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ORIGINAL RESEARCH

Evaluating the Cost-Effectiveness of Therapy Conversion to Insulin Detemir in Patients with Type 2 Diabetes in Germany: a Modelling Study of Long-Term Clinical and Cost Outcomes

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ABSTRACT

Objectives: To evaluate the long-term cost-effectiveness of transferring type 2 diabetes patients to an insulin detemir regimen after failure to achieve adequate control with oral antidiabetic agents (OADs) alone, or in combination with neutral protamine hagedorn (NPH) insulin, or with insulin glargine in Germany.

Methods: A computer simulation model of diabetes was used to make long-term projections of future clinical outcomes and direct medical costs based on findings from a German subanalysis of the PREDICTIVE trial. The study analysed the impact of converting patients failing their current treatments to an insulin detemir regimen. Therapy conversion to insulin detemir

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± OADs was associated with a significant reduction in glycosylated haemoglobin (HbA_{1c}) compared with OADs alone, NPH insulin ± OADs, and insulin glargine ± OADs. Across all three groups, hypoglycaemia rates decreased by 80% and patients lost an average of 0.9 kg of body weight during treatment with insulin detemir ± OADs

Results: Therapy conversion to insulin detemir ± OADs was projected to improve life expectancy by 0.28 years compared with OADs alone, and by 0.13 years compared with the NPH and glargine regimens. Transfer to insulin detemir was associated with improvements in quality-adjusted life expectancy of 0.21 quality-adjusted life years (QALYs) over OADs alone, 0.28 QALYs over NPH ± OADs, and 0.29 QALYs over glargine ± OADs. Insulin detemir was associated with savings over patient lifetimes due to reduced diabetes-related complications in all three comparisons.

Conclusion: Therapy conversion to insulin detemir ± OADs in type 2 diabetes patients failing OADs alone, NPH or insulin glargine regimens was associated with improvements in life expectancy, quality-adjusted life expectancy and cost savings in all three scenarios evaluated.

Keywords: cost-effectiveness; costs; Germany; insulin detemir; insulin glargine; model; NPH insulin; type 2 diabetes

INTRODUCTION

The effective management of diabetes mellitus poses an increasingly serious challenge to the German healthcare system. In a recent review of the cost of diabetes, Liebl reported that the condition is responsible for over 14% of the total direct medical cost burden in Germany, costing in excess of €60 million annually.[1] Data from the German arm of the Cost of Diabetes in Europe – Type 2 (CODE-2) study suggested that complications are by far the biggest contributor to this burden, accounting for approximately 73% of total costs, with antidiabetes medications only contributing around 7% to the total (the remaining 20% was attributable to other medications).[2] As the incidence of type 2 diabetes continues to grow, the need for effective management strategies has never been more clear.

Diabetes-related complications are a key driver of costs. Evidence from the Cost of Diabetes Mellitus (CoDiM) study published in 2006 indicated that annual costs were approximately 2.5 times higher in diabetes patients with one complication than in those without, based on data from almost 27,000 diabetes patients in Germany.[3] The presence of two complications was linked to a 2.9-fold increase in annual costs and in patients with three complications, the value was 4.7-fold higher (€12,939 vs €2756). These observations are in line with earlier data from

the CODE-2 study.[2] Based on cost data collected in 1998 from 809 patients, Liebl et al. reported that the presence of micro- or macrovascular complications doubled the annual direct medical costs for diabetes patients and the presence of both micro- and macrovascular complication increased costs more than 3-fold.[2]

The cornerstone of effective diabetes management is efficient maintenance of glycaemic control. The benefits of reducing glycosylated haemoglobin (HbA_{1c}) levels have been demonstrated in the landmark UK Prospective Diabetes Study (UKPDS), in which each 1% improvement in HbA_{1c} was associated with a 37% reduction in microvascular events and a 21% reduction in deaths related to diabetes.[4–6] Despite the unequivocal evidence supporting effective glycaemic control, a number of recent epidemiological studies in Germany have indicated that many diabetes patients fail to achieve target HbA_{1c} levels (≤6.5%) and almost half have at least one diabetes-related complication.[1,3,7–9]

The development of modern insulins, such as insulin detemir, has afforded an opportunity for earlier use of insulin in the treatment of type 2 diabetes as these agents more closely reflect physiological basal insulin. Thus, insulin detemir has consistently been associated with a significantly lower risk of hypoglycaemia than older human insulins. Moreover, insulin detemir has been associated with benefits in terms of reduced weight gain.[10–15] Addition of modern insulins to treatment with oral antidiabetic agents (OADs) has been shown to reduce HbA_{1c} levels, with glycaemic control comparable to addition of neutral protamine hagedorn (NPH) insulin, but with less hypoglycaemia.[10–12]

