**Predictors, Treatments and Outcomes of Do-Not-Resuscitate Status in Acute Myocardial Infarction patients (From a Nationwide Inpatient Cohort Study)**

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**Abstract:**

Little is known about how frequently do-not-resuscitate (DNR) orders are placed in patients with acute myocardial infarction (AMI), the types of patients in which they are placed, treatment strategies or clinical outcomes of such patients.Using theUnited States (US) National Inpatient Sample (NIS) database from 2015-2018, we identified 2,767,549 admissions that were admitted to US hospitals and during the hospitalization received a diagnosis of AMI, of which 339,270 (12.3%) patients had a DNR order (instigated both preadmission and during in-hospital stay). Patients with a DNR status were older (median age 83 vs 65, P<0.001), more likely to be female (53.4% vs 39.3%, P<0.001) and White (81.0% vs 73.3%, P<0.001). Predictors of DNR status included comorbidities such as heart failure (OR: 1.47, 95% CI: 1.45-1.48), dementia (OR: 2.53, 95% CI: 2.50-2.55), and cancer. Patients with a DNR order were less likely to undergo invasive management or be discharged home (13.5% vs 52.8%), with only 1/3 receiving palliative consultation. In hospital mortality (32.7% vs 4.6%, P<0.001) and MACCE (37.1% vs 8.8%, P<0.001) were higher in the DNR group. Factors independently associated with in-hospital mortality among patients with a DNR order included a STEMI presentation (OR: 2.90, 95% CI: 2.84-2.96) and being of Black (OR: 1.29, 95% CI: 1.26-1.33), Hispanic (OR: 1.36, 95% CI: 1.32-1.41) or Asian/Pacific Islander (OR: 1.56, 95% CI:1.49-race. In conclusion, AMI patients with a DNR status were older, multimorbid, less likely to receive invasive management, with only 1/3 of patients with DNR status referred for palliative care.

**Key words**: DNR, AMI, Mortality, Palliative

**Introduction**

Despite advances in treatment, cardiovascular disease remains the most common cause of death in the United States (US)1, accounting for almost 1 million deaths annually2. Documentation of a do-not-resuscitate (DNR) order is part of end of life care that allows patients to forgo cardiopulmonary resuscitation (CPR) in the event of a cardiac arrest3. Whilst the benefits include a reduction in suffering and allowing for the arrangement of medical care according to the patients wishes4, prior studies have shown that a DNR order can have an impact on a physicians decision to provide life-prolonging treatments other than CPR5. Limited data on the use of DNR in the setting of acute myocardial infarction (AMI) exists. Patients presenting with AMI represent a heterogenous group ranging from the young with no comorbid conditions to elderly patients who are multimorbid. Better understanding of the use of DNR orders in AMI is required to ensure for appropriate management in this group. Using data from the largest all-payer in-hospital database in the US, our study aims to look at the characteristics, predictors, treatments and outcomes of AMI patients according to DNR status.

**Methods**

The National Inpatient Sample (NIS) is the largest all-payer inpatient health care database in the United States, developed by the Healthcare Cost and Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ)6. The NIS dataset contains hospital information on between 7 and 8 million yearly hospital discharges from 2004 onwards. Since 2012, the NIS samples discharge from all hospitals participating in HUCP, approximating a 20% stratified sample of all discharges from US community hospitals.

We analyzed all adult (≥18 years) patients hospitalized for AMI from 1st October 2015 through December 2018. Patient and procedural characteristics were extracted using ICD-10 codes provided in Supplementary Table 1 (ST1). Information on patient demographics was recorded for each hospital discharge including age, gender, race, admission day (weekday or weekend), expected primary payer and median household income according to ZIP code. Missing records for age, gender, elective and weekend admission, and mortality status were excluded from the analysis (Figure 1 for study flow diagram). Patients with type 2 MI or elective admissions were also excluded from the analysis. Each discharge record had information on up to 30 diagnoses. A full list of ICD 10-CM codes used to identify a DNR order as well as other patient characteristics and complications, is provided in ST1. ICD 10-CM codes were also used to identify procedural information during hospitalization including invasive coronary angiography (ICA), percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG) surgery, thrombolysis, use of mechanical ventilation, circulatory support, mechanical ventilation and palliative care consultation.

The main outcome measured was in-hospital all-cause mortality. Other outcomes included in-hospital major adverse cardiovascular and cerebrovascular events (MACCE), acute ischemic cerebrovascular accident (CVA) and major bleeding. MACCE was defined as a composite of all-cause mortality, acute ischemic CVA or transient ischemic attack and cardiac complications. Major bleeding events were defined as a composite of gastrointestinal, retroperitoneal, intracranial, and intracerebral hemorrhage, periprocedural hemorrhage, unspecified hemorrhage, or needing a blood transfusion. Destination of discharge and receipts of invasive procedures such as coronary angiography (CA), PCI and CABG and in-patient palliative care consultation were also measured.

