Table S1a. NSAID study cohort overall and by quintiles of PS_{COH}, the propensity score estimated in the entire cohort.

	Overall		Quintile 1		Quintile 2		Quintile 3		Quintile 4		Quintile 5	
	Coxib	**ns-NSAID**	**Coxib**	**ns-NSAID**	**Coxib**	**ns-NSAID**	**Coxib**	**ns-NSAID**	**Coxib**	**ns-NSAID**	**Coxib**	**ns-NSAID**
N	32,074	17,637	4,363	5,579	5,775	4,167	6,704	3,239	7,269	2,673	7,963	1,979
Age	79.8±7.2	77.8±7.3	73.7±6.1	73.4±6.0	77.1±6.3	77.1±6.1	79.6±6.6	79.6±6.6	81.7±6.6	81.6±6.9	83.3±6.7	83.5±6.9
Male gender			28.2%	30.4%	19.4%	18.0%	14.5%	13.5%	10.2%	11.0%	5.8%	7.6%
Prior hospitalization	30.6%	26.1%	21.3%	20.3%	22.6%	21.8%	26.3%	24.7%	31.4%	32.8%	44.3%	44.5%
Nursing home residence	8.3%	5.7%	2.4%	2.0%	4.2%	3.3%	5.8%	5.8%	8.5%	8.7%	16.5%	16.7%
Prior diagnosis of												
Myocardial infarction	1.8%	1.6%	1.7%	1.5%	1.5%	1.3%	1.4%	1.3%	1.6%	2.1%	2.8%	2.7%
Hypertension	72.8%	70.1%	64.4%	65.4%	69.2%	68.3%	72.4%	70.5%	74.2%	75.4%	78.9%	79.5%
Heart failure	30.3%	24.6%	17.1%	15.3%	20.8%	20.1%	26.2%	25.7%	32.0%	33.4%	46.4%	46.0%
Coronary disease	16.4%	14.8%	13.2%	12.7%	13.8%	12.5%	15.0%	14.4%	16.3%	17.4%	21.4%	22.5%
Osteoarthritis	48.5%	33.4%	8.6%	8.8%	18.9%	18.8%	41.3%	40.9%	64.5%	63.4%	83.3%	81.1%
Rheumatoid arthritis	5.0%	2.7%	0.5%	0.3%	1.6%	0.9%	2.4%	1.7%	4.5%	4.3%	12.6%	12.5%
Severe GI disorder	0.8%	0.6%	0.2%	0.3%	0.5%	0.5%	0.7%	0.9%	0.7%	0.6%	1.3%	1.0%
Ulcer	3.7%	2.4%	0.9%	0.7%	1.6%	1.1%	2.7%	2.7%	3.7%	3.5%	7.6%	8.0%
Hemmorhage	1.7%	1.1%	0.5%	0.3%	0.7%	0.7%	1.3%	1.0%	1.4%	2.0%	3.7%	3.0%
Prior use of												
Corticosteroids	8.7%	7.8%	7.4%	6.1%	7.1%	7.0%	7.7%	7.9%	9.0%	9.7%	11.2%	11.3%
Warfarin	13.3%	6.5%	0.6%	0.5%	1.9%	1.6%	4.5%	4.3%	10.7%	10.0%	38.2%	32.9%
PPIs or H2-blockers	27.4%	20.4%	8.9%	7.9%	18.0%	16.5%	22.1%	21.5%	33.8%	33.3%	42.9%	44.9%
Charlson score	2.0±2.0	1.8±2.0	1.6±1.9	1.5±1.8	1.7±1.9	1.7±1.8	1.9±2.0	1.8±1.9	2.0±1.9	2.1±2.0	2.6±2.1	2.8±2.2
Number of office visits	8.6±6.7	7.7±6.6	6.7±6.0	6.0±5.3	7.3±5.7	7.2±5.8	8.1±6.2	8.1±7.0	9.0±6.6	9.1±6.9	10.6±7.6	11.0±8.5
Number of generic agents	8.4±5.2	7.4±5.0	6.1±4.0	5.8±3.9	7.0±4.4	6.8±4.5	7.8±4.8	7.7±4.8	8.8±5.1	8.8±5.3	10.8±5.9	11.2±6.4

Table S1b. Pennsylvania APM study cohort overall and by quintiles of PS_{COH}, the propensity score estimated in the entire cohort.