In 2007, Meneghini et al. reported the results of the German subgroup patients enrolled in the Predictable Results and Experience in Diabetes Through Intensification and Control to Target: An International Variability Evaluation (PREDICTIVE) study.[13] PREDICTIVE was an international, multicentre, open-label observational study involving more than 35,000 patients with type 1 or type 2 diabetes transferred to insulin detemir for the management of blood glucose levels. Its aim was to evaluate the safety and efficacy of insulin detemir under usual practice conditions. The authors reported data based on 12 weeks of follow-up in German patients who were transferred to a regimen of insulin detemir ± OADs from either OADs alone (n=1321), NPH insulin ± OADs (n=251), or insulin glargine ± OADs (n=260). Therapy conversion to insulin detemir was associated with a significant reduction in HbA_{1c} in all three groups (1.29%, 0.60% and 0.59%-points for patients transferring from OADs alone, NPH insulin ± OADs, and insulin glargine ± OADs, respectively). Across all three groups, the hypoglycaemic event rate decreased by 80% and patients lost an average of 0.9 kg of body weight during their time on insulin detemir ± OADs. In this German cohort, approximately 79% of patients received insulin detemir once daily and total daily basal insulin doses increased slightly from baseline for those

converting from an insulin regimen (for patients converting from NPH to insulin detemir mean daily basal dose increased from 25.7 to 27.8 IU; for those converting from insulin glargine mean daily basal dose increased from 23.8 to 27.3 IU).

The short-term benefits associated with transfer to an insulin detemir treatment regimen in German type 2 diabetes patients may well lead to long-term improvements in clinical outcomes. We therefore designed and performed a computer simulation modelling analysis to estimate the long-term health economic outcomes associated with therapy conversion to insulin detemir from OADs or other insulins (NPH insulin or insulin glargine), based on the findings of the PREDICTIVE study in the German setting.

MATERIALS AND METHODS

A computer simulation model of diabetes was used to project the long-term clinical and economic outcomes associated with the switching of type 2 diabetes patients to a combination therapy of OADs plus insulin detemir in the German setting. Findings from the German cohort of PREDICTIVE were used. Individuals were recruited into the study who were mainly inadequately controlled with a prestudy medication of OADs alone, NPH insulin ± OADs or insulin glargine ± OADs.[13] After 12 weeks of follow-up, insulin detemir-based treatment was associated with significant reductions from baseline in HbA_{1c} and body weight compared with all three prior treatments and a reduction in hypoglycaemia compared with the prior insulin regimens. Thus, comparators in this analysis are baseline values from the different treatment regimen subgroups which are then compared to the end of study results, i.e. after switching to insulin detemir.

Model

A brief overview of the CORE Diabetes Model is provided here, but a full description of the model has been previously published by Palmer et al.[14,15] The model is a non-product-specific diabetes policy analysis tool which takes into account intensive or conventional insulin therapy, oral hypoglycaemic medications, screening and treatment strategies for microvascular complications, treatment strategies for end-stage complications and multifactorial interventions. Disease progression is based on a series of interdependent submodels that simulate progression of disease-related complications (angina, myocardial infarction, congestive heart failure, stroke, peripheral vascular disease, diabetic retinopathy, macula oedema, cataract, hypoglycaemia, ketoacidosis, lactic acidosis, nephropathy, neuropathy, foot ulcer and amputation) as well as mortality from other causes. Each submodel uses time, state and diabetes type-dependent probabilities derived from published sources. The reliability of simulated outcomes has been tested, with results validated against those reported by clinical trials and epidemiological studies.[15]

Table 1. Baseline characteristics of patients in the simulated cohort.

	Value	Reference
Demographics		
Mean age, years (±SD)	62.3±10.6	13
Mean duration of diabetes, years	7±5	13
Male gender, %	50.4	13
Ethnic origin, %		
Caucasian	99.6	www.destasis.de
Black	0.2	www.destasis.de
Other	0.2	www.destasis.de
Risk factors		
Mean HbA_{1c}, %-points (±SD)	8.3±1.29	13
Systolic blood pressure, mmHg	145.97	13
Total cholesterol, mg/dl	220.02	13
High-density lipoprotein cholesterol, mg/dl	49.02	13
Low-density lipoprotein cholesterol, mg/dl	138.96	13
Triglycerides, mg/dl	194.70	13
Body mass index, kg/m^2	29.8	13

HbA_{1c}=glycosylated haemoglobin; SD=standard deviation.

