Supplementary Table 1. Definitions of cardiovascular events

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Cardiovascular Event | ICD-9-CM/ 10-CM diagnosis codes | ICD-9-CM/ 10-CM procedure or CPT-4 codes | Description | Additional Restriction | PPV |
| Primary events | | | | | |
| Acute myocardial infarction1,2 | ICD-9: 410.x1  ICD-10: I21.0-I21.4, I22.0-I22.2, I22.8, I22.9. |  | Acute MI – restriction to 5th digit of 1 restricts to the initial episode of care (distinguish from prior MI) | Require hospitalization with length of stay 2-180 days, or death if LOS is <2 days or died in the emergency department | 94% |
| Ischemic Stroke2-4 | ICD-9: 433.x1, 434.x1  ICD-10: I63.0-I63.6, I63.8, I639 |  | Restriction to 5th digit of 1 necessary to identify “with cerebral infarction” | Require hospitalization with length of stay 2-180 days, or death if LOS is <2 days or died in ED | 94-96% |
| Coronary artery bypass graft5 |  | ICD-9: 36.1x  ICD-10: 02100\*, 021048\*, 021049\*, 02104A\*, 02104J\*, 02104K\*, 02104Z\*  02110\*, 021148\*, 021149\*, 02114A\*, 02114J\*, 02114K\*, 02114Z\*,  02120\*, 021248\*, 021249\*, 02124A\*, 02124J\*, 02124K\*, 02124Z\*,  02130\*, 021348\*, 021349\*, 02134A\*, 02134J\*, 02134K\*, 02134Z\*  CPT 33510-33523, 33533-33536 |  | Require hospitalization | 95% (ICD9 codes) |
| Percutaneous coronary intervention6,7 |  | ICD-9: 00.66, 36.03, 36.06, 36.07, 36.09  ICD-10: 0270\*, 0271\*, 0272\*, 0273\*, 02C0\*, 02C1\*, 02C2\*, 02C3\*  CPT 92973, 92980–92984, 92995, 92996, G0290, G0291  New CPT codes (as of 2013) 92920-92944 |  | Either in hospital or as an observation stay |  |
| PPV, positive predictive value; MI, myocardial infarction; LOS, length of stay; TIA, transient ischemic attack; ED, emergency department; INP, inpatient; OP, outpatient | | | | | |

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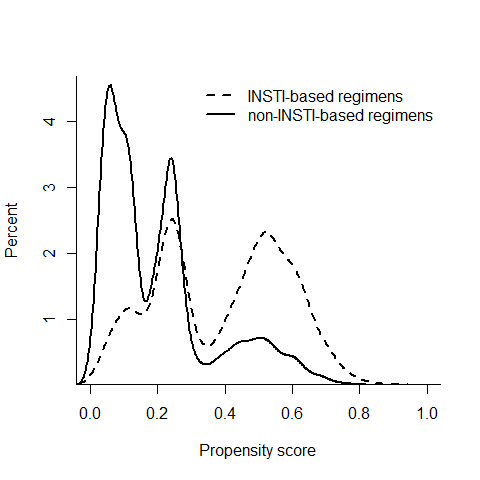
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Supplementary Table 2. Definitions of covariates

