**Cost-effectiveness of switching to insulin degludec from other basal insulins in real-world clinical practice in Italy**

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**Supplementary Supporting Information**

## Supporting information

**Supplementary Fig S1.** **Study design for EU-TREAT.**

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EU-TREAT, EUropean TREsiba AudiT; T1D, type 1 diabetes; T2D, type 2 diabetes; U, units.

**Supplementary Fig 2. Inputs into the CORE diabetes model.**

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Macrovascular complications were estimated by the EDIC risk equations for T1D and the UKPDS 82 risk equations for T2D.

EDIC, Epidemiology of Diabetes Interventions and Complications study; QALY, quality-adjusted life-year; RWE, real-world evidence; T1D, type 1 diabetes; T2D, type 2 diabetes; UKPDS, United Kingdom Prospective Diabetes Study.

**Supplementary Table 1. Clinical parameters from EU-TREAT.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Clinical parameters** | **Observed other insulins at baseline** | **Difference/rate ratio  [95% CI]** | **Degludec at 6-month follow-up** |
| **T1D** | | | |
| HbA1c (%) | 8.19 | −0.35 [−0.44; −0.27] | 7.84 |
| Insulin dose (U) | | | |
| Basal insulin | 20.64 | 0.97 [0.95; 0.99] | 19.64 |
| Bolus insulin | 24.42 | 0.86 [0.84; 0.89] | 21.25 |
| Hypoglycemic event rates (events per patient per year) | | | |
| Non-severe daytime | 13.53 | 1.02 [NS] | 13.86 |
| Non-severe nocturnal | 3.90 | 0.53 [0.40; 0.72] | 2.08 |
| Severe | 0.40 | 0.12 [0.05; 0.28] | 0.05 |
| BMI (kg/m2) | 25.00 | 0.11 [0.00; 0.21] | 25.10 |
| **T2D** | | | |
| HbA1c | 8.42 | −0.50 [−0.65; −0.35] | 7.92 |
| Insulin dose (U) | | | |
| Basal insulin | 24.71 | 0.99 [NS] | 24.64 |
| Bolus insulin | 37.56 | 0.94 [0.89; 0.99] | 36.69 |
| Hypoglycemic event rates (events per patient per year) | | | |
| Non-severe daytime | 3.89 | 0.27 [0.14; 0.50] | 1.04 |
| Non-severe nocturnal | 1.82 | 0.15 [0.07; 0.33] | 0.28 |
| Severe | 0.49 | 0.10 [R3]\* | 0.05 |
| BMI (kg/m2) | 31.14 | −0.06 [NS] | 31.08 |

\*Rule of three: for the severe hypoglycemic events, there were 123 patients with pre- and post-switch observations of severe hypoglycemic events, with 30 events in 61.29 patient-years in the pre-switch period and 0 events in 61.51 patient-years in the post-switch period. Due to no events being observed in the post-switch period, it was not possible to estimate a rate ratio using the negative binomial model. Therefore, the rate was estimated using the rates for the pre- and post-switch periods assuming the number of events in the pre- and post-switch periods were independently Poisson distributed. For the pre-switch period, the rate was estimated as (30/61.29) = 0.4895 events per patient-year. For the post-switch period, a 95% CI was estimated using an adaptation of the ’rule of three’, obtaining 95% CI of [0; 3/61.51] = [0; 0.0488]. The upper 95% CI was used as an estimate for the post-switch period rate. This led to a rate ratio of 0.0488/0.4895 = 0.0996 events per patient-year [1].  
All differences were significant unless stated otherwise. All values were rounded to two decimal points. For the cost-effectiveness analysis only significant differences where used, i.e. the follow-up parameter, was set to the pre-period parameter if the difference/rate ratio was insignificant.  
BMI, body mass index; CI, confidence interval; NS, not significant; R3, rule of three; T1D, type 1 diabetes; T2D, type 2 diabetes.

