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Supplemental Table 1. Comorbidity diagnostic codes

Hypertension	ICD-9-CM: 362.11, 401-405.xx, 437.2 ICD-10 CM: H35.039, I10, I11, I12, I13, I15, I16, I67.4
Diabetes mellitus	ICD-9-CM: 249.xx, 250.xx, 357.2, 362.0x, 366.41 ICD-10 CM: E08, E09, E10, E11, E13
Dyslipidemia	ICD-9-CM: 272.0, 272.1, 272.2, 272.3, 272.4 ICD-10 CM: E78.0x, E78.1, E78.2, E78.3, E78.4x, E78.5
Myocardial infarction	ICD-9 CM: 410.xx ICD-10 CM: I21.x(x), I22.x(x)
Stroke	ICD-9-CM: 362.3x, 430, 431, 432.x, 433.x1, 434.x1, 435.8, 435.9, 436, 438.xx, V12.54 ICD-10 CM: I60, I61, I62, I63, G45.x, I67.81, I67.82, I69.x(xx), Z86.73
Peripheral vascular disease	ICD-9-CM: 249.7x, 250.7x, 440.xx, 441.xx, 442.xx, 443.2x, 443.89, 443.9, 445.xx, 557.x, V43.4 ICD-10 CM: E10.5x, E11.5x, I70.x(xx), I71.x(x), I72.x, I73.9, I75.xx(x), I77.7x, K55.x(x), Z95.828
Prior PCI	Same as outcome code (Supplemental Table 2)
Prior CABG	Same as outcome code (Supplemental Table 2)
Heart failure	ICD-9-CM: 398.91, 402.x1, 404.x1, 404.x3, 428.x(x) ICD-10 CM: I50.x(x), I11.0, I13.0, I13.2, I09.81
Bleeding history	Same as outcome code (Supplemental Table 2)
Malignancy	ICD-9 CM: V10.xx, 14x.x, 15x.x, 16x.x, 17x.xx, 18x.x, 19x.xx, 200.xx, 201.xx, 202.xx, 203.xx, 204.xx, 205.xx, 206.xx, 207.xx, 208.xx, 209.0x, 209.1x, 209.2x, 209.3x, 209.7x ICD-10 CM: Cxx.x, Z85.xx(x)
Alcohol-related disease	ICD-9-CM: 291.xx, 303.xx, 305.0x, 357.5, 425.5, 571.x, 535.3x, 790.3, 980.0, E86.00, E86.01, V11.3 ICD-10 CM: F10, G26.1, I42.6, K29.2x, K70.x(x), R78.0, T51.0(xxx)
Liver disease	ICD-9-CM: 070.xx, 456.0, 456.1, 456.2x, 570, 571.x, 572.2, 572.3, 572.4, 572.8, 573.x, V42.7 ICD-10 CM: B15, B16, B17, B18, B19, I85, K70, K71, K72, K73, K74, K75, K76, K77, Z94.4
COPD	ICD-9 CM: 491.xx, 492.x, 496 ICD-10 CM: J41.x, J42, J43.x, J44.x

PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease

Supplemental Table 2. Outcome diagnostic codes

Cardiovascular death	Cause of death code: 23, 25, 26, 27, 28, 29, 30, 31, 32
Myocardial infarction	ICD-9 CM: 410.xx ICD-10 CM: I21.x(x), I22.x(x)
Stroke	ICD-9-CM: 362.3x, 430, 431, 432.x, 433.x1, 434.x1, 435.8, 435.9, 436 ICD-10 CM: I60, I61, I62, I63, G45.x
PCI (procedural code)	ICD-9-CM: 0066; ICD-10 CM: 027x3xx
CABG (procedural code)	ICD-9-CM: 361.x; ICD-10 CM: 021x0xx
Bleeding:	
1. Resulting in death	Cause of death code: 38, 39, 40, 41, 42, 43, 72
2. In a critical site:	
- Intracranial	ICD-9-CM: 430, 431, 432.x, 997.02 ICD-10 CM: I60, I61, I62
- Intraocular	ICD-9-CM: 360.43, 362.43, 362.81, 363.61, 363.62, 363.72, 376.32, 377.42, 379.23 ICD-10 CM: H4481, H3573, H356, H3130, H3131, H3141, H0523, H431, H4702
- Pericardial	ICD-9-CM: 423.0; ICD-10 CM: I312
- Airway	ICD-9-CM: 784.8, 786.30, 786.39; ICD-10 CM: R04
- Intra-articular	ICD-9-CM: 719.1x; ICD-10 CM: M250
- Retroperitoneal	ICD-9-CM: 568.81; ICD-10 CM: K661
3. Resulting in hospitalization:	One of the following codes in the institutional inpatient files:
- GI	ICD-9-CM: 456.0, 456.20, 530.21, 530.7, 530.82, 531.0x, 531.2x, 531.4x, 531.5x, 531.6x, 532.0x, 532.2x, 532.4x, 532.6x, 533.0x, 533.2x, 533.4x, 533.6x, 534.0x, 534.2x, 534.4x, 534.6x, 535.x1, 537.83, 537.84, 578.x, 562.x2, 562.x3, 569.3, 569.85, 569.86 ICD-10 CM: I85x1, K2211, K226, K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K31811, K3182, K29x1, K920, K921, K922, K57x1, K57x3, K625, K5521
- Urinary	ICD-9-CM: 596.7, 602.1, 599.7x ICD-10 CM: N421, R310, R319
- Gynecological	ICD-9-CM: 620.7, 621.4, 623.6, 624.5, 626.6, 626.8, 626.9, 627.0, 627.1 ICD-10 CM: N836, N837, N857, N920, N921, N924, N925, N938, N939, N950
- Other	ICD-9-CM: 459.0, 958.2, 729.92, 285.1 ICD-10 CM: R58, M7981, D62

Only cause of death codes on the primary position were used. PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting

Supplemental Table 3. Clinical outcomes in patients with acute coronary syndromes (“as-treated” analysis; N=5579).

Outcome	Clopidogrel		Prasugrel		Ticagrelor		Prasugrel vs. clopidogrel	Ticagrelor vs. clopidogrel
	Incidence rate	Events	Incidence rate	Events	Incidence rate	Events	Weighted HR (95% CI)	Weighted HR (95% CI)
CV death, MI, stroke	163	2197	144	197	168	141	0.93 (0.79-1.10)	0.94 (0.77-1.15)
Cardiovascular death	17	346	15	31	25	32	0.92 (0.58-1.47)	1.19 (0.75-1.90)
MI	87	1404	93	141	96	93	1.01 (0.81-1.26)	0.94 (0.73-1.20)
Stroke	70	1147	49	85	76	79	0.88 (0.68-1.14)	1.05 (0.80-1.36)
Revascularization	37	686	49	85	42	46	1.22 (0.91-1.65)	1.12 (0.80-1.57)
Death from any cause	29	580	26	54	35	46	0.95 (0.67-1.36)	0.99 (0.68-1.44)
Clinically relevant bleeding	79	1281	83	135	99	102	1.16 (0.93-1.44)	1.11 (0.87-1.41)
MI, stroke, CV death, or revascularization	172	2272	155	207	178	145	0.94 (0.80-1.11)	0.95 (0.78-1.15)

Incidence rates (unweighted cohort) are presented as number of events per 100 patient-years. There were 4761 patients on clopidogrel, 468 on prasugrel, and 350 on ticagrelor. Patients were followed from day 90 post drug-eluting stent (DES) implantation up to the date of death, kidney transplantation, loss of Medicare A and B coverage, end of antiplatelet agent prescription or loss of part D coverage, or 12 months after DES implantation. CV, cardiovascular; MI, myocardial infarction; HR, hazard ratio; CI, confidence interval.

Supplemental Table 4. Clinical outcomes in patients who remained on the same antiplatelet agent throughout the 90-day exposure assessment period (“as-treated” analysis; N=7331).