|  |  |
| --- | --- |
| **Covariate** | **Definition of covariate** |
| Atrial fibrillation | Diagnosis indicating atrial fibrillation prior to the start of the first stable regimen |
| Age | Age at start of first stable regimen (AGE for MarketScan CCAE and YEAR - DOBYR for MarketScan Multi-State Medicaid) |
| Arterial embolism | Diagnosis indicating arterial embolism prior to the start of the first stable regimen |
| Congestive cardiac failure | Diagnosis of CHF or prescription drug claim for loop diuretic prior to the start of the first stable regimen |
| Diabetes | Diagnosis of diabetes or prescription drug claim for anti-diabetic to the start of the first stable regimen |
| Smoking | Any of diagnosis of tobacco use, diagnosis of smoking-related disease, or prescription drug claim for nicotine replacement therapy prior to the start of the first stable regimen |
| Deep vein thrombosis | Diagnosis indicating deep vein thrombosis prior to the start of the first stable regimen |
| Alcohol abuse | Alcohol abuse (Elixhauser definition) |
| Deficiency anemias | Deficiency anemias (Elixhauser definition) |
| Rheumatoid arthritis/collagen vascular disease | Rheumatoid arthritis/collagen vascular disease (Elixhauser definition) |
| Chronic blood loss anemia | Chronic blood loss anemia (Elixhauser definition) |
| Chronic pulmonary disease | Chronic pulmonary disease (Elixhauser definition) |
| Coagulopathy | Coagulopathy (Elixhauser definition) |
| Depression | Depression (Elixhauser definition) |
| Drug abuse | Drug abuse (Elixhauser definition) |
| Hypertension (complicated) | Hypertension (complicated) (Elixhauser definition) |
| Hypertension (uncomplicated) | Hypertension (uncomplicated) (Elixhauser definition) |
| Hypothyroidism | Hypothyroidism (Elixhauser definition) |
| Liver disease | Liver disease (Elixhauser definition) |
| Lymphoma | Lymphoma (Elixhauser definition) |
| Fluid and electrolyte disorders | Fluid and electrolyte disorders (Elixhauser definition) |
| Metastatic cancer | Metastatic cancer (Elixhauser definition) |
| Other neurological disorders | Other neurological disorders (Elixhauser definition) |
| Obesity | Obesity (Elixhauser definition) |
| Paralysis | Paralysis (Elixhauser definition) |
| Peripheral vascular disease | Peripheral vascular disease (Elixhauser definition) |
| Psychoses | Psychoses (Elixhauser definition) |
| Pulmonary circulation disease | Pulmonary circulation disease (Elixhauser definition) |
| Renal failure | Renal failure (Elixhauser definition) |
| Solid tumor without metastasis | Solid tumor (Elixhauser definition) |
| Valvular disease | Valvular disease (Elixhauser definition) |
| Weight loss | Weight loss (Elixhauser definition) |
| Female patient | Female |
| Gastroesophageal reflux disease | Diagnosis indicating gastroesophageal reflux disease prior to the start of the first stable regimen |
| Hepatitis B | Diagnosis indicating hepatitis B prior to the start of the first stable regimen |
| Hepatitis C | Diagnosis indicating hepatitis C prior to the start of the first stable regimen |
| Infectious diseases consult in the proceeding 90 days | Patient was treated by an infectious diseases provider in the 90 days before the start of the first stable regimen |
| Lipid abnormality | Prescription claim for statin or other lipid-lowering drug or diagnosis of other lipidemias prior to the start of the first stable regimen |
| Lipodystrophy | Diagnosis indicating lipodystrophy prior to the start of the first stable regimen |
| Medicaid | Medicaid coverage |
| Pulmonary embolism | Diagnosis indicating pulmonary embolism prior to the start of the first stable regimen |
| Alpha-beta blocker therapy | Prescription claim for alpha-beta blocker prior to the start of the first stable regimen |
| ACE inhibitor therapy | Prescription claim for ACE inhibitor prior to the start of the first stable regimen |
| Aldosterone antagonist therapy | Prescription claim for aldosterone antagonist prior to the start of the first stable regimen |
| Angiotensin blocker therapy | Prescription claim for angiotensin blocker prior to the start of the first stable regimen |
| Antiarrhythmic therapy | Prescription claim for antiarrhythmic agent prior to the start of the first stable regimen |
| Anticoagulant therapy | Prescription claim for anticoagulant prior to the start of the first stable regimen |
| Beta blocker therapy | Prescription claim for beta blocker prior to the start of the first stable regimen |
| Calcium channel blocker therapy | Prescription claim for calcium channel blocker prior to the start of the first stable regimen |
| Cardiac glucoside therapy | Prescription claim for cardiac glycoside prior to the start of the first stable regimen |
| Hypotensive agent therapy | Prescription claim for anti-hypotensive agent prior to the start of the first stable regimen |
| Nitrate therapy | Prescription claim for nitrates prior to the start of the first stable regimen |
| Non-steroidal anti-inflammatory therapy | Prescription claim for non-steroidal anti-inflammatory drug prior to the start of the first stable regimen |
| Renin inhibitor therapy | Prescription claim for renin inhibitor prior to the start of the first stable regimen |
| Vasodilator therapy | Prescription claim for vaso-dilating agent prior to the start of the first stable regimen |
| Sickle cell disease | Diagnosis indicating sickle cell disease during the six months prior to the start of the first stable regimen |
| Sleep apnea | Diagnosis indicating sleep apnea prior to the start of the first stable regimen |
| Year | Year treatment initiated |
| Abacavir use | Abacavir included as a component of initial regimen |

Supplementary figure 1. Propensity score distributions



Supplementary table 3. Variables potentially associated with MACE events used in the inverse-weighted propensity score model.

