

Preferences for Risks and Benefits of Islet Cell Transplantation for Persons with Type 1 Diabetes with History of Episodes of Severe Hypoglycemia: A Discrete Choice Experiment to Inform Regulatory Decisions

Table 1 Supplement: CBC Experiment Attributes and Levels

ATTRIBUTES	LEVELS
Chance of achieving clinical treatment success as defined by a normal range HbA1c ($\leq 7.0\%$) and elimination of severe hypoglycemia by end of year 1 after final islet cell infusion period	40 out of 100 people
	60 out of 100 people
	90 out of 100 people
Success duration as defined by duration of time that a normal range HbA1c and elimination of severe hypoglycemia lasts after the final infusion without additional actions	0.5 years or less
	1 year
	2 years
	5 years
Extent of Insulin independence defined as not needing any insulin doses or to monitor sugars or adjust insulin to maintain your blood glucose within the first 5 years after your transplantation procedure	Never independent
	2 years of independence
	5 years of independence
Expected reduction in the risk of long term complications such as high risk of developing vision loss, or moderate risk of developing kidney damage, or low risk of developing nerve damage	Eye
	Kidney
	Nerve
Risk of Treatable procedure-related adverse effects such as nausea, vomiting, diarrhea, moderate bleeding, anemia, pain treated with medications, headache, tremors, confusion, high blood pressure or cholesterol	0 out of 100 people
	5 out of 100 people
	15 out of 100 people
	40 out of 100 people
Risk of Serious complications requiring hospital treatment and rare death (serious infections, liver bleeds, kidney damage, development of antibodies making additional transplant more difficult or cytomegalovirus infections or viral heart inflammation.	0 out of 100 people
	1 out of 100 people
	5 out of 100 people
	15 out of 100 people

Restrictions due to life time immunosuppression (anti-rejection) medications required as long as your islet cells are working (up to 5 years or longer)	Medication to prevent Mouth sores, anemia
	Constant need for Renal complications monitoring
	Need to take precautions to because of a higher infection risk
	Monitoring for increased risk of cancer
Time and support needed if 1-3 islet cell procedures are required each requiring 3 months of extra time and support to manage your diabetes including 3-5 days hospital stay, 2 weeks intensive monitoring of diabetes, and monthly physician visits each time	3 months
	6 months
	9 months

Table 2 Supplement: Hypoglycemic Scoring System Rubric and Group Membership (Number of patients in each criteria (with overlap))

Criteria	# of patients (%)
HbA1c > 8%	14 (16)
At least 1 SHE past 12 months	36 (40)
Using any type of insulin pump OR checked blood glucose > 6 times/day	63 (70)
Had a diabetes-related overnight hospital stay in past 12 months	9 (10)

Number of patients **ONLY** in each criterion (with no overlap):

Criteria	# of patients (%)
HbA1c > 8%	1 (1)
At least 1 SHE past 12 months	5 (5)
Had a diabetes-related overnight hospital stay in past 12 months	2 (2)
Using any type of insulin pump	18 (20)
Checked blood glucose > 6 times/day	6 (7)

Number of patients meeting at least 1, 2, or 3 criteria:

Criteria	# of patients (%)
At least 1 criterion (<u>HIGHER RISK SAMPLE</u>)	77 (86)
At least 2 criteria	38 (42)
At least 3 criteria	6 (7)

Number of patients meeting exact number of criteria:

Criteria	# of patients (%)
Exactly 1	39 (43)
Exactly 2	32 (36)

Exactly 3	5 (6)
Exactly 4	1 (1)

*SHE=Severe hypoglycemic episode

Note: The HIGHER RISK SAMPLE had at least 1 high risk criteria and was chosen for analysis (n=77) along with the Full sample of patients (n=90

Table 3 Supplement: Patient Preferences: Mean and Standard Deviation Estimates

3A Supplement: Full Sample– (n=90)

