

Cost comparison of insulin glargine with insulin detemir in a basal-bolus regime with mealtime insulin aspart in type 2 diabetes in Germany

Kostenvergleich von Insulin glargin mit Insulin detemir im Rahmen einer Basis-Bolus-Behandlung (ICT) mit mahlzeitenbezogenem Insulin aspart bei Typ-2-Diabetes in Deutschland

Abstract

Objective: To compare the treatment costs of insulin glargine (IG; Lantus®) to detemir (ID; Levemir®), both combined with bolus insulin aspart (NovoRapid®) in type 2 diabetes (T2D) in Germany.

Methods: Cost comparison was based on data of a 1-year randomised controlled trial [1]. IG was administered once daily and ID once (57% of patients) or twice daily (43%) according to treatment response. At the end of the trial, mean daily basal insulin doses were 0.59 U/kg (IG) and 0.82 U/kg (ID). Aspart doses were 0.32 U/kg (IG) and 0.36 U/kg (ID). Costs were calculated from the German statutory health insurance (SHI) perspective using official 2008 prices. Sensitivity analyses were performed to test robustness of the results.

Results: Annual basal and bolus insulin costs per patient were € 1,473 (IG) and € 1,940 (ID). The cost of lancets and blood glucose test strips were € 1,125 (IG) and € 1,286 (ID). Annual costs for needles were € 393 (IG) and € 449 (ID). The total annual cost per patient of administering IG was € 2,991 compared with € 3,675 for ID, translating into a 19% annual cost difference of € 684/patient. Base case results were robust to varying assumptions for insulin dose, insulin price, change in weight and proportion of ID once daily administrations.

Conclusion: IG and ID basal-bolus regimes have comparative safety and efficacy, based on the Hollander study, IG however may represent a significantly more cost saving option for T2D patients in Germany requiring basal-bolus insulin analogue therapy with potential annual cost savings of € 684/patient compared to ID.

Keywords: insulin glargine, insulin detemir, basal insulin, type 2 diabetes, cost analysis

Zusammenfassung

Ziel: Vergleich der Behandlungskosten von Insulin glargin (IG; Lantus®) und Insulin detemir (ID; Levemir®) jeweils in Kombination mit Bolusinsulin aspart (NovoRapid®) bei Typ-2-Diabetes (T2D) in Deutschland.

Methoden: Der Kostenvergleich basierte auf den Daten einer einjährigen randomisierten, kontrollierten klinischen Studie [1]. IG wurde einmal täglich verabreicht und ID einmal (57% der Patienten) oder zweimal täglich (43%) in Abhängigkeit vom Ansprechen auf die Behandlung. Die durchschnittliche Dosierung des Basalinsulins betrug 0,59 IE/kg (IG) und 0,82 IE/kg (ID) pro Tag. Die durchschnittliche Dosierung für Aspart betrug 0,32 IE/kg (IG-Patienten) und 0,36 IE/kg (ID-Patienten). Die Kosten wurden aus dem Blickwinkel der Gesetzlichen Krankenversicherung unter Verwendung offizieller Preise für 2008 berechnet. Die Robustheit der Ergebnisse wurde anhand von Sensitivitätsanalysen überprüft.

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Ergebnisse: Die jährlichen Kosten für Basal- und Bolusinsulin betragen € 1.473 (IG) und € 1.940 (ID) pro Patient. Die Kosten für Lanzetten und Blutzucker-Teststreifen beliefen sich auf € 1.125 (IG) und € 1.286 (ID). Die Kosten für Nadeln betragen € 393 (IG) und € 449 (ID) pro Patient und Jahr. Die Anwendung von IG war damit insgesamt mit Kosten von € 2.991 pro Patient und Jahr verbunden, die von ID mit Kosten von € 3.675, woraus ein Kostenunterschied von 19% oder € 684/pro Patient und Jahr resultiert. Die Ergebnisse des Basisszenarios zeigten sich robust gegenüber veränderten Annahmen hinsichtlich Insulindosis, Insulinpreis, Gewichtsveränderung und Anteil Patienten mit einmal täglicher Verabreichung von ID.

Schlussfolgerungen: Basierend auf der klinischen Studie von Hollander sind Basal-Bolus-Behandlungsregime, die auf IG und ID aufbauen, hinsichtlich Sicherheit und Wirksamkeit vergleichbar. Die Behandlung mit IG jedoch ist gegenüber ID mit einer potentiellen Einsparung von € 684 pro Patient und Jahr verbunden.