**Supplementary Table 2. Values used for baseline parameters in the CORE Diabetes Model.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **T1D** | **T2D** | **Source** |
| **Demographics** | | | |
| Mean age, years | 47.3 | 65.6 | EU-TREAT Italian cohort |
| Duration of diabetes, years | 21.2 | 17.9 | EU-TREAT Italian cohort |
| Proportion of male, % | 54.4 | 50.3 | EU-TREAT Italian cohort |
| **Risk parameters** | | | |
| HbA1c,% | 8.19 | 8.42 | EU-TREAT Italian cohort |
| Systolic blood pressure, mmHg | 121.1 | 139.2 | T1D: DCCT/EDIC study [2]; T2D: default |
| Diastolic blood pressure, mmHg | 71.1 | 80 | T1D: DCCT/EDIC study [2]; T2D: default |
| Total cholesterol, mg/dL | 175.4 | 192.8 | T1D: DCCT/EDIC study [2]; T2D: default |
| HDL, mg/dL | 61.3 | 46.3 | T1D: DCCT/EDIC study [2]; T2D: default |
| LDL, mg/dL | 97.3 | 110 | T1D: DCCT/EDIC study [2]; T2D: default |
| Triglycerides, mg/dL | 84.4 | 147 | T1D: DCCT/EDIC study [2]; T2D: default |
| BMI, kg/m2 | 25 | 31 | EU-TREAT Italian cohort |
| eGFR (mL/min/1.73 m2) | 84.5 | 77.5 | T1D: DCCT/EDIC study [2]; T2D: default |
| Hemoglobin, g/L | 145 | 145 | Default |
| White blood cell, x106/mL | 6.8 | 6.8 | Default |
| Heart rate, beats/min | 75 | 72 | T1D: DCCT/EDIC study [2]; T2D: default |
| Waist-hip ratio | 0.834 | 0.93 | T1D: DCCT/EDIC study [2]; T2D: default |
| Urinary albumin excretion rate, mg/24 h | 10.1 | 3.1 | T1D: DCCT/EDIC study [2]; T2D: default |
| Serum creatinine, mg/dL | 0.85 | 1.1 | T1D: DCCT/EDIC study [2]; T2D: default |
| Serum albumin, g/L | 39 | 39 | T1D: DCCT/EDIC study [2]; T2D: default |
| Proportion smoking, % | 25.0 | 25.0 | IMS CDM Economic Inputs: Italy [3] |
| Cigarettes/day | 5.5 | 5.5 | IMS CDM Economic Inputs: Italy [3] |
| Alcohol consumption, units | 5.64 | 5.64 | IMS CDM Economic Inputs: Italy [3] |
| **Racial characteristics** | | | |
| Proportion White, % | 100.0 | 100.0 | N/A |
| **Baseline CVD complications** | | | |
| Proportion with myocardial infarction, % | 15.0 | 15.0 | Default |
| Proportion with angina, % | 5.9 | 26.5 | EU-TREAT Italian cohort |
| Proportion with peripheral vascular disease, % | 4.5 | 12.7 | EU-TREAT Italian cohort |
| Proportion with stroke, % | 1.5 | 5.4 | EU-TREAT Italian cohort |
| Proportion with heart failure, % | 1.3 | 6.0 | EU-TREAT Italian cohort |
| Proportion with atrial fibrillation, % | 5.1 | 5.1 | Default |
| Proportion with left ventricular hypertrophy, % | 4.2 | 4.2 | Default |
| **Baseline renal complications** | | | |
| Proportion with microalbuminuria, % | 31.3 | 31.3 | Default |
| Proportion with gross proteinuria, % | 7.7 | 7.7 | Default |
| Proportion with end-stage renal disease, % | 2.5 | 2.5 | Default |
| **Baseline retinopathy complications** | | | |
| Proportion with background diabetic retinopathy, % | 11.6 | 16.9 | T1D: DCCT/EDIC study [2]; T2D: default |
| Proportion with preproliferative diabetic retinopathy, % | 4.5 | 7.1 | T1D: DCCT/EDIC study [2]; T2D: default |
| Proportion with severe visual loss, % | 0.0 | 3.0 | T1D: DCCT/EDIC study [2]; T2D: default |
| **Baseline macular edema** | | | |
| Proportion with macular edema, % | 6.0 | 9.0 | T1D: DCCT/EDIC study [2]; T2D: default |
| **Baseline cataract** | | | |
| Proportion with cataract, % | 8.3 | 11.0 | T1D: DCCT/EDIC study [2]; T2D: default |
| **Baseline foot ulcer complications** | | | |
| Proportion with uninfected ulcer, % | 0.0 | 0.0 | Default |
| Proportion with infected ulcer, % | 0.0 | 0.0 | Default |
| Proportion with healed ulcer, % | 14.6 | 14.6 | Default |
| Proportion with history of amputation, % | 02.0 | 2.0 | Default |
| **Baseline neuropathy** | | | |
| Proportion with neuropathy, % | 22.1 | 46.5 | EU-TREAT Italian cohort |
| **Baseline depression** | | | |
| Proportion with depression, % | 15.2 | 15.2 | Default |

