**Rates, Predictors and the Impact Cannabis Misuse on In-hospital Outcomes Among Patients Undergoing Percutaneous Coronary Intervention (From the National Inpatient Sample)**

Running title: Cannabis misuse and PCI outcomes

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**Abstract**

**Background:** Whether cannabis use worsens outcomes in coronary heart disease is unknown and no previous study has evaluated outcomes for patients who undergo percutaneous coronary intervention (PCI) according to cannabis use.

**Methods:** We analysed patients in the National Inpatient Sample between 2004 and 2014 who underwent PCI and evaluated rates, predictors and outcomes of patients according to cannabis misuse defined by cannabis abuse or dependence.

**Results:** A total of 7,306,012 patients were included and 32,765 cannabis misusers (0.4%). Cannabis misusers were younger (49.5 vs 64.6 years, p<0.001) and were more likely to be male (82.7% vs 66.3%, p<0.001). There was also a greater proportion of patients that were of black ethnicity in the cannabis misuse group (27.7% vs 7.9%, p<0.001) and fewer elective admissions (7.8% vs 27.6%, p<0.001). There was no difference in in-hospital mortality (OR 1.06 95%CI 0.80-1.40, p=0.67), bleeding (OR 0.94 95%CI 0.77-1.15, p=0.55) and stroke/transient ischemic attack (OR 1.19 95%CI 0.98-1.45, p=0.084) compared to non-cannabis misusers. Cannabis misusers had significantly lower odds of in-hospital vascular complications (OR 0.73 95%CI 0.58-0.90, p=0.004).

**Conclusions:** Our results suggest that cannabis misusers are more likely to be male, of black ethnicity and from the lowest quartile of income, but there was no evidence that cannabis misuse is associated with worse peri-procedural outcomes following PCI when controlling for key proxies of health status.

**What is known about this topic?**

* The impact of cannabis on PCI outcomes is not well known.
* It has been suggested that exposure to cannabis may increase the risk of thromboembolism via platelet activation and alter heart rate, blood pressure, oxygen carrying capacity and even trigger acute coronary syndrome.
* To date, there are no studies examining cannabis use in a PCI cohort.

**What does this article add?**

* Cannabis misusers represent a small portion of patients who undergo PCI but rates are increasing over time.
* Patients who misuse cannabis are distinct from the rest of the cohort as they are younger, more likely to be Black, from the lowest quartile of income and are proportionally the least likely to receive a drug eluting stent.
* Cannabis misusers appear to show no difference in adverse outcomes for in-hospital mortality, bleeding and stroke/TIA but a lower odds of vascular complications were observed.

**Introduction**

Percutaneous coronary intervention (PCI) is one of the most frequently performed procedures in the United States [1]. It has evolved to become a safe procedure with low mortality and complication rates but there remains interest in identifying factors which may affect patient outcomes. The impact of cannabis on PCI outcomes is not well known. It has been suggested that exposure to exogenous cannabinoids may interfere with the protective balance between endocannabinoids and various receptors in the coronary arteries as acute coronary syndrome has been attributed to marijuana use [2]. Cannabinoids may increase the risk of thromboembolism via platelet activation [3]. Clinically, their impact include alterations in heart rate and blood pressure and marijuana smoke can increase carboxyhemoglobin resulting in reduced oxygen carrying capacity [4]. The relationship between cannabis use and clinical outcomes in patients with cardiovascular events is conflicting, a small older study suggested increased harm associated with marijuana use among patients with acute myocardial infarction (AMI)[5] while a more recent and larger study suggested no difference [6]. To date, there are no studies examining cannabis misuse in a PCI cohort. The objectives of the current study were to evaluate the rate and trend of cannabis misuse and in-hospital outcomes for patients who misuse cannabis in a national cohort and to understand the impact of cannabis misuse among patients that undergo PCI.

**Methods**

The National Inpatient Sample (NIS) is a dataset produced by the Agency for Healthcare Research and Quality (AHRQ) as a part of the Healthcare Cost and Utilization Project (HCUP) which contains national hospitalization information from the United States [7]. We included men and women aged 18 years or older with a PCI procedure between 2004 and 2014. We excluded patients with missing data for age, sex and in-hospital death. Discharge weights were applied to the analysis sample in order to produce national estimates.

Cannabis misuse was defined using International Classification of Diseases, Ninth Revision (ICD-9) codes 3043\* (cannabis dependence) and 3052\* (cannabis abuse). Data was available on age, sex, race, elective admission, weekend admission, primary diagnosis of acute myocardial infarction, primary expected payer, median household income, year of procedure, smoking, alcohol abuse, hypercholesterolemia, hypertension, diabetes, obesity, congestive heart failure, coronary artery disease, previous myocardial infarction, previous PCI, previous coronary artery bypass graft (CABG), atrial fibrillation, previous stroke, peripheral vascular disease, renal failure, liver failure, chronic lung disease, rheumatoid arthritis/collagen vascular disease, peptic ulcer disease, tumor, lymphoma, leukemia, paralysis, acquire immune deficiency syndrome (AIDS), dementia, hospital urban classification, hospital size, multivessel disease, bifurcation disease, cardiogenic shock, need for left ventricular assist device/intra-aortic balloon pump, measurement of fractional flow reserve, intravascular ultrasound and drug eluting stent based on NIS core and severity datasets, AHRQ comorbidities measures and ICD-9 codes as described in Supplementary Table 1. The Charlson Comorbidity Index (CCI) was derived using methods previously described [8]. The outcomes of this study were in-hospital death, vascular complications, bleeding and stroke or transient ischemic attack (TIA).

