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| --- |
| Supplemental Digital Content 1: ICD-9 and 10-CM codes used to identify patients undergoing major abdominal surgery |
| Procedure | **ICD-9/10-CM Codes** |
| Large bowel resections | 4571, 4572, 4573, 4574, 4575, 4576, 4579, 4581, 4582, 4583, 1731, 1732, 1733, 1734, 1735, 1736, 1739, 0DTE, 0DTF, 0DTG, 0DTH, 0DTK, 0DTL, 0DTM, 0DTN |
| Small bowel resections | 4561, 4562, 4563, 0DT8, 0DT9, 0DTA, 0DTB, 0DTC |
| Gastrectomies | 435, 436, 437, 4381, 4382, 4389, 4391, 4399, 0DT6, 0DT7 |
| Pancreatic resections (Whipple procedures) | 526, 527, 0FTG |
| Nephrectomies | 554, 555, 5551, 5552, 5554, 0TT0, 0TT1, 0TT2 |
| Cystectomies | 576, 577, 5771, 5779, 0TTB |

|  |
| --- |
| Supplemental Digital Content 2: MarketScan® therapeutic class codes used to identify medication dispensing.  |
| Medication | **Therapeutic Class Code** |
| Cardiac Beta-blocker | 50, 51 |
| Diuretics | 120, 121, 122, 123, 124, 125 |
| Angiotensin-converting enzyme inhibitor | 47 |
| Cardiac Glycoside | 58 |
| Calcium Channel Blocker | 52 |
| Anticoagulant | 39, 40, 41 |
| Antiplatelet | 45 |
| Anti-arrhythmic | 49 |
| Antilipidemic | 53 |
| Insulin | 172 |
| Sulfonylurea and other Antidiabetics | 173, 174 |
| Bronchodilator | 216 |
| Thrombolytic | 44 |
| Cardiac Drugs | 46 |
| Hypotensive Agent | 54 |
| Vasodilator | 55 |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Supplemental Digital Content 3: ICD-9/10-CM code and Current Procedural Terminology (CPT) codes used to identify patients with a Myocardial Infarction, Cerebrovascular Event or Cardiac Arrest

|  |  |  |
| --- | --- | --- |
| Event | ICD-9/10-CM Codes | CPT Code Indicating Event |
| Myocardial Infarction | 410, I2I | None |
| Cerebrovascular Event | 435, I63 | None  |
| Cardiac Arrest | 4275, I46 | None |
| Revascularization | None  | 92920, 92921, 92924, 92925, 92929, 92933, 92934, 92937. 92938, 92941, 92943, 92944, 33510, 33511, 35512, 35513, 35514, 35515, 35516, 33533, 33534, 33535, 33536, 33517, 33518, 33519, 33521, 33522, 33523 |

Supplemental Digital Content 4: Current Procedural Terminology (CPT) codes used to identify cardiac testing.  |
| Procedure | **CPT Codes** |
| Stress echocardiography | 93350, 93351, 93355 |
| Other echocardiography  | 93303, 93304, 93306, 93307, 93308, 93312, 93313, 93314, 93315, 93316, 93317, 93318, 93320, 93321, 93325, 93355, 93356  |
| Electrocardiography | 93000, 93005, 93010 |
| Exercise Treadmill or Pharmacological Stress Test | 93015, 93016, 93017, 93018 |
| Myocardial Nuclear Imaging | 78451, 78452, 78453, 78454, 78460, 78461, 78464, 78465, 78472, 78473, 78481, 78483, 78491, 78492 |
| Stress Magnetic Resonance Imaging  | 75559, 75560, 75563, 75564  |
| Percutaneous Coronary Intervention (PCI) | 92920, 92921, 92924, 92925, 92928, 92929, 92933, 92934, 92937, 92938, 92941, 92943, 92944 |
| Heart Catheterization  | 93451, 93452, 93453, 93454, 93455, 93456, 93457, 93458, 93459, 93460, 93461, 93462, 93463, 93464, 93503, 93505  |

**Supplemental Digital Content 5**. Average treatment effect on the treated of preoperative beta blocker therapy initiation within 90 days of surgery compared to beta blocker naïve patients

|  |  |  |
| --- | --- | --- |
| Primary outcomes | Odds Ratio (95% CI) | *P* value  |
| All Major Adverse Cardiac Events | 1.18 (0.90 – 1.55) | 0.091 |
|  All-Cause Mortality | 1.50 (1.01 – 2.22) | 0.011 |
|  Myocardial Infarction | 0.83 (0.56 – 1.22) | 0.771 |
|  Cardiac Arrest | 2.24 (0.98 – 5.10) | 0.069 |
|  Revascularization  | Cannot be computed |  |
| Stroke | 0.88 (0.40 – 1.90) | 0.905 |

Odds Ratios, 95% Confidence intervals, and P-values are reported for each propensity weight analysis of the average effect of treatment on the treated. A *P* value < 0.05 was considered significant. The Mean Standardized Difference before weighting was 0.25, after it was 0.03. Revascularization could not be computed due to insufficient events.

