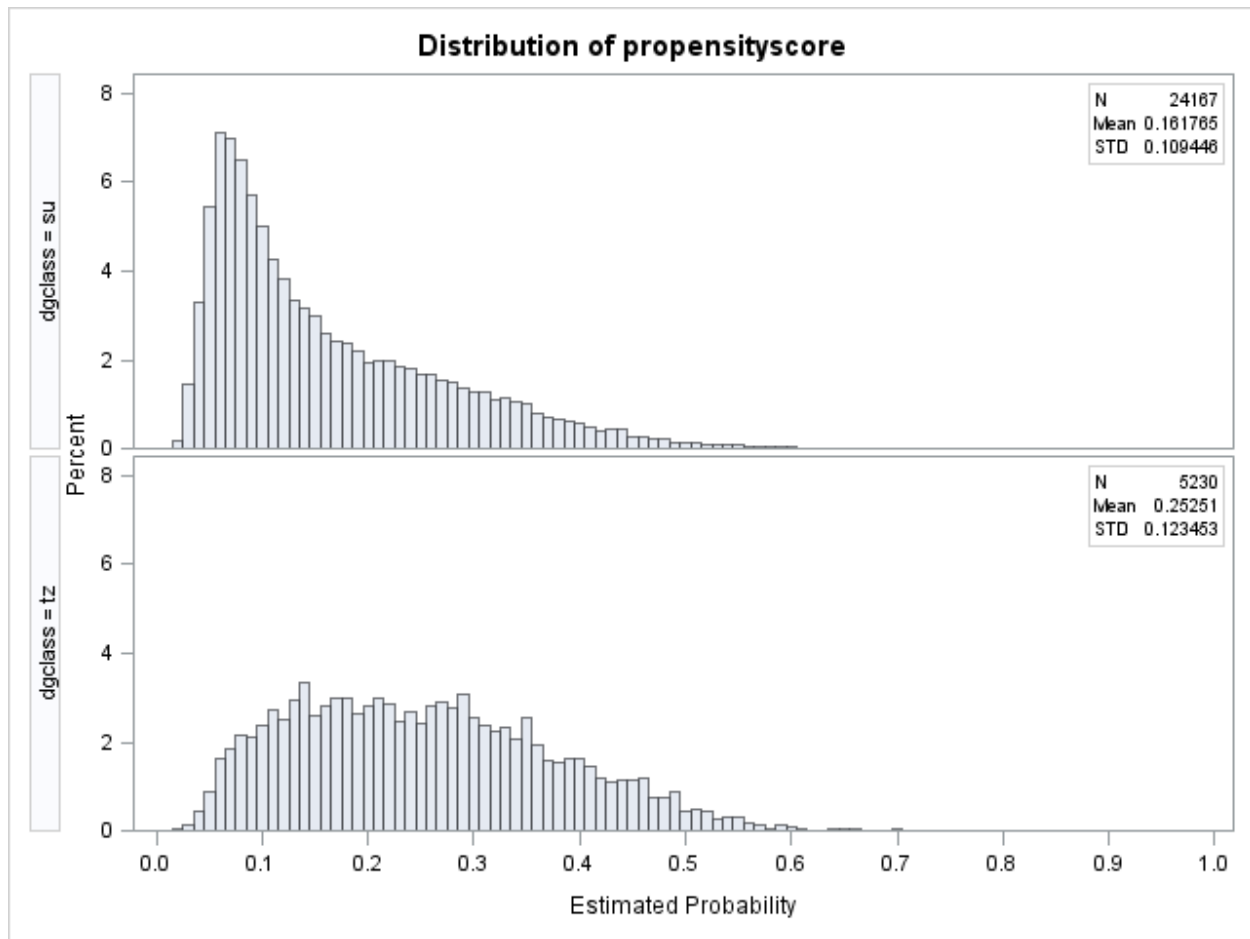
