

Supplementary online material

Table S1: Hypoglycaemic event rates

	Hypoglycaemic events per patient per year					
	T1DM		T2DM _{BOT}		T2DM _{B/B}	
	Non-severe	Severe	Non-severe	Severe	Non-severe	Severe
Base-case event rates						
T1DM UKHSG [26] T1DM (<15 years)	29.0	3.2	–	–	–	–
T2DM _{BOT} UKHSG [26] T2DM (<2 years)	–	–	4.08	0.1	–	–
T2DM _{B/B} UKHSG [26] T2DM (>5 years)	–	–	–	–	10.2	0.7
Event rates used in sensitivity analyses						
UKHSG [26] T1DM (<5 years)	35.5	1.1	–	–	–	–
UKHSG [26] T2DM (>5 years)	–	–	10.2	0.7	–	–
UKHSG [26] T2DM (<2 years)	–	–	–	–	4.08	0.1
Clinical trial	53.85	0.27	2.05	0.015	13.58	0.052
Donnelly 2005 [49]	41.74	1.15	16.02	0.35	16.02	0.35
Dornhorst 2007 [40]	44.1	3.0	8.3	0.8	8.3	0.8
Frier 2015 [41]	126.7	0.87	29.1	0.15	48	0.324

Abbreviations: UKHSG, United Kingdom Hypoglycaemia Study Group

Table S2: One-way sensitivity analyses for T1DM, T2DM_{BOT} and T2DM_{B/B}

T1DM		ΔCost (£)	ΔQALY	ICER (£/QALY)
One Way Sensitivity Analysis				
Base case analysis UKHSG hypo rates, published hypo costs		-41.23	0.0044	Dominant
Hypoglycaemia rates Base case UKHSG: Non-severe: 29/year; severe: 3.2/year	Clinical trial data: non-severe: 53.85, severe: 0.27	-43.13	0.0082	Dominant
	UKHSG (<5yrs): non-severe: 35.5, severe: 1.1	-41.73	0.0054	Dominant
	Donnelly 2005 [49]: non-severe: 41.74, severe: 1.15	-42.20	0.0064	Dominant
	Dornhorst 2007 [40]: non-severe: 44.1, severe: 3	-42.38	0.0067	Dominant
	Frier 2015 [41]: non-severe: 126.7, severe: 0.87	-48.68	0.0193	Dominant
Hypoglycaemia distribution Base case: nocturnal hypoglycaemia =13.36%	Nocturnal proportion of hypoglycaemia: 25% (+50%)	-43.16	0.0083	Dominant
	Nocturnal proportion of hypoglycaemia: 7% (-50%)	-40.18	0.0023	Dominant
Hypoglycaemia disutility Base case Evans 2013	Currie 2006 disutilities [31]	-41.23	0.0023	Dominant
Treatment cost Base case: IGlAr = £41.50/pack	IGlar price -15%	8.94	0.0044	2,026.66
	IGlar price +15%	-91.40	0.0044	Dominant
Injection Frequency Base case: IGlAr 1/day, IDeg 1/day	IGlar: BID	-76.62	0.0044	Dominant
	Weighted (25.44% IGlAr BID)*	-50.23	0.0044	Dominant
Insulin doses Base case = 33.1/35 units/day (glar/asp) Ratio 0.87/0.85	Equal doses (1:1 rate ratio)	38.89	0.0044	8,813.21
	IGlar dose from EOT dose in Heller 2009 [50]	-39.77	0.0044	Dominant
Hypoglycaemia costs Base case = published	Clinical trial derived	-39.58	0.0044	Dominant
	Clinical trial derived, Currie disutilities	-39.58	0.0023	Dominant
2 year extension data	Trial 3644 [51]	-6.15	0.0044	Dominant
No hypo benefit	Hypoglycaemia risk ratio = 1	-39.02	-	Cannot be calculated
Flexible dosing utility	Published Evans 2013 (0.013) [32]	-41.23	0.0174	Dominant
	Published Boye 2011 (0.006) [33]	-41.23	0.0104	Dominant
IGlar U300	Toujeo® price, 15% basal insulin dose increase	-47.94	0.0044	Dominant

T1DM		Δ Cost (£)	Δ QALY	ICER (£/QALY)
	Toujeo® price, 17.5% basal insulin dose increase [37]	-55.36	0.0044	Dominant
	Toujeo® price, 17.5% basal insulin dose increase [37], no hypoglycaemia benefit	-53.15	-	Cannot be calculated