Simulation Cohort and Treatment Effects

A simulated cohort was generated for the analyses based on patient data from the German arm of the PREDICTIVE study. Where possible, inputs to the model were taken directly from the study data but where no information was available this was supplemented with published country-specific data (Table 1). The prevalence of pre-existing complications in the simulation cohort was taken from recently published Germany-specific data[16–18] and, similarly, patient management practices in terms of the proportion of patients receiving concomitant cardiovascular medications and being regularly screened for retinopathy, nephropathy and foot ulcers were derived from country-specific data (IMS Stroke Analyzer Database, IMS Health, Frankfurt, Germany).

The effects of the treatments modelled in the analyses were derived from the German arm of the PREDICTIVE study.[13] Three treatment scenarios were considered and for each the change in HbA_{1c}, body mass index (BMI) and hypoglycaemic event rate was applied. In the first scenario, converting patients from OADs alone to insulin detemir ± OADs was associ-

ated with reductions in HbA_{1c} and BMI of 1.29% and 0.138 kg/m^2, respectively, and an increase in hypoglycaemic event rate of 117 events per 100 patient years. Conversion from NPH insulin ± OADs to insulin detemir ± OADs resulted in improvements of 0.60% and 0.382 kg/m^2 in HbA_{1c} and BMI, respectively, and a reduction of 676 hypoglycaemic events per 100 patient years. Conversion from insulin glargine ± OADs to insulin detemir ± OADs was similarly modelled as reductions in HbA_{1c}, BMI and hypoglycaemia event rates of 0.59%, 0.52 kg/m^2 and 728 events per 100 patient years, respectively. Only minor hypoglycaemic events were modelled in the analyses as no major hypoglycaemic events (defined as those requiring third party medical assistance) were reported in the PREDICTIVE study.

Costs

Costs were accounted from a third party payer perspective in 2006 Euros (€). Costs associated with diabetes-specific complications were obtained from published sources and are detailed in Table 2. Pharmacy costs for each treatment arm included administration devices and blood glucose monitoring and took into account OAD usage and variations in insulin dosage as noted in the study. The annual costs of treatment used in the base case were as follows: OADs alone €1382.19; NPH ± OADs €1614.91; insulin glargine ± OADs €1773.31; insulin detemir ± OADs (converted from OADs alone) €1656.28; insulin detemir ± OADs (converted from NPH) €1835.37; insulin detemir ± OADs (converted from insulin glargine) €1864.24. Variation in pharmacy costs between the three insulin detemir ± OADs arms (following therapy conversion) was driven by different resource use (e.g. different insulin doses, different OAD use) in each arm as observed in PREDICTIVE.

Discounting and Time Horizon

A discount rate of 5% per annum for the base case analysis was applied to future costs and clinical benefits in line with current recommendations.[34] The time horizon was set to 35 years to ensure long-term outcomes, such as cardiovascular disease and end-stage renal disease associated with type 2 diabetes, were captured.

Sensitivity Analyses

Sensitivity analyses were performed to examine the influence of key input parameters on the outcomes projected by the model. Changes were made to pharmacy costs, the magnitude of change in HbA_{1c}, hypoglycaemic event rates, time horizon and discount rate. To investigate the impact of variation in pharmacy costs, simulations were run using the wholesale purchase price (WPP) of medications rather than the pharmacy purchase price (PPP) used in the base case. Annual WPPs for these simulations were: OADs alone €1234.72; NPH ± OADs €1415.44; insulin glargine ± OADs €1533.83; insulin detemir ± OADs (converted from OADs alone) €1440.29; insulin detemir ± OADs (converted from NPH) €1576.94; insulin detemir ± OADs (converted from in-

Table 2. Complication costs in 2006 Euros.