Schlüsselwörter: Insulin glargin, Insulin detemir, Basalinsulin, Typ-2-Diabetes, Kostenanalyse

Introduction

Insulin therapy in patients with type 2 diabetes (T2D) has significant clinical and cost implications. The randomised controlled trial (RCT) recently published by Hollander [1] compared the efficacy and safety of the long-acting basal analogues glargine and detemir used in a basal-bolus treatment regime for T2D patients previously receiving other insulin and/or oral antidiabetic drugs (OADs). The multi-national, open-label, parallel-group, treat-to-target, non inferiority study demonstrated at 52 weeks, that there was no significant difference in terms of the primary efficacy endpoint of mean HbA1c. Both basal insulins were associated with a comparable clinically relevant reduction in hyperglycemia. At the end of the trial detemir was associated with less weight gain despite a higher total insulin dose than glargine (not significant).

The RCT included 319 subjects from 56 sites in Europe and the US. Eligible patients for inclusion were men and women aged ≥ 18 years, a diagnosis of T2D for ≥ 12 months, a BMI ≤ 40.0 kg/m², a glycosylated haemoglobin (HbA1c) of 7.0% to $\leq 11.0\%$ at screening, and had been receiving any OADs regime or insulin with or without OADs for >4 months. In the RCT patients were randomised in a 2:1 ratio to receive either detemir (n=214) or glargine (n=105). Demographic and baseline characteristics were comparable between detemir and glargine groups: % male: 60.7% vs. 52.4%; mean age (years): 59 vs. 58, mean weight (kg): 93.3 vs. 91.5; duration of diabetes (years): 13.6 vs. 13.4 years; mean HbA1c: 8.6 vs. 8.8 [1]. Existing OADs were continued, and patients were stratified by OAD. Patients receiving detemir were transferred to twice-daily dosing if titration of the evening dose did not result in a mean pre-breakfast and pre-dinner plasma glucose level of ≤ 6.0 mmol/L. Patients in the glargine group continued on once-daily dosing, according to labelled usage. In both groups insulin aspart was administered immediately before each main meal. The proportion of patients receiving different antidiabetic treatments

at baseline was comparable in the detemir and glargine groups: insulin + OAD (43.5% vs. 51.4% respectively); insulin only (36.9% vs. 32.4%); OAD only (19.6% vs. 16.2% respectively) [1].

The objective of the present study was to determine whether the use of insulin glargine (IG) would result in different total direct costs in comparison with insulin detemir (ID) in a basal-bolus regime (ICT) with mealtime insulin aspart in T2D patients in Germany.

An earlier cost analysis comparing basal insulin analogues glargine versus detemir in combination with oral antidiabetic drugs (basal supported oral therapy; BOT) in insulin naive T2D patients in Germany based on the findings of the Rosenstock trial [2] has been conducted from the perspective of the statutory health insurance (SHI) in Germany [3] and other countries [4], [5], [6], [7], [8]. Since transferability from one country to another is usually restricted, country-specific evaluations are required that take into account country-specific features such as epidemiology of diabetes, treatment guidelines, patterns of health service (resource) use, unit costs and reimbursement regulations [9].

The purpose of the current study was to perform a cost comparison based on the results of the Hollander trial [1] for once-daily insulin glargine or once- or twice daily basal insulin detemir both combined with mealtime aspart (basal-bolus therapy) in adults with T2D for the German setting. These results therefore provide estimates of potential differences in direct healthcare costs between the two therapeutic regimes in Germany.

A cost analysis in which only the costs of the alternative treatment strategies are compared is a justified economic evaluation method in the current study since evidence from the RCT [1] demonstrated that the alternative strategy is at least clinically equivalent (non inferiority trial). Such economic evaluation approaches are useful to support decision making on the financing of insulin therapies for patients with T2D in different healthcare settings.

Patients and methods

The present study conducted a direct cost comparison between the two different basal-bolus treatment strategies based on the findings of the RCT [1] for the German healthcare setting. A number of additional assumptions made in the modelling analysis have a certain degree of uncertainty, but in general the values chosen for calculation adopted a conservative approach, generally biased against the treatment arm with insulin glargine. Cost-minimisation-analysis is a valid analytical economic framework for the current study given the assumption of non-inferiority as demonstrated by the patients of the Hollander trial [1]. The cost analysis was performed according to German good practice recommendations based on the economic evaluation methods of the Institute for Quality and Efficiency in HealthCare (IQWiG) [10], on Health Economic Evaluation: third and updated version of the Hannover Consensus [11], and internationally in relation to conducting cost assessments [12].