All analyses were performed with Stata v14 (College Station, Texas). We used a flow diagram to illustrate the final cohort of included patients after applying exclusions. Trends in cannabis use over time was examined graphically. Descriptive statistics were presented according to cannabis misuse and non-misuse. Multiple logistic regressions were used to evaluate the impact of cannabis misuse on the independent odds of in-hospital mortality, vascular complication, bleeding and stroke or TIA, adjusting for age, sex, race, elective admission, weekend admission, primary diagnosis of acute myocardial infarction, primary expected payer, median household income, year of procedure, smoking, alcohol abuse, hypercholesterolemia, hypertension, diabetes, obesity, congestive heart failure, coronary artery disease, previous myocardial infarction, previous PCI, previous CABG, atrial fibrillation, previous stroke, peripheral vascular disease, renal failure, liver failure, chronic lung disease, rheumatoid arthritis/collagen vascular disease, peptic ulcer disease, tumor, lymphoma, leukemia, paralysis, AIDS, dementia, hospital urban classification, hospital size, multivessel disease, bifurcation disease, cardiogenic shock, need for left ventricular assist device/intra-aortic balloon pump, measurement of fractional flow reserve, intravascular ultrasound and drug eluting stent.

We used the function “psmatch2” to perform 1:1 nearest neighbour matching without replacement. Patients with cannabis use were matched to patients without cannabis use and the matching was based on a propensity score derived from all baseline variables. A table was generated to enable comparison of the baseline variables for the matched groups and another table was generated to evaluate the in-hospital outcome for the matched groups. Mean differences in continuous variables were evaluated using student’s T-test, while the Chi2 test was used to compare frequencies in categorical variables. Also, sensitivity analyses were performed by considering in-hospital outcomes for patients with and without cannabis use stratified by age group (≤55 years, 55-65 years, 66-75 years and >75 years), gender, tobacco smoking status and diagnosis of acute myocardial infarction.

**Results**

A total of 7,306,012 PCI procedures were included in the analysis after exclusion of patients with missing values for age, sex and in-hospital death (Figure 1). Cannabis misusers made up of a small proportion of the sample (n=32,765, 0.4%). The proportion of cannabis misusers among PCI patients has increased over time (Figure 2).

The patient characteristics according to cannabis misuse are shown in Table 1. Cannabis misusers were younger (49.5 vs 64.6 years, p<0.001) and were more likely to be male (82.7% vs 66.3%, p<0.001). There was also a greater proportion of patients that were of black ethnicity in the cannabis misuse group (27.7% vs 7.9%, p<0.001) and were less likely to be elective admissions (7.8% vs 27.6%, p<0.001). The diagnosis of AMI was significantly higher in the cannabis misuser group (67.0% vs 39.2%, p<0.001). In terms of primary expected payer, cannabis misusers had a greater proportion of patients that were on Medicaid (21.9% vs 5.7%) or self-pay (24.0% vs 4.9%) and fewer patients on Medicare (17.4% vs 51.4%). Patients who were cannabis misusers also had a greater proportion from the lowest quartile of income (40.7% vs 26.6%, p<0.001). In terms of comorbidities, cannabis misusers had a greater proportion of patients that smoked (78.2% vs 34.9%, p<0.001) and abused alcohol (20.9% vs 1.9%, p<0.001). There was also reduced use of drug eluting stents among cannabis misusers (57.4% vs 73.3%, p<0.001). Rates of all adverse outcomes was lower in the cannabis misusers group (in-hospital death 1.1% vs 1.6%, p<0.001, vascular complications 1.6% vs 3.3%, p<0.001, bleeding 1.9% vs 3.0%, p<0.001 and stroke/TIA 1.7% vs 3.0%, p<0.001).

The multivariable predictors of in-hospital death among cannabis misusers are shown in Table 2. Variables associated with in-hospital mortality included cardiogenic shock (OR 13.71 95%CI 5.76-32.60), p<0.001), paralysis (OR 7.48 95%CI 1.34-41.91, p=0.022), need for LV assist device/IABP (OR 4.62 95%CI 1.91-11.13, p=0.001) and peripheral vascular disease (OR 4.32 95%CI 1.79-10.41, p=0.001).

The stratified analysis based on age group, sex, smoking status and diagnosis of acute myocardial infarction are shown in Supplementary Table 3. The reduction in adverse events for cannabis misusers compared to non-users was most apparent in the patients with a diagnosis of acute myocardial infarction.

The association between cannabis misuse and in-hospital adverse outcomes is shown in Figure 3. After adjustments for multiple factors, cannabis misusers had no difference in in-hospital mortality (OR 1.06 95%CI 0.80-1.40, p=0.67), bleeding (OR 0.94 95%CI 0.77-1.15, p=0.55) and stroke/TIA (OR 1.19 95%CI 0.98-1.45, p=0.084) compared to non-cannabis users. Cannabis misusers had significantly lower odds of in-hospital vascular complications (OR 0.73 95%CI 0.58-0.90, p=0.004).

