

**Appendix Table 1. Baseline Characteristics of Participants in the Metformin, ILS, and Placebo groups who lost  $\geq 5\%$  body weight at year 1 compared to those that did not lose 5% body weight at year 1.**

	Metformin			ILS			Placebo		
	<5% wt loss	$\geq 5\%$ wt loss	p-value	<5% wt loss	$\geq 5\%$ wt loss	p-value	<5% wt loss	$\geq 5\%$ wt loss	p-value
N	725	289		383	640		889	137	
<b>Demographics</b>									
Age at randomization (y)	50.8 (10.1)	52.1 (10.7)	0.071	48.2 (10.8)	52.3 (11.3)	<b>&lt;0.001</b>	50.5 (10.4)	50.3 (9.8)	0.84
Sex			0.142			<b>0.001</b>			0.40
Men (n, %)	261 (36%)	90 (31%)		98 (25.6%)	228 (35.6%)		282 (31.7%)	38 (27.7%)	
Women (n, %)	464 (64%)	199 (69%)		285 (74.4%)	412 (64.4%)		607 (68.3%)	99 (72.3%)	
Race/Ethnicity			0.27			<b>&lt;0.001</b>			0.22
White (n, %)	395 (54.5%)	168 (58.1%)		179 (46.7%)	380 (59.4%)		477 (53.7%)	85 (62%)	
Black (n, %)	157 (21.7%)	54 (18.7%)		97 (25.3%)	90 (14.1%)		183 (20.6%)	22 (16.1%)	
Hispanic (n, %)	116 (16%)	40 (13.8%)		58 (15.1%)	107 (16.7%)		134 (15.1%)	22 (16.1%)	
American Indian (n, %)	32 (4.4%)	20 (6.9%)		29 (7.6%)	28 (4.4%)		54 (6.1%)	4 (2.9%)	
Asian (n, %)	25 (3.4%)	7 (2.4%)		20 (5.2%)	35 (5.5%)		41 (4.6%)	4 (2.9%)	
Education			0.58			0.75			0.42
$\leq$ High School (n, %)	183 (25.2%)	72 (24.9%)		105 (27.4%)	162 (25.3%)		237 (26.7%)	37 (27%)	
College (n, %)	354 (48.8%)	133 (46.0%)		178 (46.5%)	309 (48.3%)		419 (47.1%)	71 (51.8%)	
Post-College (n, %)	188 (25.9%)	84 (29.1%)		100 (26.1%)	169 (26.4%)		233 (26.2%)	29 (21.2%)	
<b>Anthropometrics</b>									
Weight (kg)	95 (20.3)	92.2 (18.4)	<b>0.045</b>	95 (20.8)	93.2 (20.3)	0.174	94.2 (20.2)	94.9 (20.2)	0.73
BMI (kg/m <sup>2</sup> )	34.1 (6.7)	33.1 (6.0)	<b>0.028</b>	34.5 (6.9)	33.4 (6.5)	<b>0.013</b>	34.1 (6.8)	34.5 (6.0)	0.54
Waist (cm)	105.7 (14.9)	102.6 (12.7)	<b>0.002</b>	106.0 (15.1)	104.4 (14.4)	0.097	105.2 (14.2)	105.2 (14.1)	0.99
Hip (cm)	113.7 (13.5)	112.1 (12.1)	0.078	115.6 (14.4)	112.8 (13.5)	<b>0.002</b>	114.3 (14.8)	115.4 (12.2)	0.43
Waist-hip ratio	0.93 (0.09)	0.92 (0.08)	<b>0.017</b>	0.92 (0.08)	0.93 (0.09)	0.112	0.92 (0.08)	0.91 (0.08)	0.134
<b>Baseline Health History</b>									
Family hx of diabetes (n, %)*	497 (68.6%)	204 (70.3%)	0.68	283 (73.9%)	426 (66.7%)	<b>0.019</b>	621 (69.9%)	95 (69.3%)	0.97
Alcohol use*			<b>0.048</b>			0.130			0.600
None (n, %)	384 (53.6%)	163 (57.8%)		227 (60.7%)	333 (53.2%)		494 (56.5%)	75 (55.6%)	
<1/wk (n, %)	137 (19.1%)	57 (20.2%)		66 (17.6%)	131 (20.9%)		161 (18.4%)	21 (15.6%)	
>1/wk to 1/day (n, %)	162 (22.6%)	43 (15.2%)		66 (17.6%)	127 (20.3%)		180 (20.6%)	34 (25.2%)	
$\geq 1$ /day (n, %)	33 (4.6%)	19 (6.7%)		51 (4.8%)	35 (5.6%)		39 (4.5%)	5 (3.7%)	

