SUPPLEMENTARY DATA

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SUPPLEMENTARY DATA

Supplementary Appendix S2. Missing Data by Survey

Survey	Time Point	Total N	Observed and Used N (%)	Partial and Excluded N (%)	Completely Missing N (%)
DDS	Baseline	48	44 (92%)	3 (6%)	1 (2%)
	Day 75	48	44 (92%)	2 (4%)	2 (4%)
	Day 365	48	39 (81%)	2 (4%)	7 (15%)
	Day 730	48	27 (56%)	5 (10%)	16 (33%)
HFS	Baseline	48	39 (81%)	8 (17%)	1 (2%)
	Day 75	48	40 (83%)	7 (15%)	1 (2%)
	Day 365	48	35 (73%)	6 (13%)	7 (15%)
	Day 730	48	18 (38%)	14 (29%)	16 (33%)
SF-36	Baseline	48	47 (98%)	-	1 (2%)
	Day 75	48	45 (94%)	-	3 (6%)
	Day 365	48	41 (85%)	-	7 (15%)
	Day 730	48	30 (63%)	-	18 (38%)
EQ-5D Health Preference Weight	Baseline	48	47 (98%)	0 (0%)	1 (2%)
	Day 75	48	47 (98%)	0 (0%)	1 (2%)
	Day 365	48	41 (85%)	1 (2%)	6 (13%)
	Day 730	48	32 (67%)	0 (0%)	16 (33%)
EQ-5D VAS	Baseline	48	46 (96%)	-	2 (4%)
	Day 75	48	47 (98%)	-	1 (2%)
	Day 365	48	42 (88%)	-	6 (13%)
	Day 730	48	31 (65%)	-	17 (35%)

The DDS total score, HFS total score, SF-36, EQ-5D Health Preference Weight, and EQ-5D VAS broken out by the expected number of observations at each time point and wither the observation was observed, excluded because it was partially complete, or completely missing. The QMSS software automatically handled partial SF-36 questionnaires. The EQ-5D VAS is a single item and therefore it cannot be partially complete. In order to gauge the impact of missing data, we assessed the probability of having missing data based on past survey responses. In this manner, we are able to study whether subjects with worse survey responses tend to have missing or incomplete surveys during follow-up. No associations between past survey responses and the likelihood of missing surveys during follow-up were found (analysis not shown).

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Supplementary Appendix S3. Survey by Primary Endpoint Success at Day 365

Survey	Visit	Primary Endpoint Success			Primary Endpoint Failure			p-value
		N	Mean (SD)	Median (IQR)	N	Mean (SD)	Median (IQR)	
DDS Total Score	Day 365	36	1.45 (0.47)	1.29 (0.59)	3	2.14 (0.71)	2.06 (1.41)	0.0573
	Day 730	24	1.27 (0.29)	1.21 (0.38)	3	1.69 (0.35)	1.65 (0.71)	0.0537
HFS Total Score	Day 365	32	0.47 (0.56)	0.22 (0.78)	3	1.28 (1.24)	1.35 (2.48)	0.3265
	Day 730	16	0.33 (0.47)	0.13 (0.39)	2	1.09 (1.48)	1.09 (2.09)	0.4379
SF-36 PCS	Day 365	39	52.46 (7.84)	54.39 (8.47)	2	53.54 (4.93)	53.54 (6.97)	0.9759
	Day 730	26	53.06 (9.15)	56.56 (7.81)	4	48.41 (8.40)	51.16 (12.12)	0.0818
SF-36 MCS	Day 365	39	51.95 (9.09)	54.61 (13.20)	2	50.02 (7.25)	50.02 (10.25)	0.5854
	Day 730	26	55.12 (6.68)	57.35 (7.88)	4	49.69 (10.32)	51.74 (14.52)	0.3241
EQ-5D VAS	Day 365	39	82.77 (14.97)	85.00 (22.00)	3	84.00 (5.29)	82.00 (10.00)	0.8315
	Day 730	27	86.44 (15.51)	91.00 (17.00)	4	81.00 (15.51)	84.50 (23.00)	0.2932

The DDS total score, HFS total score, SF-36 PCS, SF-36 MCS, and EQ-5D VAS broken out by primary endpoint success or failure at day 365 and day 730 following initial islet transplantation. Tests for differences between successes and failures at each visit were performed using the Mann-Whitney U test and the exact p-value is reported.