The comparison of the variables for the propensity score matched groups are shown in Supplementary Table 4. Aside from race, primary expected payer and median household income the two groups were well matched. Evaluation of the outcomes of the propensity score match groups suggest that there is no difference in in-hospital death or bleeding complications but decreased vascular complications and an increase in stroke or TIA (Table 3). These findings are similar to the multiple logistic regression model except that there was a significant increase in stroke or TIA with cannabis use for the propensity matched analysis (p=0.012) but not for the multiple logistic regression model (p=0.084).

The graphical abstract is shown in Figure 4.

**Discussion**

Our national analysis of cannabis misuse in PCI patients has several key findings. First, cannabis misusers represent a small portion of patients who undergo PCI but rates are increasing over time. Second, the patients who misuse cannabis are distinct from the general PCI population as they are younger, more likely to be black, from the lowest quartile of income and are proportionally the least likely to receive a drug eluting stent. Third, cannabis misusers appear to show no difference in adverse outcomes for in-hospital mortality, bleeding and stroke/TIA but a lower odds of vascular complications were observed. This suggests that there is insufficient evidence to conclude that patients who undergo PCI and misuse cannabis are at increased in-hospital harm compared to those who do not use cannabis.

Whether cannabis use actually causes coronary heart disease is not yet known[9] as there is limited literature in this area. Cannabis smoking activates cannabinoid receptors in various tissues of the body which include the heart and blood vessels [9]. One in-vitro study has reported that exposure of human platelets to Δ-9-tetrahydrocannabinol result in platelet activation[10] which may increase the risk of thromboembolism. Physiologically, activation of cannabinoid receptors triggers changes in heart rate and blood pressure which are dose-dependent and a reduction in oxygen carrying capacity and can cause vasospasm, vasodilation and altered coronary flow[11] and these may impact on the propensity for complications in PCI. The vascular effects of cannabis include worsening angina[12] and the study by Mittleman et al suggest that smoking marijuana is a rare trigger of acute myocardial infarction [13]. Evidence supporting increased harm with cannabis use was reported by an older study of 52 AMI patients who used marijuana compared to 1,861 controls from 1989 to 1994 in the era of thrombolysis [5]. However, a more contemporary and larger study showed no difference in in-hospital death and adverse outcome among 3,854 AMI patients who used marijuana compared to over 1 million control patients [6]. However, this study did not evaluate outcomes among patients with PCI so our study was the first to show no increased harm associated with cannabis in the PCI population.

One of the challenges with interpreting these results are the key differences between the cannabis misuse cohort and non-cannabis misuse cohort. We observed that the cannabis cohort was associated with fewer vascular complications compared to the non-cannabis cohort. It is known that older patients who undergo PCI have greater ischemic burden and complex lesions such as calcified lesions, tortuous lesions, ostial lesions and multivessel disease[14] which may increase the risk of vascular complications compared to younger patients. In addition, young patients may have greater physiological reserve and fewer comorbidities compared to the frail elderly so their outcomes may be better after the physiological stress of PCI or myocardial ischemia. In addition, we speculate that young black males may have large radial arteries so patients that smoke cannabis may be more likely to receive radial approach to PCI compared to elderly and comorbid patients with smaller radial arteries Indeed our previous work suggests that adoption of trans radial access has been more rapid in younger patients [15] and in males [16]. Previous work has shown that adoption of the radial approach for PCI is associated with a decreased risk of vascular complications[17] We observed racial differences and a greater degree of poverty among patients who use cannabis and how these factors influence clinical decisions and translates into patient outcomes is unclear. There is evidence that among PCI patients, black patients have a higher rate of mortality compared to white patients but after adjustments there is no difference [18]. Also, while analysis of procedural treatments for acute coronary syndromes have shown no differences based on patient income, it has been reported that there may be inequalities in drug eluting stent use [19]. In our study, we also observed low rates of drug eluting stents among groups with cannabis use. There is evidence that bare metal stent use was more prevalent among patients with illicit drug use[20] and we speculate that this may be related to concerns about adherence to dual antiplatelet therapy post procedure as failure to take dual antiplatelet therapy may result in stent thrombosis. While there is growing legalization of marijuana in America, it has been at one point described a gateway to more dangerous illicit drug use [21]. Even with the potential for an association between marijuana use and more illicit drug and related drug seeking behaviors we find no evidence that this translates into harm in PCI in the short term.

More than 1 in 3 patients (35%) in the current cohort smoked tobacco and 16% had chronic lung disease. Chronic cannabis use is associated with chronic bronchitis but spirometric changes differ from those observed in tobacco smoking, but the clinical implications of the changes associated with cannabis use are currently unknown [22]. Lower odds of adverse outcomes among smokers from analysis of this dataset has been previously reported as the smoker’s paradox [23]. Another study has suggested that the paradox could be mostly explained by confounding factors related to the lower risk profile of current smokers [24]. The findings from the current study suggest that cannabis misuse does not appear to be associated with increased harm in terms of in-hospital outcomes but this must be considered with the limitations associated with analysis of an administrative database. While the reason for our findings is not clear, animal studies have shown that endogenous cannabinoids may mediate myocardial preconditioning [25] and a case report suggesting amelioration of an acute coronary occlusion with coronary collateralization [26].