BMI, body mass index; CVD, cardiovascular disease; DCCT, Diabetes Control and Complications Trial; EDIC, Epidemiology of Diabetes Interventions and Complications; eGFR, estimated glomerular filtration rate; EU-TREAT, EUropean TREsiba AudiT; HDL, high-density lipoprotein; IMS CDM, IMS CORE Diabetes Model, LDL, low-density lipoprotein; N/A, not applicable; T1D, type 1 diabetes; T2D, type 2 diabetes.

**Supplementary Table 3. Treatment costs.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Input parameters** | **Input values** | **T1D** | **T2D** |
|  |  | **Quantity** | **Quantity** |
| **Basal insulin costs [4]** | **Cost/unit (€)** |  |  |
| Degludec | 0.06135 | 20.02 U/day | 24.71 U/day |
| Previous insulin T1D (weighted)\* | 0.03335 | 20.64 U/day |  |
| Previous insulin T2D (weighted)\* | 0.03310 |  | 24.71 U/day |
| Post-prandial | 0.02227 | 21.00 U/day | 27.64 U/day\*\*\* |
| Previous prandial\*\* | 0.02227 | 24.42 U/day | 29.40 U/day\*\*\* |
| **Other resource use** | **Cost/each (€)** |  |  |
| SMBG test [5] | 0.60 | 28.7/week | 28.7/week |
| Needle [6] | 0.123 | 4.1/day | 4.1/day |
| **Total annual costs** |  |  |  |
| Degludec |  | €1,702 | €1,861 |
| Previous insulin |  | €1,533 | €1,621 |

\*Based on:

IDet: 0.03395 (T1D: 24%; T2D: 54%)

Glargine U100: 0.03395 (T1D: 74%: T2D: 42%)

NPH: 0.00988 (T1D: 2%; T2D: 3%)

\*\*Weighted price based on insulin glulisine, insulin lispro, insulin aspart and others. \*\*\*The dose in the degludec arm is the observed dose in the comparator arm multiplied by the dose ratio if significant (for non-significant dose ratios, a ratio of 1 was been applied). For T2D, the bolus doses were weighted by the 78.3% who were on a basal–bolus regimen.

IDet, insulin detemir; glargine U100, insulin glargine 100 units/mL; NPH, neutral protamine Hagedorn; SMBG, self-measured blood glucose; T1D, type 1 diabetes; T2D, type 2 diabetes.