Cost	Cost (€)	Source (reference)
Cardiovascular complications		
Myocardial infarction (year of event)	15,815.75	19,20
Myocardial infarction (subsequent years)	1230.26	20,21
Angina (year of event)	3520.86	22,23
Angina (subsequent years)	3520.86	22,23
Congestive heart failure (year of event)	6290.96	24,25
Congestive heart failure (subsequent years)	837.68	26
Stroke (year of event)	20,439.05	27
Stroke (subsequent years)	6384.65	27
Stroke (death within 30 days)	9488.25	27
Peripheral vascular disease (year of event)	2695.37	22
Peripheral vascular disease (subsequent years)	393.72	22
Renal complications		
Annual cost of haemodialysis	61,230.05	28
Annual cost of peritoneal dialysis	48,776.92	28
Renal transplant (year of event)	71,828.12	29
Renal transplant (subsequent years)	11,448.50	29
Eye complications		
Annual cost of blindness	11,017.47	30
Cost of cataract removal surgery	1384.58	31
Cost of laser treatment	3662.81	21
Diabetic foot complications		
Cost of uninfected ulcer treatment	924.07	32
Cost of infected ulcer treatment	1879.28	32
Annual cost of healed ulcer	47.88	32
Cost of gangrene treatment	3356.02	32
Cost of amputation procedure	23,280.26	33
Cost of prosthesis (following amputation)	3414.40	33
Other complications		
Neuropathy (year of onset)	4019.11	22
Major hypoglycaemic event (requiring medical assistance)	378.54	22,28

sulin glargine) €1600.53. The impact of treatment-associated changes in HbA_{1c} was evaluated by reducing the reported benefit in HbA_{1c} following therapy conversion to insulin detemir ± OADs to 50% of the base case value. The influence of hypoglycaemic event rates on health economic outcomes was investigated by applying the same rates before and after conversion to the insulin detemir regimen (the rate prior to conversion was applied). The time horizon was shortened to 5 and 10 years to examine the effect of performing simulations over time periods shorter than patient lifetimes. By varying the annual discount rate between zero and 10%, the impact of this variable on costs and clinical benefits was assessed relative to the base case rate of 5% per annum.

Statistical Methodology

A simulated cohort of 1000 patients was run through the model 1000 times for each simulation (base case and sensitivity analysis) using a non-parametric bootstrapping approach, and mean values and standard deviations were generated.[35] One thousand mean values (each of 1000 patients) of incremental costs and incremental effectiveness in terms of quality-adjusted life expectancy were plotted (scatter plots) on a cost-effectiveness plane. For interventions that were not dominant (cost saving with benefits in terms of life expectancy or quality-adjusted life expectancy), it was planned to generate an acceptability curve by calculating the proportion of points below a range of willingness-to-pay thresholds.

RESULTS

Clinical Outcomes

Therapy conversion to insulin detemir ± OADs was projected to lead to improvements in life expectancy in all three scenarios (Table 3). Transferring from OADs alone to insulin detemir ± OADs produced the largest benefits in undiscounted and discounted life expectancy of 0.61 and 0.28 years, respectively. The mean improvement in life expectancy when converting to insulin detemir ± OADs from NPH insulin ± OADs and insulin glargine ± OADs was the same for both at approximately 0.27 and 0.13 years for undiscounted and discounted values, respectively.

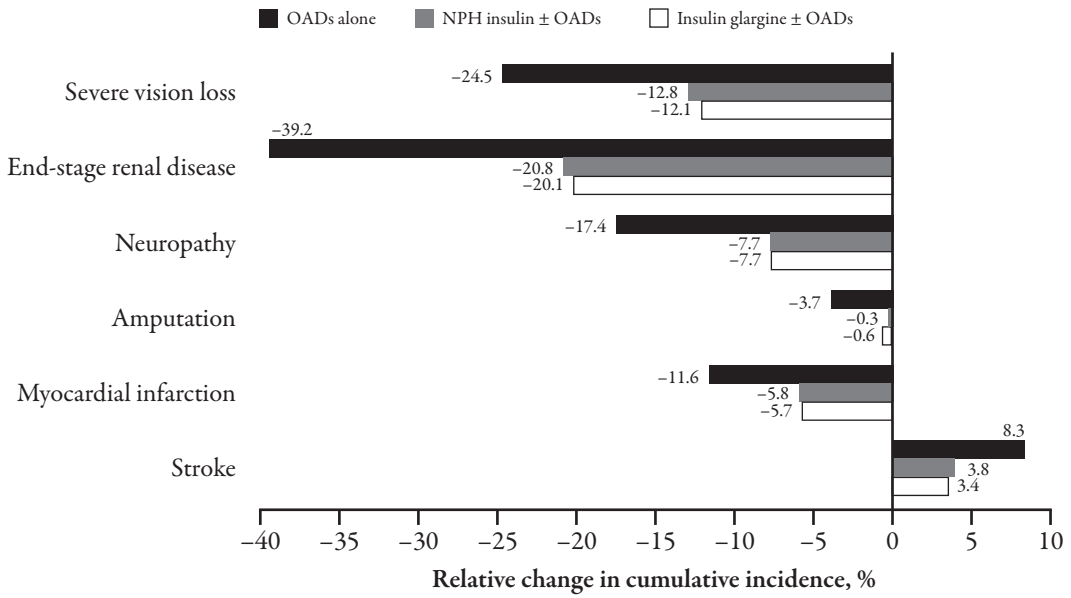
Capturing quality of life in the estimations similarly showed benefits associated with converting to an insulin detemir regimen. Therapy conversion to insulin detemir ± OADs was associated with benefits in quality-adjusted life expectancy in all three scenarios, but the greatest improvements were observed with therapy conversion from other insulin regimens (Table 3). Improvments were greatest for patients switching to insulin detemir ± OADs from insulin glargine ± OADs (0.29 quality-adjusted life years [QALYs]), then NPH insulin ± OADs (0.28 QALYs); and least improvement was seen in those converting from OADs alone (0.21 QALYs). The reduced benefit in quality-adjusted life expectancy (in relation to the corresponding improvement in life expectancy) in patients transferring from OADs alone to insulin detemir ± OADs was due to an increase in hypo-

