Diabetic Complications Consortium

Application Title: Sexual Function and Neuropathy in Pre-Diabetes and Type 2 Diabetes

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1. Project Accomplishments:

Analyses for Specific Aim 1 is largely complete with manuscripts being currently drafted. Abstracts for Male Erectile Dysfunction and Female Sexual Dysfunction in the DPPOS will be submitted to the 2022 American Diabetes Association meeting. Planning for analyses and manuscript proposal requests to the DPPOS are in progress for Specific Aim 2.

2. Specific Aims:

The finalized specific aims of the project were to use the DPPOS cohort to focus upon the burden of and risk factors for sexual dysfunction among men and women at high risk for type 2 diabetes participating in the DPPOS.

SPECIFIC AIM 1: Determine the burden of ED among men and FSD among women with pre-diabetes and incident T2DM and examine the impact of DPP treatment arm and glycemia trajectories on risk of sexual dysfunction. Prevalence of ED and FSD will be examined in men and women with pre-diabetes and incident T2DM overall and stratified by DPP treatment arm (intense lifestyle intervention, metformin, placebo) and glycemic trajectories over time (fasting glucose, 2-h post challenge glucose, HbA1c, fasting insulin). These data will offer novel insights into the extent of sexual dysfunction among adults with, and at high-risk for T2DM, and the impact of both behavioral and medical therapies for diabetes and long-term glycemic control on report of sexual dysfunction. This will allow providers to gain a deeper understanding and appreciation of high-impact co-morbidities that patients are often reluctant to discuss and ultimately provide information to design and power intervention and prevention trials.

SPECIFIC AIM 2: Examine the association between neuropathy and ED in men and FSD in women with pre-diabetes and incident T2DM. Associations between annual assessments of cardiovascular autonomic neuropathy (heart rate variability) and peripheral neuropathy (Michigan Neuropathy Screening Instrument, monofilament exams) and sexual dysfunction will be examined in men and women with pre-diabetes and incident T2DM. The potential modifying effects of treatment arm and long-term glycemic trajectories will be examined in detail. Longitudinal measures of cardiac autonomic neuropathy and peripheral neuropathy offer a unique opportunity to chart nerve function trajectories over time and relate these patterns to sexual dysfunction and further assess how glycemic control modifies these relationships. This information will help providers better understand how the complex interplay of key risk factors impacts sexual dysfunction, informing on patient education and care planning.

Initially we examined the prevalence of ED based on several definitions available using the International Index of Erectile Function (IIEF) by DPP Treatment Arm.
First, we found that 572 men had completed the IIEF questionnaire during DPPOS Year 15. We examined several definitions of ED using various validated cut points. We also examined the rate of medication use for ED and included those who indicated medication use as meeting the definition for ED. Several differences were observed when examining individual categories of ED by DPP arm. **(Table 1)** While there appeared to be a smaller proportion of men reporting severe ED in the metformin and lifestyle groups (compared to placebo), there were greater proportions of men reporting mild/moderate ED in these treatment arms. Given our hypotheses that the treatment arms would have prevented ED, it is possible that treatment may have shifted the distribution of what would have been more severe ED into the less severe categories. However, given that the ED prevalence was measured ~20 years after randomization, it is difficult to determine its true impact. Furthermore, the scoring of the IIEF has been debated in the literature given the bias towards sexual dysfunction given that men indicating no sexual activity (score of 0 on several questions) are grouped into the erectile dysfunction categories. There are several ways to avoid this bias: 1) remove all men who indicated no sexual activity prior to scoring the IIEF and 2) use responses to the single item confidence question to identify ED. The question is as follows: *How would you rate your confidence that you could get and keep an erection?* Responses include very low, low, moderate, high, and very high. After removing the no sexual activity responses from the total IIEF, we found that 205 men indicated no sexual activity significantly limiting our sample. We decided to pursue the definition of ED using the single item question on the IIEF as the responses are irrespective of sexual activity status and allowed us to maintain our full sample. ED was defined as those men who reported low or very low to the confidence question. This approach was used and validated in our previous work in the DCCT/EDIC cohort. The distribution of responses to the single item question is presented in **Figure 1** below.