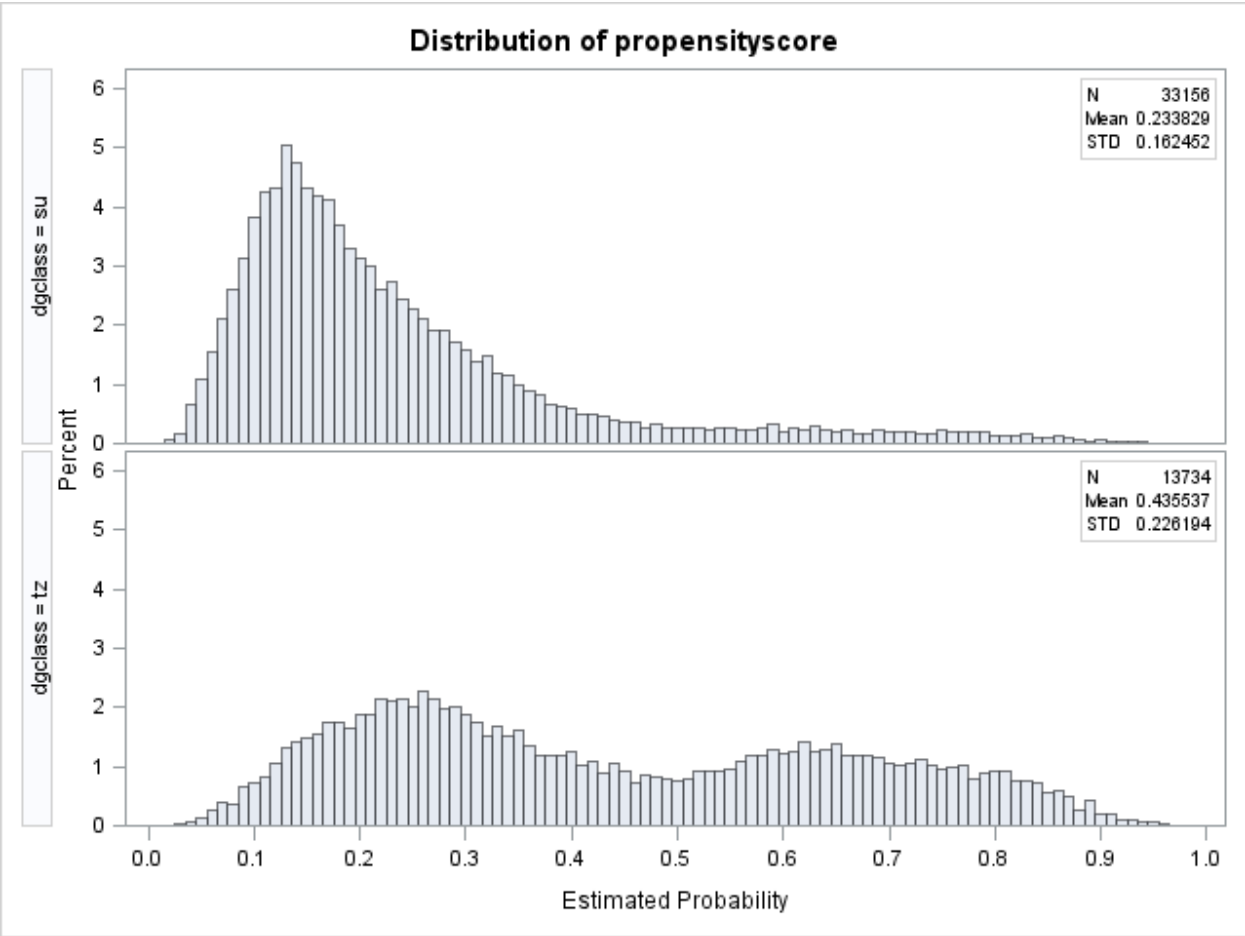