**Supplemental Digital Content 6**. Average treatment effect on the treated of preoperative beta blocker therapy initiation within 180 days of surgery compared to beta blocker naïve patients.

|  |  |  |
| --- | --- | --- |
| Primary outcomes | Odds Ratio (95% CI) | *P* value  |
| All Major Adverse Cardiac Events | 0.89 (0.70 – 1.11) | 0.830 |
|  All-Cause Mortality | 0.93 (0.68 – 1.29) | 0.908 |
|  Myocardial Infarction | 0.87 (0.64 – 1.18) | 0.978 |
|  Cardiac Arrest | 0.69 (0.34 – 1.40) | 0.383 |
|  Revascularization  | Cannot be computed |  |
| Stroke | 0.86 (0.64 – 1.15) | 0.503 |

Odds Ratios, 95% Confidence intervals, and P-values are reported for each propensity weight analysis of the average effect of treatment on the treated. A *P* value < 0.05 was considered significant. The Mean Standardized Difference before weighting was 0.28, after it was 0.03. Revascularization could not be computed due to insufficient events.

**Supplemental Digital Content 7:** *A Priori*Average Treatment Effect on the Treated of Preoperative Beta-Blocker Therapy Initiation within 60 Days of surgery compared to Beta-Blocker naïve patients

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Primary outcomes | Cohort (n = 159,557) Effect Estimate OR (95% CI) | *P* value | Revised Cardiac Risk Index Score of 0 or 1 (n = 155,857) OR (95% CI) | *P* value | Revised Cardiac Risk Index Score of 2 or more (n= 3,700)OR (95% CI) | *P* value |
| All Major Adverse Cardiac Event | 1.00 (0.99 –1.00) | 0.238 | 1.00 (0.99 – 1.00) | 0.163 | 0.99 (0.97 – 1.03) | 0.748 |
| All-Cause Mortality | 1.00 (0.99 – 1.01) | 0.304 | 1.00 (0.99 – 1.01) | 0.261 | 1.00 (0.98 – 1.03) | 0.959 |
| Myocardial Infarction | 0.99 (0.99 - 0.99) | 0.003 | 0.99 (0.99 – 0.99) | 0.002 | 0.99 (0.98 – 1.01) | 0.576 |
| Cardiac Arrest | 1.00 (0.99 - 1.00) | 0.424 | 1.00 (0.99 – 1.00) | 0.355 | 1.00 (0.99 – 1.01) | 0.996 |
| Revascularization | *Cannot be calculated because no patient in 60-day preoperative beta-blocker initiation cohort had a revascularization* |  |
| Stroke | 1.00 (0.99 - 1.00) | 0.265 | 1.00 (0.99 – 1.00) | 0.053 | 1.01 (0.99 – 1.02) | 0.128 |

Odds Ratios, 95% Confidence intervals, and P-values are reported for each propensity weight analysis of the average effect of treatment on the treated. A *P* value < 0.05 was considered significant.

**Supplemental Digital Content 8**: *A Priori* Average Treatment Effect of Treatment on the Treated of Chronic Beta-Blocker Therapy compared to Beta-Blocker naïve patients

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Primary Outcomes | Cohort (n = 200,955) Effect Estimate OR (95% CI) | *P* value | Revised Cardiac Risk Index Score of 0 or 1 (n = 190,942) OR (95% CI) | *P* value | Revised Cardiac Risk Index Score of 2 or more (n = 10,013)OR (95% CI) | *P* value |
| Major Adverse Cardiac Event | 1.01 (0.99 – 1.01) | 0.060 | 1.00 (0.99 – 1.00) | 0.429 | 1.01 (0.99 – 1.03) | 0.182 |
| All-Cause Mortality | 1.00 (1.00 – 1.01) | 0.033 | 1.00 (0.99 – 1.00) | 0.910 | 1.01 (0.99 – 1.02) | 0.097 |
| Myocardial Infarction | 1.00 (0.99 – 1.01) | 0.328 | 1.00 (0.99 – 1.00) | 0.224 | 1.01 (0.99 – 1.02) | 0.445 |
| Cardiac Arrest | 1.00 (0.99 – 1.00) | 0.474 | 1.00 (0.99 – 1.00) | 0.826 | 1.00 (0.99 – 1.00) | 0.345 |
| Revascularization | 1.00 (1.00 – 1.00) | 0.022 | 1.00 (1.00 – 1.00) | 0.129 | 1.00 (0.99 – 1.00) | 0.349 |
| Stroke | 1.00 (0.99 – 1.001) | 0.919 | 1.00 (0.99 – 1.00) | 0.955 | 1.00 (0.99 – 1.00) | 0.558 |