	Overall		Quintile 1		Quintile 2		Quintile 3		Quintile 4		Quintile 5	
	Conventional	Atypical	Conventional	Atypical	Conventional	Atypical	Conventional	Atypical	Conventional	Atypical	Conventional	Atypical
N	32,659	14,000	2,381	6,950	5,262	4,070	7,429	1,903	8,505	827	9,082	250
Age	80.5±7.3	83.5±7.1	85.3±7.0	84.6±6.8	83.2±7.0	83.0±7.1	81.4±7.0	82.4±7.2	80.0±7.0	80.9±7.2	77.4±6.4	79.2±6.4
Male gender	16.7%	16.9%	17.0%	16.8%	16.5%	17.1%	17.2%	17.0%	16.8%	17.4%	16.4%	17.6%
White race	94.4%	94.7%	94.2%	95.3%	94.2%	94.2%	94.2%	94.5%	94.4%	93.5%	94.7%	93.6%
Treated in												
1995	18.2%	2.9%	1.0%	0.2%	2.8%	1.0%	5.5%	4.4%	12.8%	17.4%	47.1%	53.2%
1996	18.4%	5.6%	3.2%	0.6%	6.0%	4.2%	10.6%	12.3%	26.0%	31.8%	28.7%	32.0%
1997	14.5%	7.7%	5.6%	2.3%	9.5%	8.4%	14.7%	18.1%	21.9%	23.5%	12.6%	11.2%
1998	12.2%	10.7%	11.8%	6.2%	11.2%	13.8%	18.7%	20.3%	14.6%	13.1%	5.4%	2.4%
1999	10.1%	11.1%	10.7%	8.5%	12.8%	13.9%	16.5%	17.9%	9.8%	6.5%	3.4%	0.4%
2000	8.3%	12.7%	13.7%	12.6%	13.6%	15.7%	13.2%	11.5%	6.5%	3.9%	1.7%	0.8%
2001	7.2%	15.3%	16.9%	19.1%	15.5%	16.2%	9.8%	7.4%	3.8%	1.3%	0.8%	0.0%
2002	6.0%	17.9%	19.4%	26.2%	15.5%	14.5%	6.1%	4.7%	2.6%	1.3%	0.2%	0.0%
Prior hospitalization	47.3%	53.6%	58.5%	60.5%	45.6%	47.5%	44.4%	47.5%	45.1%	43.7%	49.7%	41.2%
Nursing home residence	12.1%	21.6%	27.7%	27.4%	16.1%	17.8%	12.9%	13.9%	9.7%	13.7%	7.4%	8.0%
Prior diagnosis of												
Myocardial infarction	1.9%	1.4%	1.3%	1.2%	1.5%	1.4%	1.7%	1.5%	2.0%	2.7%	2.5%	2.4%
Hypertension	1.9%	1.4%	1.3%	1.2%	1.5%	1.4%	1.7%	1.5%	2.0%	2.7%	2.5%	2.4%
Heart failure	1.9%	1.4%	1.3%	1.2%	1.5%	1.4%	1.7%	1.5%	2.0%	2.7%	2.5%	2.4%
Cerebrovascular disease	1.9%	1.4%	1.3%	1.2%	1.5%	1.4%	1.7%	1.5%	2.0%	2.7%	2.5%	2.4%
Other cardiovascular disease	53.9%	59.0%	62.9%	62.1%	56.2%	56.0%	53.3%	55.8%	52.3%	56.2%	52.3%	53.2%
Arrythmia	1.9%	1.4%	1.3%	1.2%	1.5%	1.4%	1.7%	1.5%	2.0%	2.7%	2.5%	2.4%
Other dysrhythmias	53.9%	59.0%	62.9%	62.1%	56.2%	56.0%	53.3%	55.8%	52.3%	56.2%	52.3%	53.2%
HIV	53.9%	59.0%	62.9%	62.1%	56.2%	56.0%	53.3%	55.8%	52.3%	56.2%	52.3%	53.2%
Diabetes	28.3%	26.7%	24.9%	26.5%	28.2%	25.6%	27.6%	28.2%	28.5%	29.6%	29.6%	30.4%
Dementia	53.9%	59.0%	62.9%	62.1%	56.2%	56.0%	53.3%	55.8%	52.3%	56.2%	52.3%	53.2%

Delirium	53.9%	59.0%	62.9%	62.1%	56.2%	56.0%	53.3%	55.8%	52.3%	56.2%	52.3%	53.2%
Mood disorders	13.4%	36.3%	50.5%	51.5%	23.9%	25.1%	13.5%	17.0%	7.8%	16.4%	2.7%	9.6%
Psychotic disorders	13.4%	36.3%	50.5%	51.5%	23.9%	25.1%	13.5%	17.0%	7.8%	16.4%	2.7%	9.6%
Prior use of												
Anti-depressants	22.1%	43.4%	59.7%	54.7%	34.6%	36.6%	23.1%	28.5%	16.8%	24.2%	9.3%	15.6%
Charlson score	3.1±3.1	2.4±2.2	2.3±2.0	2.3±2.0	2.1±2.1	2.3±2.2	2.4±2.5	2.5±2.4	3.0±3.1	2.8±2.9	4.4±3.8	3.4±3.3
Number of office visits	5.4±4.9	3.9±3.8	3.3±3.2	3.5±3.2	3.8±3.5	3.8±3.9	4.6±3.9	4.5±4.2	5.4±4.6	5.3±5.0	7.6±5.9	6.2±5.5
Number of generic agents	8.4±5.0	7.9±4.9	8.2±4.8	7.7±4.6	7.9±4.8	7.9±4.9	8.1±4.9	8.5±5.4	8.2±4.9	8.4±5.6	9.1±5.3	8.6±5.4

Table S1c. British Columbia APM study cohort overall and by quintiles of PS_{COH}, the propensity score estimated in the entire cohort.

