

**Obstructive Sleep Apnea, Glucose Tolerance and Beta-Cell Function in Adults with
Prediabetes or Untreated Type 2 Diabetes: A Cross-Sectional Analysis of the Restoring Insulin
Secretion (RISE) Study**

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ADDITIONAL RESULTS

The associations between OSA severity categories was performed after excluding the 49 participants who reported using CPAP (regardless of the level of adherence to CPAP). OSA severity, either using continuous variables (AHI, 3% and 4% oxygen desaturation indices, T90) or categories of severity, was not associated with fasting or 2-h glucose, HOMA-IR, insulin sensitivity or beta-cell response (supplemental Table 2 and supplemental figures 2 and 3).

Supplemental Table 1. Participant characteristics based on diabetes status

	All N=221	Prediabetes N=162	Type 2 Diabetes N=59	p-value*
Demographics				
Age, years	54.5 ± 8.7	54.3 ± 8.7	55.0 ± 8.8	0.597
Men, n (%)	127 (57.5%)	92 (56.8%)	35 (59.3%)	0.736
Race/ethnicity, n (%)				0.936
White	122 (55.2%)	90 (55.6%)	32 (54.2%)	
Black	72 (32.6%)	52 (32.1%)	20 (33.9%)	
Hispanic (any)	11 (5.0%)	7 (4.3%)	4 (6.8%)	
Asian	10 (4.5%)	8 (4.9%)	2 (3.4%)	
American Indian	1 (0.5%)	1 (0.6%)	0 (0.0%)	
Mixed	5 (2.3%)	4 (2.5%)	1 (1.7%)	
Weight, kg	102.7 ± 18.5	103.4 ± 18.5	100.8 ± 18.6	0.365
Waist, cm	112.5 ± 13.2	113.3 ± 13.5	110.3 ± 12.3	0.137
Waist-to-Hip Ratio	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	0.515
BMI, kg/m ²	35.1 ± 5.5	35.3 ± 5.5	34.3 ± 5.7	0.245
Obese (BMI ≥30 kg/m ²), n (%)	176 (80.0%)	131 (81.4%)	45 (76.3%)	0.403
Systolic BP, mmHg	126.6 ± 13.3	127.0 ± 13.2	125.5 ± 13.7	0.465
Diastolic BP, mmHg	77.0 ± 10.6	76.9 ± 10.9	77.2 ± 10.0	0.838
HbA1c, %	5.76 ± 0.40	5.70 ± 0.37	5.90 ± 0.44	<.001
Epworth Sleepiness Scale	8.5 ± 4.6	8.7 ± 4.6	7.8 ± 4.7	0.192
Sleepy (Epworth >10), n (%)	82 (37.1%)	65 (40.1%)	17 (28.8%)	0.124
CPAP adherent, n (%) [†]	41 (18.6%)	31 (19.1%)	10 (16.9%)	0.711
CPAP use in subset adherent to CPAP, h/night, N=41	6.2 ± 1.1	6.1 ± 1.4	6.3 ± 1.1	0.621
Actigraphy Measurements				
Sleep time, h	6.57 ± 0.95	6.55 ± 0.98	6.63 ± 0.89	0.595
Activity duration, min	996 ± 111	1001 ± 124	982 ± 63	0.267
Percent immobility	20.4 ± 8.9	20.3 ± 8.9	20.4 ± 8.9	0.985
Total activity count	231840 ± 76307	231337 ± 77016	233219 ± 74960	0.872
Activity counts/min	233 ± 76	232 ± 76	237 ± 76	0.691
PSG Measurements				
Total recording time, min	453.4 ± 45.1	450.1 ± 47.3	462.4 ± 37.1	0.073
Total sleep time, min	360.5 ± 72.5	357.0 ± 73.8	370.1 ± 68.6	0.238
Sleep efficiency, %	79.40 ± 13.62	79.07 ± 13.86	80.31 ± 13.04	0.551
Sleep efficiency, %	84.2	83.4	84.3	
Median (25 th , 75 th percentile)	[73.8, 89.5]	[75.1, 89.8]	[71.9, 89.5]	0.674
REM sleep, %	16.93 ± 7.75	16.69 ± 7.72	17.58 ± 7.85	0.449
REM sleep, %	17.3	18.4	17.2	
Median (25 th , 75 th percentile)	[12.2, 22.2]	[12.9, 22.3]	[12.0, 22.2]	0.617
N3 sleep, %	13.3 ± 10.0	13.4 ± 10.0	12.9 ± 10.2	0.755
N3 sleep, %	12.3 [4.4, 19.9]	13.0 [4.5, 19.9]	11.8 [3.8, 21.3]	0.727
Median (25 th , 75 th percentile)				
AHI, events/h	33.8 ± 29.3	33.6 ± 29.4	34.4 ± 29.2	0.853
AHI, events/h	25.6	27.1	24.2	
Median (25 th , 75 th percentile)	[13.5, 45.9]	[12.7, 45.9]	[13.5, 44.1]	0.745
REM AHI, events/h	38.25 ± 25.03	38.30 ± 24.59	38.12 ± 26.39	0.962
REM AHI, events/h	35.5	36.9	35.5	
Median (25 th , 75 th percentile)	[17.1, 59.1]	[16.5, 60.0]	[17.3, 56.8]	0.901
Non-REM AHI, events/h	32.41 ± 31.70	31.96 ± 31.48	33.64 ± 32.54	0.729
Non-REM AHI, events/h	23.0	24.3	22.2	
Median (25 th , 75 th percentile)	[8.2, 44.1]	[8.0, 47.4]	[8.2, 43.8]	0.768

