

ORIGINAL ARTICLE

Long-term clinical and cost outcomes of treatment with biphasic insulin aspart 30/70 versus insulin glargine in insulin naïve type 2 diabetes patients: cost-effectiveness analysis in the UK setting

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ABSTRACT

Objectives: To evaluate the long-term clinical and cost outcomes associated with biphasic insulin aspart 30/70 (BIAsp 30/70, premixed 30% soluble and 70% protaminated insulin aspart in one injection) compared to insulin glargine treatment in insulin-naïve type 2 diabetes patients failing oral antidiabetic agents in the UK, based on findings recently reported from the INITIATE clinical trial.

Methods: The CORE Diabetes Model, a published, peer-reviewed and validated model of diabetes, was used to evaluate life expectancy, quality-adjusted life expectancy, cumulative incidence of complications and direct medical costs over patient lifetimes. The model simulates the range of diabetic complications and disease progression within a series of sub-models (cardiovascular disease, neuropathy, renal and eye disease) based on published data. Baseline cohort characteristics (54.5% male, mean age 52.45 years, mean diabetes duration 9 years, mean HbA_{1c} 9.77%) and treatment effects were based on INITIATE. Costs were derived from published UK sources. The analysis was run over a 35-year time horizon (patient

lifetime) from a third party payer perspective. Costs and clinical benefits were discounted at 3.5% *per annum*. Sensitivity analyses were performed.

Results: BIAsp 30/70 was associated with projected improvements in discounted life expectancy (0.19 ± 0.20 years) and quality-adjusted life expectancy (0.19 ± 0.14 quality-adjusted life years [QALYs]), as well as a reduced incidence of retinopathy and nephropathy complications, versus glargine. Total lifetime direct costs were £1319 higher with BIAsp 30/70 than with glargine leading to an incremental cost-effectiveness ratio of £6951 per QALY gained.

Conclusions: This study is the first to address the long-term health economic implications of treating type 2 diabetes patients failing oral anti-diabetics with a biphasic insulin mix versus long-acting insulin. Our projections indicate that improved HbA_{1c} levels with BIAsp 30/70 treatment are associated with improvements in life expectancy and quality-adjusted life expectancy, and that BIAsp 30/70 represents excellent value for money compared to insulin glargine in the UK.

Introduction

In patients with type 2 diabetes mellitus, diminishing beta-cell function leads to progressive decreases in insulin secretion after a number of years. As a result, oral antidiabetic agents eventually fail to provide adequate glycemic control and most patients switch to exogenous insulin treatment^{1,2}. Insulin treatment is commonly initiated with a premixed formulation containing both basal and rapid-acting insulin, or with an intermediate or long-acting basal insulin^{3,4}. It has been postulated that biphasic analog insulin mixes offer an advantage over basal insulin alone as they provide a fast-acting soluble component (insulin aspart) to resolve mealtime hyperglycemia in type 1 and type 2 diabetes patients⁵⁻⁷.