**Supplementary Table 4. Costs associated with complications.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Unit cost (€)** | **Source** | **Description/assumptions** |
| **Annual management costs** | | |  |
| Statins | 221 | AIFA November 2010 [7] | Defined daily dose according to country-specific guidelines, prices taken from country-specific formularies based on an average of the most prescribed brands |
| Aspirin | 0 | N/A | Aspirin is not reimbursed in Italy and thus the annual cost of treatment was set to 0 |
| ACE inhibitor | 177 | AIFA November 2010 [7] | Defined daily dose according to country-specific guidelines, prices taken from country-specific formularies based on an average of the most prescribed brands |
| Microalbuminuria screening | 6 | Ambulatory tariffs Lombardia 2009 [8], from the IMS CDM Economic Inputs: Italy [3] | - |
| Gross proteinuria screening | 6 | Ambulatory tariffs Lombardia 2009 [8], from the IMS CDM Economic Inputs: Italy [3] | - |
| Stopping ACE inhibitor due to side effects | 24 | Ambulatory tariffs Lombardia 2009 [8], from the IMS CDM Economic Inputs: Italy [3] | Event cost if patient is suffering from side effects from ACE inhibitors. Assumes one GP visit with the eventual prescription of an alternative drug |
| Eye screening | 113 | Ambulatory tariffs Lombardia 2009 [8], from the IMS CDM Economic Inputs: Italy [3] | Cost for eye screening (assumed once per year) |
| Foot screening program | 36 | Ambulatory tariffs Lombardia 2009 [8], from the IMS CDM Economic Inputs: Italy [3] | It was assumed that screening would imply one visit to a specialist plus three sessions of collective education for patients with diabetes. These were valued with the corresponding Lombardian Ambulatory Tariffs |
| Non-standard ulcer treatment | 2,997 | Ambulatory tariffs Lombardia 2009 [8], code 93951 from the IMS CDM Economic Inputs: Italy [3] | - |
| Anti-depression treatment | 277 | Prontuario Farmaceutico, 2010, from the IMS CDM Economic Inputs: Italy [3] | - |
| Depression screening | 31 | Ambulatory tariffs Lombardia 2009 [8], from the IMS CDM Economic Inputs: Italy [3] | Cost estimated assuming one specialist visit per year according to the Italian diabetes guidelines plus administration of a test for ability to cope |
| **Direct costs associated with CVD complications** | | |  |
| Myocardial infarction 1st year | 17,079 | Taylor *et al* [9] | Cost for a myocardial infarction (all costs incurred in first year, fatal and non-fatal events) |
| Myocardial infarction 2nd+ year | 2,966 | Adapted from Taylor *et al* [9] and Levy *et al* [10] | Cost for a myocardial infarction in subsequent years following event |
| Angina 1st year | 17,079 | Taylor *et al* [9] | Cost for unstable angina (all costs incurred in first year) |
| Angina 2nd+ year | 12,012 | Adapted from Taylor *et al* [9] and Levy *et al* [10] | Cost for unstable angina in subsequent years following event |
| Congestive heart failure 1st year | 1,884 | Politi *et al* [11] | Cost for non-fatal congestive heart failure event (all costs incurred in first year) |
| Congestive heart failure 2nd+ year | 1,884 | Politi *et al* [11] | Cost for non-fatal congestive heart failure in subsequent years following event |
| Stroke 1st year | 20,683 | Capri and Perlini [12] | Cost for non-fatal stroke (all costs incurred in first year) |
| Stroke 2nd+ year | 1,473 | Capri and Perlini [12] | Cost for stroke in subsequent years following event |
| Stroke death within 30 days | 3,700 | Hospital tariffs Lombardia 2009 [13] | Cost incurred with stroke if subject dies within 30 days |
| Peripheral vascular disease event 1st year | 15,631 | Prompers *et al* [14] | Cost for peripheral vascular disease event (all costs incurred in first year) |
| Peripheral vascular disease event 2nd+ year | 2,173 | Ambrosetti *et al* [15] | Cost for peripheral vascular disease event in subsequent years following event |
| **Direct costs associated with renal complications** | | |  |