Continuous variables are presented as a median and interquartile range, due to skewed data, and categorical data are presented as frequencies and percentages. Categorical variables were compared using Pearson chi square test, while continuous variables were compared using the Student’s t-test or the Kruskal Wallis test, as appropriate. Sampling weights were used to calculate the estimated total discharges as specified by AHRQ. Multivariable logistic regression models were used to examine the association between demographics and comorbidities and DNR status; as well as the association between demographics, comorbidities, and admission data and palliative consultation and in-hospital mortality among patients with DNR status, all expressed as odds ratios (OR) with corresponding 95% confidence intervals (CI). The models were adjusted for baseline differences between the groups, controlling for the following covariates: age, gender, weekend admission, hospital bed size, region and location/teaching status, ST-elevation myocardial infarction (STEMI), cardiogenic shock, use of intra-aortic balloon pump (IABP), CABG, PCI, CA, ventricular fibrillation (VF), ventricular tachycardia (VT), atrial fibrillation, heart failure, hypertension, dyslipidemia, diabetes mellitus, valvular heart disease, smoking status, chronic lung disease, chronic liver disease, anemia, thrombocytopenia, coagulopathies, and malignancies. All statistical analyses were performed on IBM SPSS version 26. Statistical significance was set at the 2-tailed 0.05 level, without multiplicity adjustment.

**Results**

Between October 2015 to December 2018, 2,959,244 patients were admitted to US hospitals

and during the hospitalization received a diagnosis of an AMI. Applying relevant exclusion criteria (Figure 1) produced a study cohort consisting of 2,767,549 (6.0% excluded). Of these, 339,270 (12.3%) were in the DNR group. Differences in clinical characteristics at admission between the two groups are presented in Table 1. Patients with a DNR order were older (median age 83 vs 67, P<0.001), more likely to be female (53.4% vs 39.3%, P<0.001), of White race (81.0% vs 73.1%, P<0.001), and have Medicare insurance (85.5% vs 59.2%, P<0.001). Patients with a DNR order had higher prevalence of comorbidities, including; heart failure (56.5% vs 37.7%, P<0.001), valvular disease (20.4% vs 13.6%, P<0.001), atrial fibrillation/flutter (37.1% vs 22.2%, P<0.001), chronic renal failure (39.2% vs 26.2%, P<0.001), dementia (24.8% vs 5.5%, P<0.001), solid malignancies (7.5% vs 2.8%, P<0.001) and metastatic cancer (4.6% vs 1.2%, P<0.001). Those without a DNR order were more likely to have cardiovascular risk factors including diabetes (41.5% vs 36.8%, P<0.001), dyslipidaemia (62.3% vs 49.2%, P<0.001) and smoking (47.6% vs 35.3%).

The destination of discharge for patients according to DNR status is shown in Figure 2. Patients with a DNR order were more likely to be discharged to a facility such as nursing or intermediate care (34.7% vs 15.2%) or die in hospital (32.7% vs 4.6%).

Factors independently associated with DNR status are shown in Table 2. Positive predictors included: female sex (OR: 1.34, 95% CI: 1.31-1.36), Medicaid (OR: 1.33, 95% CI: 1.30-1.36) and uninsured patients (OR: 1.23, 95% CI: 1.19-1.28), homelessness (OR:1.33, 95% CI:1.21-1.45), weekend admissions (OR: 1.05, 95% CI: 1.04-1.06) and those with comorbidities including; cerebrovascular disease (OR: 1.37, 95% CI: 1.35-1.39), heart failure (OR: 1.47, 95% CI: 1.45-1.48), dementia (OR: 2.53, 95% CI: 2.50-2.55), chronic liver disease (OR: 1.62, 95% CI: 1.56-1.68), solid (OR: 1.69, 95% CI: 1.65-1.72) and hematological malignancies (OR: 1.53, 95% CI: 1.49-1.57) and metastatic cancer (OR: 2.70, 95% CI: 2.63-2.77).

Differences in the management strategy and outcomes between the two groups are presented in Table 3. Patients with a DNR order were less likely to undergo ICA (18.8% vs 61.8%, P<0.001), PCI (10.3% vs 37.7%, P<0.001) or CABG surgery (1% vs 7%, P<0.001). They were more likely to receive palliative consultation (33.3% vs 1.8%, P<0.001) compared to those without a DNR order. In-hospital mortality (32.7% vs 4.6%, P<0.001), acute ischemic CVA (6% vs 2.5%, P<0.001), major bleeding (8.5% vs 4.4%, P<0.001) and MACCE (37.1% vs 8.8%, P<0.001) were all significantly more common in the DNR group.

We firstly looked at the characteristics of patients with DNR stratified by in-hospital mortality (Table 4), whilst predictors of in-hospital mortality for patients who had a DNR status are presented in Table 5. Of the 339,270 patients who had a DNR order, 110,945 (32.7%) patients died in-hospital. These patients were younger (median age 78 vs 85, P<0.001), were less likely to be female (46.7% vs 56.7%, P<0.001), more likely to be of Black (10.3% vs 7.1%, P<0.001), Hispanic (7.3% vs 5.0%, P<0.001) or Asian/Pacific Islander (3.2% vs 2.3%, P<0.001) race. Patients who presented with STEMI (27.4% vs 11.2%, P<0.001), in VF (8.7% vs 1.2%, P<0.001) or with VT (11.2% vs 5%, P<0.001) had greater in-hospital mortality.

