

Supplementary Tables and Figures

Trends in first-line glucose-lowering drug use in adults with type 2 diabetes in light of emerging evidence for SGLT-2i and GLP-1RA.

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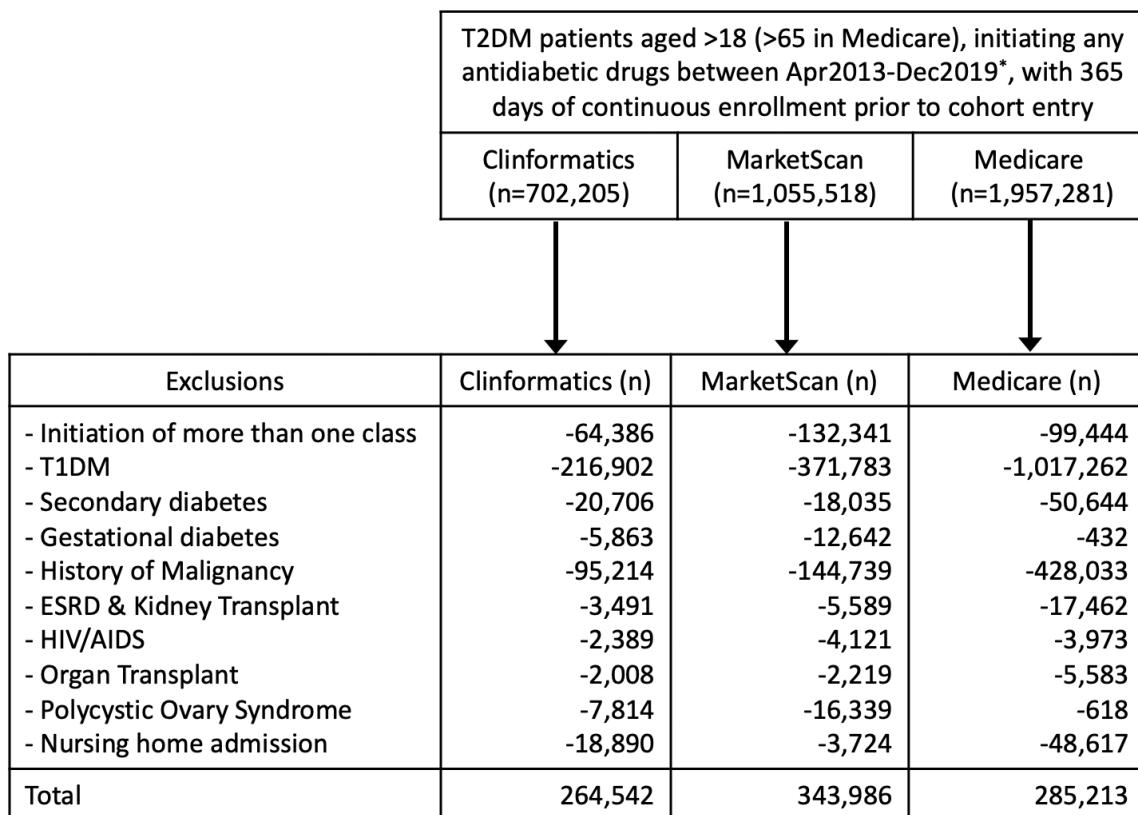
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Table S1. List of the study drugs

Therapeutic Class	Generic name(s)
Biguanides	Metformin
Sulfonylureas	Acetohexamide Chlorpropamide Tolazamide Tolbutamide Glyburide Glipizide Glimepiride
Insulin	Insulin human regular Insulin human isophane (NPH) Insulin human regular/ Insulin human isophane (NPH) Insulin Aspart Insulin Glulisine Insulin Lispro Insulin Detemir Insulin Glargine Insulin Degludec Insulin Aspart/Insulin Aspart Protamine Insulin Lispro/Insulin Lispro Protamine
Dipeptidyl peptidase-4 inhibitors (DPP-4i)	Alogliptin Linagliptin Saxagliptin Sitagliptin
Glucagon-like peptide 1 receptor agonists (GLP-1RA)	Albiglutide Exenatide Liraglutide Lixisenatide Dulaglutide Semaglutide
Sodium-glucose cotransporter 2 inhibitors (SGLT-2i)	Canagliflozin Dapagliflozin Empagliflozin Ertugliflozin
Thiazolidinediones (TZD)	Pioglitazone Rosiglitazone Troglitazone
Others	α -glucosidase inhibitors (acarbose, miglitol) Amylin agonists (pramlintide) Dopamine receptor agonists (Cycloset® (bromocriptine)) Meglitinides (nateglinide, repaglinide)

Figure S1. Consort diagram of patients initiating first-line antidiabetic medications



T2DM: type 2 diabetes mellitus; T1DM: type 1 diabetes mellitus; ESRD: end-stage renal disease; HIV/AIDS: human immunodeficiency virus/acquired immune deficiency syndrome.

* Data range: Clininformatics (Apr 2013–Dec 2019) / MarketScan (Apr 2013–Dec 2018) / Medicare (Apr 2013–Dec 2017)

Table S2. U.S. geographic region

Geographic region	States
Northeast	Connecticut Massachusetts Maine New Hampshire New Jersey New York Pennsylvania Rhode Island Vermont
South	Alabama Arkansas District of Columbia Delaware Florida Georgia Kentucky Louisiana Maryland Mississippi North Carolina Oklahoma South Carolina Tennessee Texas Virginia West Virginia
Midwest	Iowa Illinois Indiana Kansas Michigan Minnesota Missouri North Dakota Nebraska Ohio South Dakota Wisconsin
West	Alaska Arizona California Colorado Hawaii Idaho Montana New Mexico Nevada Oregon Utah Washington <u>Wyoming</u>

Figure S2. Temporal trends in first-line antidiabetic drug initiation, overall and CVD stratified plots for MarketScan

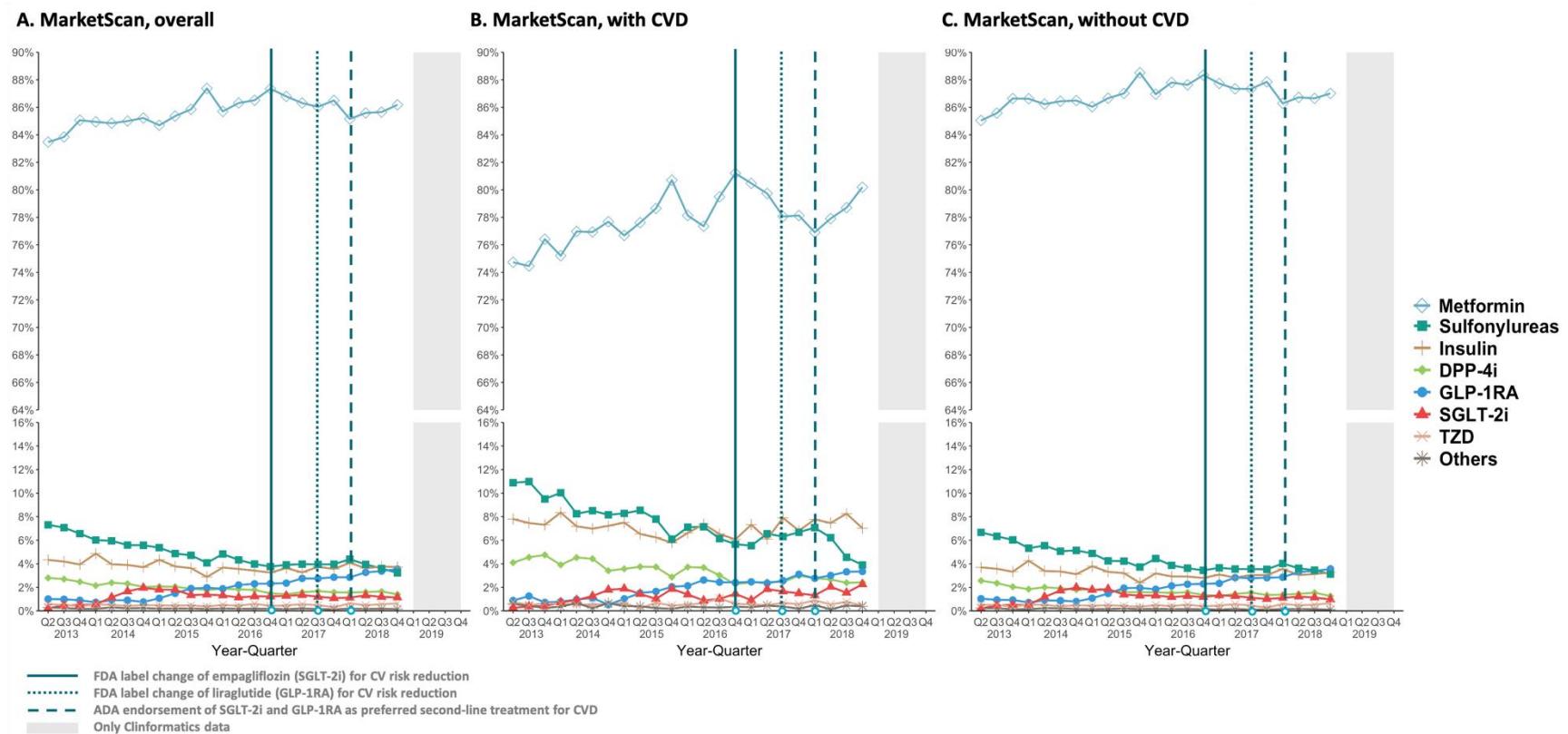
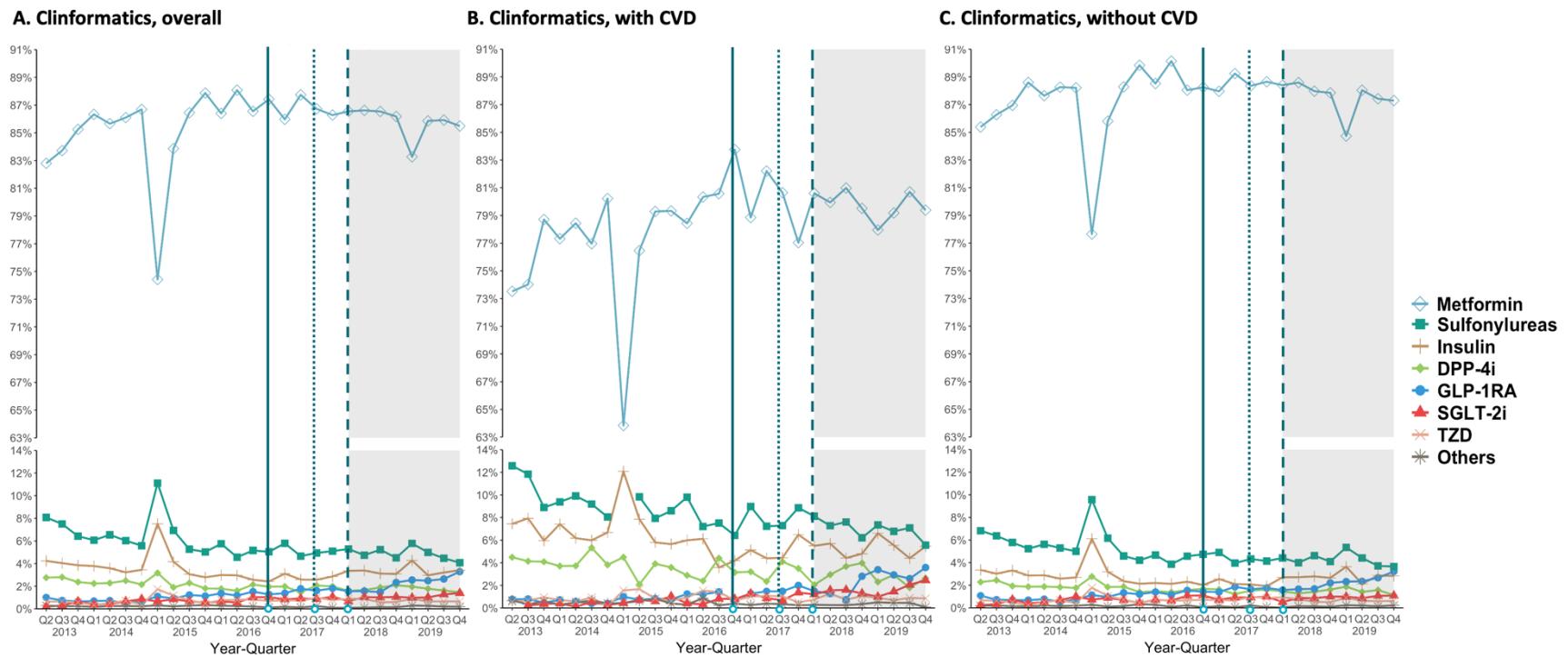
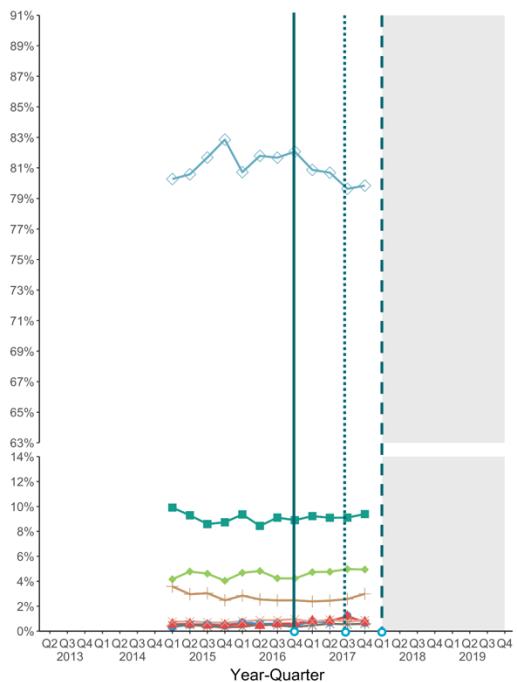


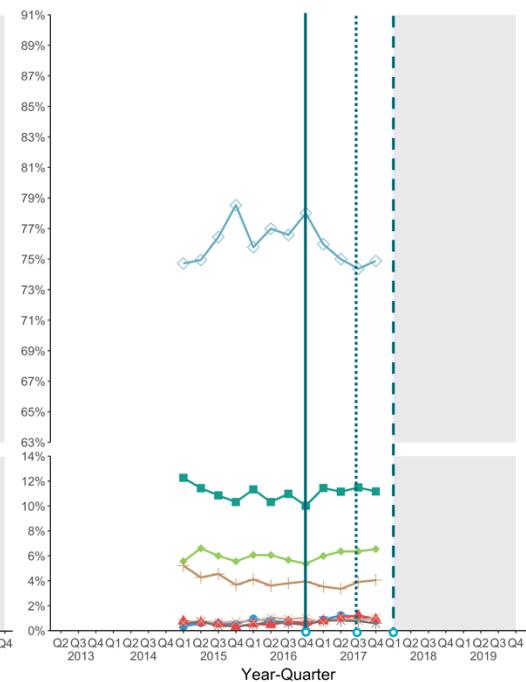
Figure S3. [Sensitivity analysis] Temporal trends in first-line antidiabetic drug initiation, overall and CVD stratified plots for all databases