Outcome	Clopidogrel		Prasugrel		Ticagrelor		Prasugrel vs. clopidogrel	Ticagrelor vs. clopidogrel
	Incidence rate	Events	Incidence rate	Events	Incidence rate	Events	Weighted HR (95% CI)	Weighted HR (95% CI)
CV death, MI, stroke	144	2813	120	173	157	120	0.91 (0.77-1.09)	1.00 (0.82-1.23)
Cardiovascular death	16	453	15	30	23	28	0.99 (0.65-1.52)	1.40 (0.87-2.26)
MI	72	1672	74	118	84	76	0.97 (0.78-1.21)	1.02 (0.79-1.33)
Stroke	67	1536	43	77	72	69	0.85 (0.65-1.11)	0.98 (0.74-1.31)
Revascularization	33	854	47	80	35	35	1.27 (0.95-1.69)	1.05 (0.73-1.51)
Death from any cause	27	763	23	48	36	43	0.92 (0.65-1.30)	1.27 (0.88-1.85)
Clinically relevant bleeding	79	1775	82	134	102	94	1.13 (0.91-1.40)	1.19 (0.94-1.51)
MI, stroke, CV death, or revascularization	153	2926	134	185	163	122	0.93 (0.79-1.10)	0.98 (0.81-1.20)

Incidence rates (unweighted cohort) are presented as number of events per 100 patient-years. There were 6535 patients on clopidogrel, 459 on prasugrel, and 337 on ticagrelor. Patients were followed from day 90 post drug-eluting stent (DES) implantation up to the date of death, kidney transplantation, loss of Medicare A and B coverage, end of antiplatelet agent prescription or loss of part D coverage, or 12 months after DES implantation. CV, cardiovascular; MI, myocardial infarction; HR, hazard ratio; CI, confidence interval.

Supplemental Table 5. Clinical outcomes in the “as-treated” population when exposure to antiplatelet agents was assessed in the first 45 days post drug-eluting stent implantation.

Outcome	Clopidogrel		Prasugrel		Ticagrelor		Prasugrel vs. clopidogrel	Ticagrelor vs. clopidogrel
	Incidence rate	Events	Incidence rate	Events	Incidence rate	Events	Weighted HR (95% CI)	Weighted HR (95% CI)
CV death, MI, stroke	143	3108	128	271	174	203	1.02 (0.88-1.18)	1.08 (0.92-1.27)
Cardiovascular death	13	442	12	41	15	31	0.90 (0.59-1.36)	1.00 (0.62-1.60)
MI	71	1917	73	178	94	135	0.98 (0.80-1.20)	1.09 (0.89-1.33)
Stroke	70	1830	49	136	78	122	0.93 (0.75-1.15)	1.02 (0.82-1.26)
Revascularization	32	981	36	100	37	63	1.10 (0.83-1.46)	1.03 (0.77-1.38)
Death from any cause	21	739	20	67	26	55	0.90 (0.64-1.25)	1.01 (0.71-1.45)
Clinically relevant bleeding	75	1985	76	194	92	145	1.11 (0.91-1.34)	1.15 (0.94-1.40)
MI, stroke, CV death, or revascularization	153	3231	137	279	184	209	1.01 (0.87-1.16)	1.09 (0.93-1.27)

Incidence rates (unweighted cohort) are presented as number of events per 100 patient-years. There were 5435 patients on clopidogrel, 521 on prasugrel, and 385 on ticagrelor. Patients were followed from day 45 post drug-eluting stent (DES) implantation up to the date of death, kidney transplantation, loss of Medicare A and B coverage, end of antiplatelet agent prescription or loss of part D coverage, or 12 months after DES implantation. CV, cardiovascular; MI, myocardial infarction; HR, hazard ratio; CI, confidence interval.

Supplemental Table 6. Interaction terms for the prevalent and incident population

Outcome	Comparison	P-value for interaction (incident versus prevalent population)
CV death, MI, stroke	Prasugrel vs. clopidogrel	0.68
	Ticagrelor vs. clopidogrel	0.33
Cardiovascular death	Prasugrel vs. clopidogrel	0.05
	Ticagrelor vs. clopidogrel	0.63
MI	Prasugrel vs. clopidogrel	0.98
	Ticagrelor vs. clopidogrel	0.93
Stroke	Prasugrel vs. clopidogrel	0.30
	Ticagrelor vs. clopidogrel	0.99
Revascularization	Prasugrel vs. clopidogrel	0.78
	Ticagrelor vs. clopidogrel	0.23
Death from any cause	Prasugrel vs. clopidogrel	0.43
	Ticagrelor vs. clopidogrel	0.58
Clinically relevant bleeding	Prasugrel vs. clopidogrel	0.75
	Ticagrelor vs. clopidogrel	0.69
MI, stroke, CV death, or revascularization	Prasugrel vs. clopidogrel	0.50
	Ticagrelor vs. clopidogrel	0.50

