SUPPLEMENTAL MATERIAL

SUPPLEMENTAL METHODS

Cohort entry criteria definitions. ACS was defined as a hospitalization with a primary
discharge ICD-9 code for MI (410.xx excluding 410.x2) or unstable angina (411); we
required that the hospitalization last at least three days and no more than 180 days. In
the United States, PCI was defined as an ICD-9 procedure code for coronary stenting
(36.06, 36.07) or angioplasty alone (00.66, 36.09) or an associated CPT-4 code for
coronary stenting (92980, 92981) or angioplasty alone (92973, 92982, 92984, 92995,
92996). In Canada, we identified PCI patients using British Columbia’s CCP codes
48.02, 48.03, and 48.09.

Outcome definitions. The MI outcome was defined as above, with the exception that we
allowed MI to appear in the secondary discharge diagnosis position. We have previously
shown this definition to have a positive predictive value in similar study populations of
94%. For the revascularization (PCI or CABG) outcome, PCI was defined as above. We
defined CABG in PA and NJ as an ICD-9 procedure code of 36.1 or 36.2 or a CPT-4
procedure code of 33510-19, 33531-23, 33530, 33533-36, 33545, or 33572; in BC, it was
defined as a CCP code 48.11-48.15. Death was assessed through vital statistics and
government agencies.

Patient characteristics measured. We assessed drug use in the 365 days prior to the
index event: use of non-selective non-steroidal anti-inflammatory drugs, cox-2 selective
inhibitors, statins, angiotensin converter enzyme inhibitors, angiotensin receptor blockers, beta blockers, warfarin, oral and injectable diabetes medications, and the number of unique medications prescribed. We further assessed specific comorbidities reported in the 365 days prior to the index event: hospitalization for stroke, MI, congestive heart failure, unstable angina/acute coronary syndrome, gastrointestinal bleed, or intracranial hemorrhage; recorded diagnosis of hypertension, diabetes, congestive heart failure, and peripheral vascular disease. We noted intensity of medical service use in the 365 days prior to the index event, including whether the patient had resided in a nursing home, the number of days spent in the hospital, and number of office visits; we also computed a Charlson co-morbidity score. We further measured the length of stay during the care for the index event (1 or more days), whether an MI occurred during that period, and whether a PCI was performed.
**SUPPLEMENTAL TABLE 1.** Association between exposure to clopidogrel with concomitant proton pump inhibitors versus clopidogrel alone after percutaneous coronary interventional or acute coronary syndrome. First exposure is carried forward over for a fixed period of 90 days of follow-up. Rate ratios and 95% confidence intervals were estimated from Cox proportional hazards regression with various methods of covariate adjustment.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>British Columbia (n=10391)</th>
<th>Pennsylvania (n=4176)</th>
<th>New Jersey (n=3998)</th>
<th>Pooled** (n=18565)</th>
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**PRIMARY ENDPOINT**
Myocardial infarction hospitalization or Death

| Number of events (risk) among PPI users | 109 (8.06%) | 112 (8.28%) | 85 (6.58%) | 306 (7.66%) |
| Number of events (risk) among PPI non-users | 468 (5.18%) | 171 (6.06%) | 152 (5.62%) | 791 (5.43%) |

**Unadjusted rate ratio**

| Rate ratio | 1.58 [1.29, 1.95] | 1.39 [1.09, 1.76] | 1.18 [0.90, 1.54] | 1.40 [1.22, 1.61] |

**Age/sex adjusted rate ratio**

| Rate ratio | 1.43 [1.16, 1.76] | 1.40 [1.11, 1.78] | 1.13 [0.87, 1.47] | 1.33 [1.16, 1.53] |

**Multivariate-adjusted rate ratio**

| Rate ratio | 1.11 [0.89, 1.38] | 1.21 [0.95, 1.56] | 0.93 [0.70, 1.22] | 1.10 [0.95, 1.26] |

**Propensity score-adjusted rate ratio**

| Rate ratio | 1.11 [0.89, 1.38] | 1.17 [0.89, 1.54] | 1.02 [0.76, 1.38] | 1.06 [0.91, 1.23] |

* In addition to the covariates noted in Table 1 and in the text, the propensity score included 400 empirically-derived covariates entered the model. PS-adjusted models adjusted for decile of propensity score.

** Pooled hazard ratios are estimated by Cox proportional hazards models stratified by database. Deciles of propensity score were computed within database.