Evidence for superior glycemic control with biphasic analog insulin mixes was provided by the recent INITIATE clinical study which compared treatment with biphasic insulin aspart 30/70 (BIAsp 30/70), a formulation of 30% soluble insulin aspart and 70% insulin aspart crystallized with protamine in one injection, with insulin glargine therapy in type 2 diabetes patients initiating insulin therapy⁸. INITIATE was a 28-week, randomized, controlled clinical trial in 233 insulin naïve patients, who were inadequately controlled on oral antidiabetic agents ($HbA_{1c} \geq 8.0\%$ on > 1000 mg/day metformin alone or in combination with other oral antidiabetic agents for at least three months). Metformin was adjusted up to 2550 mg/day before insulin therapy was initiated with 6 units of BIAsp 30/70 twice daily (pre-breakfast and pre-supper) or 12 units of glargine at bedtime, titrated to target blood glucose (80–110 mg/dL) by algorithm-directed titration assuring maximization of both insulins. Patients taking thiazolidinediones (TZD) in combination with metformin prior to enrolment continued TZD therapy throughout the study (regardless of treatment arm). At the end of the study, more patients in the BIAsp 30/70 treatment group reached target HbA_{1c} values of $< 7.0\%$ than in the glargine group (66% versus 40%, respectively, $p < 0.001$), and the mean reduction in HbA_{1c} was significantly greater in the BIAsp 30/70 group ($-2.79 \pm 0.11\%$) than in the glargine group ($-2.36 \pm 0.11\%$, $p < 0.01$). The improvement in HbA_{1c} associated with BIAsp 30/70 was particularly pronounced in the sub-group of patients with baseline $HbA_{1c} > 8.5\%$, where a decrease of $3.13 \pm 1.63\%$ was noted compared to only $2.60 \pm 1.50\%$ with glargine ($p < 0.05$). Fasting plasma glucose showed comparable decreases in the two groups. Safety monitoring showed that there were more minor hypoglycemia events (blood glucose values < 56 mg/dL) in the BIAsp 30/70 group (3.4 ± 6.6 episodes per patient-year) than in the glargine group (0.7 ± 2.0 episodes per patient-year, $p < 0.05$),

but the only major hypoglycemic event in the trial occurred in the glargine group. Weight gain (5.4 ± 4.8 versus 3.5 ± 4.5 kg, $p < 0.01$) and daily insulin dose (78.5 ± 39.5 versus 51.3 ± 26.7 units per day) were both higher in patients receiving BIAsp 30/70 than in the glargine group.

These clinical findings, from a 6-month trial, are supported by data from other clinical studies, and suggest that biphasic insulin analog mixes offer an advantage over basal insulin in large part due to their ability to control postprandial as well as fasting glucose levels⁵⁻⁸. However, no published data exist indicating the impact on long-term outcomes for type 2 diabetes patients receiving a biphasic insulin analog mix or basal insulin. We have therefore used a computer simulation modeling approach to project the short-term outcomes from the INITIATE study to evaluate the long-term clinical and cost outcomes of treatment with BIAsp 30/70 compared to insulin glargine in insulin naïve patients with type 2 diabetes failing oral antidiabetic agents.

Methods

Model

The analysis was performed using the CORE Diabetes Model, a published, peer-reviewed, validated, non-product-specific model of type 2 diabetes^{9,10}. In summary, the CORE Diabetes Model is an interactive computer simulation model designed to project the long-term health outcomes and economic consequences of different treatment policies or interventions in type 1 and type 2 diabetes. The model architecture is based on a series of sub-models that simulate the important complications of diabetes (cardiovascular disease, eye disease, hypoglycemia, nephropathy, neuropathy, foot ulcer, amputation, stroke, ketoacidosis, lactic acidosis and mortality), taking into account baseline cohort characteristics and medical history, diabetes management strategy, concomitant medications, screening strategies and changes in physiological parameters over time. Each sub-model is a Markov model using Monte Carlo simulation with time, state, time-in state, and diabetes type dependent probabilities derived from published sources. Monte Carlo simulation using tracker variables has been used to overcome the 'memory-less' properties of the standard Markov Model, and allows interconnectivity and interaction between individual complication sub-models. The model performs real time simulations to evaluate the incidence of complications, life expectancy, quality-adjusted life expectancy and total costs within defined populations. The model has been extensively validated against 'real life' data from published clinical and epidemiological studies of diabetes¹⁰.

Simulation cohorts

The baseline characteristics and risk factors of the simulation cohort were based on those of the INITIATE study population. INITIATE enrolled a total of 233 patients (117 in the BIAsp arm and 116 in the glargine arm). The baseline characteristics of this combined cohort were used to generate a virtual cohort of 1000 patients for simulation as summarized in Table 1, with 54.5% male, mean baseline age of 52.45 years, mean duration of diabetes 9 years and mean HbA_{1c} level of 9.77%. Baseline risk factors were drawn from the INITIATE study wherever possible, with additional data required for the model taken from published sources (Table 2).