Perspective and time horizon

The economic analysis involved an assessment of direct healthcare costs only and therefore takes the cost perspective of the German statutory health insurance (SHI). The time period is the first year after initiating insulin basal-bolus treatment.

Cost determinants

Identification, measurement and valuation of the key cost determinants comprise the main activities in conducting a pharmacoeconomic analysis. In the present study, all unit costs were taken from official price lists and sources based on the year 2008. The cost determinants that were included, resource utilisation in each case, and the unit costs applied, are presented in detail below. The calculations characterise the base case of the cost analysis and were further investigated in sensitivity analyses. All key model assumptions used in the analyses are summarised in Table 1.

Basal insulin analogues

The final insulin doses at the end of the RCT [1] were used for the base case analysis. These applied to consumption of glargine, detemir and aspart. It was assumed that the average final dose of each insulin over the 52 weeks treatment period and calculations of mean doses were based on patient's final weights. The RCT [1] did not report the mean insulin starting doses for glargine and detemir, but reported that the basal insulins were titrated individually throughout the trial to reach and maintain pre-breakfast and pre-dinner plasma glucose levels of ≤ 6.0 mmol/L (108 mg/dL) without hypoglycaemia. Similarly, insulin aspart was initiated and adjusted according to local practice to achieve a 2-hour

postprandial plasma glucose target of ≤ 9.0 mmol (162 mg/dL).

Insulin glargine is available on the German market as Lantus[®] (Lantus is a registered trademark of Sanofi-Aventis). The formulation for insulin detemir used in the trial was Levemir[®] (Levemir is a registered trademark of Novo Nordisk). Specific details on the actual devices used were not reported in the trial itself. For the analysis, we considered only the insulin and not the devices or pens as these are usually given to the patients free of charge as a sample. Each pen can be filled with cartridges with 3 ml solution (1 ml contains 100 U). In addition the price differences between the compared devices are very small. For insulin prices, see Table 1. For all three drugs we assumed the price of the most economical pack size, i.e.: insulin glargine (cartridge: 2700 IU, 9x3 ml); insulin detemir (cartridge: 3000 IU, 10x3 ml); insulin aspart (cartridge: 3000 IU, 10x3 ml). Prices were taken as the pharmacy sales price according to Lauer Taxe including value added tax (VAT) as reimbursed by SHI [13]. Manufacturer rebates (6%) and pharmacy rebates (€ 2.30 per prescription) were of no importance in this comparison.

Oral antidiabetic drugs, (metformin, insulin secretagogues, α -glucosidase inhibitors)

On the basis of the RCT study protocol, the use of OADs was recommended to remain stable during the study and no actual data reported in the article to the contrary. Therefore we assumed these items of resource utilisation to be the same in both groups, and thus did not include them in the current cost assessment.

Consumable items: needles, blood glucose test strips and lancets

With respect to the number of needles, test strips and lancets needed per patient we estimated as one per each insulin injection. However, findings from a recent European diabetes patient survey reported that 93% of men with diabetes in Germany used the same needle several times, on average 9.2 injections with the same needle [14], so we tested this in a sensitivity analysis. ClickFine[®] (Clickfine is a registered trademark of Ypsomed, Germany) needles were assumed for both regimes as these can be fitted in all makes of pen. The manufacturer's recommended price was used as the basis for the cost calculations [15]. One lancet and one glucose test strip is required for each blood glucose measurement. Thus, in the base case, three measurements per day were assumed linked to the aspart application, one for glargine and either one or two for detemir. Following the results in the underlying RCT [1] we assumed that 57% of patients received twice daily injections with detemir. It was assumed that Softclix[®] (Softclix is a registered trademark of Roche Diagnostics) lancets were used. As a wide range of blood glucose test strips are available at almost identical prices, a uniform price [16] could be established so that cost was independent of any particular measuring