Odds Ratios, 95% Confidence intervals, and P-values are reported for each propensity weight analysis of the average effect of treatment on the treated. A *P* value < 0.05 was considered significant.

**Supplemental Digital Content 9**:Table of Absolute Standardized Difference Scores of Covariates of the *a Priori*Analysis before and after Inverse Probability of Treatment Weighting of the Propensity Scores for Characteristics of Beta Blocker Naïve Patients and Subjects on 60 Day Preoperative Beta Blocker Therapy

|  |  |  |
| --- | --- | --- |
|  | Study Patients, (Percentage %)  |  |
| Variable | **No Beta Blocker Dispensing****(n = 155,531)** | **Preoperative Beta Blocker Initiation within 60 Days of Surgery** **(n = 4,026)**  | **Standardized Difference before Weighting Adjustment** | **Standardized Difference after Weighting Adjustment** |
| Logit Propensity Score | - | - | 1.08 | 0.08 |
| Sex |  |  |  |  |
|  Male | 69,165 (44.5%) | 2,248 (55.8%) | 0.23 | 0.00 |
|  Female | 86,366 (55.5%) | 1,778 (44.2%) |
| Age Group, years |  |  |  |  |
|  18-49 years | 51,092 (32.9%) | 583 (14.5%) | 0.44 | 0.08 |
|  50-64 years | 70,152 (45.1%) | 1,888 (46.9%) | -0.04 | 0.03 |
|  65-74 years | 18,552 (11.9%) | 759 (18.9%) | -0.19 | -0.06 |
|  ≥ 75 years | 15,735 (10.1%) | 796 (19.8%)  | -0.27 | -0.06 |
| Year  |  |  |  |  |
|  2005 | 10,545 (6.8%) | 376 (9.3%) | -0.09 | -0.02 |
|  2006 | 8,948 (5.8%) | 331 (8.2%) | -0.10 | 0.00 |
|  2007 | 9,005 (5.8%) | 376 (9.3%) | -0.13 | 0.00 |
|  2008 | 8,759 (5.6%) | 371 (9.2%) | -0.14 | 0.01 |
|  2009 | 11,954 (7.7%) | 321 (8.0%) | -0.01 | 0.01 |
|  2010 | 13,293 (8.6%) | 337 (8.4%) | 0.01 | -0.03 |
|  2011 | 18,500 (11.9%) | 500 (12.4%) | -0.02 | -0.01 |
|  2012 | 20,962 (13.5%) | 441 (11.0%) | 0.08 | -0.01 |
|  2013 | 19,022 (12.2%) | 335 (8.3%) | 0.13 | 0.00 |
|  2014 | 21,137 (13.6%) | 440 (10.9%) | 0.08 | 0.01 |
|  2015 | 13,406 (8.7%) | 198 (4.92%) | 0.15 | 0.05 |
| Procedure type |  |  |  |  |
|  Small bowel  resection | 8,840 (5.7%) | 166 (4.1%) | 0.07 | 0.02 |
|  Large bowel  resection | 80,626 (51.8%) | 1,949 (48.4%) | 0.07 | 0.04 |
|  Pancreatic  resection | 3,616 (2.32%) | 144 (3.58%) | -0.07 | 0.00 |
|  Gastrectomy | 34,813 (22.4%) | 547 (13.6%) | 0.23 | -0.03 |
|  Cystectomy | 4,186 (2.7%) | 231 (5.7%) | -0.15 | -0.01 |
|  Nephrectomy | 23,450 (15.1%) | 929 (24.57%) | -0.24 | -0.03 |
| Metropolitan Statistical Area Quintile of Beta-blocker Dispensing |  |
|  First Quintile  | 4,396 (2.8%) | 9 (0.2%) | 0.21 | 0.05 |
|  Second Quintile | 19,738 (12.7%) | 274 (6.8%) | 0.20 | 0.03 |
|  Third Quintile | 74,026 (47.6%) | 1,696 (42.1%) | 0.11 | 0.01 |
|  Fourth Quintile | 40,303 (25.9%) | 1,215 (30.2%) | -0.10 | -0.03 |
|  Fifth quintile | 17,068 (11.0%) | 832 (20.7%) | -0.27 | -0.02 |
| Region |  |  |  |  |
|  North  Central | 41,988 (27.0%) | 1,344 (33.4%) | -0.14 | -0.01 |
|  Northeast | 22,895 (14.7%) | 671 (16.7%) | -0.05 | -0.00 |
|  South | 62,309 (40.1%) | 1,337 (33.2%) | 0.14 | 0.02 |
|  West | 27,154 (17.5%) | 657 (16.3%) | 0.03 | -0.01 |
|  Unknown/  Missing | 1,185 (0.8%) | 17 (0.4%) | 0.04 | 0.02 |
| Comorbidities |  |  |  |  |
|  Insulin Dependent Diabetes Mellitus | 5,163 (3.3%) | 275 (6.8%) | -0.16 | -0.06 |
|  Cerebrovascular accident | 4,122 (2.7%) | 274 (6.8%) | -0.20 | -0.04 |
|  Chronic Kidney Disease | 2,897 (1.9%) | 199 (4.9%) | -0.17 | -0.03 |
|  Coronary Artery Disease | 8,518 (5.5%) | 805 (20.0%) | -0.45 | -0.06 |
|  Heart Failure | 2,915 (1.9%) | 298 (7.4%) | -0.27 | -0.04 |