Web Figure 1. Propensity Score Distribution for Primary Cohort:



Web Figure 2. Propensity Score Distribution for Secondary Cohort



Web Table 1. Baseline covariates of the secondary cohort

Confounder	Unmatched			Matched ^a		
	SU (N=33,156)	TZD (N=13,734)	Absolute Difference (%)	SU (N=10,953)	TZD (N=10,953)	Absolute Difference (%)
Demographics						
Age, mean (sd)	78.21 (6.99)	76.46 (6.62)	1.75	76.91 (6.77)	76.85 (6.72)	0.06
Female, n (%)	24305 (73.30)	10429 (75.94)	2.64	8219 (75.04)	8229 (75.13)	0.09
White, n (%)	28838 (86.98)	11492 (83.68)	3.30	9238 (84.34)	9234 (84.31)	0.03
Health Service Utilization, mean (sd)						
Days Hospitalized	3.10 (6.52)	2.13 (5.34)	0.97	2.44 (5.71)	2.29 (5.59)	0.15
# Hospitalizations	0.36 (0.57)	0.27 (0.51)	0.09	0.29 (0.52)	0.28 (0.52)	0.01
Days in Nursing Home	1.47 (5.98)	0.94 (4.92)	0.53	1.16 (5.18)	1.06 (5.24)	0.10
# Nursing Home Admissions	0.09 (0.31)	0.06 (0.25)	0.03	0.07 (0.27)	0.07 (0.26)	0.00
# Visits	4.87 (4.30)	5.18 (4.10)	0.31	5.11 (4.37)	5.09 (4.05)	0.02
# Generic Meds	7.50 (4.79)	8.73 (4.92)	1.23	8.37 (5.05)	8.33 (4.83)	0.04
# Diabetes Visits	2.69 (3.28)	3.54 (3.59)	0.85	3.34 (3.82)	3.27 (3.51)	0.07
# Diabetes Hospitalizations	0.30 (0.67)	0.26 (0.66)	0.04	0.29 (0.69)	0.27 (0.67)	0.02
Prior Drug Use, n (%)						
Acarbose	199 (0.60)	142 (1.03)	0.43	102 (0.93)	104 (0.95)	0.02
Exanatide	1 (0.00)	2 (0.01)	0.01	1 (0.01)	2 (0.02)	0.01
Insulin	2956 (8.92)	5550 (40.41)	31.49	2846 (25.98)	2954 (26.97)	0.99
Metformin	5310 (16.02)	3194 (23.26)	7.24	2724 (24.87)	2591 (23.66)	1.21
Miglitol	46 (0.14)	37 (0.27)	0.13	27 (0.25)	27 (0.25)	0.00
Nateglinide	251 (0.76)	304 (2.21)	1.45	215 (1.96)	224 (2.05)	0.09
Repaglinide	624 (1.88)	633 (4.61)	2.73	455 (4.15)	468 (4.27)	0.12
ACE inhibitors	11310 (34.11)	5449 (39.68)	5.57	4164 (38.02)	4146 (37.85)	0.17
Angiotensin Receptor Blockers	3856 (11.63)	2381 (17.38)	5.75	1882 (17.18)	1899 (17.34)	0.16
Alpha Blockers	2436 (7.35)	1160 (8.45)	1.10	904 (8.25)	902 (8.24)	0.01
Antiarrhythmics	1031 (3.11)	369 (2.69)	0.42	299 (2.73)	294 (2.68)	0.05
Antiplatelets	2283 (6.89)	1225 (8.92)	2.03	988 (9.02)	977 (8.92)	0.10
Beta Blockers	11927 (35.97)	5251 (38.23)	2.26	4199 (38.34)	4202 (38.36)	0.02
Bisphosphonates	1560 (4.71)	847 (6.17)	1.46	732 (6.68)	705 (6.44)	0.24
Calcium Channel Blockers	11147 (33.62)	4746 (34.56)	0.94	3646 (33.29)	3703 (33.81)	0.52
COX2 Inhibitors	3299 (9.95)	1811 (13.19)	3.24	1565 (14.29)	1484 (13.55)	0.74
Digoxin	5667 (17.09)	2039 (14.85)	2.24	1600 (14.61)	1605 (14.65)	0.04