Table 1: Assumptions used in the cost comparison model

Parameter	Base case value	Reference
Final daily insulin detemir dose (U/kg)	0.82	[1]
Final daily insulin glargine dose (U/kg)	0.59	[1]
Final daily insulin aspart dose (U/kg); glargine group	0.36	[1]
Final daily insulin aspart dose (U/kg); detemir group	0.32	[1]
Percentage of insulin detemir patients with twice daily injections (%)	57.2	[1]
Mean weight gain (kg) with insulin glargine after 52 weeks treatment	3.8	[1]
Mean weight gain (kg) with insulin detemir after 52 weeks treatment	2.8	[1]
Unit costs (€)		
glargine (100 U/ml Cartridge, sanofi-aventis, 2700 IU: 9×3 ml)	0.0491	[13]
detemir (100 U/ml Cartridge, Novo Nordisk, 3000 IU: 10×3 ml)	0.0491	[13]
aspart (100 U/ml Cartridge, Novo Nordisk, 3000 IU: 10×3 ml)	0.0419	[13]
needles	0.269/needle	[15]
blood glucose test strips	0.658/test strip	[16]
lancets	0.113/lancet	[15]

system (see Table 1). These assumptions too were varied in the sensitivity analyses.

Further resource utilisation

In the RCT, the risk of reported major hypoglycemic episodes and other adverse events was comparable between treatment regimes. Major hypoglycemic events were experienced by 4.7% of detemir patients and 5.7% glargine patients. The corresponding results for adverse events were 86.4% and 83.8% respectively. Serious adverse events were 14.5% and 13.3% respectively. We therefore assumed no difference in these related costs in our analysis between the two therapeutic groups.

Data management and calculations

Data on resource use and unit costs were entered into Microsoft Excel 2003 spreadsheets. All calculations as well as presentation of results were done using prices (Euro) to two decimal places. Calculations, tables and graphs were generated using Microsoft Excel 2003.

Allowance for parameter uncertainty: sensitivity analysis

We performed a number of sensitivity analyses to explore the robustness of the study results to changes in the value of key cost parameter estimates.

First, the assumptions made in the base case analysis were varied in simple one-way sensitivity analyses in order to test the robustness of the base case results to alternative assumptions in price, resource use, uncertainty in other assumptions and possible deviations from the underlying RCT results for routine medical care. In the first part of the sensitivity analyses, the most important cost determinants were altered independently of one another by $\pm 25\%$ around their base case values.

Additionally, since mean weight gain at 52 weeks was significantly lower with detemir than with glargine (2.8 kg vs. 3.8 kg) we also explored the impact of varying the mean weight gain by $\pm 25\%$: glargine across the range 2.85 kg to 4.75 kg; detemir across the range 2.1 kg to 3.5 kg. Specifically, this was expected to have some impact on insulin resource use and hence insulin related costs, even if the RCT publication reports no change in insulin use correlating to a change of weight of patient in the course of the study [1].

This set of one-way sensitivity analyses are summarised in a tornado plot showing the cost drivers in descending order of importance. Secondly, a number of modified scenarios were carried out to test specifically variations more applicable to routine care in Germany. These variations included: all detemir patients received once-daily injections; replacing detemir with NPH (and price) with the proportion of once daily to twice daily injections based on the recent observational trial in Germany [17]; number of blood glucose measurements and needles utilised.

Results

Base case analysis

The base case results are presented in Table 2. Once-daily insulin glargine in combination with mealtime aspart generated total annual therapy costs of € 2,991 compared to € 3,675 for patients receiving the insulin detemir basal-bolus regime. Thus, average cost savings amounting to € 684 (approx. 19% reduction) per patient per year in favour of the glargine group were generated. The most important cost component explaining the overall difference in total annual costs were the lower insulin costs (by € 467) followed by lower costs of blood glucose measurements including test strips, lancets and needles (by € 217). Insulin comprised the largest proportional

Table 2: Resource use and cost estimates in €/patient/year: base case cost analysis