Table 3. Summary of base case results.

	Conversion from OADs alone to detemir ± OADs			Conversion from NPH ± OADs to detemir ± OADs			Conversion from glargine ± OADs to detemir ± OADs		
	Detemir ± OADs	OADs alone	Difference	Detemir ± OADs	NPH ± OADs	Difference	Detemir ± OADs	Glargine ± OADs	Difference
Clinical outcomes									
Undiscounted life expectancy, years	10.48 ±0.14	9.87 ±0.12	0.61	10.15 ±0.13	9.87 ±0.12	0.27	10.14 ±0.13	9.87 ±0.12	0.27
Discounted life expectancy, years	7.23 ±0.14	6.95 ±0.12	0.28	7.08 ±0.13	6.95 ±0.12	0.13	7.08 ±0.13	6.95 ±0.12	0.13
Quality-adjusted life expectancy (QALYs)	4.61 ±0.09	4.40 ±0.08	0.21	4.51 ±0.09	4.23 ±0.08	0.28	4.53 ±0.09	4.24 ±0.08	0.29
Cost outcomes									
Direct medical costs, €	51,343 ±1724	52,877 ±1725	−1535	54,575 ±1842	54,640 ±1739	−65	54,807 ±1788	55,839 ±1749	−1032
Outcome/ICER (€ per QALY gained)		Dominant			Dominant			Dominant	

Data are shown as means ± standard deviation. Values are expressed as means from 1000 cohorts each of 1000 patients.
ICER=incremental cost-effectiveness ratio; NPH=neutral protamine hagedorn; OAD=oral antidiabetic agent; QALY=quality-adjusted life year.