 Predictors of in-hospital mortality amongst patients with a DNR order included Black (OR: 1.29, 95% CI: 1.26-1.33), Hispanic (OR: 1.36, 95% CI: 1.32-1.41), Asian/Pacific Islander (OR: 1.56, 95% CI:1.49-1.64) or Native American (OR: 1.51, 95% CI: 1.33-1.70) race, and comorbidities including atrial fibrillation/flutter (OR: 1.19, 95% CI: 1.17-1.21), thrombocytopenia (OR: 1.39, 95% CI: 1.36-1.43), and STEMI (OR: 2.9, 95% CI: 2.84-2.96). Negative predictors included heart failure (OR: 0.95, 95% CI: 0.93-0.97), dementia (OR: 0.65, 95% CI: 0.63-0.67), solid malignancy (OR: 0.79, 95% CI: 0.76 – 0.82) and metastatic cancer (OR: 0.9, 95% CI:0.86-0.94).

Our key study findings are summarised in the central illustration figure (Figure 3).

**Discussion:**

The results of this analysis of greater than 2.5 million US patients who presented with AMI between 2015-2018 revealed several important findings. First, one in eight patients hospitalized with AMI had a DNR order, with more common characteristics such as being older, female, of White race and presenting as a cardiac arrest or in cardiogenic shock, but less likely to present as a STEMI. Second, patients who received a DNR order had a high burden of comorbidities such as cerebrovascular disease, heart failure, dementia, chronic liver disease, and malignancies (solid, hematological and metastatic). Third, patients with a DNR were less likely to undergo invasive cardiac procedures such as ICA, PCI or CABG surgery, but only one third received a palliative consultation. Finally, the presence of comorbidities such as cancer, dementia and chronic lung disease were associated with reduced odds of mortality in patients with a DNR order.

 Prior studies have observed DNR orders to be more commonly used in the elderly7, 8, women9, 10 and those with comorbid conditions11. In our study, older age, female sex and comorbid conditions were associated with receipt of a DNR order. This may represent the complex interplay between a person’s own wishes and priorities about life-prolonging therapies in the face of deteriorating health and medical culture that recommends not attempting resuscitation when there is little likelihood of returning physiological function. Previous literature has suggested that women and elderly patients are less likely to want aggressive treatment when ill12 and physicians are more likely to assign DNR orders to multimorbid patients13.

*Jackson et al* looked at DNR orders in patients hospitalized with AMI as part of the Worcester Heart Attack Study and noted similar characteristics10. In their sample of 4,621 patients, approximately one fifth of patients had a DNR order. Our study highlights lower rates of DNR orders for patients with AMI compared to other cardiovascular conditions such as stroke and heart failure14 where rates of DNR at death were as high as 79%11. This may be a reflection of the advancement in the treatment of AMI, particularly coronary revascularization being associated with improved mortality outcomes15, which in turn is likely to explain why patients who presented with a STEMI, were less likely to have a DNR order. Furthermore, cardiovascular comorbidities were associated with a decreased odds of DNR status in our study. As these risk factors are largely modifiable, it may be perceived that the disease burden attributed to patients with these risk factors is more amenable to a reversible pathology and subsequently this subset of patients is more likely to receive treatment and less likely to have a DNR order.

 Whilst some studies have shown no change in the level of care delivered to patients before and after the receipt of DNR orders16, the majority of studies have shown that patients with DNR orders are less likely to receive guideline directed management, particularly with more aggressive therapies17-19. We compared the use of ICA, coronary revascularization (PCI/CABG surgery), mechanical ventilation, and receipt of palliative care according to DNR status. Patients with DNR orders were less likely to undergo ICA or receive coronary revascularization, but more likely to be on mechanical ventilation and be in receipt of palliative care. There may be increased hesitancy in performing an invasive procedure on a patient with DNR status, as the ability to respond to procedural complications, particularly life-threatening arrhythmias, is significantly attenuated. It is not clear if patients with a DNR status have a say in what treatments they would be willing to accept, however, previous literature has suggested more aggressive treatments are less likely to be favored less due to their perceived discomfort20 or poorer outcomes. Furthermore, there is large variability in a physician’s interpretation of DNR status, where it can be interpreted to mean an overall reduction in non-resuscitative measures21. Some systems are moving away from binary DNR orders in favor of more nuanced goals of care frameworks22.

Prior studies have shown that in cardiovascular conditions such as heart failure, palliative care is often less frequent and comes later in treatment compared to cancer23. In our study, one third of patients with a DNR status received palliative consultation compared to less than 2% for those without DNR status. The benefits of palliative care are well documented24-26, including to support patients and families in communicating their goals and through medical decision-making. Given the significantly higher mortality rates in the DNR group, there remains room for improvement in obtaining a palliative opinion for patients with advanced chronic illnesses, or DNR status.