3% ODI, events/h	24.4 ± 23.9	24.4 ± 23.9	24.4 ± 24.1	0.996
3% ODI, events/h	16.4	15.9	16.5	
Median (25 th , 75 th percentile)	[7.4 , 33.5]	[5.6 , 35.2]	[8.3 , 31.7]	0.760
4% ODI, events/h	18.8 ± 22.3	18.8 ± 22.2	18.9 ± 22.8	0.975
4% ODI, events/h	10.0	9.2	10.2	
Median (25 th , 75 th percentile)	[4.3 , 25.2]	[3.1 , 27.0]	[5.1 , 22.8]	0.542
Microarousal index, events/h	28.9 ± 20.7	28.7 ± 20.9	29.5 ± 20.4	0.798
Microarousal index, events/h	23.4	24.5	22.4	
Median (25 th , 75 th percentile)	[14.1 , 35.9]	[14.2 , 37.6]	[13.8 , 35.3]	0.640
T90, % [‡]	15.1 ± 21.6	15.4 ± 22.1	14.2 ± 20.4	0.722
T90, % [‡]	5.0	5.0	5.1	
Median (25 th , 75 th percentile)	[1.1 , 18.4]	[0.4 , 18.4]	[1.2 , 18.6]	0.539

Data presented as mean ± standard deviation unless otherwise specified.

* ANOVA for continuous variables and chi-square for categorical variables.

[†] CPAP adherence defined as self-report of using CPAP ≥4 hours on ≥5 nights per week

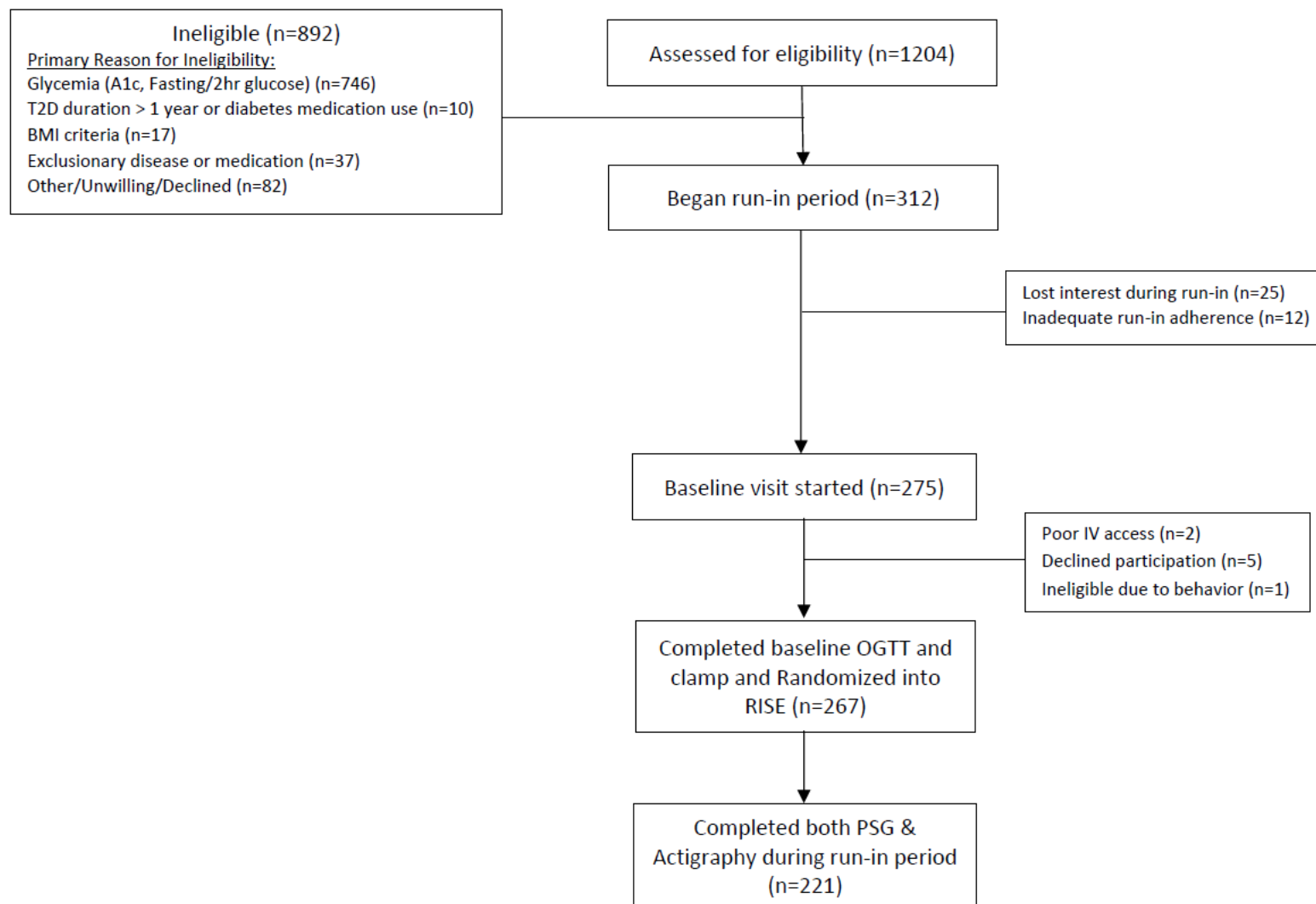
[‡] T90: Percent of total sleep time with oxygen saturation below 90%.