|  Valve Pathology | 8,316 (5.4%) | 538 (13.4%) | -0.28 | -0.04 |
| Perioperative Medications (within 60 days) |  |
|  Diuretic | 12,736 (8.2%) | 699 (17.4%) | -0.28 | -0.04 |
|  Angiotensin Converting Enzyme Inhibitor | 16,780 (10.8%) | 860 (21.4%) | -0.29 | -0.05 |
|  Cardiac Glycoside | 659 (0.4%) | 91 (2.3%) | -0.16 | -0.03 |
|  Calcium Channel  Inhibitor | 13,020 (8.4%) | 689 (17.1%) | -0.26 | -0.09 |
|  Anticoagulant  | 5,056 (3.3%) | 223 (5.8%) | -0.12 | -0.013 |
|  Anti-Platelet | 1,541 (1.0%) | 289 (4.7%) | -0.22 | -0.01 |
|  Anti-arrhythmic | 532 (0.3%) | 79 (2.0%) | -0.15 | -0.01 |
|  Anti-Lipidemic/  Statin | 26,641 (17.1%) | 1,330 (33.0%) | -0.37 | -0.04 |
|  Insulin | 3,281 (2.1%) | 223 (5.54%) | -0.18 | -0.03 |
|  Anti-diabetic | 12,496 (8.0%) | 575 (14.3%) | -0.20 | -0.05 |
|  Bronchodilator  | 225 (0.1%) | 5 (0.1%) | 0.01 | -0.03 |
|  Thrombolytic | 3 (0.0%) | 0 (0.0%) | Not included in analysis  | - |
|  Cardiac Drugs | 12,119 (7.79%) | 527 (13.1%) | -0.17 | -0.03 |
|  Hypotensive  Medication | 2,401 (1.5%) | 207 (5.15) | -0.20 | -0.03 |
|  Vasodilator | 759 (0.5%) | 178 (4.4%) | -0.26 | -0.00 |
| Existing Medications (within 365 days) |  |  |
|  Diuretic | 21,712 (14.0%) | 798 (19.8%) | -0.16 | -0.15 |
|  Angiotensin Converting Enzyme Inhibitor | 25,311 (16.3%) | 1,013 (25.2%) | -0.22 | -0.12 |
|  Cardiac Glycoside | 944 (0.6%) | 80 (2.0%) | -0.12 | -0.08 |
|  Calcium Channel  Inhibitor | 18,333 (11.8%) | 779 (19.4%) | -0.21 | -0.16 |
|  Anticoagulant  | 5,189 (3.3%) | 201 (5.0%) | -0.08 | -0.06 |
|  Anti-Platelet | 2,806 (1.8%) | 202 (5.0%) | -0.18 | -0.11 |
|  Anti-arrhythmic | 847 (0.5%) | 53 (1.3%) | -0.08 | -0.06 |
|  Anti-Lipidemic/  Statin | 41,708 (26.8%) | 1,552 (38.6%) | -0.25 | -0.14 |
|  Insulin | 4,767 (3.1%) | 219 (5.4%) | -0.12 | -0.06 |
|  Anti-diabetic | 18,369 (11.8%) | 728 (18.1%) | -0.18 | -0.09 |
|  Bronchodilator  | 404 (0.3%) | 8 (0.2%) | 0.01 | 0.00 |
|  Thrombolytic | 2 (0.0%) | 0 (0.0%) | Not included in analysis  | - |
|  Cardiac Drugs | 17,565 (11.3%) | 654 (16.2%) | -0.14 | -0.09 |
|  Hypotensive  Medication | 3,885 (2.5%) | 226 (5.6%) | -0.16 | -0.06 |
|  Vasodilator | 1,722 (1.1%) | 129 (3.2%) | -0.14 | -0.08 |
| Cardiac Testing (within 60 days) |  |  |
|  Stress echocardiography | 2,248 (1.5%) | 179 (4.5%) | -0.18 | -0.03 |
|  Other echocardiography  | 8,916 (5.7%) | 935 (23.2%) | -0.51 | -0.05 |
|  ECG  | 77,371 (49.8%) | 2,706 (67.2%) | -0.36 | -0.07 |
|  Exercise  Treadmill or  Pharmacological  Stress Test | 8,949 (5.8%) | 974 (24.2%) | -0.53 | -0.05 |
|  Myocardial  Nuclear Imaging | 6,303 (4.1%) | 791 (19.7%) | -0.50 | -0.04 |
|  Stress Magnetic Resonance Imaging | 7 (0.0%) | 0 (0.0%) | Not included in analysis  | - |
|  Percutaneous  Coronary  Intervention  (PCI) | 8 (0.0%) | 5 (0.1%) | -0.05 | 0.00 |
|  Heart  Catheterization  | 277 (0.2%) | 104 (2.6%) | -0.21 | 0.00 |
| Cardiac Testing (within 365 days) |  |  |
|  Stress echocardiography | 2,391 (1.5%) | 56 (1.4%) | 0.01 | 0.00 |
|  Other echocardiography  | 12,118 (7.8%) | 437 (10.9%) | -0.11 | -0.06 |
|  ECG  | 48,233 (31.0%) | 1,431 (35.5%) | -0.10 | -0.10 |
|  Exercise  Treadmill or  Pharmacological  Stress Test | 9,397 (6.0%) | 348 (8.6%) | -0.10 | -0.07 |
|  Myocardial  Nuclear Imaging | 6.621 (4.3%) | 307 (7.6%) | -0.14 | -0.03 |
|  Stress Magnetic Resonance Imaging  | 6 (0.0%) | 1 (0.0%) | -0.02 | 0.00 |
|  Percutaneous  Coronary  Intervention  (PCI) | 15 (0.0%) | 1 (0.0%) | -0.01 | 0.00 |
|  Heart  Catheterization  | 456 (0.3%) | 25 (0.6%) | -0.05 | -0.06 |