**Limitations**

Our study has several limitations. First, the NIS is constructed in the absence of patient identifiers so patient may appear more than once within years and between years. Second, we are limited by ICD-9 codes for cannabis use which are codes for cannabis abuse and dependence. Use of these codes may underreport the true extent of cannabis use as it is likely that infrequent users are not captured. Ideally, the frequency of cannabis use should be reported but this is not available and we do not know the time between most recent cannabis use and time of procedure. Third, the NIS does not have data on cause of death which may be interesting because it is not known if patients died because of coronary disease, complications from PCI or completely unrelated non-cardiac cause which is more common in the older non-cannabis population. Fourth, as with the nature of any observational data, there is the potential for confounding and we cannot prove any causality in our associations. Fifth, there is no post-discharge follow-up information was available in the dataset and it is possible that patients who use cannabis may have differences in long term outcomes compared to patients who do not use cannabis. It is further not clear if the findings of our study are related to the cannabis use and smoking or other related behaviors such as sedentary lifestyle and non-compliance to medications. Finally, the NIS does not have some important variables such as those related to angiographic findings or PCI approaches and periprocedural medications used, for example more potent antiplatelet use in the cannabis misusers may offset any adverse outcomes from the use of cannabis.

**Conclusions**

In conclusion, cannabis misuse is increasing among patients receiving PCI but we did not find any evidence of increased operative harm for this population. The patients using cannabis are distinct as these patients are young, more likely to be black and from lower income background. More studies are needed to better understand the potential relationship between cardiovascular disease and cannabis misuse.

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**Author contributions**

CSK conceptualized the study and performed the analysis. CSK and MAM wrote the first draft of the manuscript. MCA, MM, MR, AS, JN, KR, CWK and EK provided critical editing and review of the scientific content of the manuscript, including advice regarding statistical contents. The manuscript has neither been published nor currently under consideration for publication in any other journal. All authors have approved the final version of the manuscript.

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**Figure 1: Flow diagram of patient inclusion**

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**Figure 2: Trends in cannabis use over time**

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**Figure 3: Cannabis use and its independent impact on adverse outcomes**



Adjusted for age, sex, race, elective, weekend, diagnosis of AMI, primary expected payer, median household income, year, alcohol abuse, hypercholesterolemia, hypertension, diabetes mellitus, obesity, coronary artery disease, previous myocardial infarction, previous PCI, previous CABG, atrial fibrillation, previous stroke, peripheral vascular disease, renal failure, liver disease, rheumatoid arthritis/connective tissue disease, peptic ulcer disease, cancer, lymphoma, leukemia, hemiplegia, AIDS, dementia, urban hospital, hospital bed size, multivessel disease, bifurcation disease, cardiogenic shock, left ventricular assist device and IABP, fraction flow reserve and drug eluting stent.

**Figure 4: Graphical Abstract**

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**Table 1: Patient characteristics according to cannabis use**

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | None (n=7,273,247) | Cannabis (n=32,765) | p-value |
| Age (years) | 64.6±12.3  | 49.5 ±9.9 | <0.001 |
| Female | 33.7% | 17.3% | <0.001 |
| Race |  |  | <0.001 |
| White | 78.9% | 60.6% |  |
| Black | 7.9% | 27.7% |  |
| Hispanic | 6.8% | 6.9% |  |
| Asian or Pacific Islander | 2.2% | 0.6% |  |
| Native American | 0.5% | 0.8% |  |
| Other | 3.6% | 3.3% |  |
| Elective | 27.6% | 7.8% | <0.001 |
| Weekend | 16.0%  | 25.5% | <0.001 |
| Primary diagnosis of AMI | 39.2% | 67.0% | <0.001 |
| Primary expected payer |  |  | <0.001 |
| Medicare | 51.4% | 17.4% |  |
| Medicaid | 5.7% | 21.9% |  |
| Private insurance | 34.7% | 28.6% |  |
| Self-pay | 4.9% | 24.0% |  |
| No charge | 0.5% | 2.6% |  |
| Other | 2.8% | 5.5% |  |
| Median household income |  |  | <0.001 |
| 0th-25th | 26.6% | 40.7% |  |
| 26th-50th | 26.8% | 26.1% |  |
| 51st-75th | 24.6% | 20.6% |  |
| 76th-100th | 22.0% | 12.6% |  |
| Year |  |  | <0.001 |
| 2004 | 10.4% | 3.2% |  |
| 2005 | 10.7% | 4.0% |  |
| 2006 | 13.1% | 6.4% |  |
| 2007 | 10.3% | 6.5% |  |
| 2008 | 10.3% | 7.9% |  |
| 2009 | 9.1% | 9.3% |  |
| 2010 | 7.3% | 9.0% |  |
| 2011 | 7.8% | 11.6% |  |
| 2012 | 7.5% | 12.5% |  |
| 2013 | 7.0% | 13.4% |  |
| 2014 | 6.5% | 16.2% |  |
| Smoking | 34.9% | 78.2% | <0.001 |
| Alcohol abuse | 1.9% | 20.9% | <0.001 |
| Hypercholesterolemia | 65.8% | 60.5% | <0.001 |
| Hypertension | 69.5% | 64.0% | <0.001 |
| Diabetes | 33.3% | 22.2% | <0.001 |
| Obesity | 12.1% | 15.2% | <0.001 |
| Coronary artery disease | 93.6% | 91.4% | <0.001 |
| Previous myocardial infarction | 13.2% | 15.2% | <0.001 |
| Previous PCI | 18.7% | 16.7% | <0.001 |
| Previous CABG | 7.4% | 3.1% | <0.001 |
| Atrial fibrillation | 10.0% | 4.2% | <0.001 |
| Peripheral vascular disease | 10.4% | 6.7% | <0.001 |
| CLD | 15.5% | 16.6% | 0.011 |
| Renal failure | 9.6% | 5.8% | <0.001 |
| Liver failure | 0.9% | 2.7% | <0.001 |
| Rheumatoid arthritis/collagen vascular disease | 1.8% | 1.3% | 0.003 |
| Tumor | 1.2% | 0.5% | <0.001 |
| Lymphoma | 0.3% | 0.2% | 0.008 |
| Acquired immune deficiency syndrome | 0.1% | 0.8% | <0.001 |
| Dementia | 1.4% | 0.2% | <0.001 |
| Charlson Comorbidity Index | 1.1±1.3  | 0.9±1.3 | <0.001 |
| Urban hospital | 94.5% | 95.0% | 0.047 |
| Hospital size |  |  | 0.040 |
| Small | 8.2% | 8.0% |  |
| Medium | 20.7% | 22.0% |  |
| Large | 71.1% | 70.1% |  |
| Multivessel disease | 14.2% | 12.9% | 0.002 |
| Bifurcation disease | 1.7% | 2.2% | 0.004 |
| Measurement of FFR | 0.7% | 1.3% | <0.001 |
| IVUS | 4.8% | 5.9% | <0.001 |
| DES | 73.3% | 57.4% | <0.001 |
| In-hospital death | 1.6% | 1.1% | 0.001 |
| Vascular complication | 3.3% | 1.6% | <0.001 |
| Bleeding | 3.0% | 1.9% | <0.001 |
| Stroke/TIA | 3.0% | 1.7% | <0.001 |