We then examined the distribution of sociodemographic, clinical and diabetes-related characteristics by ED status defined as those who med ED criteria on the single item question and/or reported ED medications (n=218). After adjustment for age, we found significant differences by race in report of ED with significantly less report of ED in non-white (African- American Hispanic and Native American) men compared to white men. Traditional risk factors reported in the general population for ED were also observed to be important in this cohort. For example, men with ED were more likely to report depression, have higher waist circumference, and higher LDL and lower HDL cholesterol levels. There were no significant differences observed in the diabetes-related or glycemic measures by ED status. There were, however, significant differences in markers of peripheral and autonomic neuropathy. We hypothesize that the profile of ED in this cohort is more related to the metabolic phenotype. Further analyses are underway to examine metabolic syndrome as a whole and its individual components as risk factors. These findings are different than data presented in the type 1 population in which ED is significantly impacted by long term glycemic control. The DPPOS population while at high risk for type 2 diabetes (with some already having been diagnosed) is still in a relatively mild/early state for diabetes complications.

Table 1. Prevalence of Erectile Dysfunction at DPPOS Year 15 by Treatment Arm						
	Overall (n=572)	**Placebo (n=183)**	**Metformin (n=207)**	**p-value***	**Lifestyle (n=182)**	**p-value***
				0.129		0.092
ED (score<26 or meds)	440 (76.9%)	132 (72.1%)	163 (78.7%)		146 (79.7%)	
No ED	132 (23.1)	51 (27.9%)	44 (21.3%)		37 (20.3%)	
				0.819		0.939
Mild to moderate/moderate severe ED (score < 22 or meds)	386 (67.5)	124 (67.8)	138 (66.7)		124 (68.1)	
No ED/mild ED	186 (32.5)	59 (32.2)	69 (33.3)		58 (31.9)	
				0.021		0.046
No ED	132 (23.1%)	51 (27.9%)	44 (21.3%)		37 (20.3%)	
Mild/mild to moderate	90 (15.7%)	18 (9.8%)	40 (19.3%)		32 (17.6%)	
Moderate/Severe/ ED medication	350 (61.2%)	114 (62.3%)	123 (59.4%)		113 (62.1%)	
				0.005†		0.072†
No ED	132 (23.1%)	51 (27.9%)	44 (21.3%)		37 (20.3%)	
Mild ED	54 (9.4%)	8 (4.4%)	25 (12.1%)		21 (11.5%)	
Mild to moderate	36 (6.3%)	10 (5.5%)	15 (7.2%)		11 (6.0%)	
Moderate	73 (12.8%)	16 (8.7%)	34 (16.4%)		23 (12.6%)	
Severe	265 (46.3%)	95 (51.9%)	84 (40.6%)		86 (47.3%)	
ED medication	12 (2.1%)	3 (1.6%)	5 (2.4%)		4 (2.2%)	
Comparison to No ED (ref)						
No ED	132 (23.1%)	51 (27.9%)	44 (21.3%)	--	37 (20.3%)	--
Mild ED	54 (9.4%)	8 (13.6%)	25 (36.2%)	0.004	21 (36.2%)	0.005
Mild to moderate	36 (6.3%)	10 (16.4%)	15 (25.4%)	0.223	11 (22.9%)	0.391
Moderate	73 (12.8%)	16 (23.9%)	34 (43.6%)	0.013	23 (38.3%)	0.078
Severe	265 (46.3%)	95 (65.1%)	84 (65.6%)	0.923	86 (69.9%)	0.398
ED medication	12 (2.1%)	3 (5.6%)	5 (10.2%)	0.473†	4 (9.8%)	0.460†

*p-value for comparison between intensive lifestyle intervention and placebo and between metformin and placebo.
†Fisher's exact test