Resource use item	Consumption/year		Costs in €/year (%)		Difference in costs, € (%)	Difference in costs, %	
	Glargine + Aspart	Detemir + Aspart	Glargine + Aspart	Detemir + Aspart			
Insulin (U)	glargine	20,523	-	1,006.68	-		
	detemir	-	28,763	-	1,410.91	-404.22	-28.6
	aspart	11,131	12,628	466.58	529.30	-62.73	-11.9
Total insulin consumption (U)	31,654	41,491	1,473.26 (49.2)	1,940.21 (52.8)	-466.95	-24.1	
Consumables: basal insulins (glargine, detemir)							
needles	365	574*	98.22	154.40	-56.18	-36.4	
blood glucose test strips	365	574*	240.17	377.55	-137.38	-36.4	
lancets	365	574*	41.15	64.69	-23.54	-36.4	
Total			379.55 (12.7)	596.65 (16.2)	-217.10	-36.4	
Consumables: bolus insulin (aspart)							
needles	1,095	1,095	294.66	294.66	0	0	
blood glucose test strips	1,095	1,095	720.51	720.51	0	0	
lancets	1,095	1,095	123.46	123.46	0	0	
Total			1,138.64 (38.1)	1,138.64 (31.0)	0	0	
Total costs (€/year)			2,991.44	3,675.49	-684.05	-18.6	

*=0.572 × (2 detemir administrations per day) + (1-0.572) × (1 detemir administration per day) = average of 1.572 administration per day in the detemir group. This equates to 1.572x365 administrations over 1 year, i.e. 574.

cost for both treatment regimens: 49% vs. 53% for insulin glargine and insulin detemir respectively.

Sensitivity analysis

Univariate sensitivity analysis are summarised in Figure 1 as a tornado diagram showing the cost savings of insulin glargine resulting from changes in different cost determinants and varied assumptions. The length of the horizontal bars (x-axis) corresponds to the difference in average costs between glargine and detemir groups over the specified variables of interest depicted on the y-axis. The vertical line transecting the bars represents the cost difference between the groups in the point-estimate (average) base case. The base case with a cost saving of € 684 per patient per year is represented by the central axis. The tornado diagram ranks the cost parameters based on the magnitude of their impact on the cost differences between the two treatment groups. The results show clearly that the insulin consumptions and insulin price have the highest impact. Several reports regarding higher dose requirements of insulin detemir versus insulin glargine support the findings [18], [19], [20], [21]. For all these variations, cost advantages and thus real cost savings were seen with insulin glargine basal bolus regime (range of cost savings is € 331–€ 1,037). Factors with the least influence included price (unit costs) of needles,

test strips and lancets as well as gain in weight. For example, increasing the weight gain in the glargine group (3.8 kg) by 25%, shifted the final weight from 95.3 kg to 96.25 kg, and mean daily total insulin glargine dose from 56.2 units to 56.8 units. Thus, total glargine insulin related costs were increased by <1% (€ 1,007 to € 1,018) and decreased total costs savings from € 684 to € 669. On the other hand, decreasing the weight gain in the detemir group (2.8 kg) by 25%, shifted the final weight from 96.1 to 95.4 kg, and mean daily total detemir dose from 78.8 to 78.23 units. Total detemir insulin related costs were decreased by <1% (€ 1,411 to €1,401) and total cost savings reduced from € 684 to € 670. Finally, increasing or decreasing the proportion of detemir patients receiving once-daily insulin injections, i.e. from 42.8% to 53.5% (+25%), or from 42.8% to 32.1% (-25%), had moderate impact with annual cost savings moving ranging € 628 to € 805.

One-way sensitivity analysis on price assumptions for lancets and needles covered the range of published potential unit prices. Only in the case of glucose test strips was there still a potentially lower price (€ 0.43/test strip) [22] than the assumed price when the minus 25% assumption was applied (€ 0.49/test strip). Using the lower price reduced total annual cost savings by 7% (i.e. from € 684 to € 637).