**Supplemental Digital Content 10:** Table of Absolute Standardized Difference Scores of Covariates of the *a Priori*Analysis before and after Inverse Probability of Treatment Weighting of the Propensity Scores for Characteristics of Beta Blocker Naïve Patients and Patients on Chronic Beta Blocker Therapy

|  |  |  |
| --- | --- | --- |
|  | Study Patients, (Percentage %) |  |
| Variable | **No Beta Blocker Dispensing****(n = 155,531)** | **Chronic Beta Blocker Dispensing****(n = 45,424)** | **Standardized Difference before Weighting Adjustment** | **Standardized Difference after Weighting Adjustment** |
| Logit Propensity Score | - | - | 1.19 | 0.01 |
| Sex |  |  |  |  |
|  Male | 69,165 (44.5%) | 23,060 (50.8%)  | 0.12 | 0.03 |
|  Female | 86,366 (55.5%) | 22,364 (49.2%) |
| Age Group, years |  |  |  |  |
|  18-49 years | 51,092 (32.9%) | 5,852 (12.9%) | 0.49 | 0.03 |
|  50-64 years | 70,152 (45.1%) | 19,233 (42.3%) | 0.06 | 0.02 |
|  65-74 years | 18,552 (11.9%) | 9,704 (21.4%) | 0.26 | 0.02 |
|  ≥ 75 years | 15,735 (10.1%) | 10,605 (23.4%) | 0.45 | 0.04 |
| Year  |  |  |  |  |
|  2005 | 10,545 (6.8%) | 3,592 (7.9%) | 0.04 | 0.01 |
|  2006 | 8,948 (5.8%) | 3.038 (6.7%) | 0.04 | 0.00 |
|  2007 | 9,005 (5.8%) | 3,095 (6.8%) | 0.04 | 0.00 |
|  2008 | 8,759 (5.6%) | 3,075 (6.8%) | 0.04 | 0.00 |
|  2009 | 11,954 (7.7%) | 3,739 (8.2%) | 0.02 | 0.00 |
|  2010 | 13,293 (8.6%) | 3,869 (8.5%) | 0.00 | 0.01 |
|  2011 | 18,500 (11.9%) | 5,185 (11.4%) | 0.01 | 0.00 |
|  2012 | 20,962 (13.5%) | 5,540 (12.2%) | 0.04 | 0.01 |
|  2013 | 19,022 (12.2%) | 5,256 (11.6%) | 0.02 | 0.00 |
|  2014 | 21,137 (13.6%) | 5,450 (12.0%) | 0.05 | 0.01 |
|  2015 | 13,406 (8.7%) | 3,585 (7.9%) | 0.03 | 0.00 |
| Procedure type |  |  |  |  |
|  Small bowel  resection | 8,840 (5.7%) | 2,701 (6.0%) | 0.02 | 0.01 |
|  Large bowel  resection | 80,626 (51.8%) | 22,543 (49.6%) | 0.04 | 0.02 |
|  Pancreatic  resection | 3,616 (2.32%) | 1,100 (2.42%) | 0.00 | 0.00 |
|  Gastrectomy | 34,813 (22.4%) | 8,043 (17.7%) | 0.12 | 0.03 |
|  Cystectomy | 4,186 (2.7%) | 1,781 (3.9%) | 0.07 | 0.00 |
|  Nephrectomy | 23,450 (15.1%) | 9,256 (20.4%) | 0.14 | 0.00 |
| Metropolitan Statistical Area Quintile of Beta-blocker Dispensing |  |
|  First Quintile  | 4,396 (2.8%) | 1,172 (2.6%) | 0.02 | 0.00 |