Figure 1. Prevalence of ED Based on Responses to Confidence Question

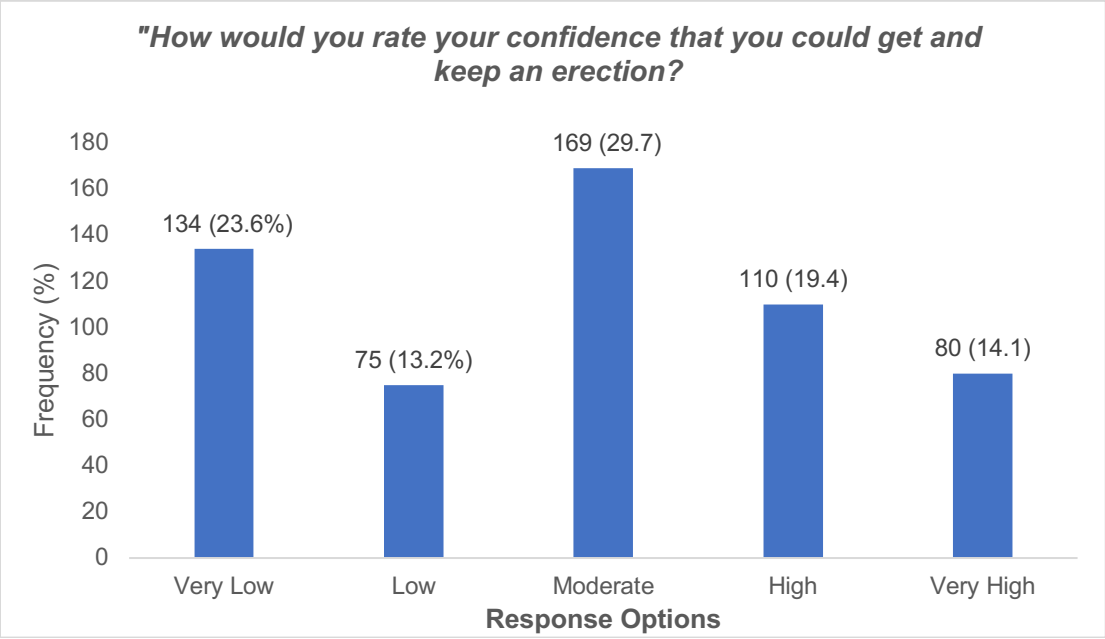

Table 2. Characteristics of Men in the DPPOS at Year 15 by ED status (N=568)				
	ED (n=218)	**No ED (n=350)**	**p-value**	**age-adjusted p-value**
Group assignment			0.599	
Placebo	74 (40.7%)	108 (59.3%)	ref	ref
Metformin	80 (38.8%)	126 (61.2%)		0.632
Lifestyle	64 (35.6%)	116 (64.4%)		0.329
Sociodemographics				
Age (years)	74.5 ± 9	68.8 ± 8.8	<0.001	--
Race/ethnicity (%)			<0.001	
White	144 (66.1%)	170 (48.6%)	ref	ref
African American	24 (11%)	66 (18.9%)		0.001
Hispanic	31 (14.2%)	71 (20.3%)		0.014
Native American/Asian	19 (8.7%)	43 (12.3%)		0.351
Marital Status			0.302	
Never married	20 (9.2%)	42 (12%)	ref	ref
Living together/Married	176 (80.7%)	263 (75.1%)		0.798
Separated/Divorced/Widowed	22 (10.1%)	45 (12.9%)		0.277
Clinical/Behavioral				
Current Smoking (%)	4 (1.9%)	5 (1.4%)	0.735*	0.323
Weekly Alcohol Use (%)	67 (31.9%)	142 (40.8%)	0.044	0.064
General Health (%)			0.004	
Excellent/very good	51 (23.5%)	87 (24.9%)	ref	ref
Good	122 (56.2%)	227 (64.9%)		0.274
Fair/poor	44 (20.3%)	36 (10.3%)		0.053
Depression (%)	41 (19.5%)	41 (12%)	0.023	0.005
Summary mean depression score	4.2 ± 4	2.7 ± 2.8	<0.001	<0.001
Physical Activity (MET/week)	19.6 ± 20.8	21.2 ± 21	0.402	0.303
Summary mean MET/week	22.3 ± 17.4	21.2 ± 15.3	0.440	0.845
Body Mass Index (kg/m2)	30.5 ± 5.7	30.8 ± 6.2	0.654	0.119
Summary mean BMI	31.2 ± 5.3	31.3 ± 6	0.833	0.129
Waist Circumference (cm)	110.2 ± 13.4	107.7 ± 14.9	0.041	0.001
Summary mean waist	109.5 ± 12.2	107.2 ± 14.1	0.041	0.002
PDE5 Inhibitor use (%)	12 (5.5%)	0 (0%)	<0.001	<0.001
Albumin:creatinine	63.4 ± 261.4	44.5 ± 240.3	0.398	0.525
Summary mean Alb/cre	34.7 ± 126	18.5 ± 42.6	0.068	0.061
Testosterone	3200.9 ± 1077.4	3256.4 ± 1209.8	0.579	0.225
CVD Risk Factors				
JNC Hypertension Status (%)			0.063	
Hypertensive	158 (79%)	238 (70.8%)		0.088
Prehypertensive	20 (10%)	57 (17%)		ref
Normotensive	22 (11%)	41 (12.2%)	ref	ref
Blood Pressure (mm/Hg)				
Systolic	122.8 ± 14.1	123.3 ± 14.8	0.697	0.569
Diastolic	70.8 ± 10.6	72.7 ± 10	0.029	0.795
Summary mean blood pressure				
Systolic	122.6 ± 9.2	121 ± 9.5	0.047	0.207
Diastolic	73.3 ± 7.2	74.8 ± 6.6	0.011	0.895
Antihypertensive use (%)	154 (77%)	227 (67.6%)	0.026	0.049
LDL cholesterol (mg/dL)	85.5 ± 28.9	88.2 ± 31.5	0.316	0.728
Summary mean LDL	95.4 ± 22.3	102.5 ± 22.4	<0.001	0.012
HDL cholesterol (mg/dL)	48.3 ± 12.4	49.4 ± 12.2	0.296	0.018
Summary mean HDL	44.8 ± 10.5	45.6 ± 9.1	0.332	0.030
Triglycerides (mg/dL)	119.9 ± 60.4	129.7 ± 82.1	0.110	0.675
Summary mean triglycerides	138.2 ± 64.4	142.1 ± 66.1	0.489	0.445
Coronary calcification (%)	149 (83.2%)	233 (74.2%)	0.028	0.437