| Hemodialysis 1st year | 49,529 | Based on resource utilization from: Palmer *et al* [16] | Annual cost for hemodialysis in first year |
| Hemodialysis 2nd+ year | 47,839 | Based on resource utilization from: Palmer *et al* [16] | Annual cost for hemodialysis in subsequent years |
| Peritoneal dialysis 1st year | 34,829 | Based on resource utilization from: Palmer *et al* [16] | Annual cost for peritoneal dialysis in first year |
| Peritoneal dialysis 2nd+ year | 33,139 | Based on resource utilization from: Palmer *et al* [16] | Annual cost for peritoneal dialysis in subsequent years |
| Renal transplant 1st year | 44,055 | Based on resource utilization from: Palmer *et al* [16] | Annual cost for renal transplant for year of transplant |
| Renal transplant 2nd+ year | 12,093 | Based on resource utilization from: Palmer *et al* [16] | Annual cost for years following successful renal transplant |
| **Directs costs associated with acute events** | | |  |
| Non-severe hypoglycemia | 2 | Geelhoed-Duijvestijn *et al* [17] | - |
| Severe hypoglycemia for T1D | 217 | Adapted from Giorda *et al* [18] (excluding indirect costs) | - |
| Severe hypoglycemia for T2D | 806 | Adapted from Giorda *et al* [18] (excluding indirect costs) | - |
| Ketoacidosis event for T1D | 2,529 | Hospital tariffs Lombardia 2009 [13] | - |
| Lactic acidosis event for T2D | 1,450 | Hospital tariffs Lombardia 2009 [13] | - |
| Edema onset and 1st year | 24 | Ambulatory tariffs Lombardia 2009 [8], from the IMS CDM Economic Inputs: Italy [3] | Edema arising as an adverse event of diabetes pharmacological treatment was assumed to involve one visit to a family doctor at the onset of the event |
| Edema follow-up | 0 | Assumed medical resource consumption is not required once medication is changed | Cost of edema as an adverse event associated with pharmacological treatment for subsequent years |
| **Direct costs associated with eye disease** | | | **-** |
| Laser treatment | 140 | Ambulatory tariffs Lombardia 2009 [8], from the IMS CDM Economic Inputs: Italy [3] | Cost for laser treatment/retinal photocoagulation |
| Cataract operation 1st year (1st or 2nd cataract extraction) | 1,014 | Ambulatory tariffs Lombardia 2009 [8], from the IMS CDM Economic Inputs: Italy [3] | The annual cost in the year following cataract operation was assumed to imply two ophthalmologist check-up visits |
| Following cataract operation | 49 | Ambulatory tariffs Lombardia 2009 [8], from the IMS CDM Economic Inputs: Italy [3] | - |
| Blindness 1st year | 6,231 | IMS CDM Economic Inputs: Italy [3] | - |
| Blindness 2nd+ year | 6,231 | IMS CDM Economic Inputs: Italy [3] | - |
| **Direct costs associated with neuropathy, foot ulcer, and amputation** | | | **-** |
| Neuropathy 1st year | 1,464 | Hospital tariffs Lombardia. 2009 [13] | - |
| Neuropathy 2nd+ year | 643 | Prontuario Farmaceutico, 2010, from the IMS CDM Economic Inputs: Italy [3] | - |
| Amputation event | 9,542 | Hospital tariffs Lombardia 2009 [13] | Cost of amputation event (all medical costs except prosthesis) |
| Amputation prosthesis | 540 | Nomenclatore tariffario delle protesi, page 62 [19] | Cost of prosthesis following amputation event |
| Gangrene treatment | 19,233 | Prompers *et al* [14] | Cost of gangrene treatment (monthly cost\*12) |
| After healed ulcer | 11 | Ambulatory tariffs Lombardia 2009 [8], CD 93822, from the IMS CDM Economic Inputs: Italy [3], | Annual cost assumed as ten sessions of collective education, valued based on the Lombardian Ambulatory Tariffs in lack of more specific information |
| Infected ulcer | 14,085 | Prompers *et al* [14] | - |
| Standard uninfected ulcer | 4,419 | Prompers *et al* [14] | - |
| Healed ulcer history of amputation | 11 | Ambulatory tariffs Lombardia 2009 [8], CD 93822, from the IMS CDM Economic Inputs: Italy [3] | Annual cost assumed as ten sessions of collective education, valued based on the Lombardian Ambulatory Tariffs in lack of more specific information |