Treatments and treatment effects

Treatment patterns from the INITIATE study were recreated for the model simulation⁸. In summary, following a 4-week run-in period where metformin was optimized and secretagogues and alpha-glucosidase inhibitors were discontinued (although pioglitazone was continued), insulin therapy (BIAsp 30/70 or glargine) was initiated at a total daily dose of 12 units. BIAsp 30/70 was administered 15 minutes before breakfast and evening meals using the FlexPen insulin delivery device (Novo Nordisk, Bagsvaerd, Denmark). The entire dose of glargine was administered at bedtime using a vial and syringe. Insulin doses were titrated weekly for the first 12 weeks, then every 2 weeks thereafter to achieve

Table 1. Baseline demographics of the simulation cohort

Characteristics	INITIATE study cohorts		Model simulation population
	BIAsp 30/70	Glargine	
Sex (%)			
Male	53.0	56.0	54.5
Female	47.0	44.0	45.5
Ethnic origin (%)			
Caucasian	54.7	51.7	53.2
Hispanic	27.4	25.9	26.6
Black	14.5	17.2	15.9
Other	3.4	5.2	4.3
Age (years), mean (SD)	52.6 (10.6)	52.3 (9.8)	52.45
BMI (kg/m ²), mean (SD)	31.5 (5.5)	31.4 (5.3)	31.45
Duration of diabetes (years), mean (SD)	9.5 (5.9)	8.9 (4.8)	9
HbA _{1c} (%), mean (SD)	9.70 (1.48)	9.84 (1.42)	9.77

Table 2. Baseline complications, relevant concomitant medications and management of patients in the simulated cohort

Parameter	Percentage at baseline (%)	Source ref. no.
Hypertensive heart disease (assumed LVH)	0	8
Angina pectoris	1.72	8
Myocardial infarction	2.15	8
Heart failure	0.43	8
Cardiac dysrhythmia (assumed atrial fibrillation)	1.29	8
Stroke	0	8
Peripheral vascular disease	0.86	8
Peripheral neuropathy	23.2	8
Foot ulcer/amputation	0.43/0.43	8
Microalbuminuria	4.0	8
Gross proteinuria	4.0	8
Background diabetic retinopathy	8.5	8
Proliferative diabetic retinopathy	0	8
Blindness and low vision	8.5	8
Cataract	4.3	8
Macula edema	0	8
Taking ACE-I/ARB	20.6	21
Taking statins	17.8	22
Taking aspirin	7.7	20
Screened for retinopathy (assumed treated with laser if detected)	63.2	23
Screened for renal disease (assumed treated with ACE-I or ARB if detected)	60	24
Screened for foot disease	37.3	24

LVH = left ventricular hypertension; ACE-I = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker

a target fasting plasma glucose and pre-supper glucose values of 80–110 mg/dL. Patients continued on this treatment regimen for the remainder of the simulation.

The treatment effects associated with BIA_{sp} 30/70 and glargine applied in the model are summarized in Table 3. Both treatments were associated with improvements in HbA_{1c} and, subsequently, gradual increases in HbA_{1c} levels were assumed to occur in both treatment arms in line with those observed in the United Kingdom Prospective Diabetes Study (UKPDS)¹¹. Body mass index (BMI) also increased in both treatment groups in the INITIATE study and this effect was applied in the simulation. After the initial increase in BMI according to treatment, BMI levels followed the natural course for type 2 diabetes patients reported in the NHANES II database¹². Doses of insulin also increased from baseline in the INITIATE study, and these increases were applied in the simulation, with specific reference to the calculation of costs.