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Supplementary Appendix S4. Survey by Insulin Independence at Day 365

Survey	Visit	Insulin Independence Success			Insulin Independence Failure			p-value
		N	Mean (SD)	Median (IQR)	N	Mean (SD)	Median (IQR)	
DDS Total Score	Day75	10	1.72 (0.49)	1.62 (0.88)	34	1.87 (0.78)	1.62 (0.76)	1.0000
	Day 365	21	1.38 (0.47)	1.24 (0.41)	18	1.65 (0.53)	1.59 (0.47)	0.0405
	Day 730	8	1.34 (0.32)	1.35 (0.32)	19	1.31 (0.33)	1.24 (0.59)	0.6478
HFS Total Score	Day 75	9	1.09 (1.06)	0.65 (2.04)	31	1.40 (0.83)	1.26 (1.30)	0.3390
	Day 365	19	0.40 (0.59)	0.09 (0.39)	16	0.72 (0.70)	0.67 (1.11)	0.2038
	Day 730	4	0.40 (0.52)	0.17 (0.54)	14	0.41 (0.66)	0.07 (0.43)	0.4484
SF-36 PCS	Day 75	10	50.61 (5.98)	52.20 (10.14)	35	49.79 (8.61)	49.55 (9.81)	0.8806
	Day 365	23	52.95 (7.76)	54.24 (9.75)	18	51.97 (7.78)	54.64 (6.97)	0.7229
	Day 730	8	56.74 (2.26)	56.62 (3.43)	22	50.88 (10.10)	54.47 (9.64)	0.1812
SF-36 MCS	Day 75	10	55.57 (3.86)	56.35 (4.61)	35	52.31 (10.69)	54.66 (11.39)	0.7639
	Day 365	23	52.29 (8.94)	55.53 (14.43)	18	51.31 (9.17)	53.24 (11.62)	0.6647
	Day 730	8	55.71 (7.33)	57.64 (8.57)	22	53.92 (7.37)	56.11 (9.88)	0.5420
EQ-5D VAS	Day 75	11	77.36 (16.63)	80.00 (21.00)	36	79.58 (15.96)	80.00 (17.50)	0.7233
	Day 365	23	81.52 (17.10)	85.00 (24.00)	19	84.47 (10.68)	87.00 (15.00)	0.7902
	Day 730	8	88.50 (11.86)	93.50 (20.50)	23	84.78 (16.53)	91.00 (16.00)	0.5711

The DDS total score, HFS total score, SF-36 PCS, SF-36 MCS, and EQ-5D VAS broken out by insulin independence success or failure at day 75, day 365, and day 730 following initial islet transplantation. Tests for differences between successes and failures at each visit were performed using the Mann-Whitney U test and the p-value based on the normal approximation is reported.

SUPPLEMENTARY DATA

Supplementary Appendix S5. Impact of Occurrence of SHE on Survey

Survey	Score	Mean (SE)	95% CI
DDS	Total	-	-
	Emotional Burden	1.08 (0.42)	(0.23, 1.92)
	Physician-Related Distress	-	-
	Regimen-Related Distress	-	-
	Interpersonal Distress	-	-
HFS	Total	-	-
	Hypoglycemia Avoidance Behavior	0.48 (0.32)	(-0.13, 1.07)
	Worry about Hypoglycemia	0.12 (0.38)	(-0.65, 0.87)
SF-36	PCS	2.64 (2.79)	(-2.83, 8.77)
	MCS	-7.85 (3.34)	(-14.79, -1.21)
EQ-5D	VAS	-1.61 (5.69)	(-12.08, 10.16)

Supplemental Appendix S5 Legend:

The mean estimates, standard errors, and associated bootstrap 95% confidence intervals for the SHE incidence indicator of the longitudinal models are shown. A dash (-) indicates that model selection removed the SHE incidence indicator from the model. Included in candidate models were patient characteristics (age, disease duration, gender, and baseline BMI), metabolic outcomes (HbA_{1C} and basal and 90-minute C-peptide from mixed meal tolerance tests), and a time-varying indicator of whether or not a subject had experienced an SHE. This indicator represents the impact on survey responses, of moving from a state of freedom from SHE to a state where at least one SHE has occurred. Model selection was performed in two steps: first by checking variance inflation factors to assess multicollinearity of the covariates; and second by using LASSO regression, making use of a leave-one-cluster-out cross-validation guided by minimizing the Akaike Information Criterion to select the tuning parameter.

SUPPLEMENTARY DATA

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92. Robien, Mark A
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94. Rosichuk, Shawn
95. Sarman, Donna
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