Peripheral and Autonomic Function				
MNSI questionnaire>4 or exam>2	118 (57.3%)	150 (44.2%)	0.004	0.109
MNSI questionnaire>7 or exam>2	118 (57.3%)	149 (44%)	0.003	0.094
MNSI questionnaire	1.2 ± 1.5	0.9 ± 1.4	0.021	0.076
MNSI questionnaire>4	9 (4.2%)	11 (3.2%)	0.680	0.595
Summary mean MNSI questionnaire	1 ± 1	0.8 ± 0.9	0.008	0.025
MNSI exam	2.7 ± 1.8	2.1 ± 1.6	<0.001	0.010
MNSI exam>2	118 (57.3%)	149 (44%)	0.003	0.094
Summary mean MNSI exam	2.1 ± 1	1.7 ± 0.9	<0.001	0.008
Heart rate	63.4 ± 11.1	63.6 ± 11.3	0.840	0.713
Summary mean heart rate	62.2 ± 8.4	63.2 ± 8.6	0.172	0.752
QTI	103.7 ± 7	101.9 ± 4.7	0.001	0.023
Summary mean QTI	101.3 ± 4.1	100.2 ± 3.3	<0.001	0.013
SDNN	23 ± 16.2	28.4 ± 24	0.003	0.048
Abnormal SDNN	6 (3.5%)	12 (3.9%)	0.989	0.473
Summary mean SDNN	12.9 ± 5.3	13.3 ± 6.2	0.462	0.917
RMSD	23.1 ± 20.7	26.2 ± 24.7	0.143	0.290
Abnormal RMSD	9 (5.2%)	16 (5.3%)	1.000	0.707
Summary mean RMSD	24.3 ± 13.9	24.4 ± 14.4	0.940	0.955
Diabetes				
Fasting plasma glucose (mg/dL)	129.4 ± 40.2	128.1 ± 32.1	0.697	0.158
Summary mean fasting glucose	118.9 ± 21.7	118.7 ± 19.6	0.923	0.225
HbA1c (%)	6.5 ± 1.6	6.5 ± 1.3	0.851	0.228
Summary mean HbA1c	2.3 ± 1.6	2.3 ± 1.5	0.794	0.233
Fasting insulin (μU/mL)	32.5 ± 32.1	29.8 ± 20.5	0.288	--
Log fasting insulin	30.3 ± 17.7	30.4 ± 15	0.933	0.226
Summary mean fasting insulin	3.2 ± 0.7	3.2 ± 0.6	0.854	--
Log of summary mean fasting insulin	3.3 ± 0.5	3.3 ± 0.5	0.434	0.433
Type 2 diabetes (%)	145 (66.5%)	246 (70.3%)	0.395	0.835
Duration of diabetes (years)	8.1 ± 7.4	7.7 ± 7	0.482	0.350
Diabetes by HbA1c	92 (42.2%)	163 (46.6%)	0.352	0.505
Duration of diabetes by HbA1c	3.8 ± 6.1	3.8 ± 5.8	0.974	0.331
Loss of glycemic control	39 (17.9%)	85 (24.4%)	0.088	0.823
% of visits with loss of glycemic control	12.3 ± 23.4	11.6 ± 20.9	0.734	0.068