Costs

Diabetes-specific costs of complications for 2004 in the UK were derived from published sources and are summarized in Table 4. Published evidence indicates that the cost of treating complications in patients with diabetes may well be higher than in the general population¹³. For example, it has been reported that the annual hospital costs associated with a fatal myocardial infarction (MI) event (£1567) and a non-fatal MI event (£5104) in a patient with diabetes were higher than the reference costs for a completed consultation episode for MI with complications in the general population (£1479)^{13,14}. In the present analysis, we therefore used costs data specific to diabetes patients as opposed to National Health Service (NHS) reference costs. All costs data that were not available in 2004 values were inflated using the composite NHS price inflation index¹⁵. Acquisition costs of the insulins used in the INITIATE clinical trial and administration devices were taken from the Monthly Index of Marketed Medicines¹⁶.

Discounting, time horizon and perspective

In the base case analysis, discount rates of 3.5% *per annum* were applied to costs and clinical benefits, in line with current recommendations for health economic analyses in the UK setting. A time horizon of 35 years was used to capture all events associated with the progression of diabetes and related complications in the simulation cohort. However, shortened time horizons of 5, 10 and 15 years were also investigated. The analysis was performed from a third party payer (NHS) perspective, taking into account only direct medical costs.

Table 3. Summary of treatment effects based on the findings of the INITIATE study

	BIA _{sp} 30/70	Glargine
Change from baseline in HbA _{1c} (%-points)	-2.79	-2.36
Change from baseline in BMI (kg/m ²)	+1.88	+1.22
Increase from baseline to end of study in total dose of insulin (units per kg body weight)	+0.82	+0.55

Sensitivity analyses

Sensitivity analyses were performed to investigate the impact of varying the key assumptions and drivers on model outcomes. The improvement in HbA_{1c} associated with BIA_{sp} 30/70 treatment was varied between +2.36%-points (the same as glargine treatment) and +3.22%-points (twice the relative improvement versus glargine) to investigate how this parameter influenced the long-term cost and clinical outcomes predicted by the model. Discount rates on costs and clinical benefits were varied between 0 and 6% *per annum* to assess how they influenced the study findings, and the time horizon of the simulation was varied between 5 and 35 years to provide data on the relative cost and clinical benefits of BIA_{sp} 30/70 and glargine treatment periods shorter than patients' lifetimes.

Statistical approach

For each simulation performed in the present study (base case and sensitivity analyses), 1000 patients were run 1000 times through the model, and mean results and standard deviations generated using a non-parametric bootstrapping approach¹⁷. Calculation of 1000 mean (and standard deviation) values allowed us to generate a scatterplot of incremental costs versus incremental effectiveness for BIA_{sp} 30/70 versus insulin glargine, which was in turn used to generate an acceptability curve, based on the percentage of points from the scatterplot falling below set willingness to pay values between 0 and £70 000.

Results

Base case analysis

Clinical outcomes

In a cohort of insulin naïve patients with type 2 diabetes and failing oral antidiabetic therapy, treatment with BIA_{sp} 30/70 was projected to improve life expectancy and quality-adjusted life expectancy compared to insulin glargine (Table 5). Discounted life expectancy

Table 4. Cost per event or state used in the analysis, expressed in British pounds sterling (£), 2004 values

Description of event or state	Annual costs (£)	Reference no.
Myocardial infarction, year of event	4598	13
Myocardial infarction, each subsequent year	757	13
Angina, year of onset	2385	13
Angina, each subsequent year	788	13
Congestive heart failure, year of onset	2659	13
Congestive heart failure, each subsequent year	932	13
Stroke, fatal	3548	13
Stroke, year of event	2813	13
Stroke, each subsequent year	532	13
Peripheral vascular disease, onset	2450	25*
Hemodialysis	26 073	26
Peritoneal dialysis	19 577	26
Kidney transplant, first year	20 500	27
Kidney transplant, each subsequent year	6749	27
Retinal photocoagulation	707	27
Severe vision loss/blindness, year of onset	914	13
Severe vision loss/blindness, each subsequent year	295	13
Cataract extraction	1629	13
Cataract annual follow-up	110	13
Neuropathy, onset	997	25*
Uninfected ulcer	1312	28
Infected ulcer	1345	28
Gangrene	2160	28
Amputation, year of event	9201	13
Amputation, prosthesis	585	13
Major hypoglycemic event	391	29
Ketoacidosis	852	30
Annual cost aspirin	65	16 (75 mg Angettes† tds)
Annual cost statins	386	16 (20 mg Crestor‡ od)
Annual costs ACE-I	235	16 (25 mg Captopril tds)
Costs of screening for retinopathy	28	31
Costs of screening for nephropathy	33	32
Costs non-standard ulcer treatment	216	16 (Regranex§ 12 g per year)

