Appendix B

Table 1: Nephropathy Status at enrollment according to study group.

Characteristic		Case Singleton	Case Trio Proband	Case Total	Control Singleton	Control Trio Proband	Control Total
ESRD							
N		369 (65%)	127 (51%)	496 (60%)	0	0	0
Dialysis		40 (11%)	8 (6.%)	48 (10%)			
Kidney Transplant		327 (89%)	119 (94%)	446 (90%)			
Diabetes Duration at ESRD							
(years)	*Mean (SD)*	24.6 (7.1)	24.5 (6.8)	24.5 (7.0)			
ESRD Duration at Enrollment							
(years)	*Mean (SD)*	9.1 (5.5)	7.6 (5.4)	8.7 (5.5)			
NON-ESRD							
N		203 (35%)	121 (49%)	324 (40%)	595 (100%)	302 (100%)	891 (100%)
ACR (ug albumin/mg creatinine)							
	Median (SD)	1045 (1577)	1083 (1292)	1061 (1475)	5.8 (3.5)	5.8 (3.6)	5.8 (3.6)
MDRD GFR (mL/min/1.73m2)*							
	Mean (SD)	53.7 (27)	49.6 (24.7)	52.3 (26.3)	87.1 (16.8)	87.9 (15.8)	87.4 (16.5)
	GFR<60	122 (62%)	68 (62%)	190 (62%)	19 (3%)	3 (1%)	22 (3%)
	GFR≥60	74 (38%)	41 (38%)	115 (38%)	562 (97%)	291 (99%)	853 (97%)
Cockcroft-Gault GFR (mL/min)*							
	Mean (SD)	72.1 (35.1)	67.5 (36.7)	70.5 (35.7)	108 (31)	114 (30)	110 (31)
	GFR<60	84 (44%)	54 (50%)	138 (46%)	7 (1%)	3 (1%)	10 (1%)
	GFR≥60	109 (56%)	55 (50%)	164 (54%)	566 (99%)	283 (99%)	849 (99%)
Serum Creatinine (mg/dL)							
	Mean (SD)	1.8 (1.1)	1.8 (1.0)	1.8 (1.05)	0.9 (0.2)	0.9 (0.1)	0.9 (0.2)
100/creatinine	*<60*	86 (44%)	48 (44%)	134 (44%)	0 (0%)	0 (0%)	0 (0%)
	≥60	110 (56%)	61 (56%)	171 (56%)	579 (100%)	292 (100%)	871 (100%)
Serum Cystatin C (mg/dL)							
	Mean (SD)	1.8 (0.9)	1.8 (1.0)	1.8 (0.9)	0.9 (0.2)	0.9 (0.2)	0.9 (0.2)
100/cystatin C	*<60*	83 (43%)	50 (47%)	133 (45%)	2 (0.4%)	0 (0%)	2 (0.2%)
	≥60	109 (57%)	56 (53%)	165 (55%)	554 (99.6%)	277 (100%)	831 (99.8%)

* References 41 and 42.

Table 2: Clinical characteristics at enrollment according to study group.

Characteristic		Case			Control			P value
		Singleton	Trio Proband	Total	Singleton	Trio Proband	Total	Total Cases vs. Total Controls
Race								
	White	505 (89%)	234 (94%)	739 (90%)	571 (97%)	292 (97%)	863 (97%)	<0.0001
Gender								
	Male	305 (54%)	106 (43%)	411 (50%)	241 (41%)	127 (42%)	368 (41%)	0.0002
Age at Entry (years)								
	Mean (SD)	43.2 (6.8)	39.6 (7.2)	42.2 (7.1)	39.9 (8.4)	34.8 (8.2)	38.2 (8.7)	<0.0001
	<40	174 (31%)	143 (58%)	317 (39%)	291 (49%)	218 (73%)	509 (57%)	<0.0001
	40+	396 (69%)	105 (42%)	501 (61%)	302 (51%)	82 (27%)	384 (43%)	
Body Mass Index (kg/m2)								
	Mean (SD)	25.9 (5.4)	25.5 (7.2)	25.8 (5.4)	26.1 (4.4)	26.5 (4.5)	26.2 (4.4)	0.0004
Waist Circumference (cm)								
	Mean (SD)	89.1 (15.8)	89.1 (14.6)	89.1 (15.5)	86.8 (13.9)	84.3 (12.5)	85.9 (13.5)	0.02
Smoker								
	Ever	281 (49%)	113 (46%)	394 (48%)	201 (34%)	96 (32%)	297 (33%)	<0.0001

Table 3: Diabetes characteristics at enrollment according to study group.