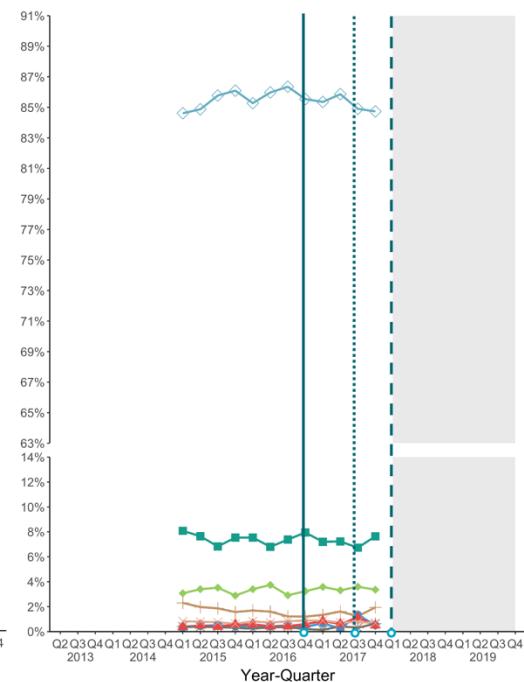
D. Medicare, overall



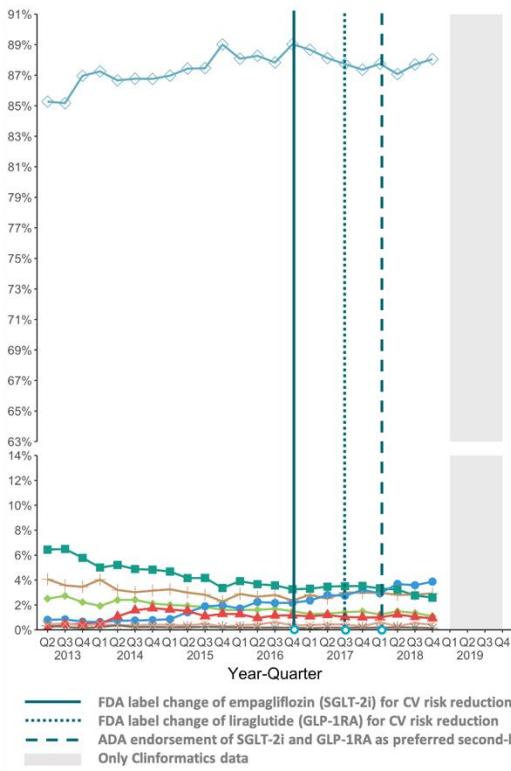
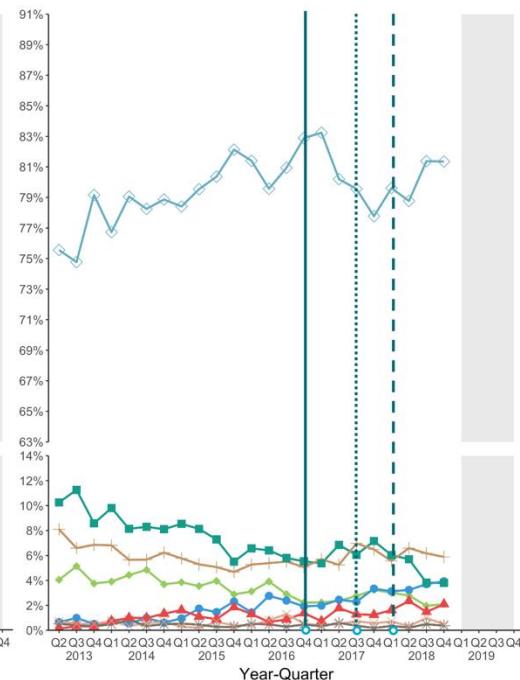
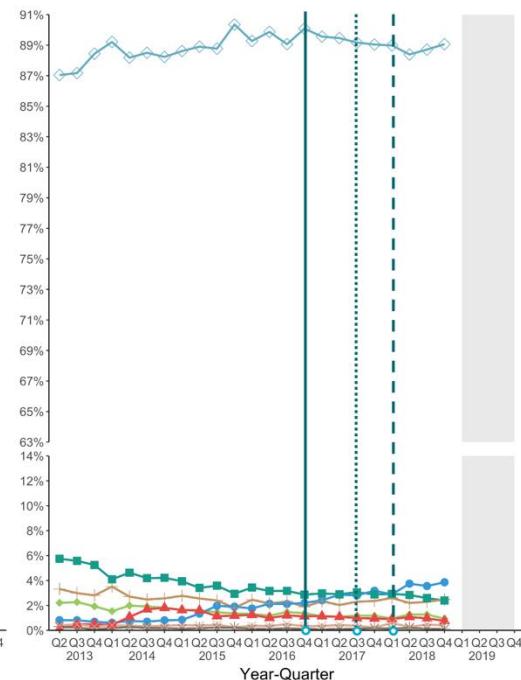
E. Medicare, with CVD



F. Medicare, without CVD



- ◆ Metformin
- Sulfonylureas
- ▲ Insulin
- ◆ DPP-4i
- GLP-1RA
- ▲ SGLT-2i
- TZD
- * Others

G. MarketScan, overall**H. MarketScan, with CVD****I. MarketScan, without CVD**

- Metformin
- Sulfonylureas
- Insulin
- DPP-4i
- GLP-1RA
- SGLT-2i
- TZD
- Others

Table S3. Patient characteristics at the time of first-line antidiabetic drug initiation (2013-2019)

Clininformatics			MarketScan			Medicare		
Apr2013-Sep2015 (n=88,873)	Oct2015-Dec2017 (n=89,484)	Jan2018-Dec2019 (n=86,185)	Apr2013-Sep2015 (n= 172,158)	Oct2015-Dec2017 (n=127,450)	Jan2018-Dec2018 (n=44,378)	Apr2013-Sep2015 (n=186,146)	Oct2015-Dec2017 (n=99,067)	
Baseline characteristics			N (%) or mean (SD)			N (%) or mean (SD)		
Demographics								
Age (mean, SD)	58.87 (13.07)	58.92 (13.10)	59.63 (13.23)	54.49 (11.47)	53.70 (11.16)	52.21 (10.47)	73.16 (6.34)	73.09 (6.26)
Male	48349 (54.4)	48751 (54.5)	48175 (55.9)	93473 (54.3)	69403 (54.5)	24977 (56.3)	84081 (45.2)	46869 (47.3)
Region								
Northeast	9172 (10.3)	9393 (10.5)	8494 (9.9)	29447 (17.1)	20680 (16.2)	7418 (16.7)	31814 (17.1)	19410 (19.6)
South	40210 (45.2)	42002 (46.9)	41774 (48.5)	75389 (43.8)	64866 (50.9)	21601 (48.7)	78099 (42.0)	40702 (41.1)
Midwest	18605 (20.9)	19439 (21.7)	18076 (21.0)	38736 (22.5)	24994 (19.6)	9318 (21.0)	43368 (23.3)	21389 (21.6)
West	20886 (23.5)	18650 (20.8)	17841 (20.7)	28586 (16.6)	16910 (13.3)	6041 (13.6)	32865 (17.7)	17566 (17.7)
Race	-	-	-	-	-	-	150883 (81.1)	80978 (81.7)
Life-style risk factors								
Alcohol/Drug abuse or dependence	2858 (3.2)	9381 (10.5)	11659 (13.5)	3793 (2.2)	9057 (7.1)	4018 (9.1)	5044 (2.7)	7990 (8.1)
Obesity or Overweight	24929 (28.1)	35225 (39.4)	41669 (48.3)	39395 (22.9)	47684 (37.4)	19572 (44.1)	43743 (23.5)	33993 (34.3)
Smoking	10787 (12.1)	15209 (17.0)	17667 (20.5)	13851 (8.0)	13527 (10.6)	5191 (11.7)	32421 (17.4)	21732 (21.9)
Comorbidities								
Diabetic microvascular complications*	9307 (10.5)	10274 (11.5)	11524 (13.4)	7887 (4.6)	6982 (5.5)	2827 (6.4)	17922 (9.6)	15189 (15.3)
Hypoglycemia	3120 (3.5)	4745 (5.3)	7033 (8.2)	4019 (2.3)	4181 (3.3)	2063 (4.6)	4831 (2.6)	3928 (4.0)
Hyperlipidemia	59320 (66.7)	55035 (61.5)	55166 (64.0)	98693 (57.3)	66300 (52.0)	23915 (53.9)	152456 (81.9)	79636 (80.4)
Hypertension	55536 (62.5)	55508 (62.0)	53958 (62.6)	92763 (53.9)	72075 (56.6)	23870 (53.8)	154358 (82.9)	84676 (85.5)
CVD†	18439 (20.7)	18142 (20.3)	19001 (22.0)	25570 (14.9)	17765 (13.9)	5482 (12.4)	78102 (42.0)	43142 (43.5)
CKD	6621 (7.4)	6745 (7.5)	7256 (8.4)	4640 (2.7)	3752 (2.9)	1161 (2.6)	20418 (11.0)	13352 (13.5)
COPD	6805 (7.7)	6929 (7.7)	7437 (8.6)	7553 (4.4)	5321 (4.2)	1495 (3.4)	29194 (15.7)	15366 (15.5)
Physician specialties‡								
Cardiologists	5801 (6.5)	5889 (6.6)	6384 (7.4)	7288 (4.2)	5751 (4.5)	1921 (4.3)	21478 (11.5)	10004 (10.1)
Endocrinologists	2193 (2.5)	2087 (2.3)	2069 (2.4)	3907 (2.3)	3200 (2.5)	1055 (2.4)	5171 (2.8)	2937 (3.0)
Internists	47579 (53.5)	48527 (54.2)	48037 (55.7)	116223 (67.5)	90272 (70.8)	30646 (69.1)	123537 (66.4)	66010 (66.6)
Healthcare utilization								
Any hospitalization§	6481 (7.3)	6113 (6.8)	6428 (7.5)	11768 (6.8)	8136 (6.4)	2780 (6.3)	23073 (12.4)	10719 (10.8)
Duration of hospitalizations (mean, SD)	0.85 (5.54)	0.74 (4.58)	0.83 (5.05)	0.66 (3.66)	0.63 (3.70)	0.60 (3.68)	1.46 (5.75)	1.34 (5.40)
Emergency department visits	30393 (34.2)	32087 (35.9)	31597 (36.7)	52366 (30.4)	39886 (31.3)	14071 (31.7)	55032 (29.6)	28747 (29.0)
Number of office visits (mean, SD)	8.08 (8.50)	7.86 (8.51)	8.13 (8.77)	8.81 (9.96)	8.92 (10.16)	8.68 (10.24)	8.34 (6.96)	8.84 (6.90)
HbA1c test orders ≥ 3	13433 (15.1)	13405 (15.0)	13186 (15.3)	18609 (10.8)	13310 (10.4)	4630 (10.4)	41286 (22.2)	28708 (29.0)

Preventive healthcare service [†]	57843 (65.1)	59374 (66.4)	57693 (66.9)	103983 (60.4)	78621 (61.7)	27290 (61.5)	149190 (80.1)	82821 (83.6)
Brand/Generic ratio [#] (mean, SD)	-1.46 (1.24)	-1.66 (1.24)	-1.74 (1.22)	-1.35 (1.18)	-1.56 (1.17)	-1.63 (1.17)	-1.68 (1.20)	-1.97 (1.16)
Concomitant medications								
ACE inhibitors or ARBs	45719 (51.4)	46910 (52.4)	45455 (52.7)	88150 (51.2)	64614 (50.7)	21760 (49.0)	115942 (62.3)	63517 (64.1)
Anticoagulants	3555 (4.0)	3511 (3.9)	4083 (4.7)	5718 (3.3)	4067 (3.2)	1215 (2.7)	18878 (10.1)	11486 (11.6)
Antiplatelet agents	5810 (6.5)	6270 (7.0)	6785 (7.9)	10721 (6.2)	8330 (6.5)	2966 (6.7)	24237 (13.0)	12684 (12.8)
Beta blockers	22996 (25.9)	22543 (25.2)	22966 (26.6)	40848 (23.7)	28840 (22.6)	9068 (20.4)	83308 (44.8)	45216 (45.6)
Calcium channel blockers	17473 (19.7)	18495 (20.7)	18892 (21.9)	32111 (18.7)	24699 (19.4)	8444 (19.0)	58746 (31.6)	31367 (31.7)
Loop diuretics	6479 (7.3)	6432 (7.2)	6684 (7.8)	10081 (5.9)	7062 (5.5)	1984 (4.5)	30080 (16.2)	16644 (16.8)
Statin	42619 (48.0)	44070 (49.2)	44284 (51.4)	78721 (45.7)	57131 (44.8)	19511 (44.0)	118767 (63.8)	66827 (67.5)
Thiazide	9968 (11.2)	10321 (11.5)	10544 (12.2)	19678 (11.4)	14957 (11.7)	5113 (11.5)	31431 (16.9)	16418 (16.6)

SD: standard deviation; CVD: Cardiovascular disease; CKD: Chronic kidney disease; HbA1c: hemoglobin A1c.

*Defined as a history of diabetic nephropathy, neuropathy, or retinopathy.

[†]Defined as a history of myocardial infarction, unstable angina, other ischemic heart diseases, transient ischemic attack, stroke, atherosclerotic peripheral vascular disease, or heart failure.

[‡]Defined as specialist visits occurred within 14 days prior to cohort entry.

[§]Defined as hospitalization occurred within 180 days prior to cohort entry.

^{||}Defined as at least one emergency department visit 365 days prior to cohort entry.

[†]Defined as administration of bone mineral density test, colonoscopy, fecal occult blood test, mammography, pap smear, prostate-specific antigen test, flu vaccine, or pneumococcal vaccine.

[#]Added 1 to both numerator and denominator, then log-transformed.

