

Supplemental Table 1. Baseline characteristics for the overall DPP cohort and stratified by inclusion in the analytic sample.

	Overall	Analytic Cohort	Unavailable for Analysis	Active but Missing DSPN Data*
N	3234	1792	1442	639
Assignment (%)				
Placebo	1082 (33.5)	597 (33.3)	485 (33.6)	227 (35.5)
Lifestyle	1079 (33.4)	582 (32.5)	497 (34.5)	211 (33.0)
Metformin	1073 (33.2)	613 (34.2)	460 (31.9)	201 (31.5)
Age (years)	50.61 (10.68)	49.36 (9.10)	52.15 (12.20)	50.74 (11.03)
Sex = Female (%)	2191 (67.7)	1265 (70.6)	926 (64.2)	444 (69.5)
Race/Ethnicity (%)				
White	1768 (54.7)	912 (50.9)	856 (59.4)	368 (57.6)
Black	645 (19.9)	367 (20.5)	278 (19.3)	133 (20.8)
Hispanic	508 (15.7)	296 (16.5)	212 (14.7)	96 (15.0)
Asian	142 (4.4)	91 (5.1)	51 (3.5)	19 ( 3.0)
American Indian	171 (5.3)	126 (7.0)	45 (3.1)	23 ( 3.6)
Ever smoker (%)	1337 (41.3)	684 (38.2)	653 (45.3)	272 (42.6)
Alcohol Drinks/Week (%)				
None	1772 (55.8)	975 (55.5)	797 (56.2)	372 (59.6)
< 1 per week	608 (19.1)	331 (18.8)	277 (19.5)	126 (20.2)
1 - 7 per week	647 (20.4)	369 (21.0)	278 (19.6)	102 (16.3)
> 7 per week	148 (4.7)	83 (4.7)	65 (4.6)	24 ( 3.8)
Weight (kg)	94.2 (20.3)	92.7 (19.0)	96.1 (21.6)	96.25 (22.1)
Height (m)	166.4 (9.2)	166.0 (9.0)	167.1 (9.4)	166.56 (9.20)
EGFR (mL/min/1.73 m <sup>2</sup> )	98.4 (16.6)	99.2 (15.9)	97.5 (17.4)	98.96 (16.8)
Triglycerides (mg/dL)**	141.0 [99.0, 201.0]	143.0 [99.5, 200.0]	139.0 [99.0, 201.0]	139.00 [99.00, 199.50]
HbA1c (%)	5.9 (0.5)	5.9 (0.5)	5.9 (0.5)	5.92 (0.52)

\*These 639 subjects are a subset of the 1442 who were enrolled in DPPOS and were still alive at the visit at which DSPN was ascertained.

\*\*Median [IQR]

Supplemental Table 2. Estimated odds ratios (95% confidence intervals) from logistic regression models with presence of DSPN as the response.

	Model 1	Model 2	Model 3	Model 4	Model 5
ILS	0.95 (0.71, 1.26)	0.92 (0.68, 1.25)	0.93 (0.69, 1.27)	0.97 (0.72, 1.32)	0.95 (0.70, 1.29)
Metformin	0.92 (0.69, 1.22)	0.94 (0.70, 1.26)	0.93 (0.69, 1.25)	1.05 (0.78, 1.41)	0.97 (0.72, 1.30)
Age (1 year)	1.05*** (1.03, 1.06)	1.07*** (1.05, 1.09)	1.07*** (1.05, 1.09)	1.08*** (1.06, 1.10)	1.07*** (1.05, 1.09)
Black	0.60*** (0.44, 0.83)	0.58*** (0.41, 0.82)	0.58*** (0.41, 0.82)	0.43*** (0.30, 0.62)	0.55*** (0.39, 0.77)
Hispanic	0.81 (0.58, 1.12)	1.05 (0.73, 1.50)	1.06 (0.73, 1.51)	0.90 (0.62, 1.30)	1.03 (0.72, 1.48)
Asian	0.26*** (0.12, 0.56)	0.32*** (0.14, 0.73)	0.30*** (0.13, 0.69)	0.27*** (0.12, 0.62)	0.31*** (0.14, 0.71)
Am. Indian	0.62* (0.36, 1.07)	0.89 (0.50, 1.57)	0.89 (0.50, 1.59)	0.68 (0.38, 1.22)	0.88 (0.50, 1.55)
Female	0.75** (0.58, 0.96)	1.35 (0.93, 1.96)	1.31 (0.90, 1.92)	1.42* (0.97, 2.08)	1.40* (0.96, 2.05)
Height (1 cm)		1.03*** (1.01, 1.05)	1.03*** (1.01, 1.05)	1.03*** (1.01, 1.06)	1.04*** (1.01, 1.06)
Ever Smoker		1.24* (0.96, 1.59)	1.21 (0.94, 1.56)	1.23 (0.95, 1.59)	1.22 (0.95, 1.57)
ln(Triglyceride)		1.35** (1.02, 1.79)	1.33** (1.00, 1.77)	1.20 (0.90, 1.60)	1.27 (0.95, 1.69)
eGFR (10ml/min)		0.96 (0.90, 1.04)	0.96 (0.89, 1.04)	0.97 (0.90, 1.04)	0.97 (0.90, 1.04)
Weight (5 kg)		1.06*** (1.02, 1.09)	1.05*** (1.02, 1.09)	1.04** (1.01, 1.08)	1.05*** (1.01, 1.09)
Low B12 or Supp.			1.68** (1.11, 2.54)		
HbA1c mean				1.82*** (1.53, 2.17)	
ln(Diabetes Years)					1.05*** (1.02, 1.08)
N	1,792	1,709	1,684	1,709	1,709

Notes:

If a covariate does not have a corresponding OR value in a column, the covariate was excluded from the model.