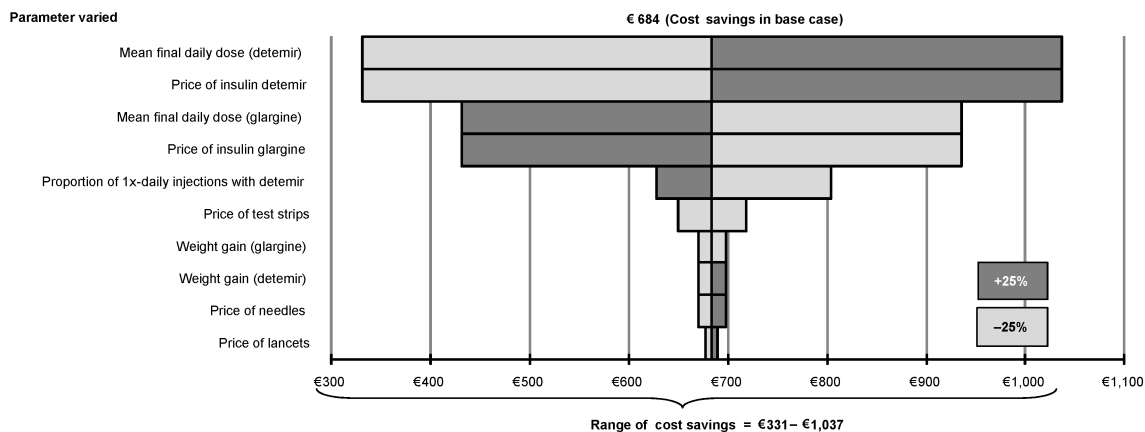


Figure 1: One-way sensitivity analysis: Cost savings of glargine versus detemir per patient per year (Parameter variation $\pm 25\%$ around base case values)

Table 3: Sensitivity analysis: results with modified scenarios

Scenario	Resulting cost savings with glargine (€/patient/year)	Change from base case
100% of insulin detemir patients with once daily injections*	243.27	440.78
Insulin detemir replaced by NPH (distribution of daily injections based on LIVE-DE [10])†	64.32	619.73
One blood glucose measurement daily with both basal-bolus regimes‡	523.13	160.92
Needle consumption in both groups, one needle per ten injections‡	633.49	50.56

*mean once-daily dose based on an exploratory analysis conducted as part of the Hollander trial [1]: 0.69 U/kg (vs. 0.95 U/kg for twice-daily)

†66.8% with once-daily dose [LIVE-DE; 17]; most economical unit price applied for Insuman Basal, 10x3 ml: € 0.324/U

‡applies to both basal-bolus regimes

Further modified scenarios to investigate assumptions more applicable to routine care confirmed the robustness of the base case results (Table 3). All scenarios still yielded considerable cost savings for the insulin glargine group compared to the insulin detemir group.

Discussion

The clinical results from the Hollander RCT [1] showed that efficacy of glargine compared with detemir both combined with mealtime aspart, were of comparable efficacy in improving overall metabolic control. However, after 52 weeks treatment, weight gain with detemir was slightly lower than with glargine. On the other hand, detemir was associated with a higher basal and bolus insulin dose compared to glargine. The results of our cost analysis comparing the direct treatment costs between the two regimes showed lower annual costs per patient for Germany in favour of insulin glargine. The results of this cost comparison are consistent with the findings of further recent German cost comparisons between insulin

glargine and insulin detemir such as the Rosenstock RCT [3], the LIVE-COM study [17], the LIVE-KK study [23] and findings from other countries [4], [5], [6], [7], [8].

A limitation of the current study might be that resource use had to be derived from a RCT setting that might not mirror every day practice. There may be a number of characteristics of the trial setting that might be different in actual German clinical practice context worthy of further exploration. We tried to overcome this problem by varying resource use in various sensitivity analyses. Our range of modified scenarios showed that the cost advantages with glargine were robust to a range of plausible variations in base case assumptions. However, it would be helpful to perform a calculation on the basis of observational data.

Further support to the finding that insulin glargine-based regimes are cost saving was demonstrated in a recent retrospective analysis of three years claims data (over years 2006–2008) among patients with type 1 and type 2 diabetes in Germany receiving insulin detemir and insulin glargine based regimes [24]. Based on resource use in an actual real-life practice setting, the study de-