Table S4. Proportions and trend test P values for Clinformatics

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	2018-1	2018-2	2018-3	2018-4	2019-1	2019-2	2019-3	2019-4	Trend (p)	
Metformin	% 79.9	81.09	82.18	83.29	82.81	83.13	84.06	75.66	82.46	83.96	85.16	81.42	84.48	84.12	84.44	81.36	84.27	83.84	83.71	83.21	82.98	82.89	83.75	80.46	83.36	83.29	83.12	0.51	
	# 6812	6824	6644	8301	6901	6596	6590	9128	7677	7050	7151	8868	8083	7642	7600	10120	9479	8258	7538	9142	8803	7980	8118	10350	9582	8967	8433		
SU	% 9.23	8.77	7.67	7.15	7.67	7.23	6.63	10.44	7.44	6.3	6.32	7.79	6.23	6.18	5.83	7.28	6.12	6.2	5.86	6.29	5.92	6.18	5.54	6.46	5.56	5.4	4.65	<.01	
	# 787	738	620	713	639	574	520	1259	693	529	531	596	561	525	905	688	611	528	691	628	595	537	831	639	581	472			
Insulin	% 4.96	4.92	4.84	5	4.69	4.26	4.4	7.32	4.55	4.04	3.76	4.7	3.85	3.76	3.71	5.13	3.67	4	4.04	4.67	4.62	4.94	4.26	5.29	4.05	4.08	4.33	0.05	
	# 423	414	391	498	391	338	345	883	424	339	316	512	368	342	334	638	413	394	364	513	490	476	413	681	466	439	439		
DPP-4i	% 3.41	2.99	2.86	2.53	2.53	2.79	2.53	2.9	2.33	2.5	1.75	2.23	2.14	2.19	2.26	2.32	1.98	2.05	2.12	2.07	2.2	1.97	2.15	2.04	1.98	1.97	1.69	<.01	
	# 291	252	231	252	211	221	198	350	217	210	147	243	205	199	203	289	223	202	191	227	233	190	208	262	228	212	171		
GLP-1RA	% 1.29	0.92	0.95	0.85	0.98	0.89	0.71	1.13	1.03	1.37	1.26	1.64	1.54	1.68	1.51	1.66	1.82	1.74	2.13	1.87	2.08	1.98	2.35	2.99	2.73	2.92	3.52	<.01	
	# 110	77	77	85	82	71	56	136	96	115	106	179	147	153	136	207	205	171	192	206	221	191	228	385	314	314	357		
SGLT2-i	% 0.19	0.32	0.61	0.45	0.54	0.83	0.88	0.76	0.91	0.74	0.75	0.9	0.79	1.09	1.24	1.17	1.08	1.07	1.15	0.77	1.09	1.02	0.98	1.52	1.25	1.37	1.65	<.01	
	# 16	27	49	45	45	66	69	92	85	62	63	98	76	99	112	145	121	105	104	85	116	98	95	196	144	148	167		
TZD	% 0.75	0.7	0.63	0.49	0.53	0.68	0.55	1.53	1.08	0.76	0.71	1	0.79	0.81	0.83	0.9	0.91	0.88	0.78	0.88	0.96	0.8	0.76	1.02	0.86	0.79	0.86	0.18	
	# 64	59	51	49	44	54	43	184	101	64	60	109	76	74	75	112	102	87	70	97	102	77	74	131	99	85	87		
Others	% 0.27	0.29	0.27	0.23	0.25	0.19	0.24	0.27	0.18	0.33	0.27	0.31	0.18	0.17	0.18	0.16	0.22	0.2	0.24	0.14	0.21	0.21	0.2	0.19	0.2	0.18	0.18	0.18	
	# 23	24	22	23	21	15	19	33	17	28	23	34	17	15	15	22	18	22	18	26	15	20	27	23	20	20			
Total #	8526	8415	8085	9966	8334	7935	7840	12065	9310	8397	8397	10892	9568	9085	9000	12438	11249	9850	9005	10987	10608	9627	9693	12863	11495	10766	10146		

Table S5. Proportions and trend test P values for Medicare

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	Trend (p)										
Metformin	% 77	77.36	78.6	78.08	79.4	79.64	79.57	79.63	80.67	81.06	82.24	79.94	81.08	81.03	81.6	80.12	80.63	79.98	80.61	<.01										
	# 14102	12388	12499	17163	16480	14466	13893	16005	16025	14258	14591	10971	10047	8455	7914	8817	7828	6102	5428											
SU	% 12.25	11.78	10.97	11.11	10.23	9.69	10.02	10.07	9.17	8.7	8.88	9.6	8.79	9.37	9	9.18	8.84	8.66	8.69	<.01										
	# 2244	1886	1744	2442	2123	1760	1750	2023	1821	1531	1575	1317	1089	978	873	1010	858	661	585											
Insulin	% 4.37	4.22	4.19	4.3	3.83	3.78	3.71	4.03	3.32	3.45	2.95	3.43	2.98	2.83	2.88	3.44	3	3.17	3.43	<.01										
	# 801	676	667	946	794	686	648	810	660	607	523	471	369	295	279	379	291	242	231											
DPP-4i	% 4.62	4.71	4.36	4.49	4.68	4.72	4.34	3.99	4.18	4.47	3.68	4.28	4.52	3.93	3.9	4.02	4.07	4.57	4.01	<.01										
	# 847	755	693	988	971	858	758	801	831	787	652	588	560	410	378	442	395	349	370											
GLP-1RA	% 0.43	0.49	0.37	0.46	0.38	0.45	0.45	0.37	0.62	0.71	0.59	0.77	0.67	0.74	0.71	0.95	0.92	1.18	1.04	<.01										
	# 79	78	59	102	78	82	79	75	124	125	104	105	83	77	69	104	89	90	70											
SGLT2-i	% 0.04	0.08	0.09	0.19	0.21	0.42	0.42	0.55	0.68	0.5	0.59	0.68	0.53	0.61	0.68	1.03	1.09	1.14	0.82	<.01										
	# 7	13	14	42	43	76	73	111	135	88	104	94	66	64	66	113	106	87	55											
TZD	% 0.7	0.76	0.89	0.87	0.73	0.86	0.93	0.91	0.84	0.75	0.74	0.93	1.01	1	0.9	0.85	0.94	0.9	0.98	0.06										
	# 128	122	141	192	152	156	163	182	166	132	132	128	125	104	87	93	91	69	66											
Others	% 0.58	0.59	0.53	0.48	0.55	0.45	0.56	0.45	0.52	0.35	0.34	0.36	0.42	0.5	0.34	0.43	0.53	0.38	0.43	<.01										
	# 107	95	85	106	114	81	97	91	104	62	60	50	52	52	33	47	51	29	29											
Total #	18315	16013	15902	21981	20755	18165	17461	20098	19866	17590	17741	13724	12391	10435	9699	11005	9709	7629	6734											

Table S6. Proportions and trend test P values for MarketScan

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	2018-1	2018-2	2018-3	2018-4	Trend (p)		
Metformin	% 83.47	83.84	85.06	84.94	84.84	85	85.22	84.69	85.36	85.85	87.37	85.7	86.31	86.51	87.35	86.79	86.31	86.03	86.5	85.15	85.59	85.65	86.18	<.01		
	# 15013	14009	14580	17567	15347	14290	14573	14295	13607	12720	13148	14689	13620	12814	12581	12444	9971	9646	10215	9770	8852	9163				
SU	% 7.31	7.07	6.56	6.02	5.95	5.59	5.57	5.37	4.87	4.72	4.08	4.83	4.33	3.98	3.76	3.91	3.97	3.95	3.96	4.39	3.95	3.6	3.23	<.01		</

Table S7. Proportions and trend test P values for Clininformatics beneficiaries with CVD

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	2018-1	2018-2	2018-3	2018-4	2019-1	2019-2	2019-3	2019-4	Trend (p)	
Metformin	%	70.2	72.07	74.76	75.64	75.53	74.43	76.86	65.32	74.53	76.79	77.33	72.62	77.62	77.71	78.26	72.47	77.12	77.45	75.92	74.85	75.53	75.79	78.03	74.72	76.7	76.51	76.72	0.05
	#	1305	1293	1232	1543	1330	1135	1159	1746	1460	1284	1235	1650	1519	1325	1256	1924	1874	1628	1381	1896	1784	1609	1602	2057	2041	1769	1691	
SU	%	13.45	13.27	10.25	10.34	10.9	10.36	9.02	14.74	10.72	8.79	9.77	11.71	7.92	8.15	8.16	10.81	8.89	8.66	7.92	9.47	8.17	8.48	7.45	8.06	6.73	8.04	5.85	<.01
	#	250	238	169	211	192	158	136	394	210	147	156	266	155	139	131	287	216	182	144	240	193	180	153	222	179	186	129	
Insulin	%	8.39	8.47	7.46	8.14	7.67	7.28	8.29	12.05	7.76	7.6	6.76	8.27	7.41	6.39	6.29	9.27	6.79	6.95	7.97	8.09	7.79	8.15	6.53	8.06	7.37	6.36	6.94	0.51
	#	156	152	123	166	135	111	125	322	152	127	108	188	145	109	101	246	165	146	145	205	184	173	134	222	196	147	153	
DPP-4i	%	5.11	4.07	4.43	3.87	3.86	5.18	3.71	4.53	3.27	3.83	3.13	3.35	3.32	3.52	3.61	3.54	2.88	3.52	3.74	3.28	3.81	3.25	3.31	2.76	3.42	2.68	2.72	<.01
	#	95	73	73	79	68	79	56	121	64	64	50	76	65	60	58	94	70	74	68	83	90	69	68	76	91	62	60	
GLP-1RA	%	1.29	0.72	1.21	0.83	0.68	0.72	0.73	1.01	0.92	1.08	0.81	1.58	1.38	1.76	1.12	1.24	1.6	1.43	1.76	1.74	1.95	1.74	2.39	2.87	2.86	3.07	3.58	<.01
	#	24	13	20	17	12	11	11	27	18	18	13	36	27	30	18	33	39	30	32	44	46	37	49	79	76	71	79	
SGLT2-i	%	NA	0.17	0.42	0.2	0.23	0.59	0.6	0.71	0.87	0.6	0.81	0.53	0.72	1	1.12	1.32	1.03	1	1.65	1.03	1.44	1.27	1.02	1.93	1.77	2.25	2.86	<.01
	#	NA	3	7	4	4	9	9	19	17	10	13	12	14	17	18	35	25	21	30	26	34	27	21	53	47	52	63	
TZD	%	0.86	0.78	0.91	0.64	0.62	0.98	0.27	1.23	1.38	0.72	0.88	1.63	1.07	1.17	0.93	1.13	1.4	0.67	0.6	0.99	1.23	0.89	0.97	1.13	0.79	0.82	1.09	0.51
	#	16	14	15	13	11	15	4	33	27	12	14	37	21	20	15	30	34	14	11	25	29	19	20	31	21	19	24	
Others	%	0.7	0.45	0.55	0.34	0.51	0.46	0.53	0.41	0.56	0.6	0.5	0.31	0.56	0.29	0.5	0.23	0.29	0.33	0.44	0.55	0.08	0.42	0.29	0.47	0.38	0.26	0.23	0.51
	#	13	8	9	7	9	7	8	11	11	10	8	7	11	5	8	6	7	7	8	14	2	9	6	13	10	6	5	
Total #		1859	1794	1648	2040	1761	1525	1508	2673	1959	1672	1597	2272	1957	1705	1605	2655	2430	2102	1819	2533	2362	2123	2053	2753	2661	2312	2204	

Table S8. Proportions and trend test P values for Clininformatics beneficiaries without CVD

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	2018-1	2018-2	2018-3	2018-4	2019-1	2019-2	2019-3	2019-4	Trend (p)	
Metformin	%	82.6	83.54	84.08	85.26	84.76	85.2	85.77	78.6	84.57	85.74	87	83.74	86.24	85.6	85.79	83.78	86.23	85.57	85.68	85.71	85.12	84.9	85.29	82.03	85.36	85.14	84.89	0.51
	#	5507	5531	5412	6758	5571	5461	5431	7382	6217	5766	5916	7218	6564	6317	6344	8196	7605	6630	6157	7246	7019	6371	6516	8293	7541	7198	6742	
SU	%	8.05	7.55	7.01	6.33	6.8	6.49	6.06	9.21	6.57	5.68	5.51	6.76	5.79	5.72	5.33	6.32	5.35	5.54	5.34	5.33	5.28	5.53	5.03	6.02	5.21	4.67	4.32	<.01
	#	537	500	451	502	447	416	384	865	483	382	375	583	441	422	394	618	472	429	384	451	435	415	384	609	460	395	343	
Insulin	%	4	3.96	4.16	4.19	3.89	3.54	3.47	5.97	3.7	3.15	3.06	3.76	2.93	3.16	3.15	4.01	2.81	3.2	3.05	3.64	3.71	4.04	3.65	4.54	3.06	3.45	3.6	0.05
	#	267	262	268	332	256	227	220	561	272	212	208	324	223	233	233	392	248	248	219	308	306	303	279	459	270	292	286	
DPP-4i	%	2.94	2.7	2.45	2.18	2.18	2.22	2.24	2.44	2.08	2.17	1.43	1.94	1.84	1.88	1.96	1.99	1.73	1.65	1.71	1.7	1.73	1.61	1.83	1.55	1.77	1.4	<.01	
	#	196	179	158	173	143	142	142	229	153	146	97	167	140	139	145	195	153	128	123	144	143	121	140	186	137	150	111	
GLP-1RA	%	1.29	0.97	0.89	0.86	1.06	0.94	0.71	1.16	1.06	1.44	1.37	1.66	1.58	1.67	1.6	1.78	1.88	1.82	2.23	1.92	2.12	2.05	2.34	3.03	2.69	2.87	3.5	<.01
	#	86	64	57	68	70	60	45	109	78	97	93	143	120	123	118	174	166	141	160	162	175	154	179	306	238	243	278	
SGLT2-i	%	0.24	0.36	0.65	0.52	0.62	0.89	0.95	0.78	0.93	0.77	0.74	1	0.81	1.11	1.27	1.12	1.09	1.08	1.03	0.7	0.99	0.95	0.97	1.41	1.1	1.14	1.31	<.01
	#	16	24	42	41	41	57	60	73	68	52	50	86	62	82	94	110	96	84	74	59	82	71	74	143	97	96	104	
TZD	%	0.72	0.68	0.56	0.45	0.5	0.61	0.62	1.61	1.01	0.77	0.68	0.84	0.72	0.73	0.81	0.84	0.77	0.94	0.82	0.85	0.89	0.77	0.71	0.99	0.88	0.78	0.79	0.18
	#	48	45	36	36	33	39	39	151	74	52	46	72	55	54	60	82	68	73	59	72	73	58	54	100	78	66	63	
Others	%	0.15	0.24	0.2	0.2	0.18	0.12	0.17	0.23	0.08	0.27	0.22	0.31	0.08	0.14	0.09	0.16	0.12	0.19	0.14	0.14	0.16	0.15	0.18	0.14	0.15	0.17	0.19	0.51
	#	10	16	13	16	12	8	11	22	6	18	15	27	6	10	7	16	11	15	10	12	13	11	14	14	13	14	15	
Total #		6667	6621	6437	7926	6573	6410	6332	9392	7351	6725	6800	8620	7611	7380	7395	9783	8819	7748	7186	8454	8246	7504	7640	10110	8834	8454	7942	

Table S9. Proportions and trend test P values for Medicare beneficiaries with CVD

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	Trend (p)
Metformin	%	70.58	70.96	72.29	71.96	74.27	74.11	73.69	73.79	74.88	75.61	77.51	74.83	76.4	76.23	77.37	76.28	76	75.42	

Table S10. Proportions and trend test P values for Medicare beneficiaries without CVD