\*\*\*Significant at the 1 percent level.

\*\*Significant at the 5 percent level.

\*Significant at the 10 percent level.

For Black, Hispanic, Asian, and Am. Indian indicators, White is the reference group

Supplemental Table 3. Estimated odds ratios (95% confidence intervals) from logistic regression models with presence of DSPN as the response for model including Age x Treatment Group interaction.

	OR (95% Confidence Interval)
Lifestyle	1.02 (1.76, 1.37)
Metformin	0.93 (0.69, 1.25)
Age (Years)	1.07*** (1.04, 1.09)
Black	0.60*** (0.44, 0.83)
Hispanic	0.80 (0.58, 1.11)
Asian	0.26*** (0.12, 0.56)
Am. Indian	0.63* (0.37, 1.09)
Female	0.75** (0.58, 0.96)
Lifestyle x Age	0.96** (0.93, 0.99)
Metformin x Age	0.99 (0.96, 1.02)
<i>N</i>	1,792

Notes:

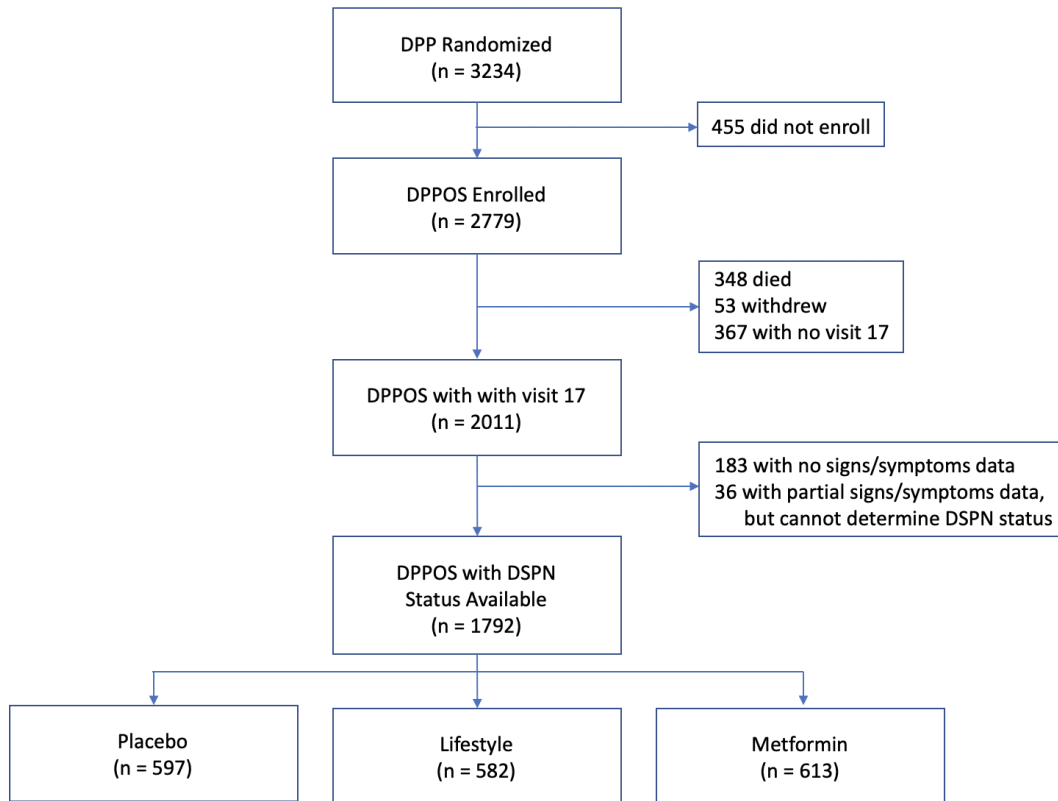
\*\*\* Significant at the 1 percent level.

\*\* Significant at the 5 percent level.

\* Significant at the 10 percent level.

The age variable was centered at the sample mean age of 70.36 years. The estimated OR for the Lifestyle variable is interpreted as the OR for DSPN comparing Lifestyle to Placebo for those who are 70.36 years of age. Similarly, the estimated OR for the Metformin variable is interpreted as the OR for DSPN comparing Metformin to Placebo for those who are 70.36 years of age.

Supplemental Figure 1. Consort Diagram



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## Appendix

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## Appendix

### DPP, DPPOS 1, DPPOS 2 & DPPOS 3 Research Group (1996-2021)

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