ACE, angiotensin-converting enzyme; AIFA, Italian Medicines Agency; CDM, CORE Diabetes Model; CVD, cardiovascular disease; GP, general practitioner; IDet, insulin detemir; glargine U100, insulin glargine 100 units/mL; N/A, not applicable; NPH, neutral protamine Hagedorn; T1D, type 1 diabetes; T2D, type 2 diabetes.

**Supplementary Table 5. Utility and disutility values.**

|  |  |  |
| --- | --- | --- |
| **Quality of life utilities/disutilities** | **Mean** | **Source** |
| Utility T1D no complications | 0.9342 | Freemantle *et al* [20] |
| Utility T2D no complications | 0.8140 | Clarke *et al* [21] |
| Disutility myocardial infarction event | −0.1290 | Clarke *et al* [21] |
| Utility post-myocardial infarction | 0.7360 | Clarke *et al* [21] |
| Utility angina | 0.6820 | Clarke *et al* [21] |
| Utility congestive heart failure | 0.6330 | Clarke *et al* [21] |
| Disutility stroke event | −0.1810 | Clarke *et al* [21] |
| Utility post-stroke | 0.5450 | Clarke *et al* [21] |
| Utility peripheral vascular disease | 0.5700 | Tengs and Wallace [22] |
| Utility microalbuminuria | 0.9342/0.8140 | No decrease in utility as per CDM default |
| Utility gross proteinuria | 0.9342/0.8140 | No decrease in utility as per CDM default |
| Utility hemodialysis | 0.6040 | Wasserfallen *et al* [23] |
| Utility peritoneal dialysis | 0.6120 | Wasserfallen *et al* [23] |
| Utility radiation therapy | 0.7500 | Tengs and Wallace [22] |
| Utility background diabetic retinopathy | 0.7900 | Sharma *et al* [24] |
| Utility background diabetic retinopathy wrongly treated | 0.7900 | Sharma *et al* [24] |
| Utility preproliferative diabetic retinopathy laser treated | 0.7900 | Sharma *et al* [24] |
| Utility preproliferative diabetic retinopathy no laser | 0.7900 | Sharma *et al* [24] |
| Utility macular edema | 0.7900 | Sharma *et al* [24] |
| Utility severe visual loss | 0.6700 | Lloyd *et al* [25] |
| Utility cataract | 0.6200 | Hopkins *et al* [26] |
| Utility neuropathy | 0.6300 | Lloyd *et al* [25] |
| Utility healed ulcer | 0.9342/0.8140 | No decrease in utility as per CDM default |
| Utility active ulcer | 0.7500 | Redekop *et al* [27] |
| Disutility amputation event | −0.5380 | Clarke *et al* [21] |
| Utility post-amputation | 0.4020 | Clarke *et al* [21] |
| Diminishing non-severe daytime hypoglycemic event | None | Lauridsen *et al* [28] (used for sensitivity analyses) |
| Disutility for non-severe daytime hypoglycemic event | −0.005 | Evans *et al* [29] |
| Disutility for non-severe nocturnal hypoglycemic event | −0.007 | Evans *et al* [29] |
| Disutility for severe daytime hypoglycemic event | −0.057 | Evans *et al* [29] |

T1D, type 1 diabetes; T2D, type 2 diabetes.

**Supplementary Table 6. Base-case long-term cost-effectiveness analysis of degludec versus other basal insulins in T1D and T2D (based on PPP $).**

|  |  |  |  |
| --- | --- | --- | --- |
| **T1D** | **Degludec ($)** | **Other insulins ($)** | **Incremental cost (degludec–other insulins) ($)** |
| **Costs** | | | |
| Treatment | 21,709 | 19,428 | 2,280 |
| Management | 4,102 | 4,173 | −71 |
| CVD | 42,608 | 44,385 | −1,777 |
| Renal | 44,063 | 45,826 | −1,762 |
| Ulcer/amputation/neuropathy | 9,850 | 10,510 | −659 |
| Eye | 13,161 | 14,574 | −1,413 |
| Non-severe hypoglycemia | 398 | 442 | −44 |
| Severe hypoglycemia | 136 | 1,082 | −946 |
| **Total costs** | **136,027** | **140,420** | **−4,394** |
| **Effects** | | | |
| **Undiscounted life expectancy (years)** | 28.087 | 27.816 | 0.271 |
| **QALY** | 10.325 | 9.544 | 0.781 |
| **ICER (cost per QALY)** |  |  | **Dominant** |
| **T2D** | **Degludec ($)** | **Other insulins ($)** | **Incremental cost (degludec–other insulins) ($)** |
| **Costs** | | | |
| Treatment | 14,341 | 12,328 | 2,012 |
| Management | 2,048 | 2,029 | 19 |
| CVD | 37,294 | 36,917 | 377 |
| Renal | 8,584 | 9,569 | −985 |
| Ulcer/amputation/neuropathy | 5,194 | 5,241 | −47 |
| Eye | 4,272 | 4,557 | −285 |
| Non-severe hypoglycemia | 20 | 87 | −67 |
| Severe hypoglycemia | 334 | 3,227 | −2,893 |
| **Total costs** | **72,089** | **73,956** | **−1,867** |
| **Effects** | | | |
| **Undiscounted life expectancy (years)** | 13.794 | 13.546 | 0.248 |
| **QALY** | 6.400 | 5.772 | 0.628 |
| **ICER (cost per QALY)** |  |  | **Dominant** |