PCI=percutaneous coronary intervention, CABG=coronary artery bypass graft, CLD=chronic lung disease, LV=left ventricular, IABP=intra-aortic balloon pump, FFR=fractional flow reserve, IVUS=intravascular ultrasound, DES=drug eluting stent, TIA=transient ischemic attack

Only statistical significant variables shown. Full table in Supplementary Table 1.

**Table 2: Predictors of in-hospital death among cannabis users**

|  |  |  |
| --- | --- | --- |
| Variable | Cannabis | p-value |
| Age (years) | 1.05 (1.01-1.08) | 0.016 |
| Weekend | 2.20 (1.18-4.12) | 0.014 |
| Hypertension | 0.30 (0.15-0.59) | 0.001 |
| Peripheral vascular disease | 4.32 (1.79-10.41) | 0.001 |
| Chronic lung disease | 2.10 (1.03-4.26) | 0.041 |
| Paralysis | 7.48 (1.34-41.91) | 0.022 |
| Cardiogenic shock | 13.71 (5.76-32.60) | <0.001 |
| Need for LV assist device/IABP | 4.62 (1.91-11.13) | 0.001 |
| IVUS | 3.20 (1.10-9.30) | 0.032 |
| DES | 0.45 (0.24-0.86) | 0.015 |

**Table 3: Propensity score matched cohort comparison of outcomes**

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | No cannabis (unweighted n=2,933) | Cannabis (unweighted n=2,933) | p-value |
| In-hospital death | 1.1% | 0.9% | 0.51 |
| Vascular complications | 2.5% | 1.5% | 0.007 |
| Bleeding complications | 1.9% | 2.0% | 0.93 |
| Stroke or TIA | 1.3% | 2.2% | 0.012 |