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	Trend (p)
Metformin	% 82.04	82.23	83.38	82.64	83.12	83.46	83.81	83.71	84.57	84.77	85.38	84.09	84.76	84.88	84.81	83.09	84.3	83.83	84.23	<.01
	# 8412	7478	7542	10405	10001	8958	8492	9916	10029	8867	9111	6373	5884	4912	4677	5155	4563	3473	3092	
SU	% 10.47	9.56	8.76	9.12	8.83	8.27	8.22	8.47	7.65	7.05	7.63	7.96	7.26	7.95	8.03	7.82	7.41	6.9	7.19	<.01
	# 1074	869	792	1148	1063	888	833	1003	907	737	814	603	504	460	443	485	401	286	264	
Insulin	% 2.79	2.9	2.81	2.99	2.87	2.95	2.46	2.74	2.42	2.38	2.05	2.43	2.12	1.8	1.67	2.66	2.18	2.15	2.56	0.06
	# 286	264	254	376	345	317	249	325	287	249	219	184	147	104	92	165	118	89	94	
DPP-4i	% 3.23	3.52	3.29	3.48	3.49	3.39	3.43	3.01	2.94	3.48	2.75	3.13	3.62	2.85	2.99	3.21	3.29	3.62	3.19	0.29
	# 331	320	298	438	420	364	348	357	349	364	293	237	251	165	165	199	178	150	117	
GLP-1RA	% 0.41	0.47	0.27	0.47	0.36	0.39	0.44	0.34	0.56	0.75	0.55	0.5	0.53	0.6	0.71	0.85	0.67	1.23	0.9	<.01
	# 42	43	24	59	43	42	45	40	67	78	59	38	37	35	39	53	36	51	33	
SGLT2-i	% 0.03	0.08	0.13	0.15	0.19	0.34	0.36	0.43	0.64	0.49	0.6	0.77	0.58	0.48	0.65	1.14	0.96	1.16	0.68	<.01
	# 3	7	12	19	23	36	36	51	76	51	64	58	40	28	36	71	52	48	25	
TZD	% 0.64	0.93	0.93	0.81	0.74	0.87	0.9	0.96	0.84	0.76	0.68	0.9	0.88	1.09	0.91	1.02	0.87	0.89	0.82	0.29
	# 66	85	84	102	89	93	91	114	100	79	73	68	61	63	50	63	47	37	30	
Others	% 0.38	0.31	0.43	0.34	0.4	0.33	0.38	0.34	0.37	0.33	0.36	0.24	0.26	0.35	0.24	0.21	0.33	0.22	0.44	0.29
	# 39	28	39	43	48	35	38	40	44	35	38	18	18	20	13	13	18	9	16	
Total #	10253	9094	9045	12590	12032	10733	10132	11846	11859	10460	10671	7579	6942	5787	5515	6204	5413	4143	3671	

Table S11. Proportions and trend test P values for MarketScan beneficiaries with CVD

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	2018-1	2018-2	2018-3	2018-4	Trend (p)
Metformin	% 74.73	74.46	76.41	75.21	76.97	76.93	77.68	76.68	77.61	78.65	80.7	78.13	77.35	79.49	81.2	80.47	79.73	78.06	78.13	76.91	77.91	78.7	80.19	0.05
	# 2040	1947	2028	2288	2089	1961	1914	1871	1782	1625	1773	1911	1745	1632	1620	1496	1424	1274	1204	1109	1139	1020	1028	
SU	% 10.88	10.98	9.5	10.03	8.25	8.51	8.16	8.28	8.54	7.79	6.1	7.11	7.14	6.14	5.66	5.54	6.55	6.31	6.68	7.07	6.22	4.55	3.9	<.01
	# 297	287	252	305	224	217	201	202	196	161	134	174	161	126	113	103	117	103	103	102	91	59	50	
Insulin	% 7.8	7.46	7.31	8.35	7.18	6.98	7.22	7.5	6.53	6.24	5.78	6.62	7.36	6.53	6.07	7.32	6.1	7.9	6.81	7.77	7.46	8.26	7.02	0.81
	# 213	195	194	254	195	178	178	183	150	129	127	162	166	134	121	136	109	129	105	112	109	107	90	
DPP-4i	% 4.1	4.55	4.75	3.91	4.53	4.43	3.41	3.57	3.75	3.73	2.87	3.72	3.68	3.02	2.26	2.42	2.46	2.45	2.99	2.77	2.67	2.39	2.42	<.01
	# 112	119	126	119	123	113	84	87	86	77	63	91	83	62	45	45	44	40	46	40	39	31	31	
GLP-1RA	% 0.88	1.26	0.72	0.79	0.96	1.1	0.53	1.02	1.52	1.65	2.05	2.13	2.62	2.44	2.41	2.47	2.35	2.57	3.11	2.77	3.01	3.32	3.35	<.01
	# 24	33	19	24	26	28	13	25	35	34	45	52	59	50	48	46	42	42	48	40	44	43	43	
SGLT2-i	% 0.26	0.38	0.41	0.72	0.92	1.26	1.79	1.89	1.44	1.02	1.87	1.39	0.89	1.02	1.45	0.91	1.85	1.65	1.49	1.32	2.05	1.54	2.26	0.05
	# 7	10	11	22	25	32	44	46	33	21	41	34	20	21	29	17	33	27	23	19	30	20	29	
TZD	% 0.77	0.5	0.64	0.62	0.52	0.55	0.57	0.66	0.22	0.68	0.46	0.53	0.66	1.07	0.6	0.54	0.5	0.67	0.58	0.9	0.55	0.77	0.47	0.81
	# 21	13	17	19	14	14	16	5	14	10	13	15	22	12	10	9	11	9	13	8	10	6		
Others	% 0.59	0.42	0.26	0.36	0.66	0.24	0.65	0.41	0.39	0.24	0.18	0.37	0.31	0.29	0.35	0.32	0.45	0.37	0.19	0.49	0.14	0.46	0.39	0.23
	# 16	11	7	11	18	6	16	10	9	5	4	9	7	6	7	6	8	6	3	7	2	6	5	
Total #	2730	2615	2654	3042	2714	2549	2464	2440	2296	2066	2197	2446	2256	2053	1995	1859	1786	1632	1541	1442	1462	1296	1282	

Table S12. Proportions and trend test P values for MarketScan beneficiaries without CVD

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	2018-1	2018-2	2018-3	2018-4	Trend (p)
Metformin	% 85.04	85.58	86.64	86.62	86.23	86.44	86.49	86.04	86.66	87.01	88.51	86.95	87.8	87.63	88.34	87.73	87.34	87.34	87.85	86.28	86.72	86.65	87.01	<.01
	# 12973	12062	12552	15279	13258	12329	12659	12424	11825	11095	11375	12778	11875	11182	10961	10948	9955	8697	8442	9106	8631	7832	8135	
SU	% 6.67	6.34	6.03	5.33	5.55	5.07	5.14	4.88	4.25	4.23	3.73	4.45	3.87	3.63	3.45	3.66	3.56	3.56	3.53	4.03	3.62	3.46	3.13	<.01
	# 1017	894	873	940	853	723	752	704	580	539	480	654	523	463	428	457	406	355	339	425	360	313	293	
Insulin	% 3.7	3.58	3.33	4.27	3.39	3.35	3.12	3.8	3.32	3.21	2.39	3.19	2.93	2.92	2.8	3.09	2.83	3.05	3.04	3.57	3.05	3.13	3.26	0.23
	# 565	505	482	753	521	478	456	549	453	409	307	469	396	373	347	385	322	304	292	377	304	283	305	
DPP-4i	% 2.57	2.36	2.05	1.85	2.01	1.93	1.8	1.81	1.77	1.59	1.58	1.53	1.58	1.37	1.27	1.44	1.56	1.35	1.39	1.45	1.55	1.27	<.01	
	# 392	333	297	326	309	275	264	262	241	203	204	232	207	201	170	159	164	155	130	147	144	140	119	
GLP-1RA	% 1.04	0.94	0.93	0.72	0.89	0.88	0.8	1.08	1.48	1.94	1.96	1.84	2.13	2.27	2.3	2.34	2.83	2.78	2.82	2.86	3.31	3.39	3.57	<.01
	# 158	133	135	127	137	125	117	156	202	248	252	270	288	290	286	292	322	277						

Table S13. [Sensitivity analysis] Proportions and trend test P values for Clininformatics

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	2018-1	2018-2	2018-3	2018-4	2019-1	2019-2	2019-3	2019-4	Trend (p)	
Metformin	%	82.8	83.72	85.25	86.33	85.66	86.1	86.69	74.42	83.86	86.45	87.87	86.4	88.08	86.55	87.42	85.97	87.74	86.73	86.28	86.55	86.62	86.54	86.18	83.27	85.86	85.92	85.49	0.18
	#	3475	3503	3561	4155	3416	3383	3342	5090	3850	3593	3651	3982	3844	3643	3607	4309	4200	3613	3382	3911	3857	3440	3666	4668	4523	4289	4001	
SU	%	8.08	7.5	6.42	6.07	6.54	6.03	5.58	11.11	6.93	5.27	5.03	5.75	4.56	5.16	5.04	5.79	4.66	4.94	5.1	5.29	4.74	5.23	4.51	5.78	4.99	4.47	4.08	<.01
	#	339	314	268	292	261	237	215	760	318	219	209	265	199	217	208	290	290	206	200	239	211	208	192	324	263	223	191	
Insulin	%	4.24	4.04	3.85	3.78	3.59	3.23	3.45	7.51	4.16	3.06	2.79	2.99	2.96	2.57	2.42	3.11	2.59	2.57	2.86	3.36	3.39	3.12	3.08	4.28	2.96	3.21	3.42	0.05
	#	178	169	161	182	143	127	133	514	191	127	116	138	129	108	100	156	124	107	112	152	151	124	131	240	156	160	160	
DPP-4i	%	2.76	2.8	2.37	2.24	2.28	2.49	2.15	3.17	1.9	2.29	1.81	1.78	1.6	2.14	1.96	1.98	1.46	2.06	1.99	1.59	1.66	1.89	2.09	1.96	1.78	1.62	1.47	<.01
	#	116	117	99	108	91	98	83	217	87	95	75	82	70	90	81	99	70	86	78	72	74	75	89	110	94	81	69	
GLP-1RA	%	1	0.74	0.65	0.69	0.73	0.51	0.67	1.1	0.91	1.23	1.13	1.37	1.17	1.52	1.28	1.38	1.78	1.61	1.81	1.55	1.57	1.48	2.33	2.55	2.49	2.64	3.29	<.01
	#	42	31	27	33	29	20	26	75	42	51	47	63	51	64	53	69	85	67	71	70	70	59	99	143	131	132	154	
SGLT2-i	%	0.19	0.31	0.65	0.39	0.43	0.66	0.86	0.66	0.85	0.67	0.55	0.65	0.57	1.02	1.04	0.84	0.92	0.86	1.07	0.69	1.03	1.01	1.06	0.98	1.01	1.28	1.39	<.01
	#	8	13	27	19	17	26	33	45	39	28	23	30	25	43	43	42	44	36	42	31	46	40	45	55	53	64	65	
TZD	%	0.64	0.65	0.57	0.33	0.53	0.71	0.36	1.73	1.18	0.75	0.48	0.78	0.8	0.83	0.7	0.76	0.73	0.98	0.79	0.89	0.88	0.58	0.61	0.89	0.65	0.66	0.66	0.18
	#	27	27	24	16	21	28	14	118	54	31	20	36	35	35	29	38	35	41	31	40	39	23	26	50	34	33	31	
Others	%	0.29	0.24	0.24	0.17	0.25	0.25	0.23	0.31	0.22	0.29	0.34	0.28	0.25	0.21	0.12	0.18	0.13	0.24	0.1	0.09	0.11	0.15	0.14	0.29	0.27	0.2	0.19	0.18
	#	12	10	10	8	10	10	9	21	10	12	14	13	11	9	5	9	6	10	4	4	5	6	6	16	14	10	9	
Total #		4197	4184	4177	4813	3988	3929	3855	6840	4591	4156	4155	4609	4364	4209	4126	5012	4787	4166	3920	4519	4453	3975	4254	5606	5268	4992	4680	

Table S14. [Sensitivity analysis] Proportions and trend test P values for Clininformatics beneficiaries with CVD

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	2018-1	2018-2	2018-3	2018-4	2019-1	2019-2	2019-3	2019-4	Trend (p)	
Metformin	%	73.52	74.02	78.71	77.32	78.44	76.96	80.22	63.84	76.46	79.29	79.33	78.43	80.33	80.57	83.75	78.85	82.21	80.64	77.03	80.6	79.94	80.98	79.51	77.95	79.18	80.7	79.38	0.05
	#	672	644	673	750	673	578	588	1024	731	670	618	760	735	676	639	861	841	708	617	864	813	660	679	944	1027	899	843	
SU	%	12.58	11.84	8.89	9.38	9.91	9.19	8.05	16.15	9.83	7.93	8.6	9.8	7.21	7.51	6.42	8.97	7.23	7.29	8.86	8.12	7.28	7.61	6.21	7.35	6.78	7.09	5.56	<.01
	#	115	103	76	91	85	69	59	259	94	67	67	95	66	63	49	98	74	64	71	87	74	62	53	89	88	79	59	
Insulin	%	7.44	7.93	5.96	7.42	6.18	5.99	6.68	12.09	7.85	5.8	5.65	5.99	6.12	3.58	4.19	5.13	4.4	4.44	6.49	5.5	5.7	4.42	4.8	6.61	5.55	4.4	5.46	0.05
	#	68	69	51	51	72	53	45	49	194	75	49	44	58	56	30	32	56	45	39	52	59	58	36	41	80	72	49	58
DPP-4i	%	4.49	4.14	4.09	3.71	3.73	5.33	3.82	4.49	2.09	3.91	3.59	2.89	2.4	4.41	3.15	3.21	2.35	4.1	3.5	2.05	2.95	3.68	3.98	2.31	2.93	1.8	2.64	0.18
	#	41	36	35	36	32	40	28	72	20	33	28	28	22	37	24	35	24	36	28	22	30	30	34	28	38	20	28	
GLP-1RA	%	0.77	0.8	0.47	0.72	0.58	0.4	0.41	1	0.73	0.83	0.77	1.24	1.2	1.43	0.66	1.28	1.47	1.48	2	1.49	1.28	0.74	2.81	3.39	2.93	2.6	3.58	<.01
	#	7	7	4	7	5	3	3	16	7	7	6	12	11	12	5	14	15	13	16	16	13	6	24	41	38	29	38	
SGLT2-i	%	0	0.23	0.35	0.41	0.12	0.53	0.27	0.44	0.73	0.59	1.03	0.41	0.33	0.83	0.79	1.28	0.88	0.68	1.37	1.21	1.57	1.6	1.29	0.99	1.46	2.06	2.45	<.01
	#	0	2	3	4	1	4	2	7	7	5	8	4	3	7	6	14	9	6	11	13	16	13	11	12	19	23	26	
TZD	%	0.55	0.69	0.94	0.72	0.58	0.93	0.14	1.56	1.67	0.83	0.64	0.93	1.53	1.43	0.66	1.01	1.08	1.03	0.5	0.75	1.28	0.74	1.05	0.91	0.69	0.9	0.85	1
	#	5	6	8	7	5	7	1	25	16	7	5	9	14	12	5	11	11	9	4	8	13	6	9	11	9	10	9	
Others	%	0.66	0.34	0.58	0.31	0.47	0.67	0.41	0.44	0.63	0.83	0.39	0.31	0.87	0.24	0.39	0.27	0.39	0.34	0.25	0.28	0	0.25	0.35	0.5	0.46	0.45	0.09	0.14
	#	6	3	5	3	4	5	3	7	6	7	3	3	8	2	3	3	4	3	2	3	0	2	3	6	6	5	1	
Total #		914	870	855	970	858	751	733	1604	956	845	779	969	915	839	763	1092	1023	878	801	1072	1017	815	854	1211	1297	1114	1062	