There are a number of important limitations to our present study. Despite the NIS using ICD-9 and 10 codes and being a validated dataset for the purposes of cardiovascular research27, 28, it is an administrative dataset, and coding error may be a source of bias. The identification of AMI, DNR status as well as other comorbidities and procedural data was based on the use of administrative codes. Second, the NIS dataset only records in-hospital outcomes and therefore longer-term follow up of mortality or other adverse outcomes are missing from our analysis. As more than two-thirds of patients with a DNR order were discharged from hospital, it is important to follow up on their outcomes. Third, the database does not include pharmacotherapy, thus we are unable to determine if there was a significant disparity in care between the two groups regarding pharmacotherapy, or to see if the use of pharmacotherapy altered clinical outcomes for those patients with a DNR status. Furthermore, the NIS does not capture when the DNR order was instituted, whether it was in place prior to admission29, at the point of admission, or during the inpatient episode following a complication / adverse outcome. In addition, there is a spectrum of options encapsulated within a DNR order, including options for chest compression, defibrillation, and type of ventilation; these differences could not be accounted for in the analysis. Finally, the process in which the DNR order was established – and how patients’ preferences were elicited in the decision-making is unknown.

 In conclusion, our study found that AMI patients who had a DNR order were more likely to be female, White, present at an older age and have comorbidities including cerebrovascular disease, heart failure, dementia, chronic liver disease, and cancer. Patients with DNR status were less likely to receive invasive management and only one third received a palliative consultation. Whilst White patients were more likely to have a DNR status, predictors of mortality for DNR patients including being of non-White race. Given the heterogeneity of patients with AMI who have a DNR order, closer working relationships between Cardiologists and Palliative care physicians will likely facilitate better individualistic end of life care for these patients.

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### **Competing interests**

Giuseppe Biondi-Zoccai has consulted for Cardionovum, Innovheart, Meditrial, Opsens Medical, and Replycare.

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**Figure 1: Flow diagram of study population.**

**Excluded (n=191,695 )**

* Missing Data:
	+ Age: n=125.
	+ Gender: n=655.
	+ Elective procedure: n=5,665.
	+ Weekend admission: n=14.
	+ Mortality: n=2450.
* Age <18: n=390.
* Type 2 MI: n=3,685.
* Elective admissions: n=179,120.

**All records taken from NIS database from Q42015 - 2018**

**Records were identified with AMI**

**(n=2,959,244 weighted cases)**

**Identified records with AMI using ICD-10**

**Records with AMI included in analysis (N=2,767,549 weighted)**

AMI; acute myocardial infarction, NIS; National Inpatient sample, ICD; International classification of diseases

**Figure 2: Destination of Discharge - stratified by DNR status.**

DNR; do not resuscitate

**Figure 3: Central Illustration Figure**

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AMI; acute myocardial infarction, DNR; do not resuscitate, ICA; invasive coronary angiogram, PCI; percutaneous coronary intervention, CABG surgery; coronary artery bypass grafting surgery, CVA; cerebrovascular accident, MACCE; major adverse cardiovascular and cerebrovascular events

\* MACCE is defined as a composite of all-cause mortality, acute ischemic CVA or transient ischemic attack and cardiac complications