TIA=transient ischemic attack

**Supplementary Table 1: Full description of variables, data source and codes**

|  |  |  |
| --- | --- | --- |
| Variable | Data source | Codes |
| Age | NRD core file | - |
| Sex | NRD core file | - |
| Elective admission | NRD core file | - |
| Weekend admission | NRD core file | - |
| Year | Individual year dataset | - |
| Income based on ZIP codes in quartiles | NRD core file | - |
| Smoking | ICD-9 | Diagnostic V1582 3051 |
| Alcohol misuse | AHRQ comorbidity measure | - |
| Hypertension | AHRQ comorbidity measure | - |
| Dyslipidemia | ICD-9 | Diagnostic 2720/2724 |
| Obesity | AHRQ comorbidity measure | - |
| Diabetes mellitus | AHRQ comorbidity measure | Composite of diabetes uncomplicated and with chronic complication |
| Coronary artery disease | ICD-9 | Diagnostic 41400/41407 |
| Previous myocardial infarction | ICD-9 | Diagnostic 412 |
| Previous PCI | ICD-9 | Diagnostic V4582 |
| Previous CABG | ICD-9 | Diagnostic V4581 |
| Atrial fibrillation | ICD-9 | Diagnostic 42731 |
| Valvular heart disease | AHRQ comorbidity measure | - |
| Peripheral vascular disease | AHRQ comorbidity measure | - |
| Previous stroke/TIA | ICD-9 | Diagnostic V1254 438\* |
| Chronic lung disease | AHRQ comorbidity measure | - |
| Renal failure | AHRQ comorbidity measure | - |
| Liver failure | AHRQ comorbidity measure | - |
| Fluid and electrolyte disorder | AHRQ comorbidity measure | - |
| Hypothyroidism | AHRQ comorbidity measure | - |
| Pulmonary circulatory disorder | AHRQ comorbidity measure | - |
| Peptic ulcer disease | AHRQ comorbidity measure | - |
| Depression | AHRQ comorbidity measure | - |
| Dementia | ICD-9 | Diagnostic 290\* 2941\* 2942\* 2948 3310/3312 33182 797 |
| Multivessel coronary disease | ICD-9 | Procedural 0041 0042 0043 0046 0047 0048 |
| Bifurcation disease | ICD-9 | Procedural 0044 |
| Use of circulatory support | ICD-9 | Procedural 3761 3768 3965 |
| FFR | ICD-9 | Procedural 0059 |
| IVUS | ICD-9 | Procedural 0024 |
| Drug eluting stent | ICD-9 | Procedural 3607 |
| Hospital bed size | NRD hospital file | - |
| Hospital urban classification | NRD hospital file | - |
| Hospital teaching status | NRD hospital file | - |
| Cardiogenic shock | ICD-9 | Diagnostic 78551 |
| In-hospital stroke/TIA | ICD-9 | Diagnostic 431 433\*1 434\*1 435\* 4336\* 99701 |
| Vascular complication | ICD-9 | Diagnostic code 900/904 9982 9992 9977 4470 86804Procedural code 3931 3941 3949 3952 4956 3957 3959 3979 |
| Bleeding | ICD-9 | Diagnostic code 431\* 4329 4590 566881 5789 Procedural code 990\* |