Table S15. [Sensitivity analysis] Proportions and trend test P values for Clininformatics beneficiaries without CVD

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	2018-1	2018-2	2018-3	2018-4	2019-1	2019-2	2019-3	2019-4	Trend (p)
Metformin	%	85.38	86.27	86.94	88.6	87.64	88.26	88.21	77.65	85.8	88.28	89.84	88.52	90.14	88.04	88.25	87.96	89.24	88.35	88.65	88.4	88.59	87.97	87.85	84.73			

Table S16. [Sensitivity analysis] Proportions and trend test P values for Medicare

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	Trend (p)
Metformin	%							80.27	80.58	81.68	82.85	80.72	81.79	81.67	82.07	80.87	80.69	79.63	79.84	0.75
	#							9084	9216	8354	8377	7160	6803	5650	5293	4408	4003	3104	2781	
SU	%							9.91	9.29	8.59	8.73	9.36	8.44	9.11	8.9	9.23	9.09	9.11	9.39	0.75
	#							1122	1062	879	883	830	702	630	574	503	451	355	327	
Insulin	%							3.58	2.96	3.04	2.47	2.85	2.54	2.46	2.47	2.38	2.44	2.57	2.99	0.20
	#							405	339	311	250	253	211	170	159	130	121	100	104	
DPP-4i	%							4.16	4.78	4.61	4.04	4.68	4.82	4.24	4.22	4.73	4.76	4.98	4.94	0.75
	#							471	547	471	408	415	401	293	272	258	236	194	172	
GLP-1RA	%							0.32	0.52	0.55	0.45	0.7	0.58	0.59	0.45	0.77	0.71	1.23	0.66	0.20
	#							36	60	56	46	62	48	41	29	42	35	48	23	
SGLT2-i	%							0.55	0.56	0.46	0.46	0.56	0.44	0.58	0.62	0.81	0.81	1.18	0.72	0.13
	#							62	64	47	47	50	37	40	40	44	40	46	25	
TZD	%							0.75	0.78	0.7	0.67	0.79	0.87	0.88	0.95	0.75	0.91	0.77	0.86	0.75
	#							85	89	72	68	70	72	61	61	41	45	30	30	
Others	%							0.46	0.52	0.37	0.32	0.34	0.53	0.48	0.33	0.46	0.6	0.54	0.6	0.62
	#							52	60	38	32	30	44	33	21	25	30	21	21	
Total #								11317	11437	10228	10111	8870	8318	6918	6449	5451	4961	3898	3483	

Table S17. [Sensitivity analysis] Proportions and trend test P values for Medicare beneficiaries with CVD

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	Trend (p)
Metformin	%							74.71	74.94	76.44	78.53	75.78	76.99	76.58	78	75.97	74.99	74.37	74.88	0.75
	#							3711	3703	3430	3401	3223	2985	2538	2311	1979	1769	1451	1294	
SU	%							12.26	11.43	10.85	10.32	11.33	10.32	10.98	10.02	11.44	11.15	11.48	11.17	0.75
	#							609	565	487	447	482	400	364	297	298	263	224	193	
Insulin	%							5.21	4.27	4.55	3.67	4.11	3.61	3.8	3.95	3.53	3.35	3.9	4.05	0.20
	#							259	211	204	159	175	140	126	117	92	79	76	70	
DPP-4i	%							5.56	6.6	6	5.56	6.07	6.06	5.67	5.37	5.99	6.36	6.36	6.54	0.75
	#							276	326	269	241	258	235	188	159	156	150	124	113	
GLP-1RA	%							0.32	0.61	0.6	0.51	0.96	0.77	0.69	0.54	0.88	1.23	1.13	0.81	0.13
	#							16	30	27	22	41	30	23	16	23	29	22	14	
SGLT2-i	%							0.77	0.65	0.53	0.32	0.54	0.46	0.72	0.64	0.77	1.02	1.23	0.93	0.62
	#							38	32	24	14	23	18	24	19	20	24	24	16	
TZD	%							0.64	0.77	0.65	0.74	0.75	1.03	0.94	1.01	0.61	1.1	0.77	1.04	0.75
	#							32	38	29	32	32	40	31	30	16	26	15	18	
Others	%							0.52	0.73	0.38	0.35	0.45	0.75	0.6	0.47	0.81	0.81	0.77	0.58	0.13
	#							26	36	17	15	19	29	20	14	21	19	15	10	
Total #								4967	4941	4487	4331	4253	3877	3314	2963	2605	2359	1951	1728	

Table S18. [Sensitivity analysis] Proportions and trend test P values for Medicare beneficiaries without CVD

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	Trend (p)
Metformin	%							84.61	84.87	85.77	86.09	85.27	85.97	86.35	85.54	85.35	85.86	84.9	84.73	0.75
	#							5373	5513	4924	4976	3937	3818	3112	2982	2429	2234	1653	1487	
SU	%							8.08	7.65	6.83	7.54	7.54	6.8	7.38	7.95	7.2	7.23	6.73	7.64	0.20
	#							513	497	392	436	348	302	266	277	205	188	131	134	
Insulin	%							2.3	1.97	1.86	1.57	1.69	1.6	1.22	1.2	1.34	1.61	1.23	1.94	0.20
	#							146	128	107	91	78	71	44	42	38	42	24	34	
DPP-4i	%							3.07	3.4	3.52	2.89	3.4	3.74	2.91	3.24	3.58	3.31	3.6	3.36	0.62
	#							195	221	202	167	157	166	105	113	102	86	70	59	
GLP-1RA	%							0.31	0.46	0.51	0.42	0.45	0.41	0.5	0.37	0.67	0.23	1.34	0.51	0.75
	#							20	30	29	24	21	18	18	13	19	6	26	9	
SGLT2-i	%							0.38	0.49	0.4	0.57	0.58	0.43	0.44	0.6	0.84	0.61	1.13	0.51	0.62
	#							24	32	23	33	27	19	16	21	24	16	22	9	
TZD	%							0.83	0.79	0.75	0.62	0.82	0.72	0.83	0.89	0.88	0.73	0.77	0.68	0.75
	#							53	51	43	36	38	32	30	31	25	19	15	12	
Others	%							0.41	0.37	0.37	0.29	0.24	0.34	0.36	0.2	0.14	0.42	0.31	0.63	0.62
	#							26	24	21	17	11	15	13	7	4	11	6	11	
Total #								6350	6496	5741	5780	4617	4441	3604	3486	2846	2602	1947	1755	

Table S19. [Sensitivity analysis] Proportions and trend test P values for MarketScan

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	2018-1	2018-2	2018-3	2018-4	Trend (p)
Metformin	% 85.27	85.17	86.96	87.25	86.66	86.77	86.76	86.97	87.43	87.46	89.01	88.08	88.27	87.83	89.03	88.67	88.12	87.73	87.36	87.75	87.07	87.7	88.05	<.01
	# 8471	8043	8587	10331	9394	8823	9151	9019	8631	8099	8564	8959	8431	8003	7927	7679	7212	6382	6130	5790	5683	5147	5484	
SU	% 6.44	6.49	5.78	5	5.21	4.88	4.83	4.68	4.15	4.17	3.36	3.91	3.66	3.57	3.26	3.3	3.47	3.51	3.52	3.33	3.23	2.76	2.59	<.01
	# 640	613	571	592	565	496	509	485	410	386	323	398	350	325	290	286	284	247	220	211	162	161		
Insulin	% 4.06	3.57	3.45	4.03	3.2	3.02	3.15	3.25	2.99	2.82	2.28	2.88	2.66	2.8	2.36	2.81	2.5	3	2.98	2.99	2.8	2.83	2.92	<.01
	# 403	337	341	477	347	307	332	337	295	261	219	293	254	255	210	243	205	218	209	197	183	166	182	
DPP-4i	% 2.5	2.73	2.22	1.92	2.4	2.41	2.11	2	1.93	1.84	1.61	1.59	1.61	1.69	1.5	1.28	1.3	1.42	1.48	1.23	1.49	1.36	1.09	<.01
	# 248	258	219	227	260	245	223	207	191	170	155	162	154	154	134	111	106	103	104	81	97	80	68	
GLP-1RA	% 0.8	0.84	0.66	0.63	0.73	0.75	0.78	0.86	1.41	1.89	1.96	1.71	2.24	2.16	2.16	2.36	2.8	2.74	3.21	2.93	3.68	3.58	3.87	<.01
	# 79	79	65	75	79	76	82	89	139	175	189	174	214	197	192	204	229	199	225	193	240	210	241	
SGLT2-i	% 0.15	0.46	0.47	0.49	1.07	1.57	1.74	1.63	1.52	1.1	1.29	1.26	0.95	1.15	1.17	1.09	1.19	1.03	1	1	1.24	1.04	0.93	0.81
	# 15	43	46	58	116	160	183	169	150	102	124	128	91	105	104	94	97	75	70	66	81	61	58	
TZD	% 0.45	0.5	0.33	0.46	0.36	0.38	0.41	0.41	0.35	0.49	0.27	0.37	0.42	0.63	0.36	0.37	0.44	0.43	0.29	0.61	0.29	0.55	0.4	0.63
	# 45	47	33	55	39	39	43	43	35	45	26	38	40	57	32	32	36	31	20	40	19	32	25	
Others	% 0.33	0.24	0.13	0.22	0.37	0.22	0.23	0.2	0.21	0.24	0.22	0.19	0.18	0.18	0.17	0.13	0.18	0.16	0.17	0.17	0.2	0.19	0.14	0.05
	# 33	23	13	26	40	22	24	21	21	22	21	19	17	16	15	11	15	12	12	11	13	11	9	
Total #	9934	9443	9875	11841	10840	10168	10547	10370	9872	9260	9621	10171	9551	9112	8904	8660	8184	7275	7017	6598	6527	5869	6228	

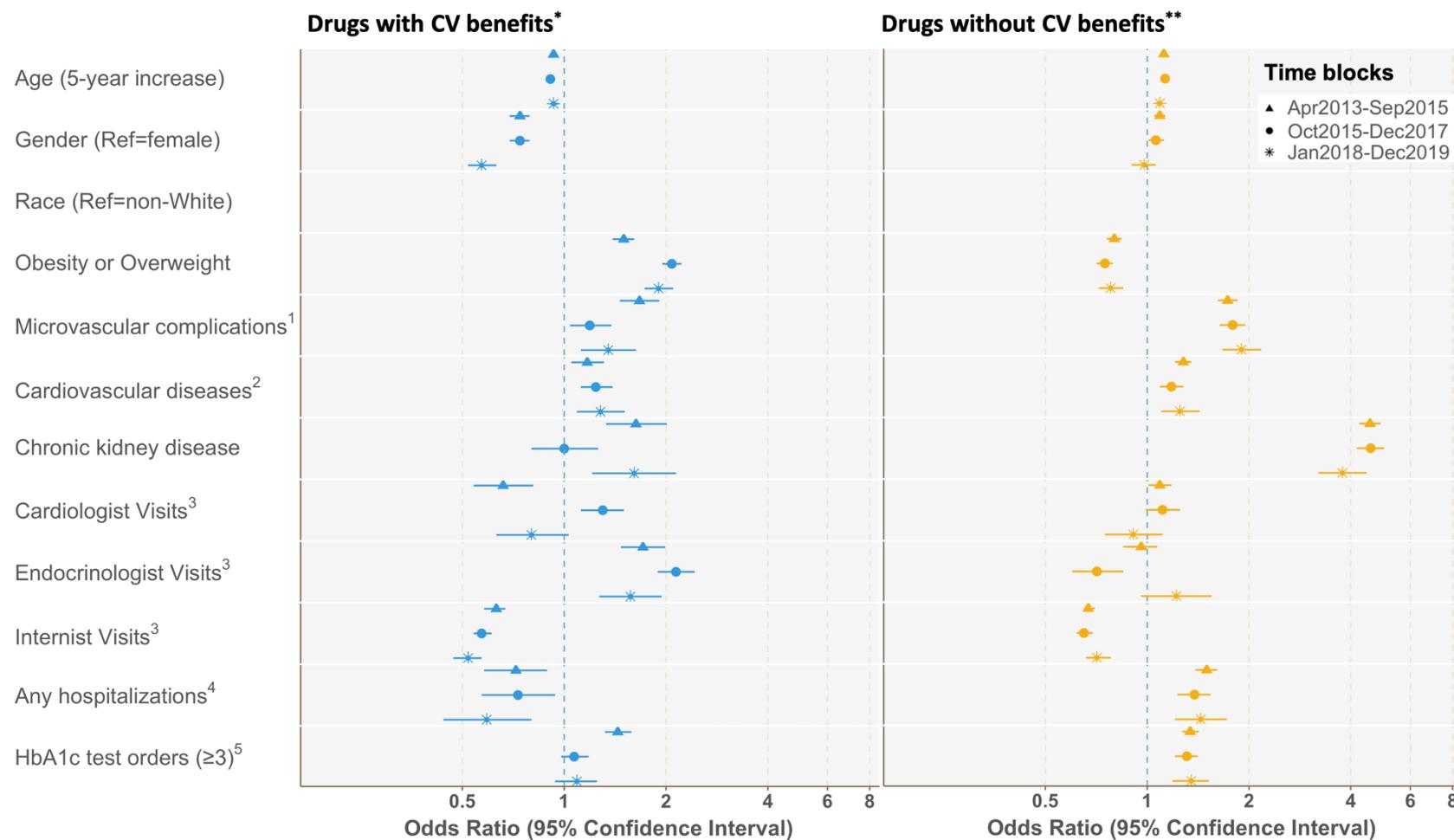
Table S20. [Sensitivity analysis] Proportions and trend test P values for MarketScan beneficiaries with CVD