*Fisher's exact test

The following dummy tables have been submitted to the DPPOS analytic team to complete. We will build a final multivariable model that will examine the factors that were significant in bivariate analyses above. Factors significant at the $p<0.1$ level will be included in a stepwise backwards model build where factors remaining at the $p<0.05$ will be retained in the final model (**Table 3**). Additionally, individual peripheral and autonomic function variables will be examined at DPPOS baseline, Year 15, change and summary mean. Categorical representations of these variables will also be explored. (**Table 4**)

Table 3. Multivariable Adjusted Odds Ratios for ED Per Unit Change in Each Covariate

	Odds Ratio (95% CI)	p-value
DPN Model		
CAN Model		

Note: Odds ratios and p-values from separate logistic regression models.

Table 4. Multivariable Adjusted Odds Ratios for ED by Diabetic Peripheral Neuropathy and Autonomic Neuropathy Indices

	Age-adjusted Odds Ratio (95% CI)	p-value
Diabetic Peripheral Neuropathy Measures		
MNSI questionnaire>4 or exam>2		
MNSI questionnaire>7 or exam>2		
MNSI questionnaire		
MNSI questionnaire>4		
Summary mean MNSI questionnaire		
MNSI exam		
MNSI exam>2		
Summary mean MNSI exam		
Autonomic Function measures		
Heart rate (bpm)		
Baseline		
Year 15		
Summary mean heart rate		
Average change		
QTI		
Summary mean QTI		
SDNN		
Abnormal SDNN		
Summary mean SDNN		
RMSD		
Abnormal RMSD		
Summary mean RMSD		

We have also examined the prevalence of FSD based on the validated FSFI by DPP Treatment Arm. We found that 184 women (43.4%) report FSD. There was no significant difference in FSD status by DPP treatment arm. **(Table 5)** In analyses adjusting for age, race, and marital status **(Table 6)** we observed women with FSD reported significantly more depression, poor general health, greater reports of hysterectomy, more UTIs and urinary leakage. Like their male counterparts, women with FSD also had greater markers of peripheral and autonomic neuropathy. No differences were observed in diabetes related measures of glycemic control by FSD status. Final analyses are ongoing and the final manuscript is being drafted.

Table 5. Prevalence of FSD at DPPOS Year 15 by Treatment Arm

	Overall (n=426)	Placebo (n=158)	Metformin (n=126)	p-value*	Lifestyle (n=142)	p-value*
				0.105		0.764
FSD	185 (43.4%)	65 (41.1%)	64 (50.8%)		56 (39.4%)	
No FSD	241 (56.6%)	93 (58.9%)	62 (49.2%)		86 (60.6%)	

Note: Data are n(%)
*p-value for comparison between intensive lifestyle intervention and placebo and between metformin and placebo.

