

**SUPPLEMENTARY MATERIAL**

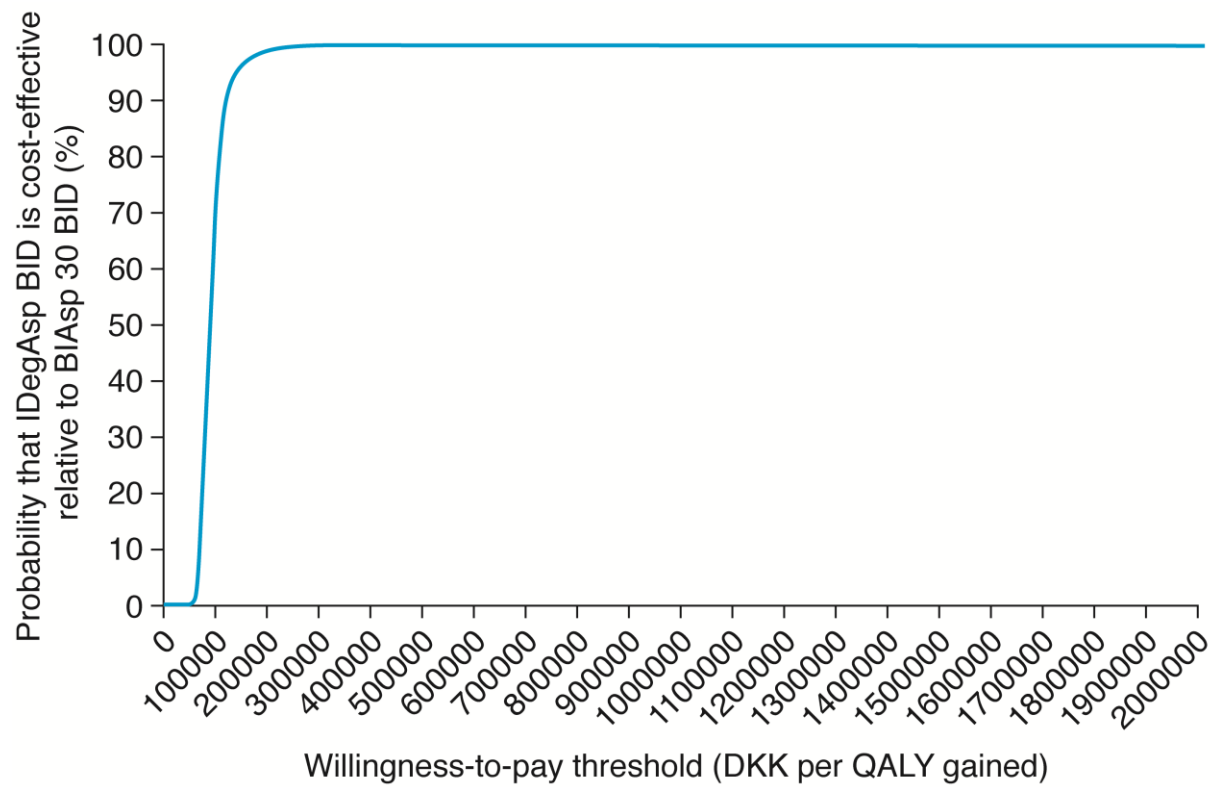
**Table S1. Results of one-way sensitivity analysis.**

		<b>ΔCost (DKK)</b>	<b>ΔQALY</b>	<b>ICER (DKK/QALY)</b>
<b>Base-case</b>		18,126	0.2224	81,508
<b>Time horizon</b> Base-case: 5 years	1 year	4003	0.0365	109,652
	2 years	7692	0.0851	90,433
	3 years	11,273	0.1322	85,279
	10 years	33,586	0.4259	78,867
<b>Discount rate</b> Base-case: 3% for both costs and effects	0%	19,201	0.2365	81,177
	5%	17,476	0.2138	81,729
<b>Hypoglycemia rates</b> Base-case: UKHSG <2 years on insulin. Non-severe 10.2/year; severe 0.7/year	Published event rates: non-severe daytime: 13.6, non-severe nocturnal: 8.3, and severe: 0.3 [35,36]	20,416	0.2875	71,012
	Clinical trial data from combined analysis: Non-severe daytime: 9.61 (titration), 10.50 (maintenance) Non-severe nocturnal: 1.96 (titration), 2.30 (maintenance) Severe: 0.13 (titration), 0.23 (maintenance)	22,006	0.1434	153,440
<b>Clinical trial data</b> Base-case: Combined analysis	Clinical trial data from global clinical trial [7]	24,947	0.2488	100,289
<b>Hypoglycemia costs</b> Base-case: Costs based on clinical trial resource use	Severe hypoglycemia event cost +20%	16,914	0.2224	76,049
	Severe hypoglycemia event cost -20%	19,338	0.2224	86,968