*Assuming one hospital admission at onset for investigation of symptoms

ACE-I = angiotensin converting enzyme inhibitor

†Angettes 75 (Bristol-Myers Squibb, New York, USA)

‡Crestor (AstraZeneca, London, UK)

§Regranex (Janssen-Cilag, Beerse, Belgium)

from the baseline cohort age of approximately 52 years was 0.19 years longer with BIAsp 30/70 (12.07 ± 0.16 years) than with insulin glargine (11.88 ± 0.16 years). A similar improvement in quality-adjusted life expectancy of approximately 0.19 quality-adjusted life years (QALYs) was observed with BIAsp 30/70 (8.46 ± 0.11 years) versus glargine (8.27 ± 0.11 years).

Analysis of the cumulative incidence of diabetes-related complications over patient lifetimes indicated that BIAsp 30/70 treatment was associated with notable reductions in retinopathy and nephropathy complications compared to glargine. For example, the cumulative incidence of severe visual loss associated with diabetic retinopathy was $11.1 \pm 1.0\%$ with BIAsp 30/70 treatment compared to $12.3 \pm 1.1\%$ with glargine. Moreover, the cumulative incidence of end-stage renal disease, one of the costliest complications associated with diabetes, was only $6.8 \pm 0.8\%$ in the BIAsp 30/70 group compared to $8.1 \pm 0.9\%$ in the glargine treatment

group. Cumulative incidence rates for cardiovascular and other complications were comparable in both treatment arms.

Costs and cost-effectiveness

Accounting of total direct costs over patients' lifetimes showed that BIAsp 30/70 therapy was £1319 per patient more expensive than insulin glargine (Table 5). This was due to higher treatment costs in the BIAsp 30/70 arm of approximately £2296 per patient, which was in part driven by improved life expectancy with BIAsp 30/70 versus glargine. However, treatment costs in the BIAsp 30/70 group were partially offset by the reduced cost of complications, in particular nephropathy complications where a mean cost saving of £569 per patient was observed, compared to glargine therapy over patients' lifetimes. The incremental cost-effectiveness ratio (ICER) was calculated to be £6788 per life year gained

or, taking into account quality of life, £6951 per QALY gained. Graphing incremental costs versus incremental effectiveness allowed us to generate a scatterplot of each of the 1000 bootstrap simulations performed in the base case analysis (Figure 1). From this, we could generate an acceptability curve which showed that BIAsp 30/70 was associated with a 88% likelihood of being cost-effective compared to glargine, with a willingness to pay of £30 000 per QALY gained in the treatment of patients with type 2 diabetes and failing oral antidiabetic treatment in the UK (Figure 2).

Sensitivity analyses

Sensitivity analyses on several key assumptions in the study showed that change from baseline in HbA_{1c} and time horizon were the major influences on clinical and cost outcomes (Table 6). Varying the reduction in mean HbA_{1c} associated with BIAsp 30/70 showed that when the effect on HbA_{1c} was the same as glargine (-2.36%),

quality-adjusted life expectancy (QALE) was very slightly greater (0.0091 QALYs) and costs were slightly lower (£2011 per patient) in the glargine treatment arm. However, when the reduction in mean HbA_{1c} with BIAsp 30/70 was set to 3.22% (base case minus 0.43%-points), the associated improvement in QALE led to the ICER falling to a value of £1966 per QALY gained for BIAsp versus glargine. Variation of discount rates had no substantial effect on the ICER (Table 6). Varying the time horizon demonstrated that BIAsp 30/70 represented good value for money even after 5, 10 and 15 years, with ICERs of £39 022, £18 991 and £10 849 per QALY gained for BIAsp 30/70 versus glargine, respectively.