Attribute	Level	Mean Estimates				Standard Deviation Estimates				Odds Ratio
		coefficient	standard error	t value	p value	coefficient	standard error	t value	p value	
Chance of clinical treatment success	40%	-	-	-	-	-	-	-	-	1.00
	60%	0.49 ***	0.13	3.66	0.00	0.11	0.40	0.29	0.77	1.63
	90%	1.09 ***	0.18	6.17	0.00	0.73 ***	0.20	3.65	0.00	2.98
Success duration	0.5 years	-	-	-	-	-	-	-	-	1.00
	1 year	0.64 ***	0.16	3.95	0.00	0.22	0.26	0.86	0.39	1.89
	2 years	0.84 ***	0.17	4.82	0.00	0.54 *	0.28	1.89	0.06	2.32
	5 years	1.39 ***	0.20	6.87	0.00	0.72 ***	0.22	3.22	0.00	4.01
Insulin independence	Never independent	-	-	-	-	-	-	-	-	1.00
	2 years	1.10 ***	0.16	6.88	0.00	0.33	0.52	0.63	0.53	3.00
	5 years	1.75 ***	0.21	8.47	0.00	0.78 ***	0.21	3.79	0.00	5.78
Long term complications	Eye	-	-	-	-	-	-	-	-	1.00
	Kidney	0.22 *	0.13	1.71	0.09	0.24	0.26	0.95	0.34	1.25
	Nerve	0.13	0.14	0.92	0.36	0.66 ***	0.18	3.69	0.00	1.14
Treatable adverse effects	0%	-	-	-	-	-	-	-	-	1.00
	5%	-0.53 ***	0.16	-3.35	0.00	0.48 **	0.23	2.07	0.04	0.59
	15%	-0.69 ***	0.16	-4.26	0.00	0.05	0.22	0.22	0.82	0.50
	40%	-1.01 ***	0.17	-5.96	0.00	0.36	0.30	1.22	0.22	0.37
Serious complications	0%	-	-	-	-	-	-	-	-	1.00
	1%	-0.30 **	0.15	-2.05	0.04	0.18	0.42	0.43	0.67	0.74
	5%	-1.02 ***	0.19	-5.33	0.00	0.82 ***	0.23	3.55	0.00	0.36
	15%	-2.03 ***	0.29	-6.98	0.00	1.97 ***	0.29	6.85	0.00	0.13
Restrictions	Mouth sores, anemia	-	-	-	-	-	-	-	-	1.00
	Renal monitoring	-0.61 ***	0.19	-3.17	0.00	1.19 ***	0.23	5.23	0.00	0.54
	Higher infection risk	0.05	0.16	0.30	0.77	0.52 **	0.23	2.22	0.03	1.05
	Cancer	0.20	0.16	1.25	0.21	0.46 **	0.22	2.13	0.03	1.22
Time and support	3 months	-	-	-	-	-	-	-	-	1.00
	6 months	-0.07	0.13	-0.51	0.61	0.16	0.27	0.59	0.56	0.94
	9 months	-0.21	0.13	-1.57	0.12	0.42 **	0.21	1.98	0.05	0.81

3B Supplement: Higher Hypoglycemic Risk Sample (n=77)