**Supplementary Table 2: Patient characteristics according to cannabis use**

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | None (n=7,273,247) | Cannabis (n=32,765) | p-value |
| Age (years) | 64.6±12.3 (n=7,273,247) | 49.5 ±9.9 (n=32,765) | <0.001 |
| Female | 2,451,235 (33.7%) | 5,652 (17.3%) | <0.001 |
| Race |  |  | <0.001 |
| White | 4,637,468 (78.9%) | 17,104 (60.6%) |  |
| Black | 464,967 (7.9%) | 7,808 (27.7%) |  |
| Hispanic | 400,575 (6.8%) | 1,945 (6.9%) |  |
| Asian or Pacific Islander | 129,749 (2.2%) | 172 (0.6%) |  |
| Native American | 31,814 (0.5%) | 236 (0.8%) |  |
| Other | 212,308 (3.6%) | 940 (3.3%) |  |
| Elective | 2,001,870 (27.6%) | 2,536 (7.8%) | <0.001 |
| Weekend | 1,160,384 (16.0%)  | 8,365 (25.5%) | <0.001 |
| Primary diagnosis of AMI | 2,854,227 (39.2%) | 21,958 (67.0%) | <0.001 |
| Primary expected payer |  |  | <0.001 |
| Medicare | 3,734,248 (51.4%) | 5,677 (17.4%) |  |
| Medicaid | 413,380 (5.7%) | 7,149 (21.9%) |  |
| Private insurance | 2,520,540 (34.7%) | 9,344 (28.6%) |  |
| Self-pay | 353,232 (4.9%) | 7,853 (24.0%) |  |
| No charge | 35,881 (0.5%) | 857 (2.6%) |  |
| Other | 204,677 (2.8%) | 1,797 (5.5%) |  |
| Median household income |  |  | <0.001 |
| 0th-25th | 1,890,603 (26.6%) | 12,968 (40.7%) |  |
| 26th-50th | 1,905,467 (26.8%) | 8,301 (26.1%) |  |
| 51st-75th | 1,748,517 (24.6%) | 6,553 (20.6%) |  |
| 76th-100th | 1,563,765 (22.0%) | 4,022 (12.6%) |  |
| Year |  |  | <0.001 |
| 2004 | 729,141 (10.4%) | 1,029 (3.2%) |  |
| 2005 | 751,813 (10.7%) | 1,280 (4.0%) |  |
| 2006 | 920,043 (13.1%) | 2,053 (6.4%) |  |
| 2007 | 717,690 (10.3%) | 2,087 (6.5%) |  |
| 2008 | 723,120 (10.3%) | 2,550 (7.9%) |  |
| 2009 | 639,350 (9.1%) | 2,988 (9.3%) |  |
| 2010 | 511,812 (7.3%) | 2,885 (9.0%) |  |
| 2011 | 546,575 (7.8%) | 3,732 (11.6%) |  |
| 2012 | 523,239 (7.5%) | 4,003 (12.5%) |  |
| 2013 | 487,831 (7.0%) | 4,313 (13.4%) |  |
| 2014 | 453,530 (6.5%) | 5,209 (16.2%) |  |
| Smoking | 2,539,327 (34.9%) | 25,616 (78.2%) | <0.001 |
| Alcohol abuse | 137,158 (1.9%) | 6,838 (20.9%) | <0.001 |
| Hypercholesterolemia | 4,785,344 (65.8%) | 19,821 (60.5%) | <0.001 |
| Hypertension | 5,057,376 (69.5%) | 20,968 (64.0%) | <0.001 |
| Diabetes | 2,420,041 (33.3%) | 7,267 (22.2%) | <0.001 |
| Obesity | 881,380 (12.1%) | 4,968 (15.2%) | <0.001 |
| Congestive heart failure | 71,905 (1.0%) | 261 (0.8%) | 0.11 |
| Coronary artery disease | 6,879,974 (93.6%) | 29,948 (91.4%) | <0.001 |
| Previous myocardial infarction | 956,327 (13.2%) | 4,963 (15.2%) | <0.001 |
| Previous PCI | 1,362,820 (18.7%) | 5,465 (16.7%) | <0.001 |
| Previous CABG | 535,981 (7.4%) | 1,024 (3.1%) | <0.001 |
| Atrial fibrillation | 726,832 (10.0%) | 1,364 (4.2%) | <0.001 |
| Previous stroke | 274,538 (3.8%) | 1,265 (3.9%) | 0.71 |
| Peripheral vascular disease | 753,792 (10.4%) | 2,196 (6.7%) | <0.001 |
| CLD | 1,127,299 (15.5%) | 5,450 (16.6%) | 0.011 |
| Renal failure | 698,720 (9.6%) | 1,905 (5.8%) | <0.001 |
| Liver failure | 61,753 (0.9%) | 876 (2.7%) | <0.001 |
| Rheumatoid arthritis/collagen vascular disease | 127,740 (1.8%) | 418 (1.3%) | 0.003 |
| Peptic ulcer disease | 2,043 (0.03%) | 10 (0.03%) | 0.92 |
| Tumor | 88,600 (1.2%) | 158 (0.5%) | <0.001 |
| Lymphoma | 24,617 (0.3%) | 49 (0.2%) | 0.008 |
| Leukemia | 19,985 (0.3%) | 64 (0.2%) | 0.22 |
| Paralysis | 50,587 (0.7%) | 217 (0.7%) | 0.74 |
| Acquired immune deficiency syndrome | 7,291 (0.1%) | 256 (0.8%) | <0.001 |
| Dementia | 100,224 (1.4%) | 64 (0.2%) | <0.001 |
| Charlson Comorbidity Index | 1.1±1.3 (n=7,273,247) | 0.9±1.3 (n=32,765) | <0.001 |
| Urban hospital | 6,801,767 (94.5%) | 30,652 (95.0%) | 0.047 |
| Hospital size |  |  | 0.040 |
| Small | 594,445 (8.2%) | 2,595 (8.0%) |  |
| Medium | 1,500,776 (20.7%) | 7,144 (22.0%) |  |
| Large | 5,151,786 (71.1%) | 22,775 (70.1%) |  |
| Multivessel disease | 1,032,964 (14.2%) | 4,214 (12.9%) | 0.002 |
| Bifurcation disease | 122,768 (1.7%) | 704 (2.2%) | 0.004 |
| Cardiogenic shock | 201,580 (2.8%) | 862 (2.6%) | 0.48 |
| Need for LV assist device/IABP | 239,534 (3.3%) | 1,108 (3.4%) | 0.69 |
| Measurement of FFR | 51,798 (0.7%) | 414 (1.3%) | <0.001 |
| IVUS | 347,699 (4.8%) | 1,935 (5.9%) | <0.001 |
| DES | 5,330,295 (73.3%) | 18,792 (57.4%) | <0.001 |
| In-hospital death | 117,283 (1.6%) | 364 (1.1%) | 0.001 |
| Vascular complication | 240,671 (3.3%) | 527 (1.6%) | <0.001 |
| Bleeding | 220,535 (3.0%) | 620 (1.9%) | <0.001 |
| Stroke/TIA | 216,945 (3.0%) | 571 (1.7%) | <0.001 |

PCI=percutaneous coronary intervention, CABG=coronary artery bypass graft, CLD=chronic lung disease, LV=left ventricular, IABP=intra-aortic balloon pump, FFR=fractional flow reserve, IVUS=intravascular ultrasound, DES=drug eluting stent, TIA=transient ischemic attack

**Supplementary Table 3: Analysis of outcomes stratified by age group, sex, smoking status, diagnosis of acute myocardial infarction and use of drug eluting stent**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Group | In-hospital death | Vascular complications | Bleeding complications | Stroke or TIA |
| No cannabis use | Cannabis use | p-value | No cannabis use | Cannabis use | p-value | No cannabis use | Cannabis use | p-value | No cannabis use | Cannabis use | p-value |
| Age ≤55Age 56-65Age 66-75Age >75 | 0.8%1.2%1.6%3.1% | 0.8%1.6%3.0%4.8% | 0.930.100.0520.66 | 1.8%2.6%3.6%5.6% | 1.3%2.0%4.4%0% | 0.0080.200.490.27 | 1.5%2.2%3.3%5.4% | 1.6%2.1%5.7%9.5% | 0.830.700.0210.40 | 1.1%2.3%3.8%5.0% | 1.1%3.1%5.4%14.3% | 0.880.0580.150.051 |
| MaleFemale | 1.4%2.0% | 1.1%1.3% | 0.0330.091 | 2.4%5.1% | 1.4%2.8% | <0.001<0.001 | 2.2%4.7% | 1.6%3.2% | 0.0050.016 | 2.6%3.8% | 1.5%2.9% | <0.0010.11 |
| Non-smokerSmoker | 2.0%1.0% | 1.7%0.9% | 0.530.75 | 3.8%2.5% | 1.7%1.6% | <0.001<0.001 | 3.5%2.2% | 2.5%1.7% | 0.0390.019 | 3.1%2.8% | 1.9%1.7% | 0.007<0.001 |
| No AMI diagnosisDiagnosis of AMI | 0.9%2.8% | 0.8%1.3% | 0.81<0.001 | 3.0%3.9% | 2.1%1.4% | 0.018<0.001 | 2.5%3.9% | 2.1%1.8% | 0.24<0.001 | 3.4%2.4% | 2.3%1.5% | 0.008<0.001 |