	Metformin			ILS			Placebo		
	<5% wt loss	≥5% wt loss	p-value	<5% wt loss	≥5% wt loss	p-value	<5% wt loss	≥5% wt loss	p-value
Smoking			0.34			<b>0.021</b>			<b>0.002</b>
Never (n, %)	417 (57.5%)	180 (62.3%)		242 (63.2%)	357 (55.8%)		527 (59.3%)	73 (53.3%)	
Current (n, %)	51 (7.0%)	16 (5.5%)		26 (6.8%)	36 (5.6%)		59 (6.6%)	21 (15.3%)	
Past (n, %)	257 (35.4%)	93 (32.2%)		115 (30.0%)	247 (38.6%)		303 (34.1%)	43 (31.4%)	
Gestational diabetes (n, %)**	63 (13.6%)	37 (18.7%)	0.093	59 (20.7%)	52 (12.6%)	<b>0.006</b>	99 (16.3%)	12 (12.1%)	0.36
Antidepressant use (n, %)	43 (5.9%)	18 (6.2%)	0.86	26 (6.8%)	25 (3.9%)	0.057	36 (4.0%)	9 (6.6%)	0.26
Beck depression	4.6 (4.6)	4.2 (3.9)	0.22	4.8 (4.7)	4.4 (4.3)	0.136	4.6 (4.7)	4.8 (4.6)	0.59
Beck anxiety	3.9 (4.6)	3.81 (4.7)	0.73	4.7 (5.9)	3.8 (4.5)	<b>0.005</b>	4.0 (5.2)	3.8 (4.3)	0.63
SF-6D	0.80 (0.10)	0.80 (0.10)	0.56	0.79 (0.11)	0.81 (0.10)	<b>0.015</b>	0.80 (0.10)	0.80 (0.10)	0.97
<b>Glucose and Insulin</b>									
Fasting glucose (mg/dl)	106.6 (8.5)	106.2 (8.3)	0.54	106.0 (8.4)	106.4 (7.9)	0.44	106.6 (8.4)	106.7 (8.2)	0.90
2-h glucose (mg/dl)	164.6 (17.0)	166.5 (17.7)	0.11	164.8 (17.2)	163.9 (16.6)	0.40	164.5 (17.2)	164.4 (16.9)	0.95
HbA1c (%)	5.9 (0.5)	5.9 (0.4)	0.30	5.9 (0.5)	5.9 (0.5)	0.39	5.9 (0.5)	5.9 (0.5)	0.84
Fasting insulin (uU/ml)	27.6 (15.4)	25.8 (13.9)	0.07	27.7 (15.9)	25.8 (15.4)	0.062	26.7 (15.4)	26.1 (13.9)	0.66
HOMA IR	7.3 (4.3)	6.8 (3.87)	0.07	7.3 (4.4)	6.8 (4.3)	0.090	7.09 (4.29)	6.91 (3.73)	0.65
<b>Blood Pressure</b>									
SBP (mmHg)	123.5 (15.0)	125.5 (14.6)	0.06	122.7 (15.0)	124.0 (14.6)	0.185	123.6 (14.5)	122.6 (14.4)	0.45
DBP (mmHg)	78.3 (9.6)	77.7 (9.3)	0.36	78.4 (9.5)	78.6 (9.0)	0.74	78.2 (9.0)	76.9 (10.2)	0.134
<b>Lipids</b>									
Cholesterol (mg/dl)	203.1 (35.7)	201.4 (34.3)	0.50	203.3 (36.0)	204.6 (37.2)	0.59	203.1 (37.6)	200.3 (32.5)	0.41
LDL (mg/dl)	124.8 (32.3)	123.4 (31.6)	0.53	124.7 (32.0)	125.5 (32.9)	0.71	124.6 (34.3)	119.9 (29.3)	0.130
HDL (mg/dl)	46.2 (11.7)	45.9 (11.1)	0.68	46.5 (13.1)	45.9 (11.9)	0.46	44.9 (11.5)	44.2 (11.5)	0.49
Triglycerides (mg/dl)	139.00 (50.6, 381.9)	139.6 (51.7, 377.2)	0.89	138.7 (50.2, 382.9)	142.5 (50.5, 402.0)	0.42	147.0 (55.3, 391.1)	156.4 (55.1, 443.8)	0.182
<b>Adipocytokines/ Chemokines</b>									
Adiponectin (ug/mL)	7.9 (3.5)	8.5 (3.4)	<b>0.018</b>	7.7 (3.6)	8.2 (3.5)	0.056	7.7 (3.2)	8.2 (4.0)	0.112