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	2018-1	2018-2	2018-3	2018-4	Trend (p)
Metformin	% 75.56	74.77	79.16	76.73	79.06	78.25	78.87	78.41	79.54	80.36	82.13	81.4	79.57	80.94	82.89	83.24	80.2	79.56	77.77	79.61	78.77	81.38	81.35	<.01
	# 1156	1135	1246	1431	1427	1338	1303	1304	1232	1158	1282	1252	1180	1117	1080	1008	948	868	815	687	705	660	663	
SU	% 10.26	11.26	8.58	9.81	8.14	8.3	8.11	8.54	8.13	7.29	5.51	6.57	6.41	5.8	5.53	5.37	6.85	6.05	7.16	6.03	5.7	3.82	3.8	<.01
	# 157	171	135	183	147	142	134	142	126	105	86	101	95	80	72	65	81	66	75	52	51	31	31	
Insulin	% 8.1	6.59	6.86	6.81	5.65	5.67	6.23	5.77	5.29	5.07	4.68	5.27	5.39	5.51	5.07	5.7	5.25	6.97	6.49	5.56	6.59	6.17	5.89	0.63
	# 124	100	108	127	102	97	103	96	82	73	73	81	80	76	66	69	62	76	68	48	59	50	48	
DPP-4i	% 4.05	5.14	3.75	3.91	4.43	4.85	3.69	3.85	3.55	3.96	2.88	3.12	3.91	2.9	2.23	2.23	2.37	2.75	3.24	3.01	2.79	1.97	2.09	<.01
	# 62	78	59	73	80	83	61	64	55	57	45	48	58	40	29	27	28	30	34	26	25	16	17	
GLP-1RA	% 0.65	0.99	0.51	0.75	0.55	0.99	0.61	0.96	1.74	1.46	2.31	1.43	2.76	2.39	1.92	1.98	2.45	2.29	3.34	3.13	3.24	3.7	3.93	<.01
	# 10	15	8	14	10	17	10	16	27	21	36	22	41	33	25	24	29	25	35	27	29	30	32	
SGLT2-i	% 0.13	0.33	0.32	0.75	1	0.99	1.33	1.62	1.1	0.9	1.86	1.3	0.67	0.87	1.38	0.74	1.78	1.28	1.24	1.62	2.35	1.48	2.09	<.01
	# 2	5	5	14	18	17	22	27	17	13	29	20	10	12	18	9	21	14	13	14	21	12	17	
TZD	% 0.72	0.53	0.51	0.75	0.33	0.58	0.67	0.3	0.19	0.69	0.38	0.39	0.81	1.3	0.54	0.41	0.51	0.73	0.57	0.7	0.34	0.99	0.49	0.81
	# 11	8	8	14	6	10	11	5	3	10	6	6	12	18	7	5	6	8	6	6	3	8	4	
Others	% 0.52	0.4	0.32	0.48	0.83	0.35	0.48	0.54	0.45	0.28	0.26	0.52	0.47	0.29	0.46	0.33	0.59	0.37	0.19	0.35	0.22	0.49	0.37	0.63
	# 8	6	5	9	15	6	8	9	7	4	4	4	8	7	4	6	4	7	4	2	3	2	4	3
Total #	1530	1518	1574	1865	1805	1710	1652	1663	1549	1441	1561	1538	1483	1380	1303	1211	1182	1091	1048	863	895	811	815	

Table S21. [Sensitivity analysis] Proportions and trend test P values for MarketScan beneficiaries without CVD

Rx class \ Year-Quarter	2013-2	2013-3	2013-4	2014-1	2014-2	2014-3	2014-4	2015-1	2015-2	2015-3	2015-4	2016-1	2016-2	2016-3	2016-4	2017-1	2017-2	2017-3	2017-4	2018-1	2018-2	2018-3	2018-4	Trend (p)
Metformin	% 87.04	87.17	88.44	89.21	88.18	88.5	88.23	88.61	88.9	88.77	90.35	89.27	89.87	89.06	90.08	89.56	89.46	89.17	89.04	88.98	88.39	88.71	89.06	0.23
	# 7315	6908	7341	8900	7967	7485	7848	7715	7399	6941	7282	7707	7251	6886	6847	6671	6264	5514	5315	5103	4978	4487	4821	
SU	% 5.75	5.58	5.25	4.1	4.63	4.19	4.22	3.94	3.41	3.59	2.94	3.44	3.16	3.17	2.87	2.97	2.9	3.06	2.88	2.93	2.84	2.59	2.4	<.01
	# 483	442	436	409	418	354	375	343	284	281	237	297	255	245	218	221	203	189	172	168	160	131	130	
Insulin	% 3.32	2.99	2.81	3.51	2.71	2.48	2.57	2.77	2.56	2.4	1.81	2.46	2.16	2.32	1.89	2.34	2.04	2.3	2.36	2.6	2.2	2.29	2.48	<.01
	# 279	237	233	350	245	210	229	241	213	188	146	212	174	179	144	174	143	142	141	149	124	116	134	
DPP-4i	% 2.21	2.27	1.93	1.54	1.99	1.82	1.64	1.63	1.45	1.36	1.32	1.19	1.47	1.38	1.13	1.11	1.18	1.17	0.96	1.28	1.27	0.94	<.01	
	# 186																							

Figure S4. Predictors of first-line antidiabetic drugs with or without CV benefits (referent: metformin) and temporal trends for MarketScan



* SGLT-2i and GLP-1RA

** Sulfonylureas, DPP-4i, TZD, and Others (alpha-glucosidase inhibitors, amylin mimetics, dopamine receptor agonists, and meglitinides)

¹ Defined as a history of diabetic nephropathy, neuropathy, or retinopathy.

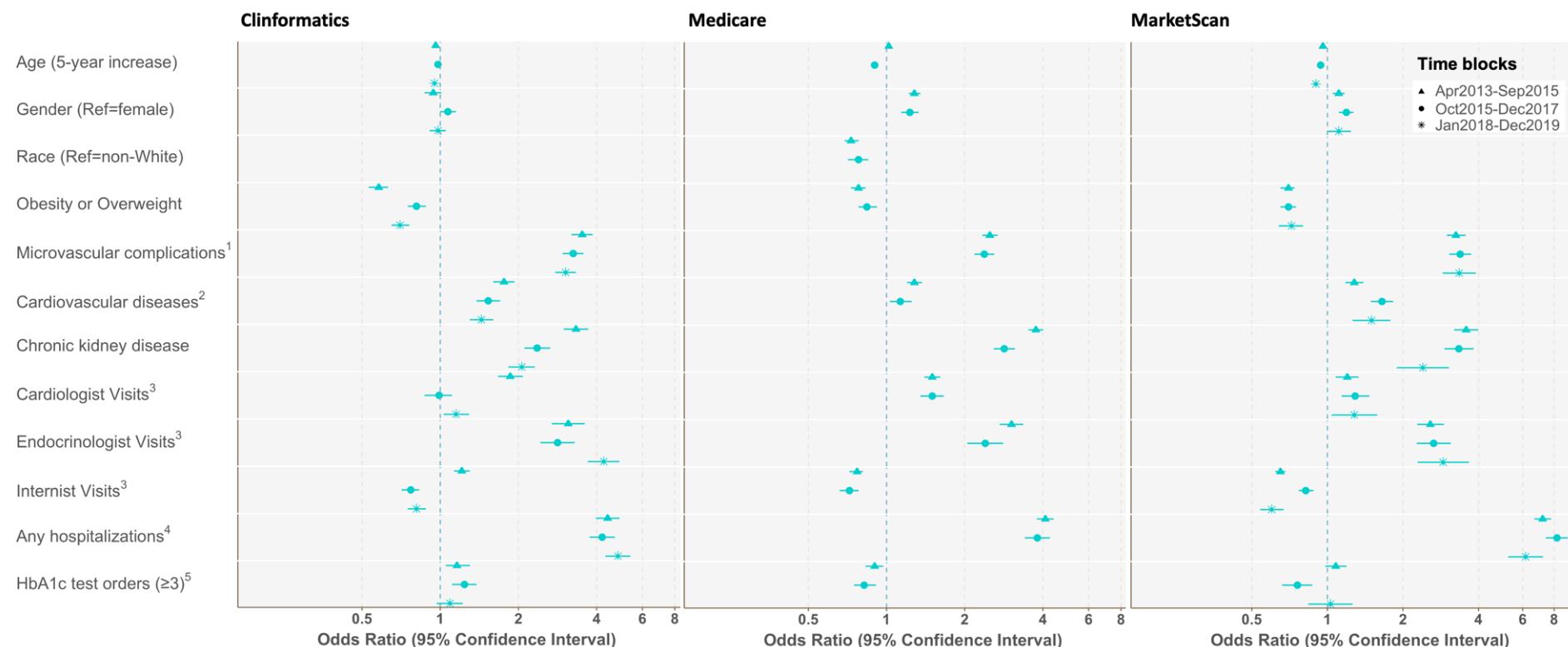
² Defined as a history of myocardial infarction, unstable angina, other ischemic heart diseases, transient ischemic attack, stroke, atherosclerotic peripheral vascular disease, or heart failure.

³ Defined as specialist visits occurred within 14 days prior to cohort entry.

⁴ Defined as hospitalization occurred within 180 days prior to cohort entry.

⁵ Defined as having HbA1c test orders greater than or equal to 3 within 365 days prior to cohort entry.

Figure S5. Predictors for first-line insulin (referent: metformin) and temporal trends



¹Defined as a history of diabetic nephropathy, neuropathy, or retinopathy.

²Defined as a history of myocardial infarction, unstable angina, other ischemic heart diseases, transient ischemic attack, stroke, atherosclerotic peripheral vascular disease, or heart failure.

³Defined as specialist visits occurred within 14 days prior to cohort entry.

⁴Defined as hospitalization occurred within 180 days prior to cohort entry.

⁵Defined as having HbA1c test orders greater than or equal to 3 within 365 days prior to cohort entry.

Table S22. Predictors of first-line antidiabetic drugs with or without CV benefits, or insulin (referent: metformin) in Clininformatics