Supplemental Table 2: Adjusted metabolic outcomes based on OSA severity categories after excluding 49 participants who reported using CPAP

Dependent	OSA Category	Adj Mean	Lower 95% CI	Upper 95% CI	p-value
HbA1c	Severe (N=67)	5.6504	5.5012	5.7996	0.1630
	Moderate (N=46)	5.5204	5.3568	5.6840	
	No/Mild (N=59)	5.6568	5.5099	5.8037	
Fasting Glucose	Severe (N=67)	111.13	106.62	115.63	0.3034
	Moderate (N=46)	114.08	109.14	119.03	
	No/Mild (N=59)	110.56	106.12	114.99	
2-Hour Glucose	Severe (N=67)	176.2	161.1	191.29	0.9967
	Moderate (N=46)	175.98	159.43	192.54	
	No/Mild (N=59)	176.65	161.79	191.51	
iAUC Glucose	Severe (N=67)	10788.8	9165.87	12411.7	0.3508
	Moderate (N=46)	9557.93	7771.88	11344	
	No/Mild (N=59)	10399.5	8804.54	11994.4	
Insulinogenic Index	Severe (N=67)	90.65	70.16	117.14	0.2185
	Moderate (N=46)	94.21	70.96	125.09	
	No/Mild (N=59)	74.59	57.99	95.95	
C-Peptide Index	Severe (N=67)	7.07	5.77	8.67	0.3177
	Moderate (N=46)	7.46	5.96	9.35	
	No/Mild (N=59)	6.3	5.16	7.7	
HOMA-IR	Severe (N=67)	3.83	3.07	4.77	0.0835
	Moderate (N=46)	4.24	3.34	5.4	
	No/Mild (N=59)	3.24	2.61	4.02	
Insulin Sensitivity (M/I)	Severe (N=67)	47.3008	36.7970	60.8030	0.3012
	Moderate (N=46)	40.3678	30.6530	53.1615	
	No/Mild (N=59)	49.3743	38.5604	63.2208	
ACPRmax	Severe (N=67)	17.7241	15.0297	20.9016	0.4781
	Moderate (N=46)	16.3479	13.6472	19.5829	
	No/Mild (N=59)	16.0251	13.6191	18.8560	
ACPRg	Severe (N=67)	3.1237	2.6154	3.7309	0.7392
	Moderate (N=46)	3.2467	2.6729	3.9437	
	No/Mild (N=59)	3.3659	2.8249	4.0105	
SS C-Peptide	Severe (N=67)	11.7704	10.7125	12.9328	0.8910
	Moderate (N=46)	11.5187	10.3901	12.7700	
	No/Mild (N=59)	11.5429	10.5188	12.6668	

