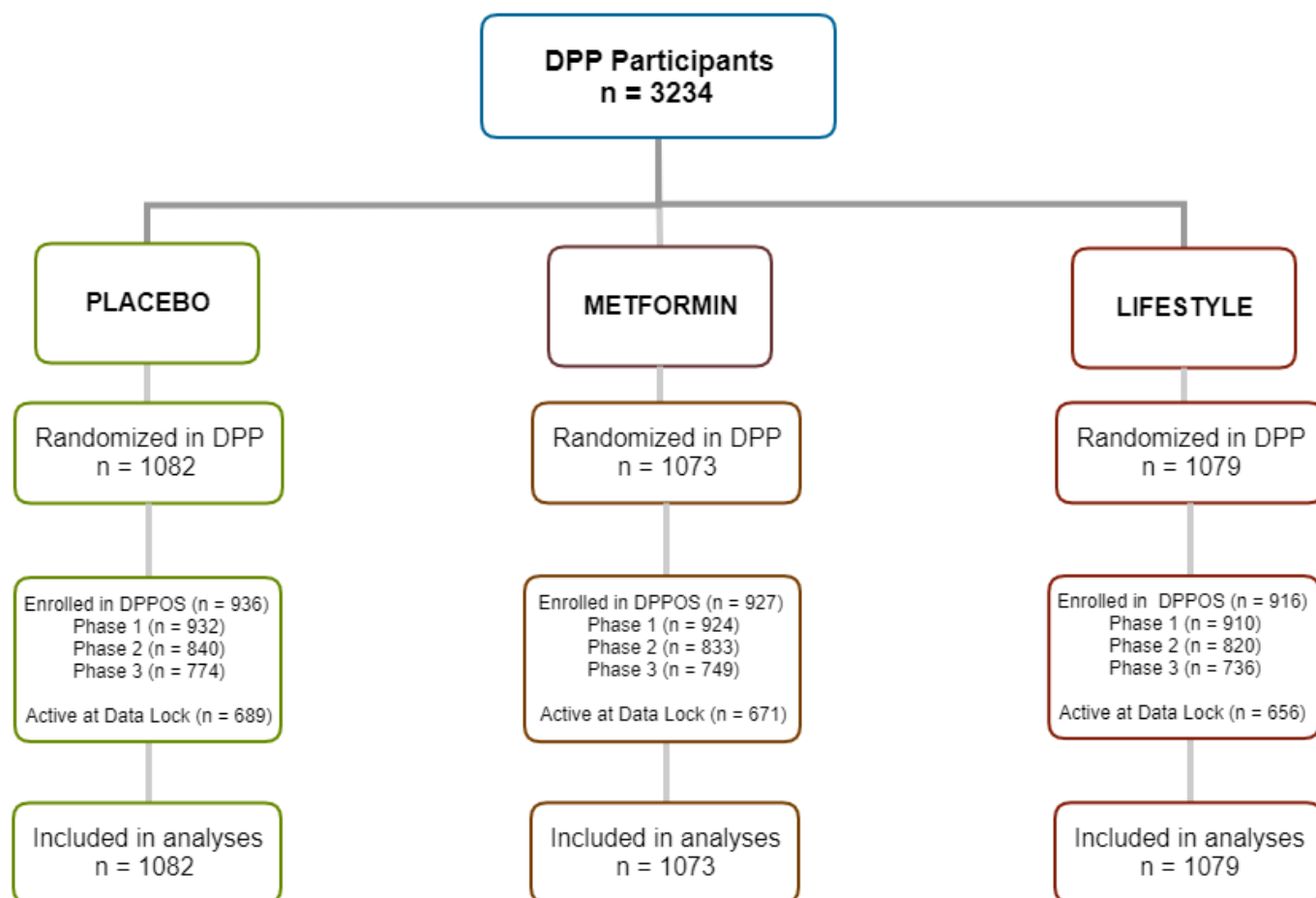




**eFigure 1.** Consort figure for DPP/DPPOS



All randomized participants were included in the analyses. The number in each phase of DPPOS represent surviving participants who had study visits. Visits were conducted in Phase 1 in 2002-2008, Phase 2 in 2008-2014, and Phase 3 in 2014-2022.