**Table 1: Demographics, record characteristics and comorbidities of patients, stratified by DNR status.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No DNR** | **DNR** | **P value** |
| Number of weighted records | 2,428,279 (87.7%) | 339,270 (12.3%) |  |
| Age (years), median (IQR) | 67 (57,77) | 83 (73,89) | <0.001 |
| Females, % | 39.3% | 53.4% | <0.001 |
| **Race** |  |  | <0.001 |
|  White | 73.1% | 81% |
|  Black | 13.1% | 8.2% |
|  Hispanic | 7.9% | 5.7% |
|  Asian/Pacific Islander | 2.5% | 2.6% |
|  Native American | 0.5% | 0.4% |
|  Other | 2.8% | 2.0% |
| **Hospital Location** |  |  | <0.001 |
|  Northeast | 20.4% | 21.8% |
|  Midwest | 24.3% | 26.8% |
|  South | 40.6% | 34.5% |
|  West | 14.7% | 16.9% |
| **Hospital Size** |  |  | <0.001 |
|  Small | 17.1% | 19.2% |
|  Medium | 30% | 30% |
|  Large | 52.9% | 50.8% |
| **Hospital Location/ teaching Status** |  |  | <0.001 |
|  Rural | 8.1% | 10.3% |
|  Urban non-teaching | 24.2% | 23.8% |
|  Teaching | 67.7% | 65.9% |
| Weekend Admission  | 26.4% | 27.4% | <0.001 |
| **Median ZIP income** |  |  | <0.001 |
|  1st quartile | 31.8% | 27.4% |
|  2nd quartile | 27.5% | 27.6% |
|  3rd quartile | 23% | 24.7% |
|  4th quartile | 17.6% | 20.3% |
| **Expected Primary Payer** |  |  | <0.001 |
|  Medicare | 59.2% | 85.5% |
|  Medicaid | 10.1% | 3.8% |
|  Private | 23.5% | 7.5% |
|  Uninsured | 4.3% | 1.3% |
|  No charge | 0.4% | 0.1% |
|  Other | 2.6% | 1.8% |
| Record Characteristics |  |
| STEMI | 22.3% | 16.5% | <0.001 |
| Cardiac Arrest | 3.2% | 8.5% | <0.001 |
| Ventricular Fibrillation | 2.7% | 3.6% | <0.001 |
| Ventricular tachycardia | 6.4% | 7% | <0.001 |
| Cardiogenic Shock | 5.1% | 11.4% | <0.001 |
| Length of stay, days, median (IQR) | 3 (2,7) | 4 (2,8) | <0.001 |
| Total charge, $, median (IQR) | 63,391 (34,303, 112,956) | 46,317 (23,212, 96478) | <0.001 |
| Comorbidities |  |
| Previous MI | 14.8% | 14% | <0.001 |
| Cerebrovascular disease | 5.4% | 8.4% | <0.001 |
| Heart failure | 37.7% | 56.5% | <0.001 |
| Valvular disease | 13.6% | 20.4% | <0.001 |
| Atrial fibrillation/flutter  | 22.1% | 37.1% | <0.001 |
| Hypertension | 80.8% | 80.8% | 0.66 |
| Dyslipidaemia | 62.3% | 49.2% | <0.001 |
| Diabetes | 41.5% | 36.8% | <0.001 |
| Smoking | 47.6% | 35.3% | <0.001 |
| Peripheral vascular disease | 9.2% | 11.3% | <0.001 |
| Chronic lung disease | 24.7% | 29.3% | <0.001 |
| Chronic renal failure | 26.2% | 39.2% | <0.001 |
| Obesity | 17.8% | 8.7% | <0.001 |
| Anaemia | 27.1% | 38.1% | <0.001 |
| Thrombocytopenia | 6.3% | 9.4% | <0.001 |
| Coagulopathy | 2.3% | 4.5% | <0.001 |
| Dementia | 5.5% | 24.8% | <0.001 |
| Chronic Liver Disease | 0.8% | 1.2% | <0.001 |
| Homelessness | 0.4% | 0.2% | <0.001 |
| Solid malignancy | 2.8% | 7.5% | <0.001 |
| Hematologic Malignancies | 1.2% | 2.7% | <0.001 |
| Metastatic cancer | 1.2% | 4.6% | <0.001 |

DNR; do not resuscitate, MI; myocardial infarction, IQR; interquartile range, STEMI; ST-segment elevation myocardial infarction

**Table 2: Predictors of DNR status.**

|  |  |  |
| --- | --- | --- |
|  | **OR (95% CI)** | **P value** |
| **Female** | 1.34 (1.31-1.36) | <0.001 |
| **Age** | 1.08 (1.08-1.08) | <0.001 |
| **Race (White – reference)** |  |  |
|  Black | 0.71 (0.7-0.72) | <0.001 |
|  Hispanic | 0.77 (0.75-0.78) | <0.001 |
|  Asian/Pacific Islander | 0.87 (0.84-0.89) | <0.001 |
|  Native American | 0.91 (0.85-0.97) | 0.003 |
|  Other | 0.76 (0.74-0.78) | <0.001 |
| **Hospital Location (Northeast – reference)** |  |  |
|  Midwest | 1.18 (1.17-1.2) | <0.001 |
|  South | 1.00 (0.99-1.01) | 0.85 |
|  West | 1.23 (1.21-1.25) | <0.001 |
| **Hospital Location/ teaching Status (Rural – reference)** |  |  |
|  Urban non-teaching | 0.9 (0.89-0.91) | <0.001 |
|  Teaching | 0.98 (0.97-0.99) | 0.031 |
| **Weekend Admission**  | 1.05 (1.04-1.06) | <0.001 |
| **Median ZIP income ( 1st quartile – reference)** |  |  |
|  2nd quartile | 1.04 (1.03-1.05) | <0.001 |
|  3rd quartile | 1.08 (1.07-1.09) | <0.001 |
|  4th quartile | 1.07 (1.06-1.09) | <0.001 |
| **Expected Primary Payer ( Medicare- reference)** |  |  |
|  Medicaid | 1.33 (1.3-1.36) | <0.001 |
|  Private | 0.87 (0.85-0.88) | <0.001 |
|  Uninsured | 1.23 (1.19-1.28) | <0.001 |
|  No charge | 0.79 (0.7-0.91) | 0.001 |
|  Other | 1.17 (1.14-1.21) | <0.001 |
| **Comorbidities** |
| Previous MI | 0.99 (0.98-0.99) | 0.035 |
| Cerebrovascular disease | 1.37 (1.35-1.39) | <0.001 |
| Heart failure | 1.47 (1.45-1.48) | <0.001 |
| Valvular disease | 0.98 (0.97-0.99) | <0.001 |
| Atrial fibrillation/flutter  | 1.1 (1.09-1.11) | <0.001 |
| Hypertension | 0.8 (0.79-0.81) | <0.001 |
| Dyslipidaemia | 0.63 (0.62-0.64) | <0.001 |
| Diabetes | 0.95 (0.94-0.96) | <0.001 |
| Smoking | 0.95 (0.94-0.96) | <0.001 |
| Peripheral vascular disease | 1.03 (1.02-1.04) | <0.001 |
| Chronic lung disease | 1.17 (1.16-1.18) | <0.001 |
| Chronic renal failure | 1.21 (1.2-1.22) | <0.001 |
| Obesity | 0.82 (0.81-0.83) | <0.001 |
| Anaemia | 1.14 (1.13-1.15) | <0.001 |
| Thrombocytopenia | 1.23 (1.21-1.25) | <0.001 |
| Coagulopathy | 2 (1.96-2.04) | <0.001 |
| Dementia | 2.53 (2.5-2.55) | <0.001 |
| Chronic Liver Disease | 1.62 (1.56-1.68) | <0.001 |
| Homelessness | 1.33 (1.21-1.45) | <0.001 |
| Solid malignancy | 1.69 (1.65-1.72) | <0.001 |
| Hematologic Malignancies | 1.53 (1.49-1.57) | <0.001 |
| Metastatic cancer | 2.7 (2.63-2.77) | <0.001 |