Table 6. Characteristics of 426 Women in the DPPOS at Year 15 by FSD status-Year 15 or most recent, summary mean from DPPOS baseline to year 15

	FSD (n=185)	No FSD (n=241)	p-value*	Adjusted p-value**
Group assignment			0.133	
Placebo	65 (35.1%)	93 (38.6%)		
Lifestyle	64 (34.6%)	62 (25.7%)		
Metformin	56 (30.3%)	86 (35.7%)		
Sociodemographics				
Age (years)	64.8 ± 7	62.4 ± 7.6	<0.001	
Race/ethnicity (%)			<0.001	
White	91 (49.2%)	131 (54.4%)		
African American	27 (14.6%)	54 (22.4%)		
Hispanic	30 (16.2%)	39 (16.2%)		
Native American/Asian	37 (20%)	17 (7.1%)		
Marital Status			0.001	
Never married	10 (5.4%)	33 (13.7%)		
Living together/Married	158 (85.4%)	171 (71%)		
Separated/Divorced/Widowed	17 (9.2%)	37 (15.4%)		
Clinical/Behavioral				
Current Smoking (%)	9 (4.9%)	6 (2.5%)	0.281	0.094
Weekly Alcohol Use (%)	47 (25.8%)	54 (22.5%)	0.498	0.126
General Health (%)			0.080	
Excellent/very good	50 (27%)	88 (36.7%)		ref
Good	107 (57.8%)	126 (52.5%)		0.053
Fair/poor	28 (15.1%)	26 (10.8%)		0.004
Depression (%)	41 (23.2%)	29 (12.4%)	0.006	<0.001
Summary mean depression score	4.2 ± 3.5	2.8 ± 3.5	<0.001	<0.001
Physical Activity (MET/week)	13.2 ± 12	14.6 ± 14.4	0.288	0.018
Summary mean MET/week	13.2 ± 9.6	15.3 ± 11.1	0.039	0.013
Body Mass Index (kg/m2)	32.1 ± 6.7	34.8 ± 7	<0.001	0.020
Summary mean BMI	32.3 ± 5.8	35.1 ± 6.5	<0.001	0.005
Waist Circumference (cm)	103.2 ± 12.8	107 ± 13.8	0.005	0.080
Summary mean waist	101.4 ± 12.5	105.9 ± 13.2	<0.001	0.031
Albumin:creatinine	13.1 ± 23.3	33.2 ± 131	0.025	0.094
Summary mean Alb/cre	11.7 ± 13.9	27.9 ± 156.4	0.111	0.018
Number of live births	2.5 ± 1.1	2.2 ± 1.2	0.038	0.052
Hysterectomy	38 (20.5%)	28 (11.6%)	0.017	0.067
UTI in the last year	25 (13.5%)	21 (8.7%)	0.154	0.075
Urinary leakage in the last week	109 (58.9%)	119 (49.4%)	0.063	0.148
Urinary leakage in the last 12 months			0.112	
None	37 (20%)	57 (23.7%)		ref
Less than once a month	43 (23.2%)	64 (26.6%)		0.532
One or more times per month	35 (18.9%)	58 (24.1%)		0.867
One or more times per week	42 (22.7%)	35 (14.5%)		0.113
Every day	28 (15.1%)	27 (11.2%)		0.135
Menopause			0.001*	
Premenopausal	116 (62.7%)	187 (77.6%)		Ref
Perimenopausal	4 (2.2%)	1 (0.4%)		0.244
Postmenopausal	65 (35.1%)	53 (22%)		0.111
Taking hormones (estrogen or progestin)	12 (6.9%)	9 (3.9%)	0.263	0.198
Estrogen	10 (5.7%)	7 (3%)	0.273	0.190
Progestin	2 (1.1%)	3 (1.3%)	1.000*	0.659