Confounder	Unmatched			Matched*		
	SU (N=34,424)	TZD (N=14,279)	Absolute Difference (%)	SU (N=10,953)	TZD (N=10,953)	Absolute Difference (%)
Estrogens	1035 (3.12)	483 (3.52)	0.40	383 (3.50)	373 (3.41)	0.09
H2 Antagonists	3656 (11.03)	1258 (9.16)	1.87	955 (8.72)	966 (8.82)	0.10
Drugs that cause hepatotoxicity	19982 (60.27)	8429 (61.37)	1.10	6600 (60.26)	6567 (59.96)	0.30
Loop diuretics	9248 (27.89)	3964 (28.86)	0.97	2940 (26.84)	3018 (27.55)	0.71
Non-selective NSAIDs	4367 (13.17)	1886 (13.73)	0.56	1397 (12.75)	1445 (13.19)	0.44
Nitrates	6820 (20.57)	2808 (20.45)	0.12	2076 (18.95)	2132 (19.46)	0.51
Other lipid lowering drugs	1584 (4.78)	986 (7.18)	2.40	806 (7.36)	791 (7.22)	0.14
Others cardiovascular drugs	1301 (3.92)	578 (4.21)	0.29	428 (3.91)	447 (4.08)	0.17
Parkinsonism inducing medication	2496 (7.53)	953 (6.94)	0.59	758 (6.92)	725 (6.62)	0.30
Potassium sparing agents	2755 (8.31)	994 (7.24)	1.07	855 (7.81)	823 (7.51)	0.30
Proton pump inhibitors	3815 (11.51)	1874 (13.64)	2.13	1636 (14.94)	1557 (14.22)	0.72
Statins	9204 (27.76)	5294 (38.55)	10.79	4249 (38.79)	4175 (38.12)	0.67
Thiazides	7648 (23.07)	3485 (25.37)	2.30	2881 (26.30)	2845 (25.97)	0.33
Thyroid	4475 (13.50)	2077 (15.12)	1.62	1642 (14.99)	1641 (14.98)	0.01
Warfarin	4197 (12.66)	1482 (10.79)	1.87	1230 (11.23)	1191 (10.87)	0.36
Metformin Combination Therapy	1708 (5.15)	709 (5.16)	0.01	693 (6.33)	661 (6.03)	0.30
Clinical Conditions, n (%) [unless otherwise noted]						
Combined Comorbidity Score, mean (sd)	1.74 (2.57)	1.46 (2.34)	0.28	1.50 (2.45)	1.47 (2.39)	0.03
Alzheimer's disease	2386 (7.20)	785 (5.72)	1.48	701 (6.40)	660 (6.03)	0.37
Atrial Fibrillation	1280 (3.86)	340 (2.48)	1.38	311 (2.84)	292 (2.67)	0.17
Alcohol Abuse	117 (0.35)	28 (0.20)	0.15	28 (0.26)	28 (0.26)	0.00
Angina	3651 (11.01)	1435 (10.45)	0.56	1105 (10.09)	1101 (10.05)	0.04
History of CABG before baseline period	1969 (5.94)	828 (6.03)	0.09	647 (5.91)	649 (5.93)	0.02
CABG during baseline period	318 (0.96)	110 (0.80)	0.16	94 (0.86)	88 (0.80)	0.06
Congestive Heart Failure	8719 (26.30)	2962 (21.57)	4.73	2392 (21.84)	2403 (21.94)	0.10
Chronic Obstructive Pulmonary Disease	3080 (9.29)	879 (6.40)	2.89	764 (6.98)	741 (6.77)	0.21
Cancer	5540 (16.71)	2014 (14.66)	2.05	1696 (15.48)	1677 (15.31)	0.17
Chronic kidney disease	1331 (4.01)	623 (4.54)	0.53	513 (4.68)	481 (4.39)	0.29
Coronary artery disease	12967 (39.11)	5186 (37.76)	1.35	4102 (37.45)	4055 (37.02)	0.43
Depression	997 (3.01)	380 (2.77)	0.24	326 (2.98)	311 (2.84)	0.14
End Stage Renal Disease	11 (0.03)	5 (0.04)	0.01	5 (0.05)	3 (0.03)	0.02
	Unmatched			Matched*		

Confounder	SU (N=34,424)	TZD (N=14,279)	Absolute Difference (%)	SU (N=10,953)	TZD (N=10,953)	Absolute Difference (%)
Gastroparesis	98 (0.30)	76 (0.55)	0.25	55 (0.50)	59 (0.54)	0.04
Gout	984 (2.97)	322 (2.34)	0.63	292 (2.67)	279 (2.55)	0.12
HIV/AIDS	19 (0.06)	5 (0.04)	0.02	6 (0.05)	5 (0.05)	0.00
Hyperlipidemia	14396 (43.42)	7328 (53.36)	9.94	5995 (54.73)	5875 (53.64)	1.09
Hypothyroidism	6250 (18.85)	2904 (21.14)	2.29	2315 (21.14)	2303 (21.03)	0.11
Illicit drug use	38 (0.11)	7 (0.05)	0.06	5 (0.05)	7 (0.06)	0.01
Inflammatory arthritis	7955 (23.99)	3050 (22.21)	1.78	2486 (22.70)	2499 (22.82)	0.12
Nephropathy	12 (0.04)	6 (0.04)	0.00	5 (0.05)	4 (0.04)	0.01
Neuropathy	2083 (6.28)	1597 (11.63)	5.35	1096 (10.01)	1083 (9.89)	0.12
History of MI before baseline period	1869 (5.64)	618 (4.50)	1.14	540 (4.93)	518 (4.73)	0.20
MI during baseline period	1494 (4.51)	436 (3.17)	1.34	373 (3.41)	399 (3.50)	0.09
Obesity	1265 (3.82)	667 (4.86)	1.04	511 (4.67)	508 (4.64)	0.03
Peripheral Vascular Disease	4746 (14.31)	2035 (14.82)	0.51	1529 (13.96)	1526 (13.93)	0.03
Palpitations	971 (2.93)	394 (2.87)	0.06	331 (3.02)	320 (2.92)	0.10
Peptic ulcer	1998 (6.03)	768 (5.59)	0.44	619 (5.65)	625 (5.71)	0.06
Retinopathy	2028 (6.12)	1985 (14.45)	8.33	1183 (10.80)	1213 (11.07)	0.27
Stroke	3224 (9.72)	1216 (8.29)	1.43	959 (8.76)	919 (8.39)	0.37
Transient Ischemic Attack	1597 (4.82)	563 (4.10)	0.72	518 (4.54)	452 (4.13)	0.41
Angiography	1224 (3.69)	457 (3.33)	0.36	366 (3.34)	377 (3.44)	0.10
Dialysis	174 (0.52)	79 (0.58)	0.06	71 (0.65)	66 (0.60)	0.05
Stent	281 (0.85)	118 (0.86)	0.01	87 (0.79)	93 (0.85)	0.06
Hypertension	23986 (72.34)	10248 (74.62)	2.28	8281 (75.60)	8200 (74.87)	0.73
Liver Disease	1213 (3.66)	418 (3.04)	0.62	372 (3.40)	350 (3.20)	0.20