	Overall		Quintile 1		Quintile 2		Quintile 3		Quintile 4		Quintile 5	
	Conventional	Atypical	Conventional	Atypical	Conventional	Atypical	Conventional	Atypical	Conventional	Atypical	Conventional	Atypical
N	16,311	26,254	1,057	7,456	1,624	6,889	2,689	5,824	4,381	4,132	6,560	1,953
Age	79.2±8.6	80.3±8.3	83.7±8.3	82.6±8.2	80.8±8.7	80.5±8.2	77.8±8.4	78.4±8.1	78.6±8.6	79.0±8.2	79.0±8.5	79.0±8.1
Male gender	43.6%	36.9%	27.7%	27.4%	36.8%	36.6%	41.9%	42.9%	42.7%	41.9%	49.1%	45.5%
Treated in												
1997	19.2%	2.9%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	3.0%	2.4%	45.8%	33.7%
1998	17.9%	5.6%	0.0%	0.0%	0.1%	0.0%	1.8%	1.1%	17.5%	15.5%	32.1%	39.2%
1999	16.3%	8.1%	0.0%	0.0%	0.7%	0.6%	8.1%	6.7%	31.8%	31.3%	15.8%	20.2%
2000	12.0%	12.1%	3.3%	1.7%	10.2%	8.0%	24.3%	23.3%	21.5%	26.5%	2.4%	2.4%
2001	10.2%	15.3%	13.8%	9.1%	23.0%	20.1%	21.8%	25.8%	9.9%	10.4%	1.7%	1.9%
2002	9.1%	16.6%	21.8%	17.7%	22.7%	23.3%	17.2%	19.1%	7.5%	6.8%	1.4%	1.8%
2003	7.8%	19.1%	28.7%	32.5%	21.5%	24.2%	14.4%	12.4%	4.8%	4.3%	0.4%	0.7%
Prior hospitalization	20.2%	14.7%	11.3%	9.2%	12.6%	11.7%	16.9%	17.2%	22.9%	22.2%	23.1%	23.3%
Nursing home residence	26.1%	25.9%	31.5%	28.1%	26.7%	25.1%	21.5%	22.9%	24.8%	26.9%	27.8%	27.1%
Prior diagnosis of												
Myocardial infarction	2.6%	2.3%	2.6%	1.3%	2.8%	2.0%	3.2%	2.9%	2.9%	3.7%	2.2%	2.7%
Hypertension	22.3%	24.1%	26.8%	25.3%	25.2%	24.2%	24.8%	24.7%	21.1%	22.8%	20.7%	20.6%
Heart failure	8.0%	6.3%	6.3%	4.3%	6.2%	5.0%	7.4%	7.7%	7.8%	9.3%	9.0%	8.0%
Cerebrovascular disease	10.2%	10.0%	11.7%	9.2%	10.5%	9.9%	10.2%	10.4%	10.1%	10.4%	10.0%	11.2%
Ischemic heart disease	3.6%	2.8%	1.4%	1.4%	2.8%	2.2%	4.4%	3.5%	4.1%	5.3%	3.6%	3.0%
Arrythmia	0.0%	0.1%	0.1%	0.2%	0.0%	0.1%	0.0%	0.0%	0.1%	0.0%	0.0%	0.0%
Other dysrhythmias												
Diabetes	14.9%	13.8%	10.8%	11.8%	15.2%	12.7%	16.1%	15.6%	15.3%	15.9%	14.6%	15.1%
Dementia	8.4%	12.4%	22.2%	18.9%	11.4%	12.3%	7.4%	8.7%	8.6%	9.0%	5.8%	6.2%
Delirium	7.4%	8.9%	12.3%	11.6%	8.7%	7.5%	8.4%	8.3%	7.1%	8.2%	5.9%	6.8%
Mood disorders	14.9%	25.2%	41.3%	46.2%	21.1%	19.3%	16.0%	15.9%	15.7%	16.8%	8.0%	11.3%
Other psychotic disorders	3.0%	4.5%	7.9%	7.4%	3.9%	3.5%	3.1%	3.5%	3.1%	3.2%	1.8%	3.0%

Prior use of												
Anti-depressants	26.6%	41.3%	63.2%	66.5%	39.9%	38.1%	28.9%	28.7%	27.5%	29.3%	15.9%	20.1%
Psychotic medications	10.4%	16.9%	31.9%	27.6%	15.0%	14.5%	11.4%	12.6%	10.1%	11.1%	5.6%	9.2%
Other pyschiatric medications	4.0%	3.6%	3.9%	3.5%	3.7%	3.3%	3.7%	3.7%	3.9%	3.8%	4.2%	4.8%
Charlson score	1.1±1.4	0.8±1.2	0.6±0.8	0.5±0.8	0.7±1.0	0.7±1.0	1.0±1.2	1.0±1.2	1.2±1.6	1.1±1.5	1.2±1.5	1.1±1.6
Number of generic agents	7.9±5.3	7.5±5.1	7.0±4.7	7.1±4.6	7.6±5.1	7.2±4.9	7.7±5.1	7.8±5.3	8.0±5.4	8.1±5.6	8.1±5.4	8.0±5.7

Table S2a. Empirical results for the NSAID study. Key within-PS interactions were omitted from PS models.