|  Second Quintile | 19,738 (12.7%) | 5,182 (11.4%) | 0.04 | 0.00 |
|  Third Quintile | 74,026 (47.6%) | 21,082 (46.4%) | 0.02 | 0.00 |
|  Fourth Quintile | 40,303 (25.9%) | 12.298 (27.1%) | 0.03 | 0.00 |
|  Fifth quintile | 17,068 (11.0%) | 5.690 (22.6%) | 0.05 | 0.00 |
| Region |  |  |  |  |
|  North  Central | 41,988 (27.0%) | 14,808 (32.6%) | 0.12 | 0.00 |
|  Northeast | 22,895 (14.7%) | 6,634 (14.6%) | 0.00 | 0.00 |
|  South | 62,309 (40.1%) | 16,306 (35.9%) | 0.09 | 0.00 |
|  West | 27,154 (17.5%) | 7,412 (16.3%) | 0.03 | 0.00 |
|  Unknown/  Missing | 1,185 (0.8%) | 264 (0.6%) | 0.02 | 0.00 |
| Comorbidities |  |  |  |  |
|  Insulin Dependent Diabetes Mellitus | 5,163 (3.3%) | 4,049 (8.9%) | 0.24 | 0.01 |
|  Cerebrovascular accident | 4,122 (2.7%) | 3,562 (7.8%) | 0.23 | 0.01 |
|  Chronic Kidney Disease | 2,897 (1.9%) | 3,430 (7.6%) | 0.27 | 0.02 |
|  Coronary Artery Disease | 8,518 (5.5%) | 12,467 (27.5%) | 0.62 | 0.04 |
|  Heart Failure | 2,915 (1.9%) | 5,043 (11.1%) | 0.38 | 0.05 |
|  Valve Pathology | 8,316 (5.4%) | 6,298 (13.9%) | 0.30 | 0.01 |
| Perioperative Medications (within 60 days) |  |
|  Diuretic | 12,736 (8.2%) | 10,059 (22.1%) | -0.40 | -0.02 |
|  Angiotensin Converting Enzyme Inhibitor | 16,780 (10.8%) | 9,454 (20.8%) | -0.28 | -0.02 |
|  Cardiac Glycoside | 659 (0.4%) | 1,255 (2.8%) | -0.32 | -0.01 |
|  Calcium Channel  Inhibitor | 13,020 (8.4%) | 8,642 (19.0%) | -0.31 | -0.03 |
|  Anticoagulant  | 5,056 (3.3%) | 3,841 (8.5%) | -0.22 | -0.01 |
|  Anti-Platelet | 1,541 (1.0%) | 3,432 (7.6%) | -0.33 | -0.03 |
|  Anti-arrhythmic | 532 (0.3%) | 967 (2.1%) | -0.16 | -0.02 |
|  Anti-Lipidemic/  Statin | 26,641 (17.1%) | 17,780 (39.1%) | -0.50 | -0.02 |
|  Insulin | 3,281 (2.1%) | 2,633 (5.8%) | -0.19 | -0.01 |
|  Anti-diabetic | 12,496 (8.0%) | 7,281 (16.0%) | -0.25 | -0.02 |
|  Bronchodilator  | 225 (0.1%) | 74 (0.2%) | 0.00 | 0.00 |
|  Thrombolytic | 3 (0.0%) | 0 (0.0%) | Not included in analysis  | - |
|  Cardiac Drugs | 12,119 (7.79%) | 7,180 (15.8%) | -0.25 | -0.02 |
|  Hypotensive  Medication | 2,401 (1.5%) | 2,820 (6.2%) | -0.24 | -0.01 |
|  Vasodilator | 759 (0.5%) | 2,060 (4.5%) | -0.37 | -0.03 |
| Existing Medications (within 365 days) |  |  |
|  Diuretic | 21,712 (14.0%) | 17,053 (37.5%) | -0.56 | -0.02 |