	Metformin			ILS			Placebo		
	<5% wt loss	≥5% wt loss	p-value	<5% wt loss	≥5% wt loss	p-value	<5% wt loss	≥5% wt loss	p-value
Fibrinogen (mg/dL)	378.8 (86.6)	380.0 (81.3)	0.83	385.7 (87.4)	385.7 (85.0)	0.99	385.4 (86.4)	394.8 (81.7)	0.234
IL6 (pg/mL)	2.5 (2.4)	2.2 (1.7)	<b>0.029</b>	2.6 (2.1)	2.4 (2.2)	0.100	2.5 (2.1)	2.4 (1.5)	0.66
tPA (ng/mL)	11.3 (4.4)	11.0 (4.1)	0.38	11.6 (4.3)	11.2 (4.3)	0.25	11.5 (4.1)	10.9 (3.4)	0.132
CRP (mg/dL)	0.35 (0.04, 3.07)	0.29 (0.04, 2.31)	<b>0.009</b>	0.41 (0.05, 3.01)	0.32 (0.04, 2.55)	<b>&lt;0.001</b>	0.35 (0.04, 2.97)	0.43 (0.06, 3.33)	<b>0.034</b>
Leptin (ng/mL)	24.2 (15.4)	22.5 (13.4)	0.105	26.7 (15)	21.8 (13.7)	<b>&lt;0.001</b>	24.5 (14.1)	24.9 (13.4)	0.72
eSelectin (ng/mL)	46.4 (17.8)	44.8 (16.2)	0.180	45.8 (17.3)	44.7 (17.6)	0.36	47.3 (19.6)	45.2 (18.3)	0.25
MCP-1 (pg/mL)	152.8 (112.7)	154.0 (102.8)	0.88	148.6 (71.6)	145.2 (50.8)	0.37	148.5 (61.4)	159.6 (172.0)	0.161
sICAM (ng/mL)	248.5 (75.8)	253.5 (82.5)	0.36	253.3 (87.5)	246.4 (71.1)	0.167	247.6 (76.1)	256.5 (77.9)	0.21
<b>Sex Hormones</b>									
FSH (women; mIU/L)	31.5 (25.8)	35.9 (27.5)	0.090	28.4 (25.8)	32.9 (28.5)	0.068	32.3 (28.8)	36.5 (27.6)	0.25
DHEA (ng/mL)	2397 (1625)	2397 (1454)	0.99	2543 (1558)	2552 (1854)	0.94	2480 (1665)	2637 (2048)	0.38
DHEA-S (ng/mL)	911 (615)	911 (695)	0.99	996 (683)	919 (656)	0.094	909 (599)	998 (733)	0.136
Androstenedione (men, pg/mL)	778 (240)	815 (295)	0.27	789 (283)	773 (267)	0.65	785 (265)	851.8 (389)	0.20
Testosterone (pg/mL)	553 (30, 10286)	473 (27, 8123)	0.172	424 (29, 6119)	556 (28, 11188)	<b>0.010</b>	460 (27, 7893)	359 (26, 4920)	0.082
SHBG (nmol/L)	55.7 (45.4)	58.3 (44.0)	0.44	54.7 (41.2)	55.2 (39.8)	0.87	55.1 (43.4)	51.3 (36.2)	0.35
Estrone (E1) (pg/mL)	54.7 (51.4, 58.1)	51.0 (45.6, 56.9)	0.28	63.3 (18.8, 213)	51.29 (14.3, 183)	<b>&lt;0.001</b>	54.1 (15.6, 187)	64.5 (18.3, 226.8)	0.132
Estradiol (E2) (pg/mL)	25.9 (24.0, 28.0)	24.5 (21.7, 27.7)	0.45	28.7 (4.03, 204)	22.9 (3.5, 149.8)	<b>&lt;0.001</b>	24.6 (3.55, 170)	29.3 (3.6, 238)	0.081

Data are mean (SD) or geometric mean (95% confidence intervals) for non-normally distributed data; p-values for non-normally distributed data based on log-transformed values. ILS, Intensive Lifestyle intervention; SF-6D, Short-Form Six Dimension Questionnaire; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; tPA, tissue Plasminogen Activator; CRP, C-Reactive Protein; IL6, Interleukin-6; MCP-1, Monocyte Chemoattractant Protein; sICAM, Soluble Intercellular Adhesion Molecule; FSH, Follicle Stimulating Hormone; DHEA, Dehydroepiandrosterone; DHEA-S, Dehydroepiandrosterone Sulfate; SHBG, Sex

Hormone Binding Globulin. \*Some participants were unable or refused to answer some questions at baseline; percents are among responders only.  
\*\*Among parous women only.