DNR; do not resuscitate, MI; myocardial infarction, IQR; interquartile range, STEMI; ST-segment elevation myocardial infarction,

**Table 3: In-Hospital Procedures and Outcomes, stratified by DNR status.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No DNR** | **DNR** | **P value** |
| **Number of weighted records** | 2,428,279 (87.7%) | 339,270 (12.3%) |  |
| **In Hospital Procedures** |
| Coronary Angiography | 61.8% | 18.8% | <0.001 |
| PCI | 37.7% | 10.3% | <0.001 |
| CABG  | 7% | 1% | <0.001 |
| Thrombolysis | 0.2% | 0.1% | <0.001 |
| Circulatory support (inc. IABP, LV assist device and ECMO).  | 3.9% | 3.9% | 0.68 |
| Mechanical Ventilation | 9.4% | 22.1% | <0.001 |
| Palliative consultation | 1.8% | 33.3% | <0.001 |
| **In Hospital Outcomes** |
| MACCE1 | 8.8% | 37.1% | <0.001 |
| Mortality | 4.6% | 32.7% | <0.001 |
| Acute Ischemic CVA | 2.5% | 6% | <0.001 |
| Major Bleeding  | 4.4% | 8.5% | <0.001 |
|  GI bleed | 3.2% | 6.3% | <0.001 |
|  Procedural related bleeding | 0.7% | 0.4% | <0.001 |
|  Retroperitoneal Bleed | 0.2% | 0.2% | <0.001 |
|  Intracranial Hemorrhage | 0.5% | 1.7% | <0.001 |

DNR; do not resuscitate, PCI; percutaneous coronary intervention, CABG surgery; coronary artery bypass grafting surgery, CVA; cerebrovascular accident, IABP; intra-aortic balloon pump, LV; left ventricle, ECMO; extracorporeal membrane oxygenation, GI; gastrointestinal, MACCE; major adverse cardiovascular and cerebrovascular events

\* MACCE is defined as a composite of all-cause mortality, acute ischemic CVA or transient ischemic attack and cardiac complications

