Supplementary Appendix

ENDPOINT DEFINITIONS

Death

Deaths is classified as cardiovascular or non-cardiovascular. The cause of death will be determined by the principal condition that resulted in the death, not the immediate mode of death. Managing physicians will utilize all available information provided, along with clinical expertise, in their adjudication of the cause of death.

Stroke

Stroke is defined as an acute episode of focal or global neurological dysfunction caused by cerebral vascular injury as a result of infarction or hemorrhage not caused by trauma. Ischemic stroke is defined as an acute episode of focal cerebral dysfunction caused by cerebral infarction. Hemorrhagic stroke is defined as an acute episode of focal or global cerebral dysfunction caused by intraparenchymal, intraventricular, or subarachnoid hemorrhage not caused by trauma. Subdural hematomas are intracranial hemorrhage events but not strokes.

Intracranial hemorrhage

Intracranial hemorrhage is defined as an acute or subacute episode of bleeding within the intracranial space, including hemorrhagic stroke, subdural hemorrhage and epidural hemorrhage.

Major bleeding

Major bleeding was defined as any episode of fatal bleeding event, bleeding that occurred in the critical sites (intracranial, intra-articular or intramuscular with compartment syndrome, intraocular, pericardial, retroperitoneal), bleeding necessitating transfusion, or bleeding that caused a drop in hemoglobin of ≥ 2 g/dL, in accordance to the International Society on Thrombosis and Haemostasis.

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BASELINE VARIABLES DEFINITIONS

Estimated glomerular filtration rate

Estimated glomerular filtration rate (eGFR) is calculated based on MDRD equation, expressed as:

186 x (Creatinine/88.4) - 1.154 x (Age) - 0.203 x (0.742 if female) x (1.210 if black)

where Creatinine is expressed in μmol/L.

Anemia

Anemia is defined as hemoglobin <13g/dL for men and hemoglobin <12g/dL for women.

Tables

Table S1.   Results of falsification analysis with pair-wise comparison

Outcomes	Neither	MI only		MB only		Both	
		Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Falsification							
New diagnosis of cancer	Reference	1.10 (0.86 – 1.40)	0.451	0.84 (0.59 – 1.19)	0.321	1.55 (0.85 – 2.82)	0.154
		Reference		0.76 (0.50 – 1.16)	0.201	1.41 (0.74 – 2.67)	0.293
				Reference		1.85 (0.93 – 3.66)	0.079

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Table S2.   Baseline characteristics of patients after 1:1 propensity score matching.

Characteristics	MI only	MB only	P value	Standardized difference
N	1118	1118		
Female sex	341 (30.5%)	351 (31.4%)	0.65	-0.019
Age, mean (SD)	68.1 (11.1)	68.5 (11.1)	0.41	-0.035
Age >75	694 (62.1%)	718 (64.2%)	0.29	
Tobacco use	454 (40.6%)	427 (38.2%)	0.24	0.049
Diabetes mellitus	508 (45.4%)	515 (46.1%)	0.77	-0.013
Hypertension	865 (77.4%)	861 (77.0%)	0.84	0.009
Dyslipidemia	700 (62.6%)	686 (61.4%)	0.54	0.026
Cerebrovascular disease	162 (14.5%)	161 (14.4%)	0.95	0.003
Chronic obstructive pulmonary disease	39 (3.5%)	35 (3.1%)	0.64	0.020
Peripheral artery disease	36 (3.2%)	40 (3.6%)	0.64	-0.020
Prior myocardial infarction	214 (19.1%)	200 (17.9%)	0.45	0.032
Prior CABG	21 (1.9%)	19 (1.7%)	0.75	0.013
Congestive heart failure	177 (15.8%)	168 (15.0%)	0.60	0.028
Atrial fibrillation or flutter	94 (8.4%)	103 (9.2%)	0.50	-0.028
Chronic kidney disease (eGFR <60ml/min/m2)	416 (37.2%)	435 (38.9%)	0.41	-0.035
Anemia at baseline*	582 (52.1%)	615 (55.0%)	0.16	-0.059
History of cancer	80 (7.2%)	102 (9.1%)	0.089	-0.072
Acute coronary syndrome	916 (81.9%)	898 (80.3%)	0.33	0.041
Number of epicardial arteries affected			0.45	0.052
One vessel	412 (36.9%)	440 (39.4%)		
Two vessels	391 (35.0%)	382 (34.2%)		
Three vessels	315 (28.2%)	296 (26.5%)		
Potent P2Y12 inhibitor on discharge#	96 (8.6%)	94 (8.4%)	0.88	0.006
Anti-coagulation on discharge	57 (5.1%)	83 (7.4%)	0.023	-0.096

Table S3.   Results of sensitivity analysis using multiple imputation with chained equations to handle missing variables.

Outcomes	Neither	MI only		MB only		Both	
		Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Primary							
All-cause mortality	Reference	1.64 (1.46 – 1.83)	<0.001	2.13 (1.90 – 2.40)	<0.001	2.89 (2.38 – 3.51)	<0.001
		Reference		1.30 (1.12 – 1.52)	0.001	1.77 (1.43 – 2.19)	<0.001
				Reference		1.36 (1.10 – 1.68)	0.006
Secondary							
Cardiovascular mortality	Reference	2.12 (1.76 – 2.55)	<0.001	1.86 (1.48 – 2.32)	<0.001	3.52 (2.59 – 4.78)	<0.001
		Reference		0.87 (0.67 – 1.14)	0.330	1.66 (1.18 – 2.32)	0.003
				Reference		1.89 (1.32 – 2.71)	<0.001