|  Angiotensin Converting Enzyme Inhibitor | 25,311 (16.3%) | 15,447 (34.0%) | -0.42 | -0.03 |
|  Cardiac Glycoside | 944 (0.6%) | 2,046 (4.5%) | -0.25 | -0.05 |
|  Calcium Channel  Inhibitor | 18,333 (11.8%) | 13,406 (29.5%) | -0.45 | -0.02 |
|  Anticoagulant  | 5,189 (3.3%) | 5,568 (12.3%) | -0.33 | -0.03 |
|  Anti-Platelet | 2,806 (1.8%) | 6,079 (13.4%) | -0.45 | -0.05 |
|  Anti-arrhythmic | 847 (0.5%) | 1,686 (3.7%) | -0.22 | -0.03 |
|  Anti-Lipidemic/  Statin | 41,708 (26.8%) | 27,142 (59.8%) | -0.70 | -0.03 |
|  Insulin | 4,767 (3.1%) | 3,851 (8.5%) | -0.23 | -0.01 |
|  Anti-diabetic | 18,369 (11.8%) | 10,642 (23.4%) | -0.31 | -0.02 |
|  Bronchodilator  | 404 (0.3%) | 139 (0.3%) | -0.01 | -0.02 |
|  Thrombolytic | 2 (0.0%) | 1 (0.0%) | - | - |
|  Cardiac Drugs | 17,565 (11.3%) | 11,128 (24.5%) | -0.35 | -0.02 |
|  Hypotensive  Medication | 3,885 (2.5%) | 4,523 (10.0%) | -0.31 | -0.02 |
|  Vasodilator | 1,722 (1.1%) | 4,696 (10.3%) | -0.41 | -0.05 |
| Cardiac Testing (within 60 days) |  |  |
|  Stress echocardiography | 2,248 (1.5%) | 923 (2.0%) | -0.05 | -0.01 |
|  Other echocardiography  | 8,916 (5.7%) | 4,751 (10.5%) | -0.17 | -0.00 |
|  ECG  | 77,371 (49.8%) | 26,046 (57.3%) | -0.15 | -0.02 |
|  Exercise  Treadmill or  Pharmacological  Stress Test | 8,949 (5.8%) | 5,367 (11.8%) | -0.05 | -0.01 |
|  Myocardial  Nuclear Imaging | 6,303 (4.1%) | 4,627 (10.25) | -0.24 | 0.00 |
|  Stress Magnetic Resonance Imaging | 7 (0.0%) | 4 (0.0%) | 0.00 | 0.00 |
|  Percutaneous  Coronary  Intervention  (PCI) | 8 (0.0%) | 21 (0.15) | -0.03 | 0.00 |
|  Heart  Catheterization  | 277 (0.2%) | 336 (0.7%) | -0.08 | 0.00 |
| Cardiac Testing (within 365 days) |  |  |
|  Stress echocardiography | 2,391 (1.5%) | 1,215 (2.7%) | -0.08 | -0.01 |
|  Other echocardiography  | 12,118 (7.8%) | 9,479 (20.9%) | -0.38 | -0.01 |
|  ECG  | 48,233 (31.0%) | 23,099 (50.9%) | -0.41 | -0.02 |
|  Exercise  Treadmill or  Pharmacological  Stress Test | 9,397 (6.0%) | 7,309 (16.1%) | -0.10 | -0.07 |
|  Myocardial  Nuclear Imaging | 6.621 (4.3%) | 6,342 (14.0%) | -0.34 | -0.01 |
|  Stress Magnetic Resonance Imaging  | 6 (0.0%) | 10 (0.0%) | -0.02 | 0.00 |
|  Percutaneous  Coronary  Intervention  (PCI) | 15 (0.0%) | 70 (0.2%) | -0.05 | 0.00 |
|  Heart  Catheterization  | 456 (0.3%) | 901 (2.05) | -0.16 | -0.03 |