**Table 4: Characteristics of patients with DNR stratified by occurrence of in-hospital Mortality.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **No Mortality** | **Mortality** | **P value** |
| Number of weighted records | 228,325 (67.3%) | 110,945 (32.7%) |  |
| Age (years), median (IQR) | 85 (76,90) | 78 (68,87) | <0.001 |
| Females, % | 56.7% | 46.7% | <0.001 |
| **Race** |  |  | <0.001 |
|  White | 83.5% | 76% |
|  Black | 7.1% | 10.3% |
|  Hispanic | 5% | 7.3% |
|  Asian/Pacific Islander | 2.3% | 3.2% |
|  Native American | 0.3% | 0.5% |
|  Other | 1.7% | 2.7% |
| **Hospital Location** |  |  | <0.001 |
|  Northeast | 22.1% | 21% |
|  Midwest | 27.8% | 24.6% |
|  South | 33% | 37.7% |
|  West | 17.1% | 16.6% |
| **Hospital Size** |  |  |  |
|  Small | 20.7% | 16.1% |
|  Medium | 30.1% | 29.9% |
|  Large | 49.3% | 54% |
| **Hospital Location/ teaching Status** |  |  | <0.001 |
|  Rural | 11.5% | 7.8% |
|  Urban non-teaching | 24.2% | 22.9% |
|  Teaching | 64.3% | 69.3% |
| Weekend Admission  | 27.6% | 26.8% | <0.001 |
| **Median ZIP income** |  |  | <0.001 |
|  1st quartile | 26.1% | 30.2% |
|  2nd quartile | 28.1% | 26.7% |
|  3rd quartile | 25.1% | 23.8% |
|  4th quartile | 20.7% | 19.4% |
| **Expected Primary Payer** |  |  | <0.001 |
|  Medicare | 89.3% | 77.6% |
|  Medicaid | 2.7% | 6.1% |
|  Private | 5.8% | 11.1% |
|  Uninsured | 0.8% | 2.5% |
|  No charge | <0.1% | 0.1% |
|  Other | 1.4% | 2.5% |
| Comorbidities |  |
| Previous MI | 15.5% | 11% | <0.001 |
| Cerebrovascular disease | 9.0% | 7.1% | <0.001 |
| Heart failure | 58.5% | 52.5% | <0.001 |
| Valvular disease | 22.7% | 15.8% | <0.001 |
| Atrial fibrillation/flutter  | 37.3% | 36.5% | <0.001 |
| Hypertension | 83.6% | 74.9% | <0.001 |
| Dyslipidaemia | 53% | 41.4% | <0.001 |
| Diabetes | 36.8% | 36.9% | 0.365 |
| Smoking | 36% | 33.8% | <0.001 |
| Peripheral vascular disease | 11.5% | 10.8% | <0.001 |
| Chronic lung disease | 29.9% | 27.9% | <0.001 |
| Chronic renal failure | 40.8% | 36% | <0.001 |
| Obesity | 8.2% | 9.5% | <0.001 |
| Anaemia | 38.4% | 37.5% | <0.001 |
| Thrombocytopenia | 7.9% | 12.5% | <0.001 |
| Coagulopathy | 2.5% | 8.6% | <0.001 |
| Dementia | 28.5% | 17.3% | <0.001 |
| Chronic Liver Disease | 1% | 1.6% | <0.001 |
| Homelessness | 0.2% | 0.3% | <0.001 |
| Solid malignancy | 7.5% | 7.7% | 0.006 |
| Hematologic Malignancies | 2.5% | 3.1% | <0.001 |
| Metastatic cancer | 4.3% | 5.1% | <0.001 |
| Record Characteristics |
| STEMI | 11.2% | 27.4% | <0.001 |
| Ventricular Fibrillation | 1.2% | 8.7% | <0.001 |
| Ventricular Tachycardia | 5.0% | 11.2% | <0.001 |
| In-hospital Procedures |
| Coronary angiography | 18.3% | 19.7% | <0.001 |
| PCI | 9.7% | 11.6% | <0.001 |
| CABG | 0.8% | 1.5% | <0.001 |
| Thrombolysis | 0.1% | 0.1% | 0.136 |

DNR; do not resuscitate, PCI; percutaneous coronary intervention, CABG surgery; coronary artery bypass grafting surgery, CVA; cerebrovascular accident, MI; myocardial infarction, IQR; interquartile range, STEMI; ST-segment elevation myocardial infarction

**Table 5: Predictors of In-Hospital Mortality among patients with DNR status.**

|  |  |  |
| --- | --- | --- |
|  | **OR (95% CI)** | **P value** |
| **Female** | 0.75 (0.74-0.76) | <0.001 |
| **Age** | 0.97 (0.97-0.97) | <0.001 |
| **Race (White – reference)** |  |  |
|  Black | 1.29 (1.26-1.33) | <0.001 |
|  Hispanic | 1.36 (1.32-1.41) | <0.001 |
|  Asian/Pacific Islander | 1.56 (1.49-1.64) | <0.001 |
|  Native American | 1.51 (1.33-1.7) | <0.001 |
|  Other | 1.48 (1.4-1.56) | <0.001 |
| **Hospital Bedsize (Small- reference)** |  |  |
| Medium | 1.21 (1.18-1.24) | <0.001 |
| Large | 1.26 (1.23-1.29) | <0.001 |
| **Hospital Location (Northeast – reference)** |  |  |
|  Midwest | 0.93 (0.9-0.95) | <0.001 |
|  South | 1.02 (0.99-1.05) | 0.11 |
|  West | 0.9 (0.87-0.92) | <0.001 |
| **Hospital Location/ teaching Status (Rural – reference)** |  |  |
|  Urban non-teaching | 1.41 (1.37-1.46) | <0.001 |
|  Teaching | 1.51 (1.46-1.55) | <0.001 |
| **Median ZIP income ( 1st quartile – reference)** |  |  |
|  2nd quartile | 0.92 (0.9-0.94) | <0.001 |
|  3rd quartile | 0.9 (0.88-0.92) | <0.001 |
|  4th quartile | 0.93 (0.9-0.95) | <0.001 |
| **Expected Primary Payer ( Medicare- reference)** |  |  |
|  Medicaid | 1.04 (1-1.09) | 0.05 |
|  Private | 1.28 (1.24-1.31) | <0.001 |
|  Uninsured | 1.42 (1.32-1.52) | <0.001 |
|  No charge | 1.77 (1.31-2.4) | <0.001 |
|  Other | 1.45 (1.37-1.53) | <0.001 |
| **Comorbidities**  |
| Previous MI | 0.77 (0.75-0.79) | <0.001 |
| Cerebrovascular disease | 0.78 (0.76-0.81) | <0.001 |
| Heart failure | 0.95 (0.93-0.97) | <0.001 |
| Valvular disease | 0.82 (0.81-0.81) | <0.001 |
| Atrial fibrillation/flutter  | 1.19 (1.17-1.21) | <0.001 |
| Hypertension | 0.81 (0.8-0.83) | <0.001 |
| Dyslipidaemia | 0.75 (0.74-0.76) | <0.001 |
| Diabetes |  |  |
| Smoking | 0.79 (0.78-0.8) | <0.001 |
| Chronic renal failure |  |  |
| Chronic lung disease | 0.95 (0.94-0.97) | <0.001 |
| Obesity |  |  |
| Peripheral vascular disease | 1.09 (1.06-1.11) | <0.001 |
| Anaemia | 0.91 (0.9-0.93) | <0.001 |
| Thrombocytopenia | 1.39 (1.36-1.43) | <0.001 |
| Dementia | 0.65 (0.63-0.67) | <0.001 |
| Solid malignancy | 0.79 (0.76-0.82) | <0.001 |
| Hematologic Malignancies |  |  |
| Metastatic cancer | 0.9 (0.86-0.94) | <0.001 |
| **Record Characteristics and in hospital procedures** |
| STEMI | 2.9 (2.84-2.96) | <0.001 |
| CABG | 1.96 (1.82-2.12) | <0.001 |
| Coronary angiography | 0.64 (0.63-0.66) | <0.001 |