Model		Entire Cohort (n=49,711)	Males (n=7,854)	Females (n=41,857)	Age <75 (n=14,103)	Age ≥75 (n=35,608)	High Risk (n=12,627)[a]
Exposed outcomes	N	503	71	432	83	420	348
Unexposed outcomes	N	243	57	186	49	194	157
Unadjusted	OR [CI]	1.14 [0.98, 1.33]	0.92 [0.65, 1.30]	1.21 [1.02, 1.44]	1.30 [0.91, 1.86]	1.04 [0.87, 1.23]	0.91 [0.75, 1.10]
Age/sex adjusted	OR [CI]	1.08 [0.92, 1.26]	0.87 [0.61, 1.24]	1.14 [0.95, 1.35]	1.32 [0.93, 1.89]	1.02 [0.86, 1.21]	0.88 [0.73, 1.07]
Adjusted by all covariates	OR [CI]	0.87 [0.71, 1.08]	0.68 [0.42, 1.12]	0.93 [0.73, 1.17]	1.07 [0.67, 1.72]	0.83 [0.65, 1.05]	0.74 [0.53, 1.04]
PS estimated within subgroup (PS_{SS}) ***"Referent Standard"***							
Adj. by deciles of PS_{SS}	OR [CI]	0.94 [0.80, 1.10]	0.81 [0.56, 1.16]	0.97 [0.81, 1.16]	1.04 [0.72, 1.50]	0.91 [0.76, 1.09]	0.92 [0.75, 1.12]
	Distance[b]	0.028	0.106	0.031	0.067	0.040	0.082
Matched on PS_{SS}	N Matched	33,264	5,840	27,416	10,816	22,352	7,226
	OR [CI]	0.91 [0.76, 1.10]	0.92 [0.61, 1.38]	1.04 [0.85, 1.27]	0.93 [0.61, 1.43]	0.81 [0.66, 1.01]	0.88 [0.70, 1.11]
	Distance	0.001	0.004	0.001	0.002	0.001	0.002
PS estimated overall (PS_{COH}) and applied within subgroup							
Adj. by deciles of PS_{COH}	OR [CI]	0.94 [0.80, 1.10]	0.75 [0.52, 1.09]	0.98 [0.82, 1.17]	1.19 [0.82, 1.72]	0.89 [0.74, 1.06]	0.89 [0.73, 1.08]
	Difference (%)[c]	**0.00 (0.0%)**	**-0.05 (-6.6%)**	**0.01 (1.3%)**	**0.15 (14.3%)**	**-0.02 (-2.3%)**	**-0.03 (-2.8%)**
	Distance	0.028	0.109	0.031	0.062	0.038	0.091
Matched on PS_{COH}	N Matched	33,264	5,840	27,434	10,874	22,366	7,242
	OR [CI]	0.91 [0.76, 1.10]	0.81 [0.54, 1.21]	0.99 [0.81, 1.22]	1.16 [0.78, 1.73]	0.92 [0.75, 1.13]	0.81 [0.63, 1.02]
	Difference (%)	**0.00 (0.0%)**	**-0.11 (-11.5%)**	**-0.04 (-4.3%)**	**0.23 (24.3%)**	**0.11 (13.0%)**	**-0.07 (-8.5%)**
	Distance	0.001	0.009	0.002	0.009	0.001	0.009
Matched pairs from PS_{COH} matches							
Matched on PS_{COH}	N Matched	33,264	1,402	22,876	4,886	16,446	2,166
	OR [CI]	0.92 [0.77, 1.11]	0.53 [0.21, 1.35]	0.99 [0.80, 1.24]	1.30 [0.69, 2.45]	0.99 [0.78, 1.26]	0.71 [0.46, 1.08]
	Difference (%)	**0.01 (0.9%)**	**-0.38 (-41.8%)**	**-0.04 (-4.3%)**	**0.37 (39.3%)**	**0.18 (22.0%)**	**-0.17 (-19.7%)**
	Distance	0.001	0.046	0.002	0.028	0.001	0.016

[a] Patients with prior gastrointestinal-related diagnoses or hospitalizations.

[b] Mahalanobis distance between patients in the exposure and referent categories. In the decile analyses, the distance is measured within each decile and then averaged.

[c] Difference between the observed odds ratio after adjusting by or matching on PS_{COH} versus PS_{SS}.

Table S2b. Empirical results for the Pennsylvania APM study. Key within-PS interactions were omitted from PS models.