Costs were converted to PPP $ based on the conversion rate of 0.69628 [30].Dominant, higher effectiveness with lower cost. Cost and QALYs discounted with a discount rate of 3%.  
CVD, cardiovascular disease; ICER, incremental cost-effectiveness ratio; PPP, purchasing power parity; QALY, quality-adjusted life-year; T1D, type 1 diabetes; T2D, type 2 diabetes.

**Supplementary Table 7. Net monetary benefit by ICER threshold.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Net monetary benefit by ICER threshold (€)** | | | | | |
| **T1D** | **€0** | **€10,000** | **€20,000** | **€30,000** | **€40,000** | **€50,000** |
| Base case | 6,310 | 14,110 | 21,910 | 29,710 | 37,510 | 45,310 |
| 0% discount rate | 13,128 | 26,108 | 39,088 | 52,068 | 65,048 | 78,028 |
| 8% discount rate | 2,202 | 6,402 | 10,602 | 14,802 | 19,002 | 23,202 |
| 30-year time horizon | 5,504 | 12,504 | 19,504 | 26,504 | 33,504 | 40,504 |
| 10-year time horizon | 147 | 3,247 | 6,347 | 9,447 | 12,547 | 15,647 |
| 8 year time horizon (threshold for dominance)\*\* | 57 | 2,577 | 5,097 | 7,617 | 10,137 | 12,657 |
| 5-year time horizon | −250 | 1,350 | 2,950 | 4,550 | 6,150 | 7,750 |
| 1-year time horizon | -88 | 212 | 512 | 812 | 1,112 | 1,412 |
| 1-year time horizon (deterministic model)\* | −91 | 209 | 509 | 809 | 1,109 | 1,409 |
| Difference in HbA1c excluded | −2,197 | 3,903 | 10,003 | 16,103 | 22,203 | 28,303 |
| Upper 95% CI HbA1c | 7,906 | 16,216 | 24,526 | 32,836 | 41,146 | 49,456 |
| Lower 95% CI HbA1c | 5,415 | 12,665 | 19,915 | 27,165 | 34,415 | 41,665 |
| Difference in BMI excluded | 6,481 | 14,281 | 22,081 | 29,881 | 37,681 | 45,481 |
| Upper 95% CI BMI | 6,481 | 14,321 | 22,161 | 30,001 | 37,841 | 45,681 |
| Lower 95% CI BMI | 6,357 | 14,157 | 21,957 | 29,757 | 37,557 | 45,357 |
| Difference in non-severe hypoglycemia excluded | 6,370 | 11,770 | 17,170 | 22,570 | 27,970 | 33,370 |
| Difference in severe hypoglycemia excluded | 4,802 | 9,102 | 13,402 | 17,702 | 22,002 | 26,302 |
| Upper 95% CI hypoglycemia | 6,431 | 15,341 | 24,251 | 33,161 | 42,071 | 50,981 |
| Lower 95% CI hypoglycemia | 6,098 | 12,358 | 18,618 | 24,878 | 31,138 | 37,398 |
| Difference in dose (basal and bolus) excluded | 5,540 | 13,340 | 21,140 | 28,940 | 36,740 | 44,540 |
| Disutilities +10% | 6,310 | 14,790 | 23,270 | 31,750 | 40,230 | 48,710 |
| Disutilities -10% | 6,310 | 13,510 | 20,710 | 27,910 | 35,110 | 42,310 |
| Diminishing hypoglycemia disutility model | 6,310 | 12,410 | 18,510 | 24,610 | 30,710 | 36,810 |
| Assuming new needle and SMBG test for every injection | 6,965 | 14,765 | 22,565 | 30,365 | 38,165 | 45,965 |
| Glargine U100 at baseline | 8,680 | 20,280 | 31,880 | 43,480 | 55,080 | 66,680 |
| IDet at baseline | 6,607 | 14,607 | 22,607 | 30,607 | 38,607 | 46,607 |
| 12 months efficacy data† | 5,584 | 9,484 | 13,384 | 17,284 | 21,184 | 25,084 |
| **T2D** |  |  |  |  |  |  |