CV, cardiovascular; MI, myocardial infarction

Supplemental Table 7. Baseline characteristics in the propensity-score matched cohorts

	Clopidogrel vs. prasugrel			Clopidogrel vs. ticagrelor		
	Clopidogrel	Prasugrel	Standardized mean difference	Clopidogrel	Ticagrelor	Standardized mean difference
Patients	619	619		449	449	
Follow-up (days)	155 (34-275)	170 (38-275)		153 (27-275)	93 (17-258)	
<i>Demographics</i>						
Age	60 ± 12	60 ± 11	0.02	65 ± 11	64 ± 12	-0.09
Male sex	365 (59%)	355 (57%)	-0.03	245 (55%)	226 (50%)	-0.08
Black race	141 (23%)	153 (25%)	0.05	121 (27%)	134 (30%)	0.06
Hemodialysis	554 (89%)	550 (89%)	-0.02	401 (89%)	406 (90%)	0.04
Vintage (months)	37 (20-65)	37 (18-62)	0.03	32 (19-55)	38 (21-60)	0.14
<i>Comorbidities</i>						
Hypertension	618 (100%)	619 (100%)	0.06	449 (100%)	449 (100%)	0.00
Diabetes	534 (86%)	547 (88%)	0.06	403 (90%)	395 (88%)	-0.06
Dyslipidemia	579 (94%)	582 (94%)	0.02	428 (95%)	427 (95%)	-0.01
MI	440 (71%)	435 (70%)	-0.02	358 (80%)	344 (77%)	-0.08
Prior PCI	130 (21%)	132 (21%)	0.01	52 (12%)	55 (12%)	0.02
Prior CABG	34 (5%)	28 (5%)	-0.04	21 (5%)	22 (5%)	0.01
Stroke history	167 (27%)	171 (28%)	0.01	182 (41%)	198 (44%)	0.07
PVD	391 (63%)	400 (65%)	0.03	302 (67%)	309 (69%)	0.03
Heart failure	489 (79%)	493 (80%)	0.02	372 (83%)	373 (83%)	0.01

Bleeding history	320 (52%)	313 (51%)	-0.02	253 (56%)	256 (57%)	0.01
Malignancy	102 (16%)	104 (17%)	0.01	92 (20%)	102 (23%)	0.05
Alcohol-related disease	53 (9%)	57 (9%)	0.02	45 (10%)	50 (11%)	0.04
Liver disease	169 (27%)	180 (29%)	0.04	127 (28%)	127 (28%)	0.00
COPD	229 (37%)	220 (36%)	-0.03	182 (41%)	187 (42%)	0.02
<i>Medication</i>						
ACEI	246 (40%)	270 (44%)	0.08	188 (42%)	181 (40%)	-0.03
ARB	131 (21%)	124 (20%)	-0.03	96 (21%)	96 (21%)	0.00
Beta-blocker	545 (88%)	548 (89%)	0.02	391 (87%)	388 (86%)	-0.02
Statin	505 (82%)	507 (82%)	0.01	360 (80%)	365 (81%)	0.03
MRA	<11 (<2%)	<11 (<2%)	0.03	<11 (<3%)	<11 (<3%)	0.04
P2Y12	257 (42%)	261 (42%)	0.01	153 (34%)	149 (33%)	-0.02
Anticoagulation	59 (10%)	61 (10%)	0.01	18 (4%)	22 (5%)	0.04
<i>Setting</i>						
ACS	472 (76%)	466 (75%)	-0.02	355 (79%)	350 (78%)	-0.03

Results are presented as mean $\pm$ standard deviation, median (interquartile range) or number (percentage).

MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonists; P2Y12, P2Y12 inhibitors (antiplatelets); ACS, acute coronary syndrome

Supplemental Table 8. Clinical outcomes of the “intention-to-treat” analysis in the matched cohorts.