AMI=acute myocardial infarction, TIA=transient ischemic attack

p-values determined from the Chi2 test

**Supplementary Table 4: Propensity score matching comparison of variables in groups**

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | No cannabis (unweighted n=2,933) | Cannabis (unweighted n=2,933) | p-value |
| Mean age (years) | 48.6±9.6 | 48.5±9.7 | 0.93 |
| Female | 15.1% | 16.2% | 0.27 |
| Race |  |  | <0.001 |
| White | 71.2% | 60.5% |  |
| Black | 12.9% | 27.4% |  |
| Hispanic | 7.8% | 7.6% |  |
| Asian or Pacific Islander | 2.1% | 0.6% |  |
| Native American | 1.0% | 0.8% |  |
| Other | 5.0% | 3.2% |  |
| Elective | 8.3% | 9.2% | 0.20 |
| Weekend | 22.6% | 23.3% | 0.51 |
| Primary diagnosis of AMI | 64.5% | 64.1% | 0.79 |
| Primary expected payer |  |  | <0.001 |
| Medicare | 13.7% | 15.1% |  |
| Medicaid | 12.3% | 19.1% |  |
| Private insurance | 46.7% | 30.5% |  |
| Self-pay | 18.8% | 26.1% |  |
| No charge | 2.3% | 2.9% |  |
| Other | 6.1% | 6.3% |  |
| Median household income |  |  | 0.003 |
| 0th-25th | 37.2% | 40.9% |  |
| 26th-50th | 28.2% | 24.2% |  |
| 51st-75th | 20.7% | 20.6% |  |
| 76th-100th | 13.8% | 14.3% |  |
| Smoking | 78.3% | 77.0% | 0.23 |
| Alcohol abuse | 19.8% | 20.5% | 0.54 |
| Hypercholesterolemia | 58.4% | 58.9% | 0.71 |
| Hypertension | 62.2% | 62.3% | 0.94 |
| Diabetes | 20.3% | 20.1% | 0.80 |
| Obesity | 13.4% | 14.1% | 0.43 |
| Congestive heart failure | 0.5% | 0.6% | 0.59 |
| Coronary artery disease | 92.1% | 92.1% | 0.92 |
| Previous myocardial infarction | 15.2% | 15.3% | 0.89 |
| Previous PCI | 15.0% | 15.9% | 0.35 |
| Previous CABG | 3.3% | 2.9% | 0.41 |
| Atrial fibrillation | 3.5% | 4.0% | 0.37 |
| Previous stroke | 3.6% | 3.1% | 0.28 |
| Peripheral vascular disease | 6.6% | 6.5% | 0.83 |
| CLD | 14.4% | 14.9% | 0.58 |
| Renal failure | 5.7% | 5.0% | 0.27 |
| Liver failure | 2.3% | 2.3% | 0.86 |
| Rheumatoid arthritis/collagen vascular disease | 1.1% | 1.1% | 1.00 |
| Peptic ulcer disease | 0% | 0% | - |
| Tumor | 0.3% | 0.3% | 1.00 |
| Lymphoma | 0.1% | 0.1% | 0.71 |
| Leukemia | 0.1% | 0.1% | 0.71 |
| Paralysis | 0.7% | 0.9% | 0.45 |
| Acquired immune deficiency syndrome | 1.0% | 0.9% | 0.79 |
| Dementia | 0.3% | 0.3% | 1.00 |
| Urban hospital | 97.1% | 96.6% | 0.27 |
| Hospital size |  |  | 0.77 |
| Small | 7.3% | 6.8% |  |
| Medium | 20.9% | 21.0% |  |
| Large | 71.8% | 72.1% |  |
| Multivessel disease | 12.9% | 12.3% | 0.50 |
| Bifurcation disease | 1.8% | 1.9% | 0.70 |
| Cardiogenic shock | 2.2% | 2.1% | 0.79 |
| Need for LV assist device/IABP | 3.5% | 3.6% | 0.78 |
| Measurement of FFR | 0.5% | 0.4% | 0.71 |
| IVUS | 4.5% | 4.7% | 0.66 |
| DES | 55.6% | 54.1% | 0.26 |
| Mean propensity score | 0.03±0.04 | 0.03±0.04 | 1.00 |

PCI=percutaneous coronary intervention, CABG=coronary artery bypass graft, CLD=chronic lung disease, LV=left ventricular, IABP=intra-aortic balloon pump, FFR=fractional flow reserve, IVUS=intravascular ultrasound, DES=drug eluting stent