Attribute	Level	Mean Estimates				Standard Deviation Estimates				Odds Ratio
		coefficient	standard error	t value	p value	coefficient	standard error	t value	p value	
Chance of clinical treatment success	40%	-	-	-	-	-	-	-	-	1.00
	60%	0.47 ***	0.17	2.82	0.00	0.16	0.27	0.60	0.55	1.60
	90%	1.24 ***	0.21	5.81	0.00	0.82 ***	0.21	3.96	0.00	3.45
Success duration	0.5 years	-	-	-	-	-	-	-	-	1.00
	1 year	0.81 ***	0.20	4.11	0.00	0.26	0.26	0.99	0.32	2.24
	2 years	1.03 ***	0.22	4.77	0.00	0.68 **	0.28	2.45	0.01	2.81
	5 years	1.65 ***	0.24	6.88	0.00	0.88 ***	0.29	3.09	0.00	5.19
Insulin independence	Never independent	-	-	-	-	-	-	-	-	1.00
	2 years	1.24 ***	0.20	6.24	0.00	0.97 ***	0.23	4.21	0.00	3.47
	5 years	1.96 ***	0.25	7.92	0.00	1.26 ***	0.28	4.55	0.00	7.10
Long term complications	Eye	-	-	-	-	-	-	-	-	1.00
	Kidney	-0.01	0.15	-0.09	0.93	0.02	0.21	0.09	0.93	0.99
	Nerve	0.12	0.17	0.67	0.50	0.67 ***	0.25	2.68	0.01	1.12
Treatable adverse effects	0%	-	-	-	-	-	-	-	-	1.00
	5%	-0.53 ***	0.19	-2.83	0.00	0.29	0.38	0.76	0.44	0.59
	15%	-0.72 ***	0.19	-3.77	0.00	0.23	0.24	0.98	0.33	0.49
	40%	-1.00 ***	0.21	-4.85	0.00	0.22	0.67	0.34	0.74	0.37
Serious complications	0%	-	-	-	-	-	-	-	-	1.00
	1%	-0.29	0.18	-1.62	0.11	0.35	0.39	0.91	0.36	0.75
	5%	-1.16 ***	0.22	-5.33	0.00	1.03 ***	0.24	4.31	0.00	0.31
	15%	-2.51 ***	0.35	-7.09	0.00	2.32 ***	0.36	6.36	0.00	0.08
Restrictions	Mouth sores, anemia	-	-	-	-	-	-	-	-	1.00
	Renal monitoring	-0.64 **	0.25	-2.55	0.01	1.36 ***	0.25	5.47	0.00	0.53
	Higher infection risk	-0.07	0.21	-0.32	0.75	0.81 **	0.26	3.07	0.00	0.93
	Cancer	0.12	0.18	0.63	0.53	0.47 **	0.24	1.97	0.05	1.12
Time and support	3 months	-	-	-	-	-	-	-	-	1.00
	6 months	-0.14	0.16	-0.86	0.39	0.39 *	0.20	1.93	0.05	0.87
	9 months	-0.29 *	0.16	-1.82	0.07	0.47 **	0.20	2.34	0.02	0.75

Note: Analysis is a Random Parameters Logit, (dummy coded)

Table 4 Supplement: Utility Preference Scores by Subgroups of Individual Demographic and Clinical Characteristics (Full sample)

		Females		Males		PAID: High Diabetes Distress		PAID: Low/Normal Diabetes Distress	
Attributes	Levels	Coefficients / SE	Z-value/sig,	Coefficients/SE	Z-value/sig,	Coefficients/SE	Z-value/sig,	Coefficients/SE	Z-value/sig,
Chance Clin RX Success	40%								
	60%	1.137730/ 0.367744	3.0938 0.001976 0 **	0.298397 0.235050	1.2695 0.204260 9	0.223175 0.498638	0.4476 0.654464 7	0.8529493 0.2357312	3.6183 0.000296 5 ***
	90%	2.096946/ 0.559512	3.7478 0.000178 4 ***	1.240711 0.265281	4.6770 2.911e-06 ***	3.309911 0.764791	4.3279 1.506e-05 ***	1.5939011 0.2773674	5.7465 9.109e-09 ***
Success Duration	0.5 years								
	1 year	0.929478 0.377542	2.4619 0.013819 6 *	0.846171 0.271090	3.1214 0.001800 1 **	-0.295538 0.626381	-0.4718 0.637056 2	1.1210385 0.2390364	4.6898 2.734e-06 ***
	2 years	1.739836 0.444563	3.9136 9.094e-05 ***	0.932532 0.302357	3.0842 0.002040 9 **	-0.041450 0.646433	-0.0641 0.948873 5	1.1678571 0.2526824	4.6218 3.804e-06 ***
	5 years	2.506835 0.503521	4.9786 6.404e-07 ***	1.718140 0.360583	4.7649 1.890e-06 ***	2.312850 0.697561	3.3156 0.000914 4 ***	2.1290455 0.3150176	6.7585 1.394e-11 ***
Insulin Independence	None								
	2 years	2.441503 0.513976	4.7502 2.032e-06 ***	1.129990 0.263864	4.2825 1.848e-05 ***	2.448290 0.670298	3.6525 0.000259 7 ***	1.5914348 0.2419414	6.5778 4.776e-11 ***
	5 years	3.376511 0.596844	5.6573 1.538e-08 ***	2.130769 0.361981	5.8864 3.947e-09 ***	7.373971 1.592198	4.6313 3.633e-06 ***	2.5241223 0.4107860	6.1446 8.016e-10 ***
Reduction LT Complications	Eye								
	Kidney	0.397240 0.294534	1.3487 0.177431 6	0.320311 0.243127	1.3175 0.187683 6	-0.195210 0.552856	-0.3531 0.724017 6	0.2224672 0.2080667	1.0692 0.284974 6