eTable 1. All-cause Mortality by Pre-Specified Subgroups

	N (%)	Event Rate per 1000 person-years			Hazard Ratio (95% CI)*	
		Placebo	Lifestyle	Metformin	Metformin vs. Placebo	Lifestyle vs. Placebo
Overall	3234 (100%)	6.59	7.37	7.13	1.08 (0.86,1.36)	1.12 (0.90,1.41)
Age randomized in years						
25 to < 45	1000 (30.9%)	2.39	1.99	2.04	0.83 (0.40,1.73)	0.85 (0.42,1.73)
45 to <60	1586 (49.0%)	4.68	5.65	5.07	1.21 (0.84,1.75)	1.08 (0.74,1.60)
60 plus	648 (20.0%)	20.19	19.65	22.04	0.96 (0.70,1.33)	1.12 (0.82,1.51)
Sex						
Women	2191 (67.7%)	5.03	5.34	4.96	0.99 (0.72,1.37)	1.07 (0.78,1.46)
Men	1043 (32.3%)	10.19	11.89	11.55	1.13 (0.82,1.57)	1.17 (0.84,1.62)
Race						
White	1768 (54.7%)	7.75	9.56	8.89	1.14 (0.86,1.52)	1.24 (0.94,1.64)
African American	645 (19.9%)	6.57	6.67	4.75	0.72 (0.41,1.26)	1.02 (0.60,1.72)
Hispanic	508 (15.7%)	4.66	4.76	4.83	1.04 (0.52,2.08)	1.03 (0.52,2.04)
American Indian	171 (5.3%)	2.48	0.80	3.80	1.56 (0.35,6.99)	0.31 (0.03,3.03)
Asian American	142 (4.4%)	4.91	3.39	8.38	1.72 (0.52,5.63)	0.68 (0.18,2.55)
BMI in kg/m <sup>2</sup>						
25 to 29	953 (30.4%)	7.45	7.48	8.67	1.16 (0.79,1.72)	1.00 (0.67,1.50)
30 to 34	993 (31.6%)	7.15	8.70	7.53	1.05 (0.71,1.57)	1.23 (0.83,1.82)
35+	1193 (38.0%)	5.21	6.21	5.67	1.08 (0.71,1.64)	1.18 (0.79,1.77)

\*All hazard ratios are unadjusted.

eTable 2. Adjusted Effects of Metformin and Lifestyle on All-Cause Mortality

Models*	Hazard ratio (95% CI) for Metformin vs Placebo	Hazard ratio (95% CI) for Lifestyle vs Placebo
Model A1: Unadjusted	1.08 (0.86, 1.36)	1.12 (0.90,1.41)
Model A2: Demographics	0.99 (0.79, 1.25)	1.02 (0.81, 1.28)
Model A3: Model A2+ Out-of-study metformin	0.97 (0.77, 1.23)	1.02 (0.81, 1.27)
Model A4: Model A3 + Diabetes status and duration	0.97 (0.77, 1.23)	1.02 (0.81, 1.28)
Model A5: Model A4+ Body mass index	0.97 (0.77, 1.23)	1.02 (0.81, 1.28)
Model A6: Model A5 + Hemoglobin A1c	0.97 (0.77, 1.23)	1.02 (0.81, 1.28)
Model A7: Model A6 + fully adjusted	0.98 (0.77, 1.23)	1.03 (0.82, 1.29)

\* Models A3-A7 include time dependent risk factors. Model A7 include additional adjustment for time-dependent log (albumin-to-creatinine ratio), estimated glomerular filtration rate, hypertension, dyslipidemia, smoking and alcohol use.