terminated the direct costs associated with short acting insulins, OADs, test strips, lancets and needles. The authors reported that the annual direct costs for insulin glargine were lower than for insulin detemir (€ 1,282 versus € 1,818, which is a mean cost saving difference of € 536). Compared to our results we estimated an annual cost saving of € 684 in direct costs with insulin glargine based on the Hollander trial. It is notable that the absolute costs based on the Hollander trial were higher in our analyses (i.e. glargine: € 2,992 versus € 1,282; detemir: € 3,676 versus € 1,818). A possible explanation for these differences may be due to the actual existence of differences in resource use between patients with diabetes participating in a clinical trial setting and diabetes patients in actual clinical practice [25], [26]. For example, Dixon [25] reported that "... pivotal trials of glargine (for the treatment of type 1 and type 2 diabetes) designed specifically to show non-inferiority with the comparator insulin, may not show the true value of glargine which was found to be less costly and resulted in improved outcomes in real-life use than detemir...". Also, based on data from a proprietary database of people treated in general practice in the UK (The Health Improvement Network (THIN)) Poole [26] reported that the median annual cost of treatment with glargine and detemir for people with type 2 diabetes was £ 1,014 versus £ 1,410 ($\Delta=28\%$; $p<0.001$), respectively. In type 2 diabetes, a glargine-based regimen also resulted consistently in reduced costs of treatment: "...insulin (32%; $p<0.001$), reagents (16%; $p=0.002$), hypoglycaemia rescue medication (34%; $p=0.260$), pen delivery devices (40%; $p<0.001$) and sharps (17%; $p=0.006$)..." and there was also no statistically significant increase in cost of treatment with oral hypoglycaemic agents using a glargine-based regime. In a recent cost analysis in type-1-diabetes [27] during the first year after the switch to the respective long acting insulin as part of basal-bolus therapy with insulin glargine or detemir showed cost savings not only resulting from differences in the application frequency (once or twice daily) but mainly from the lower insulin dosage of glargine compared to detemir. This is also true in T2D patients in our current analysis.

Nonetheless, both trial based cost comparisons for insulin glargine and insulin detemir [3], [4], [5], [6], [7], [8] as well as comparisons based on "real-life" data [23], [24], [28] have consistently reported a cost-advantage for glargine based regimes. Moreover, clinical trials designed to specifically show non-inferiority with the comparator insulin, may not show the true value of glargine in real-life use than detemir [25]. On the other hand, IQWiG notes the time-horizon limitation of economic data (if) collected in clinical trials [29] "... these data are often insufficient for the comprehensive costing of a health technology. Clinical trials seldom provide information on the long-term consequences of a technology. In addition, they do not always adequately and comprehensively reflect all cost aspects relevant to the German health care setting [30], [31]. Moreover, protocol-induced resource consumption in clinical trials may bias cost estimation. Thus, modelling

the effects of a health technology is an essential component of health economic evaluations..."

In the sensitivity analysis we included an alternative scenario which involved the assumption of one blood glucose measurement daily in both groups (Table 3). The annual costs of both treatments were changed but the overall conclusion remains unchanged, that is that patients treated with glargine yield cost savings. The annual cost of glargine is reduced from € 2,991 to € 2,429 and for detemir from € 3,675 to € 2,952. The cost saving is therefore reduced from € 684 to € 523. Adopting an even more conservative approach and eliminating any differences in costs due to blood glucose measurements, as disposable items as a whole, then cost savings are reduced to of € 467 and are associated with differences in insulin consumption alone.

In the Hollander RCT publication [1] the authors stated in the methods that "...existing OAD regimens were continued, and patients were stratified by OAD treatment...". However, it may well be the case that patients receiving treatment including OADs at baseline may have changed during the course of the trial since no details are given in the Hollander article itself. Therefore it should be acknowledged that there remains some uncertainty surrounding the observed (very similar) clinical effects since any changes (or otherwise) in treatment with OADs is not reported.

The Hollander trial reported that after 52 weeks of treatment, patients receiving detemir experienced a significantly lower weight gain compared to the glargine group (2.8 vs. 3.8 kg, respectively; mean difference -1.04). This result may have possible implications for insulin-consumption over the long-term and any impact on differences in resource use should be considered in future economic analyses over a longer time horizon than the short 12 months of the current study.

In the context of glargine versus detemir in the treatment of type 2 diabetes, a number of recent studies suggested in addition cost-effectiveness advantages in favour of basal analogue insulin glargine compared with detemir due to improved outcome parameters [32], [33], [34]. This is also an important area for future research to the German-specific setting with regard evaluating the relative costs and benefits of basal-bolus regimes in T2D.

Conclusion

In Germany, insulin glargine combined with mealtime aspart is associated with annual cost savings of € 684/patient (around 20%) compared to the use of insulin detemir basal bolus therapy. These findings are robust to variations in key model parameter assumptions.

Notes

Conflicts of interest

The study was funded by Sanofi-Aventis Deutschland GmbH.

ESD and ARN have been consultants for Sanofi-Aventis Deutschland GmbH.

SP is executive physician (nephrology, diabetology, rheumatology) at the Traunstein city hospital.

FWD is an employee of Sanofi-Aventis Deutschland GmbH.

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