Ref = Metformin, Apr2013-Sep2015 (n=72,523) / Oct2015-Dec2017 (n=74,739) / Jan2018-Dec2019 (n=71,375)									
Variables	Drugs with CV benefit			Drugs without CV benefit			Insulin		
	Apr2013-Sep2015 (n=1,461)	Oct2015-Dec2017 (n=2,419)	Jan2018-Dec2019 (n=3,265)	Apr2013-Sep2015 (n=10,443)	Oct2015-Dec2017 (n=8,645)	Jan2018-Dec2019 (n=7,628)	Apr2013-Sep2015 (n=4,446)	Oct2015-Dec2017 (n=3,681)	Jan2018-Dec2019 (n=3,917)
Age (5-year increase)	0.81 (0.78,0.84)	0.91 (0.89,0.93)	0.90 (0.88,0.91)	1.13 (1.11,1.14)	1.10 (1.09,1.12)	1.10 (1.09,1.11)	0.96 (0.94,0.97)	0.98 (0.97,1.00)	0.95 (0.94,0.97)
Gender (Male vs female)	0.85 (0.74,0.99)	0.87 (0.80,0.96)	0.69 (0.64,0.75)	1.11 (1.06,1.16)	1.11 (1.06,1.16)	1.01 (0.96,1.07)	0.94 (0.87,1.01)	1.07 (1.00,1.15)	0.98 (0.91,1.05)
Region									
Northeast	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
South	3.74 (2.56,5.48)	1.36 (1.15,1.60)	1.32 (1.16,1.51)	0.84 (0.78,0.90)	1.17 (1.08,1.27)	1.14 (1.05,1.25)	1.23 (1.08,1.40)	1.63 (1.40,1.89)	1.06 (0.93,1.20)
Midwest	2.57 (1.71,3.85)	1.19 (0.99,1.43)	1.15 (0.99,1.34)	0.77 (0.70,0.83)	1.21 (1.11,1.32)	0.99 (0.90,1.09)	1.38 (1.20,1.59)	1.97 (1.69,2.30)	1.03 (0.90,1.19)
West	1.49 (0.98,2.28)	1.01 (0.83,1.22)	0.71 (0.60,0.84)	0.72 (0.66,0.78)	0.93 (0.85,1.02)	0.81 (0.74,0.89)	1.25 (1.08,1.44)	1.38 (1.18,1.62)	0.93 (0.81,1.07)
Race (White vs non-White)	NA	NA	NA	NA	NA	NA	NA	NA	NA
Alcohol/Drug abuse or dependence	3.36 (2.50,4.52)	0.43 (0.35,0.53)	0.76 (0.66,0.87)	0.81 (0.71,0.93)	1.01 (0.92,1.11)	0.94 (0.86,1.03)	0.96 (0.81,1.12)	0.92 (0.81,1.03)	0.85 (0.76,0.96)
Obesity or Overweight	1.91 (1.65,2.22)	1.85 (1.69,2.03)	1.44 (1.33,1.55)	0.76 (0.72,0.80)	0.82 (0.78,0.86)	0.76 (0.72,0.80)	0.58 (0.53,0.63)	0.81 (0.75,0.88)	0.70 (0.65,0.76)
Smoking	0.42 (0.31,0.56)	1.29 (1.12,1.48)	1.02 (0.91,1.14)	0.89 (0.82,0.95)	0.87 (0.80,0.94)	1.02 (0.95,1.10)	0.80 (0.72,0.89)	1.18 (1.06,1.31)	1.15 (1.03,1.28)
Diabetic microvascular complications*	0.90 (0.69,1.19)	1.74 (1.52,1.99)	2.03 (1.84,2.25)	1.46 (1.37,1.57)	1.72 (1.61,1.84)	1.53 (1.43,1.64)	3.52 (3.20,3.86)	3.25 (2.96,3.56)	3.04 (2.77,3.33)
Hypoglycemia	1.67 (1.23,2.28)	0.51 (0.39,0.65)	1.17 (1.03,1.33)	1.31 (1.18,1.46)	1.04 (0.94,1.14)	1.26 (1.16,1.37)	1.91 (1.67,2.19)	1.32 (1.15,1.51)	1.27 (1.12,1.44)
Hyperlipidemia	1.87 (1.57,2.23)	1.60 (1.43,1.78)	1.47 (1.35,1.61)	0.98 (0.93,1.03)	1.07 (1.01,1.13)	1.09 (1.02,1.15)	0.83 (0.76,0.90)	0.98 (0.90,1.06)	0.73 (0.67,0.79)
Hypertension	2.73 (2.26,3.29)	2.10 (1.87,2.37)	1.71 (1.55,1.89)	1.20 (1.13,1.27)	1.29 (1.22,1.37)	1.17 (1.09,1.25)	1.07 (0.98,1.17)	1.08 (0.98,1.18)	1.19 (1.08,1.31)
CVD†	1.26 (1.01,1.58)	1.31 (1.15,1.50)	1.32 (1.19,1.47)	1.18 (1.11,1.25)	1.28 (1.20,1.36)	1.31 (1.22,1.40)	1.76 (1.60,1.93)	1.53 (1.38,1.70)	1.44 (1.30,1.60)
CKD	2.66 (1.98,3.56)	1.37 (1.14,1.64)	1.27 (1.11,1.46)	3.41 (3.18,3.66)	3.26 (3.03,3.50)	3.45 (3.20,3.71)	3.33 (2.99,3.71)	2.36 (2.11,2.65)	2.06 (1.83,2.31)
COPD	0.83 (0.58,1.20)	0.93 (0.77,1.13)	0.71 (0.61,0.83)	1.15 (1.06,1.25)	0.94 (0.86,1.02)	0.92 (0.84,1.01)	1.07 (0.95,1.20)	1.11 (0.98,1.25)	0.93 (0.83,1.06)
Cardiologist visit‡	0.33 (0.20,0.54)	0.55 (0.43,0.71)	0.62 (0.52,0.74)	1.07 (0.97,1.17)	0.90 (0.82,1.00)	0.99 (0.90,1.09)	1.86 (1.67,2.08)	0.99 (0.87,1.11)	1.15 (1.03,1.29)
Endocrinologist visit‡	6.21 (4.95,7.79)	1.84 (1.49,2.27)	2.12 (1.80,2.49)	1.03 (0.89,1.21)	1.27 (1.10,1.47)	1.45 (1.25,1.70)	3.11 (2.69,3.60)	2.83 (2.43,3.29)	4.26 (3.70,4.89)
Internist visit‡	0.65 (0.56,0.76)	0.49 (0.45,0.54)	0.54 (0.50,0.58)	0.86 (0.82,0.90)	0.77 (0.74,0.81)	0.81 (0.77,0.86)	1.21 (1.13,1.30)	0.77 (0.71,0.83)	0.81 (0.75,0.88)
Any hospitalization§	0.48 (0.33,0.71)	0.96 (0.75,1.23)	0.76 (0.64,0.92)	1.54 (1.40,1.69)	1.23 (1.10,1.36)	1.25 (1.12,1.40)	4.41 (3.97,4.90)	4.20 (3.76,4.70)	4.83 (4.32,5.39)
Duration of hospitalizations	1.02 (1.01,1.03)	0.99 (0.98,1.01)	1.00 (0.99,1.01)	1.00 (1.00,1.00)	1.01 (1.01,1.02)	0.99 (0.98,0.99)	1.02 (1.01,1.02)	1.02 (1.02,1.03)	1.00 (0.99,1.00)
Emergency department visits	1.41 (1.21,1.64)	0.88 (0.80,0.98)	0.89 (0.82,0.97)	1.04 (0.99,1.10)	1.02 (0.96,1.07)	1.04 (0.99,1.10)	1.42 (1.31,1.53)	1.34 (1.24,1.45)	1.20 (1.10,1.30)
Number of office visits	0.94 (0.93,0.95)	1.00 (0.99,1.01)	1.03 (1.03,1.03)	1.00 (0.99,1.00)	1.00 (0.99,1.00)	0.99 (0.99,1.00)	1.00 (1.00,1.01)	0.98 (0.97,0.98)	0.98 (0.98,0.99)
HbA1c tests ordered >= 3	2.77 (2.34,3.29)	1.58 (1.42,1.77)	1.26 (1.14,1.38)	1.40 (1.32,1.49)	1.49 (1.40,1.58)	1.31 (1.23,1.40)	1.16 (1.05,1.30)	1.24 (1.11,1.38)	1.09 (0.97,1.22)
Preventive healthcare service¶	0.88 (0.75,1.02)	0.97 (0.88,1.07)	1.11 (1.02,1.21)	0.76 (0.72,0.79)	0.78 (0.74,0.82)	0.81 (0.77,0.86)	0.45 (0.42,0.49)	0.75 (0.69,0.80)	0.67 (0.62,0.72)
Brand/Generic ratio#	1.26 (1.18,1.34)	1.07 (1.03,1.12)	1.08 (1.04,1.12)	1.09 (1.07,1.11)	1.14 (1.12,1.16)	1.03 (1.01,1.05)	1.20 (1.16,1.24)	1.09 (1.06,1.13)	1.10 (1.07,1.14)
ACE inhibitors of ARBs	0.63 (0.54,0.74)	0.70 (0.64,0.78)	0.67 (0.61,0.73)	0.78 (0.75,0.82)	0.73 (0.70,0.77)	0.78 (0.74,0.83)	0.52 (0.48,0.57)	0.62 (0.57,0.67)	0.58 (0.53,0.63)
Anticoagulants	2.94 (2.07,4.18)	0.55 (0.40,0.74)	1.05 (0.88,1.26)	1.10 (0.99,1.22)	0.98 (0.88,1.09)	1.14 (1.03,1.27)	1.19 (1.03,1.38)	0.77 (0.65,0.91)	0.98 (0.85,1.14)
Antiplatelet agents	1.67 (1.21,2.31)	1.12 (0.93,1.34)	1.93 (1.70,2.19)	1.33 (1.22,1.45)	0.87 (0.79,0.96)	1.12 (1.03,1.23)	1.20 (1.05,1.37)	1.07 (0.94,1.22)	1.07 (0.94,1.22)
Beta blockers	0.97 (0.80,1.18)	1.04 (0.92,1.16)	1.06 (0.97,1.17)	1.05 (0.99,1.11)	1.00 (0.94,1.06)	1.05 (0.99,1.12)	0.66 (0.60,0.73)	0.92 (0.83,1.01)	1.02 (0.93,1.12)
Calcium channel blockers	0.74 (0.60,0.92)	0.94 (0.83,1.06)	0.80 (0.73,0.89)	1.06 (1.00,1.12)	1.01 (0.95,1.07)	1.10 (1.03,1.17)	0.95 (0.86,1.05)	1.05 (0.95,1.15)	0.83 (0.75,0.91)
Loop diuretics	1.22 (0.89,1.67)	1.71 (1.45,2.01)	1.35 (1.18,1.54)	1.28 (1.18,1.39)	1.73 (1.59,1.87)	1.15 (1.05,1.26)	2.20 (1.97,2.46)	1.81 (1.61,2.04)	1.95 (1.74,2.19)
Statin	0.46 (0.39,0.54)	0.67 (0.60,0.74)	0.61 (0.56,0.67)	0.70 (0.67,0.74)	0.76 (0.72,0.80)	0.63 (0.60,0.67)	0.54 (0.50,0.59)	0.56 (0.52,0.61)	0.71 (0.65,0.78)
Thiazide	1.49 (1.20,1.84)	0.76 (0.66,0.89)	0.80 (0.71,0.91)	0.84 (0.78,0.90)	0.89 (0.82,0.96)	0.83 (0.77,0.90)	0.93 (0.82,1.05)	0.85 (0.75,0.96)	0.91 (0.80,1.03)
(Intercept)	0.03 (0.02,0.05)	0.05 (0.04,0.07)	0.10 (0.08,0.13)	0.05 (0.04,0.05)	0.04 (0.03,0.05)	0.04 (0.03,0.05)	0.09 (0.08,0.12)	0.04 (0.03,0.06)	0.14 (0.11,0.17)

OR: Odds ratio; CVD: Cardiovascular disease; CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease; HbA1c: hemoglobin A1c; ARB: Angiotensin receptor blocker.

^{*}Defined as a history of diabetic nephropathy, neuropathy, or retinopathy.

[†]Defined as a history of myocardial infarction, unstable angina, other ischemic heart diseases, transient ischemic attack, stroke, atherosclerotic peripheral vascular disease, or heart failure.

[‡]Defined as specialist visits occurred within 14 days prior to cohort entry.

[§]Defined as hospitalization occurred within 180 days prior to cohort entry.

^{||}Defined as at least one emergency department visit 365 days prior to cohort entry.

[¶]Defined as administration of bone mineral density test, colonoscopy, fecal occult blood test, mammography, pap smear, prostate-specific antigen test, flu vaccine, or pneumococcal vaccine.

[#]Added 1 to both numerator and denominator, then log-transformed.

Table S23. Predictors of first-line antidiabetic drugs with or without CV benefits, or insulin (referent: metformin) in Medicare

Ref = Metformin, Apr2013-Sep2015 (n=147,279) / Oct2015-Dec2017 (n=80,153)

	Drugs with CV benefit		Drugs without CV benefit		Insulin	
	Apr2013-Sep2015 (n=1,483)	Oct2015-Dec2017 (n=1,546)	Apr2013-Sep2015 (n=30,089)	Oct2015-Dec2017 (n=14,288)	Apr2013-Sep2015 (n=7,295)	Oct2015-Dec2017 (n=3,080)
Variables	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (5-year increase)	0.58 (0.54,0.62)	0.72 (0.68,0.76)	1.28 (1.27,1.29)	1.19 (1.17,1.21)	1.02 (1.00,1.04)	0.90 (0.87,0.93)
Gender (Male vs female)	0.98 (0.87,1.11)	1.06 (0.95,1.17)	1.20 (1.17,1.23)	1.12 (1.07,1.16)	1.28 (1.22,1.35)	1.23 (1.14,1.33)
Region						
Northeast	Ref	Ref	Ref	Ref	Ref	Ref
South	0.94 (0.80,1.10)	1.06 (0.93,1.21)	0.90 (0.87,0.94)	0.98 (0.93,1.03)	1.26 (1.17,1.37)	1.39 (1.24,1.56)
Midwest	0.65 (0.54,0.80)	0.71 (0.60,0.85)	0.88 (0.84,0.92)	0.96 (0.91,1.02)	1.34 (1.23,1.46)	1.42 (1.25,1.61)
West	0.93 (0.76,1.13)	0.93 (0.79,1.09)	0.72 (0.69,0.76)	0.73 (0.69,0.78)	1.02 (0.92,1.12)	1.09 (0.95,1.25)
Race (White vs non-White)	1.95 (1.61,2.36)	1.25 (1.08,1.44)	0.76 (0.73,0.78)	0.78 (0.75,0.82)	0.73 (0.69,0.78)	0.78 (0.71,0.85)
Alcohol/Drug abuse or dependence	1.16 (0.85,1.58)	0.97 (0.79,1.17)	0.98 (0.91,1.07)	0.96 (0.89,1.03)	1.00 (0.89,1.13)	0.96 (0.85,1.09)
Obesity or Overweight	2.11 (1.86,2.38)	1.39 (1.25,1.54)	0.80 (0.78,0.83)	0.81 (0.78,0.85)	0.78 (0.73,0.83)	0.84 (0.78,0.92)
Smoking	0.80 (0.68,0.95)	0.93 (0.81,1.07)	0.98 (0.94,1.02)	1.01 (0.96,1.07)	0.95 (0.89,1.01)	0.96 (0.87,1.06)
Diabetic microvascular complications*	1.67 (1.42,1.96)	1.37 (1.20,1.56)	1.42 (1.36,1.48)	1.50 (1.43,1.58)	2.50 (2.34,2.68)	2.38 (2.18,2.60)
Hypoglycemia	1.32 (0.97,1.81)	0.88 (0.68,1.14)	1.23 (1.14,1.33)	1.08 (0.98,1.18)	2.07 (1.86,2.31)	1.78 (1.54,2.07)
Hyperlipidemia	1.41 (1.17,1.71)	1.19 (1.03,1.38)	0.98 (0.94,1.02)	0.94 (0.90,0.99)	0.81 (0.75,0.86)	0.85 (0.77,0.94)
Hypertension	1.61 (1.32,1.96)	1.42 (1.20,1.69)	1.20 (1.15,1.25)	1.25 (1.17,1.33)	0.98 (0.90,1.06)	1.23 (1.08,1.40)
CVD†	1.39 (1.21,1.60)	1.25 (1.11,1.41)	1.15 (1.12,1.19)	1.11 (1.06,1.16)	1.28 (1.20,1.37)	1.13 (1.03,1.25)
CKD	1.99 (1.67,2.38)	1.80 (1.55,2.08)	3.94 (3.80,4.08)	3.54 (3.38,3.71)	3.76 (3.52,4.01)	2.84 (2.59,3.12)
COPD	0.88 (0.74,1.05)	0.91 (0.78,1.06)	1.08 (1.04,1.12)	1.05 (0.99,1.10)	1.15 (1.08,1.23)	1.10 (1.00,1.22)
Cardiologist visit‡	0.91 (0.74,1.12)	0.83 (0.69,1.00)	1.02 (0.98,1.06)	1.07 (1.01,1.14)	1.50 (1.40,1.61)	1.50 (1.35,1.66)
Endocrinologist visit‡	1.40 (1.09,1.79)	1.93 (1.58,2.36)	1.47 (1.36,1.58)	1.18 (1.06,1.31)	3.03 (2.73,3.36)	2.40 (2.05,2.81)
Internist visit‡	0.44 (0.39,0.49)	0.64 (0.57,0.71)	0.85 (0.82,0.87)	0.83 (0.80,0.86)	0.77 (0.72,0.81)	0.72 (0.66,0.78)
Any hospitalization§	0.61 (0.45,0.82)	0.86 (0.68,1.08)	1.30 (1.24,1.37)	1.22 (1.14,1.31)	4.09 (3.79,4.40)	3.81 (3.41,4.26)
Duration of hospitalizations	0.99 (0.96,1.01)	1.00 (0.98,1.01)	1.01 (1.00,1.01)	1.00 (1.00,1.01)	1.02 (1.01,1.02)	1.02 (1.01,1.02)
Emergency department visits	0.88 (0.76,1.02)	0.83 (0.73,0.94)	1.00 (0.97,1.03)	1.04 (0.99,1.08)	1.47 (1.38,1.56)	1.41 (1.28,1.54)
Number of office visits	1.03 (1.02,1.04)	1.04 (1.03,1.04)	1.00 (1.00,1.01)	1.00 (1.00,1.01)	0.98 (0.97,0.98)	0.98 (0.98,0.99)
HbA1c tests ordered >= 3	1.27 (1.12,1.45)	1.18 (1.06,1.32)	1.18 (1.14,1.22)	1.11 (1.07,1.16)	0.90 (0.83,0.97)	0.82 (0.75,0.91)
Preventive healthcare service¶	1.06 (0.90,1.24)	0.91 (0.79,1.05)	0.81 (0.78,0.83)	0.79 (0.75,0.83)	0.61 (0.58,0.65)	0.58 (0.53,0.63)
Brand/Generic ratio#	1.22 (1.16,1.29)	1.20 (1.15,1.26)	1.07 (1.06,1.08)	1.04 (1.02,1.06)	1.10 (1.07,1.12)	1.10 (1.06,1.13)
ACE inhibitors of ARBs	0.73 (0.65,0.83)	0.84 (0.75,0.94)	0.90 (0.87,0.92)	0.89 (0.85,0.92)	0.75 (0.71,0.80)	0.68 (0.62,0.73)
Anticoagulants	0.93 (0.75,1.14)	0.80 (0.67,0.95)	1.02 (0.97,1.06)	0.96 (0.90,1.02)	0.86 (0.79,0.93)	0.84 (0.75,0.94)
Antiplatelet agents	1.21 (1.01,1.44)	1.16 (1.00,1.35)	1.11 (1.07,1.16)	1.11 (1.04,1.17)	0.98 (0.90,1.05)	1.09 (0.97,1.22)
Beta blockers	0.98 (0.86,1.11)	0.97 (0.87,1.09)	1.02 (0.99,1.05)	1.06 (1.02,1.11)	0.88 (0.83,0.93)	0.91 (0.83,0.99)
Calcium channel blockers	0.99 (0.87,1.14)	0.93 (0.83,1.05)	1.07 (1.04,1.10)	1.00 (0.96,1.04)	1.00 (0.94,1.06)	0.93 (0.85,1.01)
Loop diuretics	1.74 (1.49,2.03)	1.20 (1.04,1.39)	1.38 (1.33,1.43)	1.40 (1.33,1.47)	1.66 (1.56,1.77)	1.76 (1.60,1.94)
Statin	0.63 (0.56,0.72)	0.75 (0.67,0.84)	0.79 (0.77,0.82)	0.80 (0.76,0.83)	0.58 (0.54,0.61)	0.62 (0.57,0.68)
Thiazide	0.73 (0.61,0.87)	0.91 (0.79,1.04)	0.93 (0.89,0.96)	0.91 (0.86,0.96)	1.08 (1.00,1.16)	0.87 (0.78,0.97)
(Intercept)	8.65 (3.07,24.33)	1.83 (0.83,4.03)	0.01 (0.01,0.01)	0.02 (0.01,0.02)	0.05 (0.04,0.07)	0.23 (0.14,0.37)

OR: Odds ratio; CVD: Cardiovascular disease; CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease; HbA1c: hemoglobin A1c; ARB: Angiotensin receptor blocker.