|  |  |  |
| --- | --- | --- |
| **Propensity Score Variable** | **Standardized Difference, Unweighted** | **Standardized Difference, Weighted** |
| Atrial fibrillation | 0.003 | 0.003 |
| Age | 0.003 | 0.003 |
| Arterial embolism | 0.006 | 0.006 |
| Congestive cardiac failure\* | 0.016 | 0.016 |
| Diabetes# | 0.012 | 0.012 |
| Smoking¥ | 0.024 | 0.024 |
| Deep vein thrombosis | 0.013 | 0.013 |
| Alcohol abuse | 0.015 | 0.015 |
| Deficiency anemias | 0.004 | 0.004 |
| Rheumatoid arthritis/collagen vascular disease | 0.006 | 0.006 |
| Chronic blood loss anemia | 0.005 | 0.005 |
| Chronic pulmonary disease | 0.002 | 0.002 |
| Coagulopathy | 0.008 | 0.008 |
| Depression | 0.009 | 0.009 |
| Drug abuse | 0.005 | 0.005 |
| Hypertension (uncomplicated or complicated) | 0.002 | 0.002 |
| Hypothyroidism | 0.007 | 0.007 |
| Liver disease | 0.010 | 0.010 |
| Lymphoma | 0.002 | 0.002 |
| Fluid and electrolyte disorders | 0.013 | 0.013 |
| Metastatic cancer | 0.002 | 0.002 |
| Other neurological disorders | 0.010 | 0.010 |
| Obesity | 0.009 | 0.009 |
| Paralysis | 0.020 | 0.020 |
| Peripheral vascular disease | 0.007 | 0.007 |
| Psychoses | 0.000 | 0.000 |
| Pulmonary circulation disease | 0.008 | 0.008 |
| Renal failure | 0.005 | 0.005 |
| Solid tumor without metastasis | 0.002 | 0.002 |
| Valvular disease | 0.005 | 0.005 |
| Weight loss | 0.004 | 0.004 |
| Female patient | 0.013 | 0.013 |
| Gastroesophageal reflux disease | 0.005 | 0.005 |
| Hepatitis B | 0.013 | 0.013 |
| Hepatitis C | 0.009 | 0.009 |
| Infectious diseases consult in the proceeding 90 days | 0.014 | 0.014 |
| Lipid abnormality± | 0.021 | 0.021 |
| Lipodystrophy | 0.020 | 0.020 |
| Medicaid | 0.003 | 0.003 |
| Pulmonary embolism | 0.005 | 0.005 |
| Alpha-beta blocker therapy | 0.000 | 0.000 |
| ACE inhibitor therapy | 0.014 | 0.014 |
| Aldosterone antagonist therapy | 0.015 | 0.015 |
| Angiotensin blocker therapy | 0.015 | 0.015 |
| Antiarrhythmic therapy | 0.014 | 0.014 |
| Anticoagulant therapy | 0.014 | 0.014 |
| Beta blocker therapy | 0.003 | 0.003 |
| Calcium channel blocker therapy | 0.002 | 0.002 |
| Cardiac glucoside therapy | 0.017 | 0.017 |
| Hypotensive agent therapy | 0.011 | 0.011 |
| Nitrate therapy | 0.002 | 0.002 |
| Non-steroidal anti-inflammatory therapy | 0.018 | 0.018 |
| Renin inhibitor therapy | 0.006 | 0.006 |
| Vasodilator therapy | 0.010 | 0.010 |
| Sickle cell disease | 0.001 | 0.001 |
| Sleep apnea | 0.002 | 0.002 |
| \*Diagnosis of CHF or prescription drug claim for loop #Diagnosis of diabetes or prescription drug claim for anti-diabetic during ¥Any of diagnosis of tobacco use, diagnosis of smoking-related disease, or prescription drug claim for nicotine replacement therapy ±Prescription claim for statin or other lipid-lowering drug or diagnosis of other lipidemias | | |

Supplementary figure 2. Annual trends in ART initiation by type



Supplementary table 4. Distribution of outcome events, censoring events, and person-time by exposure group

|  |  |  |
| --- | --- | --- |
| **Outcomes** | **Non-INSTI**  **n=15,173** | **INSTI**  **n=5,069** |
| Composite MACE events | 154 | 49 |
| Acute myocardial infarction | 66 | 16 |
| Stroke | 54 | 24 |
| Coronary artery bypass | 9 | 2 |
| Percutaneous coronary intervention | 25 | 7 |
| Censoring events | 15,019 | 5,020 |
| Person-time, years | 30,994 | 8,859 |
| INSTI, integrase strand transfer inhibitor; MACE, major adverse cardiac outcomes | | | |