	Nerve	0.029920 0.305765	0.0979 0.922049 1	0.272043 0.266899	1.0193 0.308074 2	0.042963 0.467723	0.0919 0.926813 1	0.1105089 0.1942172	0.5690 0.569358 5
Treatable AEs	0%								
	5%	-0.004322 0.313816	-0.0138 0.989011 7	-1.182770 0.327594	-3.6105 0.000305 6 ***	-0.484414 0.525793	-0.9213 0.356892 5	-0.7085136 0.2139269	-3.3119 0.000926 5 ***
	15%	-0.797374 0.407802	-1.9553 0.050548 1	-1.103335 0.291602	-3.7837 0.000154 5 ***	-0.867250 0.586646	-1.4783 0.139322 3	-0.7832597 0.2287289	-3.4244 0.000616 2 ***
	40%	-0.623759 0.323081	-1.9307 0.053525 3	-1.893343 0.341583	-5.5429 2.976e-08 ***	-1.915031 0.619548	-3.0910 0.001994 7 **	-1.3662627 0.2782496	-4.9102 9.098e-07 ***
Serious Complications	0%								
	1%	-0.527056 0.310343	-1.6983 0.089450 9	-0.462607 0.260186	-1.7780 0.075406 0	0.630672 0.542296	1.1630 0.244843 5	-0.5160149 0.2091468	-2.4672 0.013616 0 *
	5%	-1.028090 0.340598	-3.0185 0.002540 4 **	-1.184468 0.326649	-3.6261 0.000287 7 ***	-3.872279 1.021406	-3.7911 0.000150 0 ***	-1.4180334 0.2978175	-4.7614 1.922e-06 ***
	15%	-3.981710 0.861909	-4.6196 3.844e-06 ***	-3.088143 0.571179	-5.4066 6.423e-08 ***	-6.167967 1.411271	-4.3705 1.240e-05 ***	-2.8023487 0.4430966	-6.3245 2.541e-10 ***
Immunosupp . Restrictions	Mouth, Anemia								
	Renal monitor -ing	0.065076 0.379524	0.1715 0.863855 3	-0.542507 0.313628	-1.7298 0.083669 7	-5.326533 1.238308	-4.3015 1.697e-05 ***	-0.5806011 0.2885271	-2.0123 0.044189 1 *
	Higher Inf. Risk	0.504427 0.406514	1.2409 0.214656 9	-0.149437 0.270130	-0.5532 0.580123 9	2.906552 0.943812	3.0796 0.002072 9 **	-0.0037735 0.2221054	-0.0170 0.986444 8
	Cancer Risk	0.754083 0.414716	1.8183 0.069016 3	0.222869 0.265181	0.8404 0.400659 4	-0.927047 0.620499	-1.4940 0.135166 6	0.5895887 0.2725669	2.1631 0.030533 7 *
Time & Support for Multiple ICT	3 months								
	6 m M onths	0.056550 0.291519	0.1940 0.846189 0	0.165208 0.219822	0.7516 0.452320 0	-0.412925 0.543487	-0.7598 0.447392 8	0.0787228 0.2029694	0.3879 0.698123 2
	9 months	-0.360170 0.315915	-1.1401 0.254251 3	-0.238334 0.212895	-1.1195 0.262929 0	-1.840205 0.597547	-3.0796 0.002072 8 **	-0.2823336 0.1904490	-1.4825 0.138217 1

Figure 1 Supplement: Patient Recruitment