CVD Risk Factors				
JNC Hypertension Status (%)			0.884	0.897
Hypertensive	108 (62.1%)	142 (61.5%)		
Prehypertensive	30 (17.2%)	37 (16%)		
Normotensive	36 (20.7%)	52 (22.5%)		
Blood Pressure (mm/Hg)				
Systolic	121.1 ± 14.1	121 ± 13.7	0.941	0.098
Diastolic	71.6 ± 10.2	72.1 ± 9.3	0.596	0.731
Summary mean blood pressure				
Systolic	118.7 ± 9.9	119.6 ± 9.3	0.370	0.335
Diastolic	72.4 ± 6.5	74.1 ± 5.8	0.004	0.060
Antihypertensive use (%)	107 (61.1%)	137 (59.1%)	0.746	0.669
LDL cholesterol (mg/dL)	98 ± 33.2	103.9 ± 33.7	0.078	0.347
Summary mean LDL	107.2 ± 22.7	110.8 ± 23.6	0.112	0.222
HDL cholesterol (mg/dL)	57.1 ± 14.5	57.3 ± 15.2	0.917	0.944
Summary mean HDL	52.9 ± 11.7	52.4 ± 11.2	0.647	0.839
Triglycerides (mg/dL)	139.4 ± 74.3	147.4 ± 204.2	0.584	0.451
Summary mean triglycerides	144.1 ± 58.4	140.8 ± 80.7	0.620	0.696
Coronary calcification (%)	73 (45.1%)	87 (39%)	0.278	0.570
Autonomic Function measures				
MNSI questionnaire>4 or exam>2	63 (35.6%)	78 (33.9%)	0.804	0.597
MNSI questionnaire>7 or exam>2	63 (35.6%)	74 (32.2%)	0.537	0.777
MNSI questionnaire	1.1 ± 1.6	0.8 ± 1.3	0.031	0.008
MNSI questionnaire>4	5 (2.8%)	7 (3%)	1.000	0.784
Summary mean MNSI questionnaire	1.1 ± 1.3	0.8 ± 1	<0.001	0.009
MNSI exam	1.5 ± 0.8	1.4 ± 0.8	0.229	0.393
MNSI exam>2	63 (35.6%)	74 (32.2%)	0.537	0.597
Summary mean MNSI exam	2 ± 1	1.5 ± 0.8	<0.001	<0.001
Heart rate	64.3 ± 6.8	66.6 ± 7.7	<0.001	0.090
Summary mean heart rate	62.9 ± 8.7	62.5 ± 8.2	0.629	0.053
QTI	102.9 ± 3.9	102.7 ± 4.6	0.566	0.909
Summary mean QTI	101.8 ± 3.1	101.8 ± 3	0.889	0.055
SDNN	26.1 ± 13.6	29 ± 20.4	0.102	0.224
Abnormal SDNN	3 (1.8%)	2 (0.9%)	0.657*	0.216
Summary mean SDNN	14.2 ± 4.7	14.4 ± 5.9	0.586	0.686
RMSD	22.8 ± 13.2	26 ± 22.2	0.083	0.143
Abnormal RMSD	5 (3%)	7 (3.3%)	1.000	0.770
Summary mean RMSD	25.3 ± 9.7	26.3 ± 12.8	0.376	0.929
Diabetes				
Fasting plasma glucose (mg/dL)	126.2 ± 36	133.1 ± 45.2	0.080	0.211
Summary mean fasting glucose	114.8 ± 20.1	121.1 ± 25.3	0.004	0.0497
HbA1c (%)	6.5 ± 1.3	6.7 ± 1.5	0.144	0.337
Summary mean HbA1c	2.2 ± 1.4	2.4 ± 1.6	0.089	0.298
Log fasting insulin (μU/mL)	3.3 ± 0.6	3.3 ± 0.7	0.655	0.493
Summary mean log fasting insulin	3.2 ± 0.5	3.3 ± 0.5	0.299	0.574
Type 2 diabetes (%)	123 (66.5%)	159 (66%)	0.994	0.644
Duration of diabetes (years)	7.5 ± 7.1	7.8 ± 7.3	0.655	0.961
Diabetes by HbA1c	74 (40%)	114 (47.3%)	0.160	0.240
Duration of diabetes by HbA1c	3.2 ± 5.7	4.5 ± 6.1	0.023	0.099
Loss of glycemic control	34 (18.6%)	57 (23.8%)	0.245	0.419

*Fisher's exact test
**p-values adjusted for age, race, and marital status

3. Publications:

- **American Diabetes Association Abstract Submissions**
  Two abstracts are planned, one on the ED data and one on the FSD data.

- **Manuscript 1 Planned Submission to *Diabetes Care***
  A single manuscript that will describe ED in males (Specific Aim 1) and provide detailed neuropathy data (Specific Aim 2) is planned and in progress. Once female data analyses are complete, manuscripts will be outlined and submitted for approval.