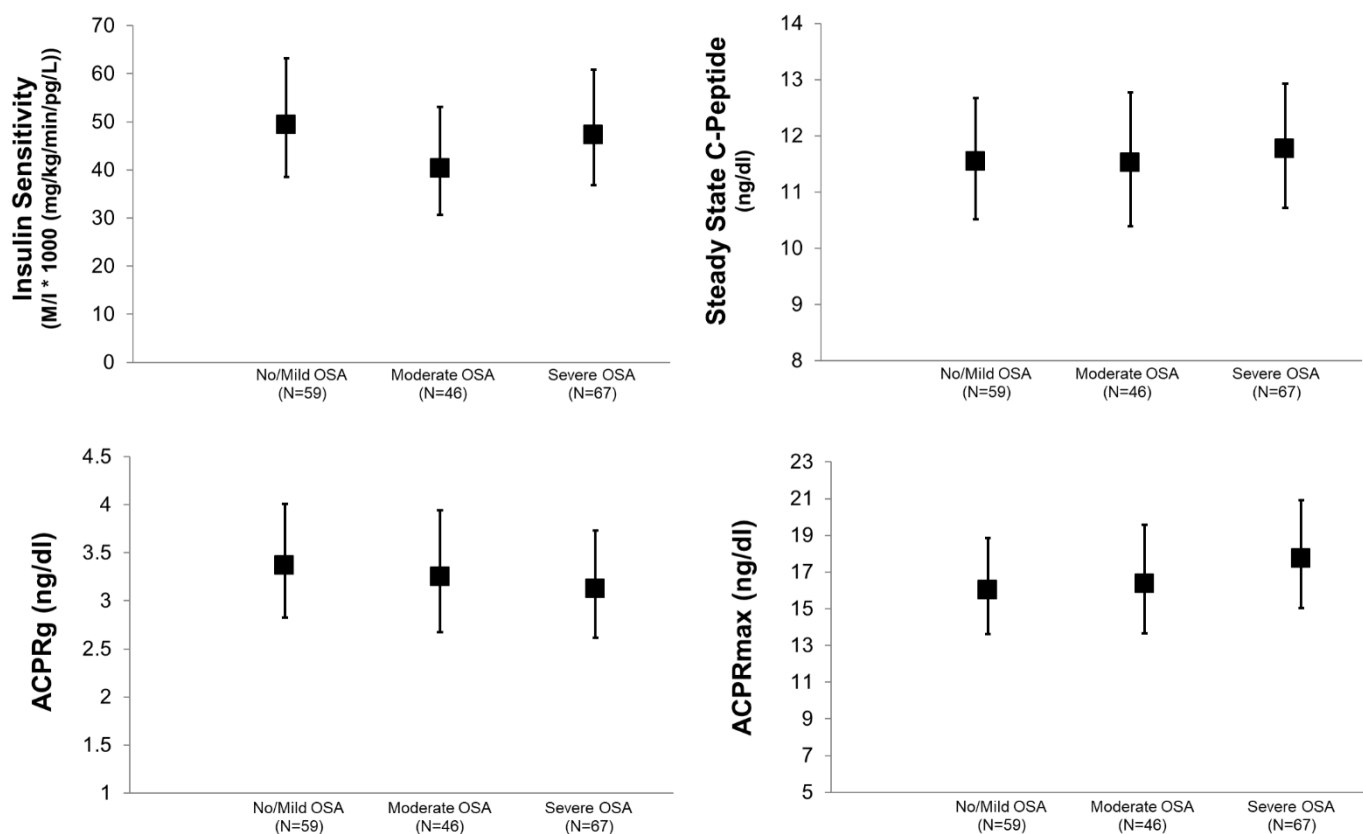
ACPRg: Acute (first phase) C-peptide response to glucose; ACPRmax: Acute C-peptide response to arginine at maximal glycemic potentiation; iAUC: incremental glucose area under the curve; HOMA-IR: homeostatic model assessment insulin resistance; SS C-Peptide: steady state C-peptide

Supplemental Figure 1. Consort diagram



Supplemental Figure 2. Effect of obstructive sleep apnea on insulin sensitivity and beta-cell function as assessed by the hyperglycemic clamp after the exclusion of participants who reported using CPAP

Supplemental Figure 2 legend: Adjusted means from multiple linear regression models for relationship of log-transformed dependent variables (insulin sensitivity and beta-cell function as assessed by the hyperglycemic clamp) with categories of OSA severity. Data shown are least square means and 95% CI adjusted for age, sex, race/ethnicity, BMI, waist-to-hip ratio, and actigraphically measured sleep duration and physical activity. Steady state C-peptide, ACPRg, and ACPRmax are also adjusted for log insulin sensitivity (M/I).



Supplemental Figure 3. Effect of obstructive sleep apnea on HbA1c and measures of glycaemia as assessed by the oral glucose tolerance test after the exclusion of participants who reported using CPAP

Supplemental Figure 3 legend: Adjusted means from multiple linear regression models for relationship of dependent variables (glycemia as assessed by the 3-h OGTT) with categories of OSA severity. Data shown are least square means and 95% CI adjusted for age, sex, race/ethnicity, BMI, waist-to-hip ratio, and actigraphically measured sleep duration and physical activity. IGI, CPI, and HOMA-IR were log-transformed for analyses.