* Defined as a history of diabetic nephropathy, neuropathy, or retinopathy.

† Defined as a history of myocardial infarction, unstable angina, other ischemic heart diseases, transient ischemic attack, stroke, atherosclerotic peripheral vascular disease, or heart failure.

‡ Defined as specialist visits occurred within 14 days prior to cohort entry.

§ Defined as hospitalization occurred within 180 days prior to cohort entry.

|| Defined as at least one emergency department visit 365 days prior to cohort entry.

*Defined as administration of bone mineral density test, colonoscopy, fecal occult blood test, mammography, pap smear, prostate-specific antigen test, flu vaccine, or pneumococcal vaccine.

Added 1 to both numerator and denominator, then log-transformed.

Table S24. Predictors of first-line antidiabetic drugs with or without CV benefits, or insulin (referent: metformin) in MarketScan

Ref = Metformin, Apr2013-Sep2015 (n=146,001) / Oct2015-Dec2017 (n=110,292) / Jan2018-Dec2018 (n=38,000)

	Drugs with CV benefit			Drugs without CV benefit			Insulin		
	Apr2013-Sep2015 (n=3,728)	Oct2015-Dec2017 (n=4,576)	Jan2018-Dec2018 (n=1,972)	Apr2013-Sep2015 (n=15,389)	Oct2015-Dec2017 (n=8,198)	Jan2018-Dec2018 (n=2,719)	Apr2013-Sep2015 (n=7,040)	Oct2015-Dec2017 (n=4,384)	Jan2018-Dec2018 (n=1,687)
Variables	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (5-year increase)	0.93 (0.91,0.94)	0.91 (0.90,0.93)	0.93 (0.91,0.96)	1.12 (1.11,1.12)	1.13 (1.11,1.14)	1.09 (1.06,1.11)	0.96 (0.95,0.97)	0.94 (0.92,0.95)	0.90 (0.88,0.92)
Gender (Male vs female)	0.74 (0.69,0.79)	0.74 (0.69,0.79)	0.57 (0.52,0.63)	1.09 (1.05,1.13)	1.06 (1.01,1.12)	0.98 (0.90,1.06)	1.11 (1.05,1.17)	1.19 (1.11,1.27)	1.11 (1.00,1.24)
Region									
Northeast									
South	1.27 (1.16,1.39)	0.91 (0.83,0.98)	0.59 (0.53,0.66)	1.08 (1.03,1.13)	1.37 (1.27,1.47)	1.16 (1.03,1.30)	1.12 (1.04,1.21)	1.15 (1.04,1.27)	1.23 (1.05,1.44)
Midwest	0.78 (0.69,0.87)	0.57 (0.51,0.63)	0.51 (0.44,0.59)	0.96 (0.91,1.01)	0.90 (0.82,0.98)	0.98 (0.86,1.12)	1.15 (1.06,1.25)	1.28 (1.14,1.43)	1.21 (1.02,1.45)
West	0.59 (0.52,0.67)	0.56 (0.50,0.64)	0.31 (0.26,0.38)	0.75 (0.71,0.80)	0.81 (0.73,0.90)	0.79 (0.68,0.92)	0.88 (0.80,0.96)	1.09 (0.96,1.24)	0.88 (0.71,1.08)
Race (White vs non-White)	NA	NA	NA	NA	NA	NA	NA	NA	NA
Alcohol/Drug abuse or dependence	1.02 (0.81,1.28)	0.65 (0.54,0.77)	1.28 (1.03,1.59)	1.13 (1.01,1.27)	0.77 (0.68,0.87)	1.03 (0.87,1.23)	1.16 (1.02,1.33)	1.08 (0.94,1.24)	0.97 (0.79,1.20)
Obesity or Overweight	1.50 (1.39,1.61)	2.08 (1.95,2.22)	1.90 (1.73,2.10)	0.80 (0.76,0.84)	0.75 (0.71,0.79)	0.78 (0.72,0.85)	0.70 (0.65,0.74)	0.70 (0.65,0.75)	0.72 (0.64,0.80)
Smoking	0.86 (0.75,0.98)	0.84 (0.73,0.96)	0.75 (0.61,0.92)	0.92 (0.86,0.98)	0.87 (0.79,0.97)	1.06 (0.90,1.24)	0.92 (0.85,1.01)	0.75 (0.66,0.85)	0.83 (0.68,1.02)
Diabetic microvascular complications*	1.67 (1.46,1.91)	1.19 (1.04,1.38)	1.35 (1.12,1.63)	1.73 (1.62,1.85)	1.79 (1.64,1.95)	1.90 (1.67,2.17)	3.25 (2.99,3.55)	3.38 (3.06,3.74)	3.35 (2.88,3.90)
Hypoglycemia	0.86 (0.68,1.09)	0.74 (0.61,0.90)	0.83 (0.65,1.05)	1.41 (1.27,1.56)	1.65 (1.47,1.85)	1.35 (1.14,1.60)	1.89 (1.68,2.14)	2.14 (1.86,2.47)	1.22 (0.96,1.54)
Hyperlipidemia	1.40 (1.30,1.51)	1.17 (1.09,1.26)	1.22 (1.09,1.35)	0.97 (0.93,1.01)	0.95 (0.90,1.01)	1.11 (1.01,1.21)	0.76 (0.72,0.81)	0.89 (0.82,0.96)	0.77 (0.68,0.87)
Hypertension	1.44 (1.33,1.57)	1.43 (1.32,1.56)	1.39 (1.23,1.57)	1.19 (1.14,1.24)	1.16 (1.09,1.24)	1.19 (1.07,1.32)	1.00 (0.93,1.06)	0.94 (0.86,1.02)	1.08 (0.94,1.23)
CVD†	1.17 (1.05,1.31)	1.24 (1.12,1.39)	1.28 (1.09,1.51)	1.28 (1.21,1.35)	1.18 (1.09,1.28)	1.25 (1.10,1.43)	1.28 (1.18,1.39)	1.65 (1.49,1.83)	1.50 (1.26,1.78)
CKD	1.63 (1.33,2.01)	1.00 (0.80,1.26)	1.61 (1.21,2.14)	4.56 (4.24,4.90)	4.58 (4.17,5.02)	3.78 (3.21,4.46)	3.57 (3.20,3.99)	3.34 (2.93,3.82)	2.40 (1.89,3.05)
COPD	0.88 (0.73,1.05)	0.90 (0.75,1.07)	0.78 (0.58,1.04)	0.99 (0.92,1.07)	1.06 (0.94,1.19)	1.01 (0.82,1.23)	1.01 (0.91,1.13)	0.94 (0.81,1.09)	1.09 (0.85,1.40)
Cardiologist visit‡	0.66 (0.54,0.81)	1.30 (1.12,1.50)	0.80 (0.63,1.03)	1.09 (1.01,1.18)	1.11 (0.99,1.25)	0.91 (0.75,1.11)	1.20 (1.08,1.33)	1.29 (1.14,1.47)	1.28 (1.04,1.58)
Endocrinologist visit‡	1.71 (1.47,1.99)	2.14 (1.89,2.43)	1.57 (1.27,1.94)	0.96 (0.85,1.07)	0.71 (0.60,0.85)	1.22 (0.96,1.55)	2.57 (2.28,2.91)	2.65 (2.27,3.10)	2.89 (2.29,3.66)
Internist visit‡	0.63 (0.58,0.67)	0.57 (0.54,0.61)	0.52 (0.47,0.57)	0.67 (0.65,0.70)	0.65 (0.62,0.69)	0.71 (0.66,0.78)	0.65 (0.62,0.68)	0.82 (0.77,0.88)	0.60 (0.54,0.67)
Any hospitalization§	0.72 (0.58,0.89)	0.73 (0.57,0.94)	0.59 (0.44,0.80)	1.50 (1.39,1.61)	1.38 (1.23,1.54)	1.44 (1.21,1.72)	7.20 (6.67,7.78)	8.21 (7.42,9.07)	6.16 (5.25,7.22)
Duration of hospitalizations	1.00 (0.98,1.01)	0.91 (0.88,0.94)	0.99 (0.97,1.01)	1.01 (1.01,1.02)	1.01 (1.00,1.01)	1.00 (0.99,1.01)	1.02 (1.02,1.02)	1.01 (1.01,1.02)	1.02 (1.01,1.03)
Emergency department visits	0.88 (0.82,0.95)	0.87 (0.81,0.94)	0.88 (0.79,0.98)	1.06 (1.01,1.10)	1.14 (1.07,1.20)	1.10 (1.01,1.21)	1.48 (1.40,1.57)	1.19 (1.10,1.29)	1.44 (1.28,1.63)
Number of office visits	1.02 (1.01,1.02)	1.02 (1.02,1.02)	1.02 (1.02,1.02)	1.00 (1.00,1.00)	1.01 (1.00,1.01)	1.00 (0.99,1.00)	0.98 (0.98,0.99)	0.98 (0.98,0.99)	0.99 (0.98,1.00)
HbA1c tests ordered >= 3	1.44 (1.32,1.58)	1.07 (0.98,1.18)	1.09 (0.94,1.25)	1.34 (1.27,1.42)	1.31 (1.21,1.41)	1.35 (1.19,1.52)	1.08 (0.98,1.19)	0.76 (0.66,0.87)	1.03 (0.84,1.26)
Preventive healthcare service¶	0.98 (0.92,1.06)	1.05 (0.98,1.12)	1.03 (0.93,1.14)	0.80 (0.78,0.83)	0.81 (0.77,0.86)	0.82 (0.75,0.89)	0.62 (0.59,0.66)	0.62 (0.58,0.67)	0.69 (0.62,0.77)
Brand/Generic ratio#	1.11 (1.08,1.15)	0.98 (0.96,1.01)	1.00 (0.95,1.04)	1.09 (1.08,1.11)	1.11 (1.09,1.14)	1.09 (1.05,1.13)	1.13 (1.10,1.16)	1.15 (1.12,1.19)	1.17 (1.12,1.23)
ACE inhibitors of ARBs	0.76 (0.71,0.82)	0.65 (0.61,0.70)	0.70 (0.63,0.79)	0.79 (0.76,0.82)	0.85 (0.80,0.90)	0.79 (0.72,0.87)	0.75 (0.71,0.80)	0.62 (0.57,0.67)	0.84 (0.74,0.95)
Anticoagulants	1.06 (0.86,1.29)	0.50 (0.38,0.65)	0.92 (0.68,1.24)	1.07 (0.98,1.16)	1.08 (0.95,1.22)	1.03 (0.83,1.28)	0.80 (0.70,0.91)	0.99 (0.85,1.15)	0.82 (0.62,1.08)
Antiplatelet agents	1.00 (0.85,1.18)	0.99 (0.85,1.15)	1.13 (0.92,1.39)	1.04 (0.97,1.11)	0.92 (0.83,1.02)	1.05 (0.89,1.23)	1.03 (0.93,1.14)	0.68 (0.60,0.78)	0.86 (0.70,1.07)
Beta blockers	0.91 (0.83,0.99)	0.99 (0.91,1.08)	0.98 (0.86,1.11)	1.00 (0.96,1.05)	0.93 (0.87,0.99)	1.04 (0.94,1.16)	0.87 (0.81,0.94)	1.07 (0.97,1.17)	0.86 (0.74,1.00)
Calcium channel blockers	0.90 (0.82,0.98)	0.94 (0.86,1.02)	0.92 (0.81,1.05)	1.05 (1.01,1.10)	1.03 (0.97,1.10)	1.21 (1.09,1.34)	0.99 (0.92,1.06)	0.84 (0.76,0.93)	1.01 (0.87,1.17)
Loop diuretics	1.27 (1.10,1.46)	1.56 (1.37,1.77)	1.16 (0.93,1.44)	1.46 (1.37,1.56)	1.00 (0.90,1.11)	1.40 (1.18,1.65)	1.65 (1.50,1.81)	1.32 (1.17,1.50)	1.28 (1.03,1.59)
Statin	0.71 (0.66,0.77)	0.73 (0.68,0.79)	0.72 (0.64,0.80)	0.76 (0.73,0.79)	0.68 (0.64,0.72)	0.69 (0.63,0.76)	0.63 (0.60,0.68)	0.84 (0.78,0.92)	0.78 (0.69,0.89)
Thiazide	0.73 (0.65,0.83)	0.90 (0.81,0.99)	0.76 (0.65,0.89)	0.82 (0.77,0.87)	0.81 (0.75,0.89)	0.77 (0.67,0.88)	0.93 (0.85,1.01)	1.05 (0.93,1.17)	0.92 (0.76,1.11)
(Intercept)	0.07 (0.06,0.09)	0.12 (0.10,0.15)	0.21 (0.16,0.28)	0.05 (0.04,0.05)	0.03 (0.02,0.03)	0.04 (0.03,0.06)	0.11 (0.10,0.13)	0.09 (0.08,0.12)	0.18 (0.13,0.25)

OR: Odds ratio; CVD: Cardiovascular disease; CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease; HbA1c: hemoglobin A1c; ARB: Angiotensin receptor blocker.

* Defined as a history of diabetic nephropathy, neuropathy, or retinopathy.

[†]Defined as a history of myocardial infarction, unstable angina, other ischemic heart diseases, transient ischemic attack, stroke, atherosclerotic peripheral vascular disease, or heart failure.

[‡]Defined as specialist visits occurred within 14 days prior to cohort entry.

[§]Defined as hospitalization occurred within 180 days prior to cohort entry.

[¶]Defined as at least one emergency department visit 365 days prior to cohort entry.

[¶]Defined as administration of bone mineral density test, colonoscopy, fecal occult blood test, mammography, pap smear, prostate-specific antigen test, flu vaccine, or pneumococcal vaccine.

[#]Added 1 to both numerator and denominator, then log-transformed.