Model		Entire Cohort (n=46,659)	Males (n=7,841)	Females (n=38,818)	Age <75 (n=10,035)	Age ≥75 (n=36,624)	High Risk (n=29,994)[a]
Exposed outcomes	N	6214	1546	4668	1213	5001	4454
Unexposed outcomes	N	2061	510	1551	127	1934	1667
Unadjusted	OR [CI]	1.36 [1.29, 1.44]	1.44 [1.28, 1.61]	1.35 [1.27, 1.43]	2.26 [1.87, 2.74]	1.37 [1.29, 1.45]	1.37 [1.29, 1.46]
Age/sex adjusted	OR [CI]	1.58 [1.50, 1.67]	1.62 [1.44, 1.83]	1.57 [1.47, 1.67]	2.36 [1.95, 2.86]	1.51 [1.43, 1.61]	1.56 [1.46, 1.66]
Adjusted by all covariates	OR [CI]	1.25 [1.16, 1.33]	1.21 [1.05, 1.40]	1.25 [1.16, 1.35]	1.29 [1.02, 1.63]	1.26 [1.17, 1.36]	1.27 [1.18, 1.38]
PS estimated within subgroup (PS_{SS}) ***"Referent Standard"***							
Adj. by deciles of PS_{SS}	OR [CI]	1.25 [1.17, 1.34]	1.20 [1.04, 1.38]	1.27 [1.18, 1.37]	1.19 [0.95, 1.50]	1.27 [1.18, 1.36]	1.28 [1.19, 1.39]
	Distance[b]	0.356	0.834	0.361	2.326	0.323	0.435
Matched on PS_{SS}	N Matched	18,584	3,166	15,376	2,684	15,832	12,690
	OR [CI]	1.24 [1.14, 1.34]	1.19 [1.00, 1.40]	1.30 [1.19, 1.42]	0.99 [0.75, 1.31]	1.23 [1.13, 1.34]	1.33 [1.22, 1.46]
	Distance	0.005	0.012	0.005	0.022	0.002	0.004
PS estimated overall (PS_{COH}) and applied within subgroup							
Adj. by deciles of PS_{COH}	OR [CI]	1.25 [1.17, 1.34]	1.19 [1.04, 1.37]	1.27 [1.18, 1.38]	1.34 [1.07, 1.69]	1.26 [1.17, 1.35]	1.27 [1.18, 1.38]
	Difference (%)[c]	**0.00 (0.0%)**	**-0.01 (-0.5%)**	**0.00 (0.1%)**	**0.15 (12.8%)**	**-0.01 (-0.5%)**	**-0.01 (-0.8%)**
	Distance	0.356	1.033	0.352	2.033	0.335	0.442
Matched on PS_{COH}	N Matched	18,584	3,192	15,412	2,696	15,890	12,718
	OR [CI]	1.24 [1.14, 1.34]	1.20 [1.02, 1.42]	1.28 [1.17, 1.40]	1.18 [0.90, 1.56]	1.25 [1.15, 1.35]	1.26 [1.15, 1.38]
	Difference (%)	**0.00 (0.0%)**	**0.02 (1.4%)**	**-0.02 (-1.5%)**	**0.19 (19.5%)**	**0.01 (1.1%)**	**-0.08 (-5.7%)**
	Distance	0.005	0.063	0.008	0.086	0.010	0.018
Matched pairs from PS_{COH} matches							
Matched on PS_{COH}	N Matched	18,584	564	12,916	482	13,564	8,336
	OR [CI]	1.24 [1.14, 1.34]	0.98 [0.66, 1.45]	1.33 [1.20, 1.46]	1.55 [0.86, 2.78]	1.24 [1.13, 1.36]	1.30 [1.17, 1.45]
	Difference (%)	**0.00 (0.0%)**	**-0.21 (-17.3%)**	**0.03 (2.2%)**	**0.56 (56.2%)**	**0.01 (0.7%)**	**-0.03 (-2.5%)**
	Distance	0.005	0.248	0.008	0.322	0.012	0.026

[a] Patients with a history of cerebrovascular disease, myocardial infarction, or arrhythmias.

[b] Mahalanobis distance between patients in the exposure and referent categories. In the decile analyses, the distance is measured within each decile and then averaged.

[c] Difference between the observed odds ratio after adjusting by or matching on PS_{COH} versus PS_{SS}.

Table S2c. Empirical results for the British Columbia APM study. Key within-PS interactions were omitted from PS models.