Discussion

This health economic modeling study was the first to evaluate long-term clinical and cost outcomes associated with a biphasic insulin analogue versus long-acting

Table 5. Summary of base case results. Values shown are means with standard deviation in parentheses

Characteristics	BIAsp 30/70	Glargine	Difference
Life expectancy (years), mean (SD)	12.07 (0.16)	11.88 (0.16)	+0.19 (0.20)
QALE (QALYs), mean (SD)	8.46 (0.11)	8.27 (0.11)	+0.19 (0.14)
Total lifetime costs	£36 715 (824)	£35 396 (853)	£1319 (1083)
ICER – based on life expectancy (£ per life year gained)	–	–	£6788
ICER – based on QALE (£ per QALY gained)	–	–	£6951

QALE = quality-adjusted life expectancy; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life years
All values are rounded to two decimal places; apparent discrepancies are due to rounding

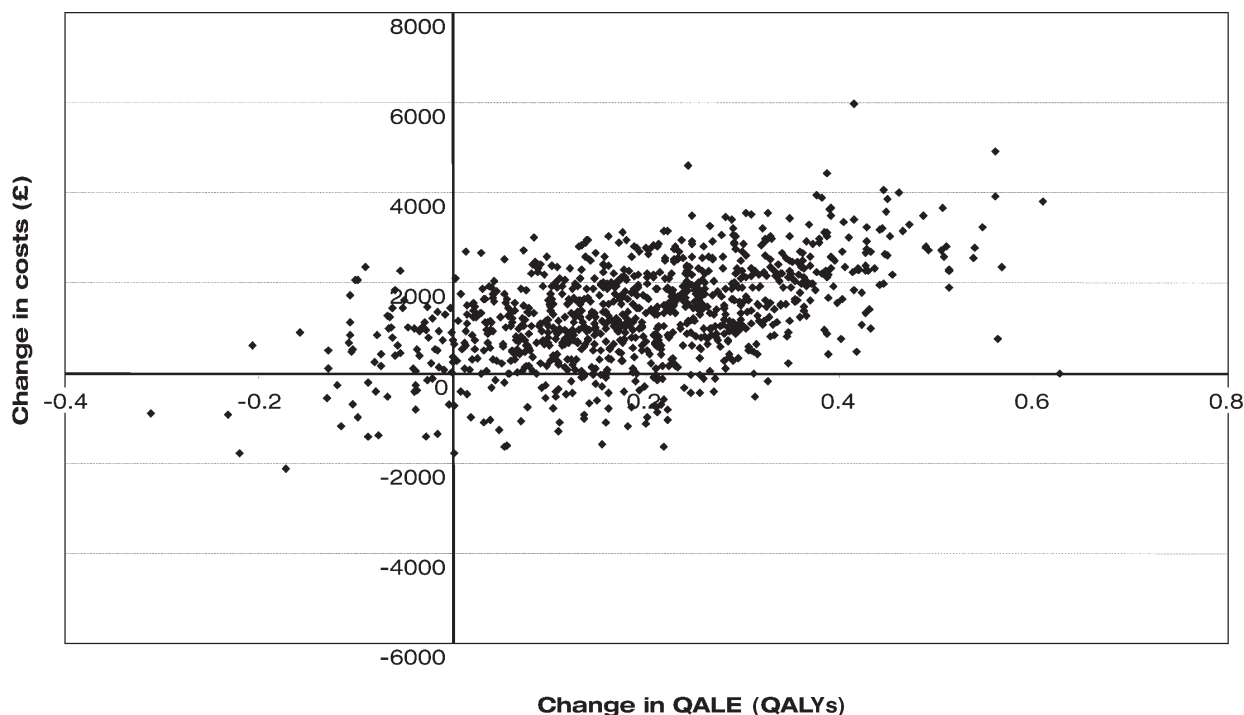


Figure 1. Scatterplot of change in costs versus change in life expectancy for BIAsp 30/70 versus glargine treatment.
QALE = quality-adjusted life expectancy