T2DM _{BOT}		Δ Cost (£)	Δ QALY	ICER (£/QALY)
One Way Sensitivity Analysis				
Base case analysis UKHSG hypo rates, published hypo costs		-32.37	0.0073	Dominant
Hypoglycaemia rates Base case UKHSG: Non-severe: 4.08/year; severe: 0.1/year	Clinical trial data: non-severe: 2.05, severe: 0.015	-0.96	0.0019	Dominant
	UKHSG (>5yrs): non-severe: 10.2, severe: 0.7	-249.49	0.0401	Dominant
	Donnelly 2005 [49]: non-severe: 16.02, severe: 0.35	-128.13	0.0265	Dominant
	Dornhorst 2007 [40]: non-severe: 8.3, severe: 0.8	-284.03	0.0438	Dominant
	Frier 2015 [41]: non-severe: 29.1, severe: 0.15	-64.28	0.0246	Dominant
Hypoglycaemia distribution Base case: nocturnal hypoglycaemia =24.66%	Nocturnal proportion of hypoglycaemia: 12.33% (-50%)	-31.22	0.0061	Dominant
	Nocturnal proportion of hypoglycaemia: 37% (+50%)	-33.52	0.0085	Dominant
Hypoglycaemia disutility Base case Evans 2013	Currie 2006 disutilities [31]	-32.37	0.0023	Dominant
Treatment cost Base case: IGl _{ar} = £41.50/pack	IGlar price -15%	45.99	0.0073	6,312.79
	IGlar price +15%	-110.74	0.0073	Dominant
Injection Frequency Base case: IGl _{ar} 1/day, IDeg 1/day	IGlar: BID	-67.77	0.0073	Dominant
	Weighted (23.51% IGl _{ar} BID)*	-40.80	0.0073	Dominant
Insulin doses Base case = 51.7 units/day (IGlar) Ratio 0.90	Equal doses (1:1 rate ratio)	26.29	0.0073	3,608.66
	Published doses Riddle 2003 [52], trial ratios	-32.85	0.0073	Dominant
	Published doses Riddle 2003 [52], equal doses	20.70	0.0073	2,841.64
Hypoglycaemia costs Base case = published	Clinical trial derived	-39.10	0.0044	Dominant
No hypo benefit	Hypoglycaemia risk ratio = 1	5.54	-	Cannot be calculated

T2DM _{BOT}		ΔCost (£)	ΔQALY	ICER (£/QALY)
Flexible dosing utility	Published Evans 2013 (0.013) [32]	-32.37	0.0203	Dominant
	Published Boye 2011 (0.006) [33]	-32.37	0.0133	Dominant
IGlar U300	Toujeo price, 17% basal insulin dose increase [53]	-52.12	0.0073	Dominant
	Toujeo price, 17% basal insulin dose increase [53], no hypoglycaemia benefit	-14.21	-	Cannot be calculated

T2DM _{B/B}		ΔCost (£)	ΔQALY	ICER (£/QALY)
One Way Sensitivity Analysis				
Base case analysis UKHSG hypo rates >5 years, published hypo costs		135.05	0.0084	15,983.37
Hypoglycaemia rates Base case UKHSG: Non-severe: 10.2/year; severe: 0.7/year	Clinical trial data: non-severe: 13.58, severe: 0.05	132.35	0.0113	11,764.60
	Donnelly 2005 [49]: non-severe: 16.02, severe: 0.35	130.41	0.0133	9,827.57
	Dornhorst 2007 [40]: non-severe: 8.3, severe: 0.8	136.56	0.0069	19,862.19
	Frier 2015 [41]: non-severe: 48, severe: 0.324	104.96	0.0398	2,639.73
Hypoglycaemia distribution Base case: nocturnal hypoglycaemia =13.36%	Nocturnal proportion of hypoglycaemia: 7% (-50%)	134.58	0.0089	15,076.91
	Nocturnal proportion of hypoglycaemia: 25% (+50%)	135.51	0.0080	16,998.39
Hypoglycaemia disutility Base case Evans 2013	Currie 2006 disutilities [31] (published hypo costs)	135.05	0.0065	20,928.97
Treatment cost Base case: IGlar = £41.50/pack	IGlar price -15%	236.00	0.0084	27,931.53
	IGlar price +15%	34.09	0.0084	4,035.21
Injection Frequency Base case: IGlar 1/day, IDeg 1/day	IGlar: 2/day	99.65	0.0084	11,794.45
	Weighted (20.98% IGlar BID)*	127.62	0.0084	15,104.53
Insulin doses Base case = 66.6/72.7 units/day (glar/asp) Ratio 1.08/1.00	Equal doses (1:1 rate ratio)	74.59	0.0084	8,827.91
	IGlar dose from EOT dose in Hollander 2008 [54]	107.96	0.0084	12,777.69
	EOT IGlar dose Hollander 2008 [54]; assumed equal doses	58.94	0.0084	6,975.97
No hypo benefit	Hypoglycaemia risk ratio = 1	143.16	-	Cannot be calculated
Flexible dosing utility	Published Evans 2013 (0.013) [32]	135.05	0.0214	6,296.08

T2DM_{B/B}		ΔCost (£)	ΔQALY	ICER (£/QALY)
	Published Boye 2011 (0.006) [33]	135.05	0.0144	9,346.27
IGlar U300	Toujeo price, 10% basal insulin dose increase [39]	151.39	0.0084	17,917.68
	Toujeo price, 10% basal insulin dose increase [39], no hypoglycaemia benefit	159.51	–	Cannot be calculate