Model		Entire Cohort (n=42,565)	Males (n=16,790)	Females (n=25,775)	Age <75 (n=11,899)	Age ≥75 (n=30,666)	High Risk (n=6,519)[a]
Exposed outcomes	N	3883	2052	1831	1190	2693	619
Unexposed outcomes	N	3015	1445	1570	430	2585	568
Unadjusted	OR [CI]	2.41 [2.29, 2.54]	2.31 [2.14, 2.50]	2.37 [2.21, 2.55]	4.37 [3.88, 4.91]	2.09 [1.97, 2.22]	1.79 [1.58, 2.03]
Age/sex adjusted	OR [CI]	2.44 [2.32, 2.58]	2.41 [2.23, 2.60]	2.47 [2.29, 2.66]	4.44 [3.95, 5.00]	2.06 [1.94, 2.19]	1.84 [1.62, 2.09]
Adjusted by all covariates	OR [CI]	2.10 [1.97, 2.23]	1.96 [1.79, 2.16]	2.22 [2.04, 2.43]	2.83 [2.44, 3.27]	1.90 [1.77, 2.04]	1.60 [1.38, 1.86]
PS estimated within subgroup (PS_{SS}) ***"Referent Standard"***							
Adj. by deciles of PS_{SS}	OR [CI]	1.93 [1.82, 2.05]	1.82 [1.66, 1.98]	2.05 [1.89, 2.23]	2.51 [2.20, 2.87]	1.80 [1.68, 1.92]	1.54 [1.33, 1.77]
	Distance[b]	0.129	0.176	0.143	0.234	0.114	0.282
Matched on PS_{SS}	N Matched	22,410	9,104	13,268	6,546	15,632	3,672
	OR [CI]	1.94 [1.81, 2.09]	1.72 [1.56, 1.90]	2.04 [1.85, 2.25]	2.46 [2.12, 2.87]	1.69 [1.56, 1.84]	1.55 [1.31, 1.83]
	Distance	0.003	0.003	0.004	0.004	0.003	0.008
PS estimated overall (PS_{COH}) and applied within subgroup							
Adj. by deciles of PS_{COH}	OR [CI]	1.93 [1.82, 2.05]	1.81 [1.66, 1.97]	2.06 [1.90, 2.24]	2.81 [2.47, 3.20]	1.76 [1.64, 1.88]	1.44 [1.25, 1.66]
	Difference (%)[c]	**0.00 (0.0%)**	**-0.00 (-0.2%)**	**0.01 (0.3%)**	**0.30 (12.0%)**	**-0.03 (-1.9%)**	**-0.10 (-6.6%)**
	Distance	0.129	0.175	0.153	0.315	0.145	0.387
Matched on PS_{COH}	N Matched	22,410	9,128	13,286	6,694	15,686	3,704
	OR [CI]	1.94 [1.81, 2.09]	1.73 [1.57, 1.92]	2.10 [1.90, 2.32]	2.71 [2.34, 3.14]	1.73 [1.60, 1.88]	1.39 [1.18, 1.64]
	Difference (%)	**0.00 (0.0%)**	**0.01 (0.8%)**	**0.06 (2.8%)**	**0.25 (10.2%)**	**0.04 (2.2%)**	**-0.16 (-10.5%)**
	Distance	0.003	0.012	0.005	0.082	0.018	0.081
Matched pairs from PS_{COH} matches							
Matched on PS_{COH}	N Matched	22,410	4,318	8,286	2,340	11,582	640
	OR [CI]	1.95 [1.81, 2.09]	1.82 [1.57, 2.11]	2.14 [1.88, 2.44]	3.28 [2.50, 4.30]	1.71 [1.56, 1.88]	1.06 [0.72, 1.58]
	Difference (%)	**0.00 (0.1%)**	**0.10 (5.8%)**	**0.10 (5.1%)**	**0.82 (33.1%)**	**0.02 (0.9%)**	**-0.49 (-31.4%)**
	Distance	0.003	0.018	0.013	0.093	0.018	0.188

[a] Patients with a history of cerebrovascular disease, myocardial infarction, or arrhythmias.

[b] Mahalanobis distance between patients in the exposure and referent categories. In the decile analyses, the distance is measured within each decile and then averaged.

[c] Difference between the observed odds ratio after adjusting by or matching on PS_{COH} versus PS_{SS}.

Table S3. Simulation Results: Difference in the log of the treatment effect after adjusting by PS_{SS} and PS_{COH} versus true propensity.