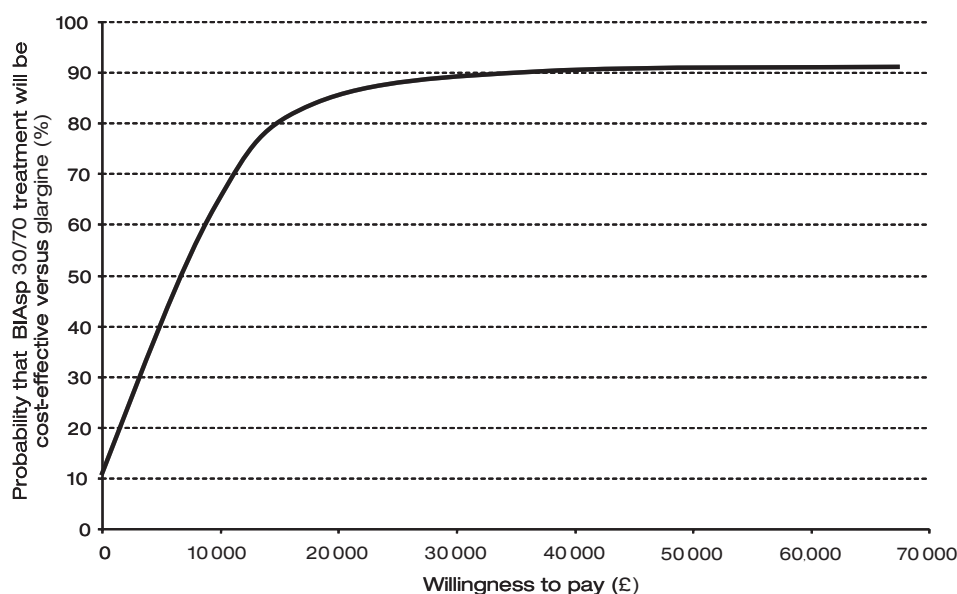


Figure 2. Acceptability curve

Table 6. Sensitivity analyses

	QALE (QALYs)		Total costs (£)		ICER (cost per QALY gained with BIAsp 30/70)
	BIAsp 30/70, mean (SD)	Glargine, mean (SD)	BIAsp 30/70, mean (SD)	Glargine, mean (SD)	
Base case analysis	8.46 (0.11)	8.27 (0.11)	£36 715 (824)	£35 396 (853)	£6951
Variation of change in HbA _{1c}					
Effect of BIAsp 30/70 reduced by 0.43%-points (same as glargine)	8.27 (0.11)	8.27 (0.11)	£37 407 (856)	£35 396 (853)	Glargine dominant
Effect of BIAsp 30/70 increased by 0.43%-points above base case	8.67 (0.11)	8.27 (0.11)	£36 170 (807)	£35 396 (853)	£1966
Variation of discount rates					
Discounting on costs and clinical benefits set to 0%	11.89 (0.19)	11.54 (0.19)	£58 469 (1570)	£56 497 (1601)	£5701
Discounting on costs and clinical benefits set to 6% and 1.5%, respectively	10.19 (0.15)	9.92 (0.15)	£27 801 (572)	£26 731 (595)	£4044
Discounting on costs and clinical benefits set to 6%	6.90 (0.08)	6.77 (0.08)	£27 801 (572)	£26 731 (595)	£8201
Variation of time horizon					
Time horizon set to 5 years	3.21 (0.02)	3.19 (0.02)	£8959 (204)	£8367 (207)	£39022
Time horizon set to 10 years	5.49 (0.05)	5.44 (0.05)	£17 345 (372)	£16 407 (393)	£18991
Time horizon set to 15 years	6.99 (0.07)	6.89 (0.08)	£24 423 (529)	£23 372 (531)	£10849