ACE - Angiotensin converting enzyme inhibitor; COX2 – Cyclooxygenase 2; NSAID - Nonsteroidal anti-inflammatory drug; CABG - Coronary artery bypass graft; MI - Myocardial infarction; sd – standard deviation

^a Note: Matched covariate comparison is based on patients included in the 'any exposure' analysis. Covariate information for sulfonylurea patients is based on a random sample of one sulfonylurea user from each matched set, as described in the statistical analysis section.

Web Table 2. Results from ITT analysis of secondary cohort

	Haz. Ratio (95% CI)	# Patients	# Total Events	# TZD Users	# TZD Events	# SU Users	# SU Events
Any Exposure	1.18 (0.89, 1.56)	42680	295	10953	74	31727	221
3 months	1.28 (0.94, 1.72)	38359	243	9881	65	28478	178
4 months	1.17 (0.83, 1.64)	29066	199	7476	49	21590	150
5 months	1.23 (0.86, 1.77)	26672	176	6813	45	19859	131
6 months	1.09 (0.73, 1.62)	24115	152	6112	36	18003	116
7 months	1.02 (0.67, 1.56)	21908	138	5517	31	16391	107
8 months	1.25 (0.82, 1.88)	20413	134	5146	34	15267	100
9 months	1.11 (0.72, 1.71)	18977	125	4773	30	14244	95
10 months	1.30 (0.84, 2.02)	17687	118	4360	30	13327	88

Web Table 3. Results from AT analysis of primary cohort

	Haz. Ratio (95% CI)	# Patients	# Total Events	# TZD Users	# TZD Events	# SU Users	# SU Events
Any exposure	0.74 (0.36, 1.51)	25508	74	5225	9	20283	65
3 months	0.60 (0.24, 1.53)	23158	60	4746	5	18412	55
4 months	0.66 (0.26, 1.70)	17504	54	3590	5	13914	49
5 months	0.55 (0.19, 1.56)	16076	48	3267	4	12809	44
6 months	0.54 (0.16, 1.77)	14551	43	2956	3	11595	40
7 months	0.59 (0.18, 1.95)	13317	40	2664	3	10653	37
8 months	0.60 (0.18, 1.99)	12450	40	2477	3	9973	37
9 months	0.66 (0.20, 2.21)	11541	38	2289	3	9252	35
10 months	0.84 (0.25, 2.83)	10785	35	2128	3	8657	32

Web Table 4. Results from AT analysis of secondary cohort

	Haz. Ratio (95% CI)	# Patients	# Total Events	# TZD Users	# TZD Events	# SU Users	# SU Events
Any Exposure	1.01 (0.65, 1.56)	42680	137	10953	28	31727	109
3 months	1.04 (0.60, 1.79)	38359	94	9881	18	28478	76
4 months	0.98 (0.55, 1.72)	29066	92	7476	16	21590	76
5 months	1.19 (0.68, 2.07)	26672	83	6813	18	19859	65
6 months	0.97 (0.52, 1.83)	24115	75	6112	13	18003	62
7 months	0.98 (0.50, 1.93)	21908	68	5517	11	16391	57
8 months	0.94 (0.46, 1.92)	20413	62	5146	10	15267	52
9 months	1.03 (0.52, 2.04)	18977	64	4733	11	14244	53
10 months	1.32 (0.65, 2.65)	177687	59	4360	11	13327	48