Grouping of Simulation Runs	Number of Runs	PS_{SS} versus True Propensity[a]		PS_{COH} versus True Propensity[b]	
		Absolute Difference (Median [Interquartile Range])	Percent Difference (Median [Interquartile Range])	Absolute Difference (Median [Interquartile Range])	Percent Difference (Median [Interquartile Range])
All simulation runs	10,092,231	0.046 [0.021, 0.086]	3.9% [1.5%, 11.4%]	0.021 [0.010, 0.038]	1.7% [0.7%, 5.1%]
Baseline exposure prevalence (β_0)					
β_0 = 25%	5,050,241	0.047 [0.021, 0.088]	3.9% [1.5%, 11.6%]	0.022 [0.010, 0.040]	1.8% [0.7%, 5.3%]
β_0 = 50%	5,041,990	0.045 [0.021, 0.084]	3.8% [1.5%, 11.1%]	0.020 [0.009, 0.037]	1.7% [0.6%, 4.9%]
Baseline outcome event rate (γ_0)					
γ_0 = 0.01 events per unit of person-time	2,486,731	0.050 [0.023, 0.095]	3.4% [1.2%, 9.8%]	0.023 [0.010, 0.042]	1.6% [0.6%, 4.4%]
γ_0 = 0.1 events per unit of person-time	2,533,750	0.045 [0.021, 0.084]	4.1% [1.6%, 12.0%]	0.021 [0.009, 0.038]	1.8% [0.7%, 5.3%]
γ_0 = 0.25 events per unit of person-time	2,493,000	0.045 [0.021, 0.083]	4.0% [1.6%, 12.1%]	0.020 [0.009, 0.037]	1.8% [0.7%, 5.3%]
γ_0 = 0.50 events per unit of person-time	2,578,750	0.045 [0.020, 0.082]	4.0% [1.5%, 11.9%]	0.020 [0.009, 0.037]	1.8% [0.7%, 5.3%]
Within-PS interactions ($\beta_{PS\text{-}INT}$)					
$\beta_{PS\text{-}INT}$ = log(1.0) (No interaction)	1,669,748	0.047 [0.021, 0.086]	3.8% [1.5%, 10.9%]	0.021 [0.010, 0.038]	1.7% [0.7%, 4.9%]
$\beta_{PS\text{-}INT}$ = log(3.0)	1,682,247	0.046 [0.021, 0.085]	3.8% [1.5%, 11.0%]	0.021 [0.010, 0.039]	1.7% [0.7%, 5.0%]
$\beta_{PS\text{-}INT}$ = log(3.5)	1,705,495	0.046 [0.021, 0.085]	3.9% [1.5%, 11.4%]	0.021 [0.010, 0.038]	1.8% [0.7%, 5.1%]
$\beta_{PS\text{-}INT}$ = log(4.0)	1,673,249	0.047 [0.021, 0.087]	3.9% [1.5%, 11.6%]	0.021 [0.010, 0.039]	1.8% [0.7%, 5.2%]
$\beta_{PS\text{-}INT}$ = log(4.5)	1,670,245	0.046 [0.021, 0.085]	3.9% [1.5%, 11.6%]	0.021 [0.010, 0.038]	1.8% [0.7%, 5.1%]
$\beta_{PS\text{-}INT}$ = log(5.0)	1,691,247	0.046 [0.021, 0.086]	3.9% [1.5%, 11.6%]	0.021 [0.010, 0.038]	1.8% [0.7%, 5.2%]
Treatment interactions (β_{INT})					
β_{INT} = log(1.0) (No interaction)	1,679,739	0.048 [0.022, 0.090]	5.1% [2.0%, 12.8%]	0.022 [0.010, 0.040]	2.3% [0.9%, 5.6%]
β_{INT} = log(3.0)	1,687,495	0.046 [0.021, 0.085]	4.1% [1.6%, 12.0%]	0.021 [0.010, 0.038]	1.9% [0.7%, 5.4%]
β_{INT} = log(3.5)	1,685,249	0.046 [0.021, 0.085]	3.8% [1.5%, 11.4%]	0.021 [0.010, 0.038]	1.7% [0.7%, 5.1%]
β_{INT} = log(4.0)	1,670,248	0.046 [0.021, 0.085]	3.7% [1.4%, 11.6%]	0.021 [0.010, 0.038]	1.7% [0.6%, 5.2%]
β_{INT} = log(4.5)	1,704,500	0.046 [0.021, 0.084]	3.5% [1.3%, 10.7%]	0.021 [0.009, 0.038]	1.6% [0.6%, 4.8%]
β_{INT} = log(5.0)	1,665,000	0.046 [0.021, 0.084]	3.2% [1.2%, 9.4%]	0.021 [0.009, 0.038]	1.4% [0.6%, 4.2%]
Treatment effect (β_X)					
β_X = log(1.0) (No effect)	1,991,749	0.046 [0.021, 0.085]	4.1% [1.7%, 9.0%]	0.021 [0.010, 0.038]	1.9% [0.8%, 4.0%]
β_X = log(2.0)	2,035,996	0.046 [0.021, 0.085]	4.0% [1.6%, 9.1%]	0.021 [0.010, 0.038]	1.8% [0.7%, 4.1%]