QALE = quality-adjusted life expectancy; QALY = quality-adjusted life years; ICER = incremental cost-effectiveness ratio

basal insulin in patients with type 2 diabetes failing oral antidiabetic agents. Based on the findings of the INITIATE clinical trial, the model predicted that insulin treatment with BIAsp 30/70 was associated with improvements in life expectancy and QALE compared to glargine in patients with type 2 diabetes. Moreover, notable reductions in the cumulative incidence of nephropathy and retinopathy complications were reported for the BIAsp 30/70 treatment arm. These clinical benefits were driven by improved HbA_{1c} levels associated with BIAsp 30/70 versus glargine as observed in INITIATE, despite associated gains in BMI. Over

patient lifetimes, treatment with BIAsp 30/70 was more expensive than glargine, although this difference was partially offset by reduced complication costs. The ICER was £6951 per QALY gained for BIAsp 30/70 versus glargine, which represents excellent value for money by current standards in the UK¹⁸. Sensitivity analysis demonstrated that the key driver in terms of clinical benefits and main difference between the treatments was the improvement in HbA_{1c} levels associated with BIAsp 30/70 treatment.

A potential criticism of the present analysis, and of a great many modeling analyses, is that it makes long-term

predictions based on short-term clinical findings. Indeed, the basic premise of the present study was to project the long-term clinical cost outcomes of treatment with biphasic insulin aspart versus long-acting insulin alone based on data from a relatively short-term clinical study. Inherently this is a shortcoming in the present analysis, as there is no direct clinical evidence to support the assumption that the differences between BIAsp 30/70 and glargine treatment in HbA_{1c} and BMI would be maintained over long-term treatment in type 2 diabetes patients. However, in the absence of long-term clinical or epidemiological follow up data, modeling is a valuable tool that provides us with the best available estimation of long-term clinical and cost outcomes. To succeed in this role, and to be accepted by clinicians and medical decision makers, models must be transparent and validated against published clinical and epidemiological data. In the present study, we used the CORE Diabetes Model which has been described in detail in a previous peer-reviewed publication and has been extensively validated against published data sources^{9,10}.

Another potential limitation of the present study was that the long-term projections were based on the findings of a single clinical trial⁸. One possible concern is that the treatments investigated might not be representative of common treatment practice in the UK. However, the treatments investigated in INITIATE conform to NICE guidelines in as much as patients failing treatment with metformin alone, or in combination with other oral agents, were started on insulin analogues (BIAsp 30/70 or glargine) and continued with metformin¹⁹. A second concern is that the clinical findings of a single trial have not been confirmed in multiple studies. However, the findings of the INITIATE study are not unique. For example, Malone *et al.*²⁰ recently reported a randomized, open-label study in 597 patients comparing twice-daily biphasic insulin lispro 75/25 or once-daily glargine, both taken concomitantly with metformin. After 16 weeks of treatment, more subjects reached target HbA_{1c} of < 7% in the group receiving lispro premix than in those taking glargine (41% versus 22%, *p* < 0.001). This evidence suggests that the clinical improvements observed in the INITIATE study may well prove to be robust as further evidence on the relative benefits of insulin treatments in type 2 diabetes patients from large scale and long-term studies accumulates in coming years.

Conclusions

This study is the first to address the long-term health economic implications of treating type 2 diabetes patients failing oral anti-diabetics with a biphasic insulin mix versus long-acting insulin. Based on the findings of the INITIATE study, our projections indicated

that treatment with BIAsp 30/70 is associated with improvements in life expectancy and QALE, as well as a reduced incidence of complications, compared to insulin glargine over patients' lifetimes. Moreover, cost-effectiveness analysis demonstrated that BIAsp 30/70 represents excellent value for money in the UK setting compared to insulin glargine, and should be considered for the treatment of insulin-naïve type 2 diabetes patients failing oral antidiabetic agents.

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