Characteristic		Case			Control			P value
		Singleton	Trio Proband	Total	Singleton	Trio Proband	Total	Total Cases vs. Total Controls
Age at Diagnosis of Diabetes								
(years)	*Mean (SD)*	12.2 (6.9)	10.5 (5.8)	11.7 (6.6)	12.8 (7.3)	13.6 (7.5)	11.2 (6.6)	0.0046
	0-9	216 (38%)	117 (47%)	333 (41%)	202 (34%)	130 (43%)	332 (37%)	0.003
	10-14	173 (30%)	77 (31%)	250 (31%)	136 (23%)	100 (33%)	236 (26%)	
	15+	181 (32%)	54 (22%)	235 (29%)	255(43%)	70 (23%)	325 (36%)	
Diabetes Duration								
(years)	*Mean (SD)*	31.0 (8.2)	29.1 (7.3)	30.4 (8.0)	26.3 (7.9)	23.6 (7.1)	25.4 (7.7)	<0.0001
	10-14	11 (2%)	4 (2%)	15 (2%)	NA	NA	NA	<0.0001
	15-24	125 (22%)	61 (26%)	186 (23%)	287 (48%)	187 (62%)	474 (53%)	
	25+	434 (76%)	183 (74%)	617 (75%)	306 (52%)	113 (38%)	419 (47%)	
Pancreas transplant								
	Yes	156 (27%)	52 (21%)	208 (25%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<0.0001
HbA1c (%)								
	Mean (SD)	7.7 (1.9)	7.9 (2.0)	7.8 (1.9)	7.4 (1.1)	7.5 (1.3)	7.5(1.2)	
without pancreas transplant	*Mean (SD)*	8.3 (1.5)	8.4 (1.8)	8.4 (1.6)*	7.4 (1.1)	7.5 (1.3)	7.5 (1.2)	0.0001
with pancreas transplant	*Mean (SD)*	6.0 (1.7)	6.0 (2.0)	6.0 (1.7)*				
Insulin Regimen								
	Single shot	43 (9%)	15 (7%)	58 (8%)	31 (5%)	12 (4%)	43 (5%)	<0.0001
	Multiple	318 (67%)	150 (68%)	468 (67%)	333 (57%)	145 (49%)	478 (54%)	
	Pump	103 (22%)	53 (24%)	156 (23%)	214 (36%)	139 (47%)	353 (40%)	
	Other	9 (2%)	3 (1%)	12 (2%)	11 (2%)	2 (1%)	13 (1%)	
Dose (Units/Kg/Day)								
	Mean (SD)	0.5 (0.3)	0.6 (0.3)	0.5 (0.4)	0.6 (0.2)	0.6 (0.2)	0.6 (0.2)	0.053
Other Autoimmune diseases								
	Yes	110 (19%)	34 (14%)	144 (18%)	126 (21%)	66 (22%)	192 (22%)	0.043

* p < 0.0001, for cases without pancreas transplants compared with those who had transplants

Table 4: Related Characteristics at enrollment according to study group.

Characteristic		Case			Control			P value
		Singleton	Trio Proband	Total	Singleton	Trio Proband	Total	Total Cases vs. Total Controls
Hypertension								
	Yes	482 (85%)	204 (82%)	686 (84%)	43 (7%)	11 (4%)	54 (6%)	<0.0001
Antihypertensive treatment								
	Yes	468 (83%)	203 (83%)	671 (83%)	NA	NA	NA	<0.0001
Blood Pressure								
Systolic BP (mm Hg)								
	Mean (SD)	131.1 (20)	129.7 (18)	130.7 (19)	118.5 (12)	115.7 (11)	117.6(12)	<0.0001
Diastolic BP (mm Hg)								
	Mean (SD)	74.1 (11.0)	75.1 (10.6)	74.4 (10.9)	71.4 (8.1)	71.3 (8.3)	71.4 (8.1)	<0.0001
Serum Lipids								
Total Cholesterol (mg/dL)								
	Mean (SD)	188.3 (47)	199.6 (44)	191.6 (46)	185.1 (31)	186.5 (34)	185.5 (32)	0.029
HDL Cholesterol (mg/dL)								
	Mean (SD)	53.3 (18.0)	56.2 (16.6)	54.1 (17.6)	59.0 (15.9)	56.6 (14.7)	58.2 (15.5)	<0.0001
Lipid-lowering drug								
	Yes	302 (53%)	149 (60%)	451 (55%)	500 (85%)	251 (85%)	751 (85%)	<0.0001
Parents' Living								
	0	180 (32%)	0	180 (22%)	119 (20%)	0	119 (13%)	<0.0001*
	1	208 (37%)	0	208 (26%)	182 (31%)	0	182 (21%)	
	2	159 (28%)	247 (100%)	404 (50%)	258 (44%)	303 (100%)	559 (63%)	
	Unkonwn	14 (3%)	0	14 (2%)	26 (4%)	0	26 (3%)	

* Note: The Chi-square test is done by comparing the numbers of parents' living of case and control singletons.

Table 5: Other Complications of Diabetes according to study group*

Complication		Case Singleton	Case Trio Proband	Case Total	Control Singleton	Control Trio Proband	Control Total	P value Total Cases vs. Total Controls
Retinopathy								
Laser Treatment	*Yes*	476 (86%)	201 (83%)	677 (85%)	109 (19%)	40 (13%)	149 (17%)	<0.0001
Cardiovascular Disease								
	Yes	504 (89%)	206 (83%)	710 (87%)	67 (11%)	27 (9%)	94 (11%)	<0.0001
Neuropathy								
	Yes	383 (67%)	156 (63%)	539 (66%)	81 (14%)	23 (8%)	104 (12%)	<0.0001

*The complications are self-reported.