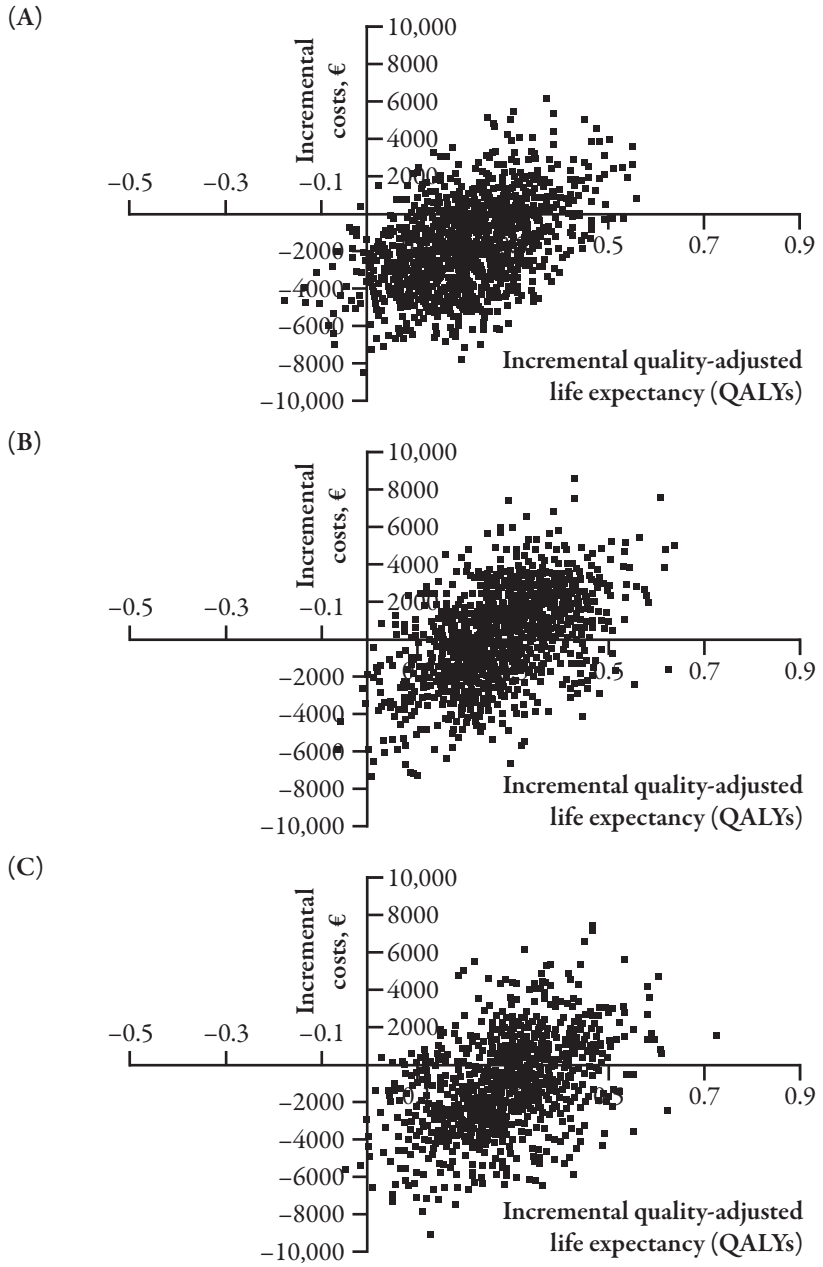
Figure 1. Relative change in the cumulative incidence of selected complications associated with therapy conversion to insulin detemir ± oral antidiabetic agents (OADs). Values shown are relative changes in the cumulative incidence of complications over patients' lifetimes associated with transfer to insulin detemir ± OADs from regimens of OADs alone (black), neutral protamine hagedorn (NPH) insulin ± OADs (grey) or insulin glargine ± OADs (white).



glycaemia. In this group, therapy conversion to an insulin detemir regimen led to a substantial improvement in HbA_{1c}, which in turn drives improvements in life expectancy and quality-adjusted life expectancy, but also a corresponding increase in minor hypoglycaemic events; this has no direct effect on life expectancy but decreases patient quality of life and therefore quality-adjusted life expectancy.

Therapy conversion to insulin detemir ± OADs was projected to reduce the cumulative incidence of most diabetes-related complications in all three scenarios (Figure 1). Benefits in terms of HbA_{1c} reduced the incidence of microvascular complications. For example, the cumulative incidence of end-stage renal disease was reduced by almost 40% versus OADs and around 20% versus the insulin regimens following transfer to insulin detemir ± OADs. A more complex pattern was observed in macrovascular complications. Transfer to an insulin detemir regimen was associated with reductions in the incidence of myocardial infarction, for example, but an increased incidence of stroke. This higher incidence of stroke was due to the survival paradox, whereby patients on insulin detemir ± OADs live longer and are exposed to the risk of stroke for a longer period of time, and the fact that stroke risk is driven by age and duration of diabetes amongst other risk factors, and not by a marker of glycaemic control such as HbA_{1c}.

Figure 2. Incremental costs versus incremental effectiveness (quality-adjusted life expectancy). Scatter plots show incremental costs versus incremental quality-adjusted life expectancy for 1000 mean values, each of which was derived from a cohort of 1000 patients. Incremental values are based on simulations of therapy conversion to insulin detemir ± oral antidiabetic agents (OADs) from regimens of (**A**) OADs alone, (**B**) neutral protamine hagedorn (NPH) insulin ± OADs, or (**C**) insulin glargine ± OADs.



Economic Outcomes

Projection over patients' lifetimes indicated that therapy conversion to insulin detemir ± OADs would be associated with lower direct medical costs in all three scenarios (Table 3). Cost savings varied between €65 for patients converting from NPH insulin ± OADs to €1032 and €1535 for those switching from insulin glargine ± OADs and OADs alone, respectively. In all three scenarios, cost savings were driven by a decreased incidence of diabetes-related complications, associated with improved HbA_{1c} levels, following transfer to an insulin detemir regimen. Complication costs accounted for 70%–76% of total direct costs in all scenarios, with patient management (approximately 4%) and pharmacy costs (20%–26%) making up the remainder. In all three scenarios investigated, switching patients to treatment with insulin detemir ± OADs was the dominant choice, being both life- and cost-saving in comparison with prior treatment regimens.