**Supplemental Digital Content 11:** *A Priori*Average Effect of Treatment on the Treated of Preoperative Beta-Blocker Therapy Initiation within 90 Days of Surgery compared to beta-blocker naïve patients

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Primary outcomes** | **Cohort** **(n = 160,851) Effect** **Estimate OR (95% CI)** | ***P* value** | **Revised Cardiac Risk Index Score of 0 or 1 (n = 156,979)** **OR (95% CI)** | ***P* value** | **Revised Cardiac Risk Index Score of 2 or more (n= 3,872)****OR (95% CI)** | ***P* value** |
| **Major Adverse Cardiac Events** | 1.00 (0.99 – 1.00) | 0.497 | 1.00 (0.99 – 1.00) | 0.261 | 1.00 (0.97 – 1.02) | 0.748 |
| **All-Cause Mortality** | 1.00 (0.99 – 1.01) | 0.224 | 1.00 (0.99 – 1.00) | 0.241 | 1.00 (0.98 – 1.02) | 0.947 |
| **Myocardial Infarction** | 0.99 (0.99 – 0.99) | 0.012 | 0.99 (0.99 – 0.99) | 0.003 | 0.99 (0.98 – 1.01) | 0.807 |
| **Cardiac Arrest** | 1.00 (0.99 – 1.00) | 0.352 | 1.00 (0.99 – 1.00) | 0.161 | 1.00 (0.99 – 1.01) | 0.912 |
| **Revascularization** | *Cannot be calculated because sample size of patients with revascularization is too small.*  |  |
| **Stroke** | 1.00 (0.99 – 1.00) | 0.415 | 1.00 (0.99 – 1.00) | 0.072 | 1.00 (0.99 – 1.01) | 0.208 |

Odds Ratios, 95% Confidence intervals, and P-values are reported for each propensity weight analysis of the average effect of treatment on the treatment estimates. A *P* value < 0.05 was considered significant.

**Supplemental Digital Content 12**: *A Priori*Average Effect of Treatment on the Treated of Preoperative Beta-Blocker Therapy Initiation within 180 days of Surgery compared to beta-blocker naïve patients

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Primary outcomes** | **Cohort** **(n = 164,529) Effect** **Estimate OR (95% CI)** | ***P* value** | **Revised Cardiac Risk Index Score of 0 or 1 (n = 160,111)** **OR (95% CI)** | ***P* value** | **Revised Cardiac Risk Index Score of 2 or more (n= 4,418)****OR (95% CI)** | ***P* value** |
| **Major Adverse Cardiac Events** | 1.00 (0.99 – 1.01) | 0.615 | 1.00 (0.99 – 1.00) | 0.142 | 1.01 (0.99 – 1.03) | 0.187 |
| **All-Cause Mortality** | 1.00 (1.00 – 1.01) | 0.093 | 1.00 (0.99 – 1.00) | 0.686 | 1.01 (0.99 – 1.02) | 0.136 |
| **Myocardial Infarction** | 1.00 (0.99 – 1.00) | 0.542 | 0.99 (0.99 – 0.99) | 0.008 | 1.01 (0.99 – 1.02) | 0.410 |
| **Cardiac Arrest** | 1.00 (0.99 – 1.00) | 0.897 | 1.00 (0.99 – 1.00) | 0.718 | 1.00 (0.99 – 1.01) | 0.966 |
| **Revascularization** | *Cannot be calculated because sample size of patients with revascularization is too small.*  |  |
| **Stroke** | 1.00 (0.99 – 1.00) | 0.381 | 1.00 (0.99 – 1.00) | 0.066 | 1.00 (0.99 – 1.01) | 0.466 |

Odds Ratios, 95% Confidence intervals, and P-values are reported for each propensity weight analysis of the average effect of treatment on the treatment estimates. A *P* value ≤ 0.05 was considered significant.