		<b>ΔCost (DKK)</b>	<b>ΔQALY</b>	<b>ICER (DKK/QALY)</b>
<b>BMI treatment difference</b> Base-case: IDegAsp – BIAsp 30; BMI treatment difference of –0.19.	BMI treatment difference: 0	18,126	0.2174	83,383
<b>Hypoglycemia disutility</b> Base-case: severe 0.0565, non-severe daytime 0.0041 and non-severe nocturnal 0.0067	Published disutilities: severe 0.0118, non-severe 0.0036 [37]	18,126	0.0865	209,446
<b>SMBG disutility</b> Base-case: SMBG disutility 0.0000221	Disutility: 0	18,126	0.2216	81,797
<b>BMI disutility</b> Base-case: 0.0061	Disutility: 0	18,126	0.2174	83,383

*ICER* incremental cost-effectiveness ratio, *QALY* quality-adjusted life year, *SMBG* self-measured blood glucose, *UKHSG* UK Hypoglycaemia Study Group.

**Fig. S1 Cost-effectiveness acceptability curve.** *BIAsp 30* biphasic insulin aspart, *BID* twice daily, *IDegAsp* insulin degludec/insulin aspart, *QALY* quality-adjusted life year.



**Table S2. Probabilistic sensitivity analyses.**

<b>Hypoglycemia rate ratios</b>	<b>Rate ratio</b>	<b>P value</b>	<b>SE</b>	<b>Distribution</b>
<i>Titration (0–16 weeks)</i>				
Daytime non-severe hypoglycemia	1.00 <sup>†</sup>	0.7782	0.111	Lognormal
Nocturnal non-severe hypoglycemia	0.46	<0.0001	0.182	Lognormal
Severe hypoglycemia	1.00 <sup>†</sup>	0.7802	0.502	Lognormal
<i>Maintenance (16–26 weeks)</i>				
Daytime non-severe hypoglycemia	0.76	0.0207	0.121	Lognormal
Nocturnal non-severe hypoglycemia	0.39	<0.0001	0.214	Lognormal
Severe hypoglycemia	0.16	0.0061	0.671	Lognormal
<b>Doses (BIAsp 30)</b>	<b>Mean</b>	<b>P value</b>	<b>SE</b>	<b>Distribution</b>
At baseline	45.7		1.513	Normal
After titration (week 16)	81.8		2.558	Normal
After total trial period (week 26)	86.2		2.795	Normal
<b>Dose ratio</b>	<b>Dose ratio</b>	<b>P value</b>	<b>SE</b>	<b>Distribution</b>
At baseline	1.00 <sup>§</sup>			Assumed
After titration (week 16)	0.84	<0.0001	0.026	Lognormal
After total trial period (week 26)	0.84	<0.0001	0.027	Lognormal
<b>BMI change (BIAsp 30)</b>	<b>Mean</b>	<b>P value</b>	<b>SE</b>	<b>Distribution</b>
At baseline	0.0		0.0	Assumed
After titration (week 16)	0.5		0.047	Normal
After total trial period (week 26)	0.7		0.058	Normal
<b>BMI change difference</b>	<b>Mean diff.</b>	<b>P value</b>	<b>SE</b>	<b>Distribution</b>
At baseline	0.0			Assumed
After titration (week 16)	0.0 <sup>‡</sup>	0.143	0.060	Normal
After total trial period (week 26)	−0.19	0.012	0.070	Normal
<b>Hypoglycemia disutilities</b>	<b>Mean</b>	<b>P value</b>	<b>SE</b>	<b>Distribution</b>
Non-severe – daytime	0.0041		0.000	Normal
Non-severe – Nocturnal	0.0067		0.000	Normal
Severe	0.0565		0.002	Normal
<b>SMBG disutility</b>	<b>Mean</b>	<b>P value</b>	<b>SE</b>	<b>Distribution</b>
Disutility per test	−0.0000221		0.0000058	Normal
<b>BMI disutility</b>	<b>Mean</b>	<b>P value</b>	<b>SE</b>	<b>Distribution</b>
TTO index prediction	0.0061	<0.001	0.001	Normal

*BIAsp 30* biphasic insulin aspart, *BMI* body mass index, *CI* confidence interval, *SE* standard error, *SMBG* self-measured blood glucose, *TTO* time trade off.

<sup>†</sup> Set to 1 because of non-significance; <sup>‡</sup> Set to 0 because of non-significance; <sup>§</sup> Assumed.