Scatter plots of the 1000 mean outcomes for 1000 patients plotted for each treatment scenario show that almost all points fall on the right side of the vertical axis indicating improved incremental effectiveness in terms of quality-adjusted life expectancy (Figure 2). The general distributions of the mean individual cohort outcomes reflect the difference in improvements in overall mean quality-adjusted life expectancy. The majority of points from the scatter plots are also below the horizontal axes confirming the overall reduction in incremental costs for patients switching to insulin detemir ± OADs.

Sensitivity Analyses

Utilisation of WPP prices for pharmacy costs in the analysis increased the magnitude of projected cost savings associated with therapy conversion to insulin detemir ± OADs in all three scenarios (Table 4). Transfer from OADs alone was associated with a saving of €2111 per patient (approximately €600 more than in the base case). Therapy conversion from NPH insulin ± OADs was projected to save approximately €544 per patient (almost €480 more than base case) and for transfer from insulin glargine ± OADs the saving was €1248 (around €220 more than base case).

Reducing the HbA_{1c} benefit associated with conversion to insulin detemir ± OADs by 50% resulted in the therapy conversion being highly cost-effective from OADs alone and from NPH insulin ± OADs, but remaining dominant to insulin glargine ± OADs. In this sensitivity analysis, transfer to an insulin detemir regimen from OADs alone was associated with a smaller benefit in quality-adjusted life expectancy and costs were higher than in the base case (due to increased risk of complications vs base case). This led to an incremental cost-effectiveness ratio (ICER) of €706 per QALY gained for transfer to an insulin detemir regimen versus OADs alone. Similar effects were observed in the conversion from NPH insulin ± OADs and insulin glargine ± OADs scenarios, resulting in an ICER of approximately €3494 per QALY gained in the former scenario and insulin de-

Table 4. Summary of sensitivity analysis findings.

	Conversion from OADs alone to detemir ± OADs			Conversion from NPH ± OADs to detemir ± OADs			Conversion from glargine ± OADs to detemir ± OADs		
Incremental changes:	**QALYs**	**Costs**	**ICER**	**QALYs**	**Costs**	**ICER**	**QALYs**	**Costs**	**ICER**
Base case	**0.21**	**−1535**	**Dominant**	**0.28**	**−65**	**Dominant**	**0.29**	**−1032**	**Dominant**
WPP prices for pharmacy costs	0.21	−2111	Dominant	0.28	−544	Dominant	0.29	−1248	Dominant
HbA_{1c} benefit reduced by 50%	0.085	60	706	0.23	791	3494	0.24	−194	Dominant
Same hypoglycaemic event rate	0.24	−1535	Dominant	0.10	−65	Dominant	0.10	−1032	Dominant
5-year time horizon	0.022	−80	Dominant	0.11	279	2629	0.11	−209	Dominant
10-year time horizon	0.086	−759	Dominant	0.19	111	581	0.20	−655	Dominant
Discount rate of 0%	0.42	−1644	Dominant	0.45	−127	Dominant	0.46	−1137	Dominant
Discount rate of 10%	0.12	−1050	Dominant	0.19	−4	Dominant	0.20	−753	Dominant

Values are expressed as means from 1000 cohorts each of 1000 patients.

HbA_{1c}=glycosylated haemoglobin; ICER=incremental cost-effectiveness ratio (expressed in € per QALY gained); NPH=neutral protamine hagedorn; OAD=oral antidiabetic agent; QALY=quality-adjusted life year; WPP=wholesale purchase price.

temir ± OADs remaining dominant in the latter. Applying the same hypoglycaemic event rates both before and after therapy conversion had different effects on quality-adjusted life expectancy across the three scenarios. In the conversion from OADs alone scenario, the benefit in quality-adjusted life expectancy associated with insulin detemir ± OADs was increased (as the hypoglycaemic event rate was lowered to match that of patients on OADs alone). In the other two scenarios, hypoglycaemic event rates were increased to match those associated with NPH insulin ± OADs and insulin glargine ± OADs, leading to a smaller quality-adjusted life expectancy benefit following transfer to insulin detemir ± OADs. There was no impact on costs as these events were assumed not to accumulate any direct medical costs (hypoglycaemic events requiring medical assistance were reported in PREDICTIVE).