β_X = log(3.0)	2,040,746	0.046 [0.021, 0.086]	4.1% [1.5%, 13.3%]	0.021 [0.010, 0.038]	1.8% [0.7%, 6.0%]
β_X = log(4.0)	2,025,247	0.046 [0.021, 0.086]	3.8% [1.4%, 16.9%]	0.021 [0.010, 0.038]	1.7% [0.6%, 7.4%]
β_X = log(5.0)	1,998,493	0.047 [0.021, 0.086]	3.4% [1.2%, 13.5%]	0.021 [0.010, 0.039]	1.5% [0.6%, 6.0%]
Confounder-to-exposure association (β_{C1})					
β_{C1} = log(1.5)	1,651,744	0.044 [0.020, 0.081]	3.7% [1.4%, 11.1%]	0.020 [0.009, 0.037]	1.7% [0.7%, 5.0%]
β_{C1} = log(2.0)	1,679,998	0.045 [0.020, 0.083]	3.7% [1.4%, 10.6%]	0.021 [0.009, 0.038]	1.7% [0.7%, 4.9%]
β_{C1} = log(2.5)	1,696,996	0.046 [0.021, 0.085]	3.9% [1.5%, 11.5%]	0.021 [0.010, 0.038]	1.8% [0.7%, 5.1%]
β_{C1} = log(3.0)	1,672,995	0.047 [0.021, 0.087]	3.9% [1.5%, 11.5%]	0.021 [0.010, 0.039]	1.7% [0.7%, 5.1%]
β_{C1} = log(3.5)	1,687,998	0.048 [0.022, 0.088]	4.0% [1.5%, 11.8%]	0.022 [0.010, 0.039]	1.8% [0.7%, 5.3%]
β_{C1} = log(4.0)	1,702,500	0.049 [0.022, 0.091]	4.0% [1.5%, 11.7%]	0.021 [0.010, 0.040]	1.8% [0.7%, 5.1%]
Confounder-to-outcome association (γ_{C1})					
γ_{C1} = log(1.5)	1,681,999	0.046 [0.021, 0.086]	4.0% [1.5%, 11.7%]	0.021 [0.010, 0.038]	1.8% [0.7%, 5.2%]
γ_{C1} = log(2.0)	1,700,750	0.046 [0.021, 0.085]	3.8% [1.5%, 11.2%]	0.021 [0.010, 0.038]	1.7% [0.7%, 5.0%]
γ_{C1} = log(2.5)	1,683,748	0.046 [0.021, 0.085]	3.8% [1.5%, 11.0%]	0.021 [0.010, 0.038]	1.7% [0.7%, 4.9%]
γ_{C1} = log(3.0)	1,658,998	0.047 [0.021, 0.086]	3.9% [1.5%, 11.4%]	0.021 [0.010, 0.039]	1.8% [0.7%, 5.1%]
γ_{C1} = log(3.5)	1,671,245	0.047 [0.021, 0.086]	3.9% [1.4%, 11.4%]	0.021 [0.010, 0.039]	1.7% [0.7%, 5.1%]
γ_{C1} = log(4.0)	1,695,491	0.046 [0.021, 0.086]	3.9% [1.5%, 11.4%]	0.021 [0.010, 0.038]	1.7% [0.7%, 5.1%]
Expected n in C_1 subgroup (P_{C1})					
Expected n in subgroup = 500	2,011,249	0.079 [0.036, 0.143]	6.1% [2.3%, 17.3%]	0.027 [0.012, 0.051]	2.1% [0.8%, 6.1%]
Expected n in subgroup = 1000	2,027,982	0.054 [0.025, 0.097]	4.3% [1.7%, 12.2%]	0.022 [0.010, 0.040]	1.8% [0.7%, 5.1%]
Expected n in subgroup = 1500	2,039,250	0.044 [0.020, 0.078]	3.7% [1.4%, 10.3%]	0.020 [0.009, 0.037]	1.7% [0.7%, 4.9%]
Expected n in subgroup = 2000	2,003,500	0.038 [0.017, 0.067]	3.2% [1.2%, 9.1%]	0.019 [0.009, 0.035]	1.6% [0.6%, 4.7%]
Expected n in subgroup = 2500	2,010,250	0.034 [0.016, 0.059]	2.8% [1.1%, 8.3%]	0.018 [0.009, 0.033]	1.6% [0.6%, 4.6%]
Actual n in C_1 subgroup					
Actual n in subgroup ≤ 500	1,029,345	0.081 [0.037, 0.146]	6.2% [2.3%, 17.6%]	0.027 [0.012, 0.051]	2.1% [0.8%, 6.2%]
500 < Actual n in subgroup ≤ 1000	2,013,071	0.065 [0.030, 0.118]	5.1% [1.9%, 14.6%]	0.024 [0.011, 0.045]	1.9% [0.7%, 5.6%]
1000 < Actual n in subgroup ≤ 1500	2,030,107	0.049 [0.022, 0.087]	4.0% [1.5%, 11.2%]	0.021 [0.010, 0.038]	1.7% [0.7%, 5.0%]
1500 < Actual n in subgroup ≤ 2000	2,020,338	0.041 [0.019, 0.072]	3.4% [1.3%, 9.7%]	0.020 [0.009, 0.036]	1.7% [0.6%, 4.8%]
2000 < Actual n in subgroup ≤ 2500	2,004,923	0.036 [0.016, 0.063]	3.0% [1.2%, 8.7%]	0.019 [0.009, 0.034]	1.6% [0.6%, 4.6%]
Actual n in subgroup > 2500	994,447	0.033 [0.015, 0.059]	2.8% [1.1%, 8.2%]	0.018 [0.009, 0.033]	1.6% [0.6%, 4.5%]
Number of exposed outcomes in full cohort (a)					
a ≤ 200	2,308,579	0.052 [0.023, 0.098]	5.9% [1.9%, 17.8%]	0.023 [0.010, 0.043]	2.6% [0.8%, 7.9%]
200 < a ≤ 400	1,226,072	0.047 [0.021, 0.087]	5.7% [1.9%, 18.7%]	0.021 [0.010, 0.038]	2.5% [0.9%, 8.2%]
400 < a ≤ 750	1,500,218	0.046 [0.021, 0.085]	5.8% [2.1%, 18.5%]	0.021 [0.010, 0.038]	2.6% [0.9%, 8.2%]
a > 750	5,057,362	0.044 [0.020, 0.081]	2.8% [1.2%, 6.7%]	0.020 [0.009, 0.037]	1.3% [0.5%, 3.1%]

Number of exposed outcomes in C_1 subgroup ($a_{C1=1}$)					
$a_{C1=1} \leq 10$	1,001,185	0.069 [0.030, 0.135]	6.4% [1.9%, 19.0%]	0.028 [0.012, 0.054]	2.6% [0.7%, 7.8%]
$10 < a_{C1=1} \leq 25$	795,308	0.054 [0.025, 0.101]	6.7% [2.4%, 19.3%]	0.023 [0.010, 0.042]	2.8% [1.0%, 8.1%]
$25 < a_{C1=1} \leq 50$	917,105	0.052 [0.023, 0.096]	6.2% [2.2%, 18.2%]	0.022 [0.010, 0.041]	2.6% [0.9%, 7.9%]
$a_{C1=1} > 50$	7,378,633	0.043 [0.020, 0.078]	3.3% [1.3%, 9.0%]	0.020 [0.009, 0.036]	1.5% [0.6%, 4.1%]

a Difference in the log of the observed rate ratio between models adjusted by PS_{SS} versus those adjusted by the known-true propensity.

b Difference in the log of the observed rate ratio between models adjusted by PS_{COH} versus those adjusted by the known-true propensity.