DNR; do not resuscitate, PCI; percutaneous coronary intervention, CABG surgery; coronary artery bypass grafting surgery, CVA; cerebrovascular accident, MI; myocardial infarction, STEMI; ST-segment elevation myocardial infarction

**Supplementary Table 1: ICD 9 and ICD 10 codes used to extract data**

|  |  |
| --- | --- |
| **Variable** | **Codes** |
| **Patient and Record Characteristics** |
| DNR status | Z66 |
| Ischemic Heart disease | I25.2;I25.5; Z95.1; I25.7x.; Z98.61; Z95.5 |
| Cerebrovascular disease | I65-69 |
| Chronic renal failure | N18 |
| Aortic Disease | I70.0 |
| Peripheral Vascular Disease of extremities | I70.2x-I70.9x; I73.x; Z98.62 |
| STEMI | I21.0-3 |
| Cardiac Arrest | I46.x |
| Ventricular Fibrillation | I49.01 |
| Ventricular tachycardia | I47.2 |
| Cardiogenic Shock | R57.0 |
| Heart failure | I50 |
| Valvular disease | I05-08; I34-37 |
| Atrial fibrillation/flutter  | I48 |
| Hypertension | I10-16 |
| Dyslipidaemia | E78 |
| Diabetes | E08-13 |
| Smoking | Z87.891 , Z72.0 |
| Chronic lung disease | J40-47 |
| Obesity | E66 |
| Anaemia | D55-59 |
| Thrombocytopenia | D69.3-.6 |
| Coagulopathy | D65-68;D69.0-.2 |
| Dementia | F01-03 |
| Chronic Liver Disease | K73-74 |
| Homelessness | Z59.0 |
| Solid malignancy | C00.x-C76.x; C80.x |
| Hematologic Malignancies | C81-96 |
| Metastatic cancer | C77.x-79.x |
| **In Hospital Procedures** |
| Palliative consultation  | Z51.5 |
| Coronary Angiography | B211x |
| PCI | 02703x/13x/23x/33x |
| CABG | 02100\*/04\*/10\*/14\*/20\*/24\*/30\*/34\* |
| Thrombolysis | 3E07317 |
| Circulatory support (inc. IABP, LV assist device and ECMO).  | 5A02x, 5A1522G, 5A15A2G, 5A15A2H |
| Mechanical Ventilation | 5A19054/35Z/45Z/55Z |
| **In Hospital Outcomes** |
| Acute Ischemic CVA | I63 |
| Coronary artery dissection | I2542 |
| Pericardial effusion (incl tamponade) | I23.0 I31.2 I31.4 I31.3 |
| Tamponade | I31.4 |
| Dressler’s syndrome | I24.1 |
| Post MI angina | I23.7 |
| Intracardiac Thrombus | I23.6 |
| Mechanical complications | I23.1-I23.5 |
| GI bleed | K92.0-92.2; K25.0-25.2; K25.4-25.6; K26.0-26.2; K27.0-27.2; K27.4-27.6; K28.0-28.2; K28.4-28.6 |
| Retroperitoneal Bleed | K66.1 |
| Intracranial Haemorrhage | I60-62 |

DNR; do not resuscitate, ICD; International classification of diseases, PCI; percutaneous coronary intervention, CABG surgery; coronary artery bypass grafting surgery, MI; myocardial infarction, CVA; cerebrovascular accident, IABP; intra-aortic balloon pump, LV; left ventricle, ECMO; extracorporeal membrane oxygenation, GI; gastrointestinal, STEMI; ST-segment elevation myocardial infarction