Shortening the time horizon to 5 and 10 years reduced the benefits associated with transfer to insulin detemir ± OADs in all three scenarios because the shorter time horizons failed to capture many of the long-term complications avoided with the insulin detemir regimens. This was particularly noticeable in the conversion from NPH insulin ± OADs scenario, where insulin detemir ± OADs went from being cost saving to being more expensive than NPH insulin ± OADs. Variation in discount rates between zero and 10% had no substantial impact on the overall outcomes.

DISCUSSION

Based on the short-term findings of the PREDICTIVE observational study, the present modelling analysis provides evidence that therapy conversion to insulin detemir ± OADs is a cost- and life-saving treatment strategy for type 2 diabetes patients, poorly controlled on OADs alone, or in combination with NPH insulin or insulin glargine in the German setting. Transfer to insulin detemir ± OADs was associated with benefits in BMI and hypoglycaemic event rates (for patients switching from other insulins), and also associated with improvements in glycaemic control, which were projected to reduce the incidence of diabetes-related complications and thereby improve health economic outcomes.

The recently published review of diabetes costs in Germany by Liebl suggests that in 2004 there were approximately 6 million Germans with diabetes, approximately 1.9 million of whom were on insulin.[1] Clearly, selecting the most cost-efficient treatment strategies will be a key factor in terms of controlling ever-increasing costs in this growing population. The modelling analysis presented in this paper suggests that, based on benefits in HbA_{1c} as well as hypoglycaemic event rates against other insulins, switching patients to insulin detemir treatment regimens may actually save money over the long term. This observation may be particularly pertinent in light of the fact that 33.6% of total diabetes-related costs are accumulated by only 5.3% of the population.[1] Improved glycaemic control at an earlier stage of treatment

may help reduce the burden represented by the most ill patients.

A number of published studies have indicated that treatment of type 2 diabetes patients with modern insulins can lead to similar or moderately improved glycaemic control compared with NPH insulin.[11,12,36,37] Importantly, this is accompanied by reduced rates of both nocturnal and daytime hypoglycaemia, and, in the case of insulin detemir, reduced weight gain and benefits in intra-subject reproducibility. Furthermore, recent evidence suggests that there may be differences between modern insulins, with data indicating that insulin detemir could be more soluble and have reduced intra-patient variability compared with other modern insulins.[38,39] With this type of clinical data available, it is prudent to begin to evaluate the health economic merits of a range of treatment options for patients in Germany. Moreover, it will be important to make economic evaluations separately for the individual modern insulin analogues, as is evident from the present analysis.

A potential criticism of our study is that it relied on short-term data from an observational study as opposed to a randomised controlled trial to make long-term projections. However, the aim of the analysis was to generate a realistic indication of the potential value (or otherwise) of transferring patients failing their current treatments to an insulin detemir-based regimen in clinical practice. To the best of our knowledge, PREDICTIVE is the only published study providing the necessary data to make such an evaluation. Moreover, while it can be argued that an observational study provides less-reliable data than a randomised controlled trial, it could be countered that an observational study may provide data that better reflects the real-life situation. The value of randomised controlled trials lies in the ability to establish causal relationships between different treatment regimens; however, such comparisons rely on selected and tightly controlled patient groups. The demonstration of efficacy in a setting where patients are treated under usual clinical conditions is also important, confirming that such effects can be achieved in a real-world situation and providing information on likely outcomes in the target population. It could be argued that this type of data may even be more pertinent for a modelling evaluation. In terms of the uncertainty around making long-term projections from short-term trial data, this remains one of the essential tenets of health economic modelling and arguably the best available option in the absence of long-term clinical trial data. Whilst there is always an element of clinical doubt around the accuracy of such an approach, we have made every effort to minimise this in the present analysis by using a model of diabetes that has been extensively published and validated against real-life data.[15]

The aim of the analysis reported here was to evaluate the long-term cost-effectiveness of converting type 2 diabetes patients to an insulin detemir regimen after failure to achieve adequate control with OADs alone or in combination with NPH insulin or insulin glargine in a routine clinical practice environment. With

recent discussion around the use of different insulins for the treatment of type 2 diabetes patients in Germany, health economic evaluations of this kind may have an important role in terms of informing decisions on optimal treatment strategies in coming years. The results of this evaluation indicate that, based on the findings of the PREDICTIVE observational study, therapy conversion to an insulin detemir-based regimen in type 2 diabetes patients failing OADs alone, NPH or insulin glargine regimens, would be life- and cost-saving in Germany.

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