| Base case | 2,682 | 8,982 | 15,282 | 21,582 | 27,882 | 34,182 |
| 0% discount rate | 3,338 | 12,008 | 20,678 | 29,348 | 38,018 | 46,688 |
| 8% discount rate | 1,908 | 6,028 | 10,148 | 14,268 | 18,388 | 22,508 |
| 30-year time horizon | 2,788 | 8,888 | 14,988 | 21,088 | 27,188 | 33,288 |
| 10-year time horizon | 1,920 | 5,620 | 9,320 | 13,020 | 16,720 | 20,420 |
| 5-year time horizon | 1,038 | 3,138 | 5,238 | 7,338 | 9,438 | 11,538 |
| 1-year time horizon (threshold for dominance)\*\* | 177 | 677 | 1,177 | 1,677 | 2,177 | 2,677 |
| 1-year time horizon (deterministic model)\* | 150 | 650 | 1,150 | 1,650 | 2,150 | 2,650 |
| Difference in HbA1c excluded | 1,156 | 6,456 | 11,756 | 17,056 | 22,356 | 27,656 |
| Upper 95% CI HbA1c | 2,775 | 9,335 | 15,895 | 22,455 | 29,015 | 35,575 |
| Lower 95% CI HbA1c | 2,474 | 8,424 | 14,374 | 20,324 | 26,274 | 32,224 |
| Difference in BMI excluded | 2,682 | 8,982 | 15,282 | 21,582 | 27,882 | 34,182 |
| BMI upper and lower 95% CI analyses not conducted due to insignificance | 2,682 | 8,962 | 15,242 | 21,522 | 27,802 | 34,082 |
| Difference in non-severe hypoglycemia excluded | 2,585 | 6,385 | 10,185 | 13,985 | 17,785 | 21,585 |
| Difference in severe hypoglycemia excluded | −1,660 | 1,940 | 5,540 | 9,140 | 12,740 | 16,340 |
| Upper 95% CI hypoglycemia | 2,696 | 9,306 | 15,916 | 22,526 | 29,136 | 35,746 |
| Lower 95% CI hypoglycemia | 2,655 | 8,275 | 13,895 | 19,515 | 25,135 | 30,755 |
| Difference in dose (basal and bolus) excluded | 2,516 | 8,816 | 15,116 | 21,416 | 27,716 | 34,016 |
| Disutilities +10% | 2,682 | 9,462 | 16,242 | 23,022 | 29,802 | 36,582 |
| Disutilities -10% | 2,682 | 8,442 | 14,202 | 19,962 | 25,722 | 31,482 |
| Diminishing hypoglycemia disutility model | 2,682 | 8,182 | 13,682 | 19,182 | 24,682 | 30,182 |
| UKPDS HbA1c progression equation | 2,431 | 8,031 | 13,631 | 19,231 | 24,831 | 30,431 |
| Assuming new needle and SMBG test for every injection | 2,813 | 9,113 | 15,413 | 21,713 | 28,013 | 34,313 |
| Glargine U100 at baseline | 7,537 | 15,737 | 23,937 | 32,137 | 40,337 | 48,537 |
| IDet at baseline | −1,039 | 3,561 | 8,161 | 12,761 | 17,361 | 21,961 |

\*1-year model based on hypoglycemia as the only complication. \*\*Time horizon necessary for dominance. †12-month efficacy data (change from baseline in HbA1c, rates of hypoglycemia, and basal and bolus insulin dose) were used in this sensitivity analysis of the T1D group. The same analysis was not feasible for the T2D group due the low number of patients and number of hypoglycemic events.

BMI, body mass index; CI, confidence interval; glargine U100, insulin glargine 100 units/mL; ICER, incremental cost-effectiveness ratio; IDet, insulin detemir; QALY, quality-adjusted life-year; SMBG, self-monitored blood glucose; T1D, type 1 diabetes; T2D, type 2 diabetes; UKPDS, United Kingdom Prospective Diabetes Study.

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