Outcome	Prasugrel vs. clopidogrel (619 patients per group)					Ticagrelor vs. clopidogrel (449 patients per group)				
	Clopidogrel		Prasugrel		HR (95% CI)	Clopidogrel		Ticagrelor		HR (95% CI)
	Incidence rate	Events	Incidence rate	Events		Incidence rate	Events	Incidence rate	Events	
CV death, MI, stroke	141	354	143	365	1.02 (0.88-1.18)	154	271	166	272	1.06 (0.90-1.26)
Cardiovascular death	32	121	28	110	0.89 (0.68-1.15)	28	77	28	76	1.00 (0.73-1.37)
MI	73	211	79	231	1.11 (0.92-1.34)	74	156	84	165	1.10 (0.89-1.37)
Stroke	56	169	50	159	0.92 (0.74-1.14)	63	137	69	141	1.07 (0.84-1.35)
Revascularization	32	107	40	133	1.27 (0.99-1.64)	34	81	39	88	1.13 (0.84-1.53)
Death from any cause	53	202	46	180	0.87 (0.71-1.06)	54	149	56	154	1.05 (0.84-1.31)
Clinically relevant bleeding	79	225	85	241	1.10 (0.91-1.31)	82	166	92	181	1.14 (0.93-1.41)
MI, stroke, CV death, or revascularization	151	371	155	381	1.03 (0.89-1.19)	163	280	176	281	1.06 (0.90-1.26)

Incidence rates are presented as number of events per 100 patient-years. After propensity-score matching, the cohorts included 619 patients on clopidogrel and 619 on prasugrel, or 449 on clopidogrel and 449 on ticagrelor. Patients were followed from day 90 post drug-eluting stent (DES) implantation up to the date of death, kidney transplantation, loss of Medicare A and B coverage, or 12 months after DES implantation. Exposure was examined as a time-varying covariate. Death was considered as a competing risk for the outcomes of myocardial infarction, stroke, revascularization, and clinically significant bleeding. CV, cardiovascular; MI, myocardial infarction; HR, hazard ratio; CI, confidence interval.

Supplemental Table 9. Clinical outcomes of the “as-treated” analysis in the matched cohorts.

Outcome	Prasugrel vs. clopidogrel (619 patients per group)					Ticagrelor vs. clopidogrel (449 patients per group)				
	Clopidogrel		Prasugrel		HR (95% CI)	Clopidogrel		Ticagrelor		HR (95% CI)
	Incidence rate	Events	Incidence rate	Events		Incidence rate	Events	Incidence rate	Events	
CV death, MI, stroke	134	264	126	235	0.93 (0.78-1.11)	144	197	160	159	1.07 (0.86-1.31)
Cardiovascular death	21	57	15	37	0.71 (0.47-1.08)	21	40	19	27	0.92 (0.57-1.50)
MI	75	169	75	154	0.99 (0.79-1.23)	81	125	89	103	1.05 (0.81-1.36)
Stroke	57	131	46	101	0.81 (0.62-1.05)	57	93	71	82	1.19 (0.89-1.60)
Revascularization	34	85	45	100	1.34 (1.01-1.79)	38	66	40	52	1.04 (0.73-1.49)
Death from any cause	28	75	23	58	0.85 (0.60-1.20)	34	64	31	44	0.93 (0.64-1.37)
Clinically relevant bleeding	76	171	83	166	1.07 (0.87-1.33)	73	111	94	108	1.27 (0.97-1.65)
MI, stroke, CV death, or revascularization	144	276	140	252	0.96 (0.81-1.14)	155	206	169	164	1.05 (0.86-1.29)

Incidence rates are presented as number of events per 100 patient-years. After propensity-score matching, the cohorts included 619 patients on clopidogrel and 619 on prasugrel, or 449 on clopidogrel and 449 on ticagrelor. Patients were followed from day 90 post drug-eluting stent (DES) implantation up to the date of death, kidney transplantation, loss of Medicare A and B coverage, end of antiplatelet agent prescription or loss of part D coverage, or 12 months after DES implantation. Exposure was examined as a time-varying covariate. Death was considered as a competing risk for the outcomes of myocardial infarction, stroke, revascularization, and clinically significant bleeding.

CV, cardiovascular; MI, myocardial infarction; HR, hazard ratio; CI, confidence interval.

Supplemental Figure 1. Propensity score distribution per treatment group.

