# SIBS 2022 Group D


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July 21, 2022

# Research Question

Which types of clinical interventions are most associated with recurrence of MI?

# Overview

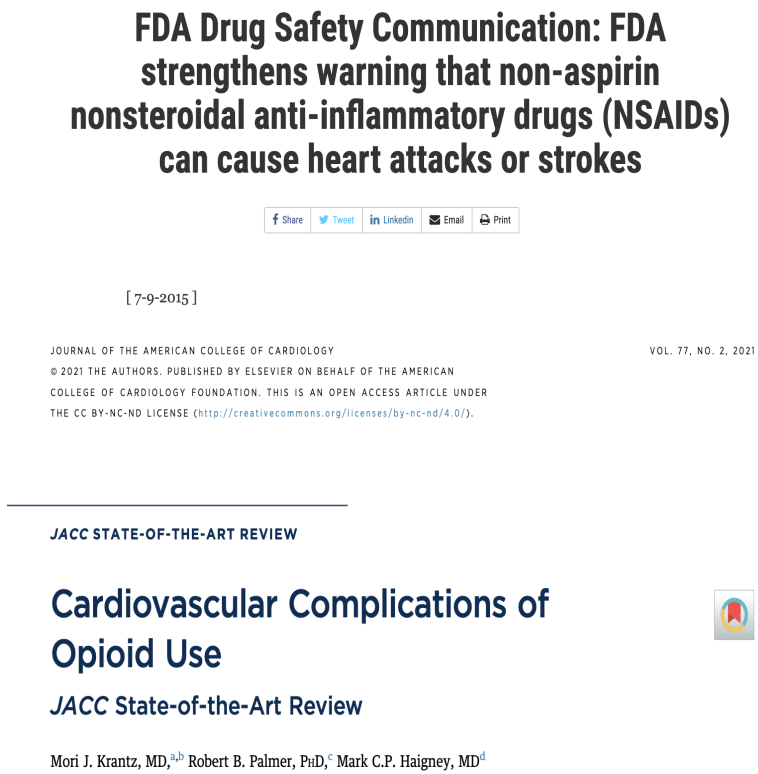
- Background & Significance
- Methods
- Model
- Clinical Significance
- Limitations & Future Directions

# The Problem

- Coronary heart disease is leading cause of death in US
- 7.2% of adults in US have coronary heart disease
- 1 in 5 people have MI recurrence within 5 years (AHA)

# Pain Medications

- Non-aspirin pain medications can lead to heart attacks



**FDA Drug Safety Communication: FDA strengthens warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) can cause heart attacks or strokes**

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JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 77, NO. 2, 2021


*JACC* STATE-OF-THE-ART REVIEW

**Cardiovascular Complications of Opioid Use**

*JACC* State-of-the-Art Review

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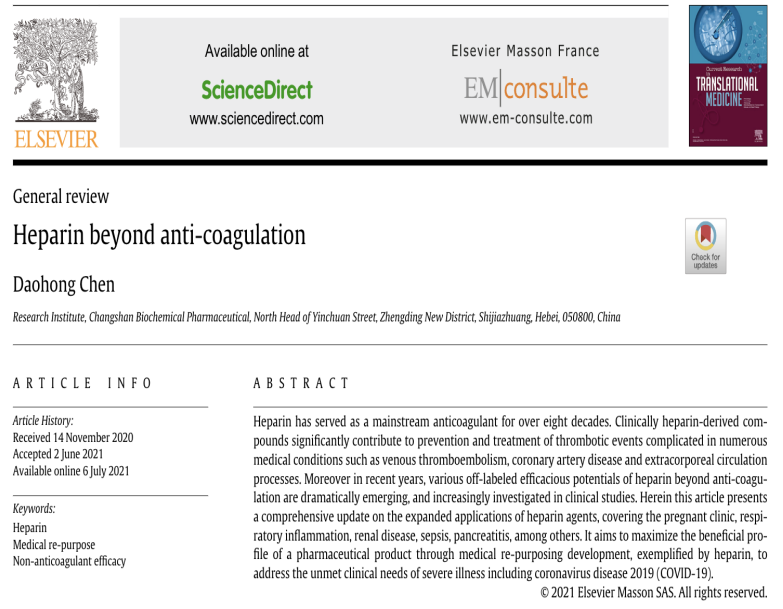
# Blood Thinners

- Anti-clotting medications may be effective at reducing MI recurrence



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General review

## Heparin beyond anti-coagulation

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ARTICLE INFO

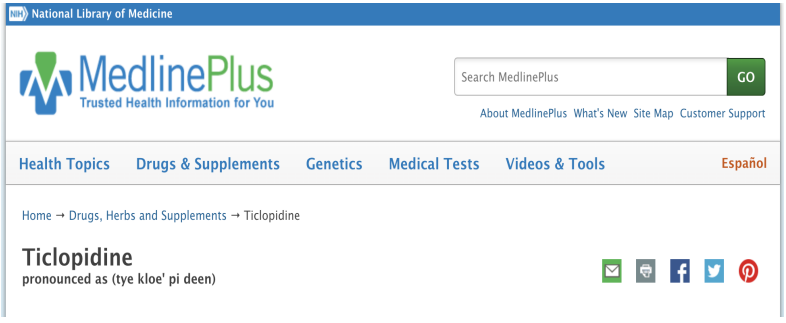
*Article History:*
Received 14 November 2020
Accepted 2 June 2021
Available online 6 July 2021

*Keywords:*
Heparin
Medical re-purpose
Non-anticoagulant efficacy

ABSTRACT

Heparin has served as a mainstream anticoagulant for over eight decades. Clinically heparin-derived compounds significantly contribute to prevention and treatment of thrombotic events complicated in numerous medical conditions such as venous thromboembolism, coronary artery disease and extracorporeal circulation processes. Moreover in recent years, various off-labeled efficacious potentials of heparin beyond anti-coagulation are dramatically emerging, and increasingly investigated in clinical studies. Herein this article presents a comprehensive update on the expanded applications of heparin agents, covering the pregnant clinic, respiratory inflammation, renal disease, sepsis, pancreatitis, among others. It aims to maximize the beneficial profile of a pharmaceutical product through medical re-purposing development, exemplified by heparin, to address the unmet clinical needs of severe illness including coronavirus disease 2019 (COVID-19).





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**Ticlopidine**
pronounced as (tye kloe' pi deen)

# Significance

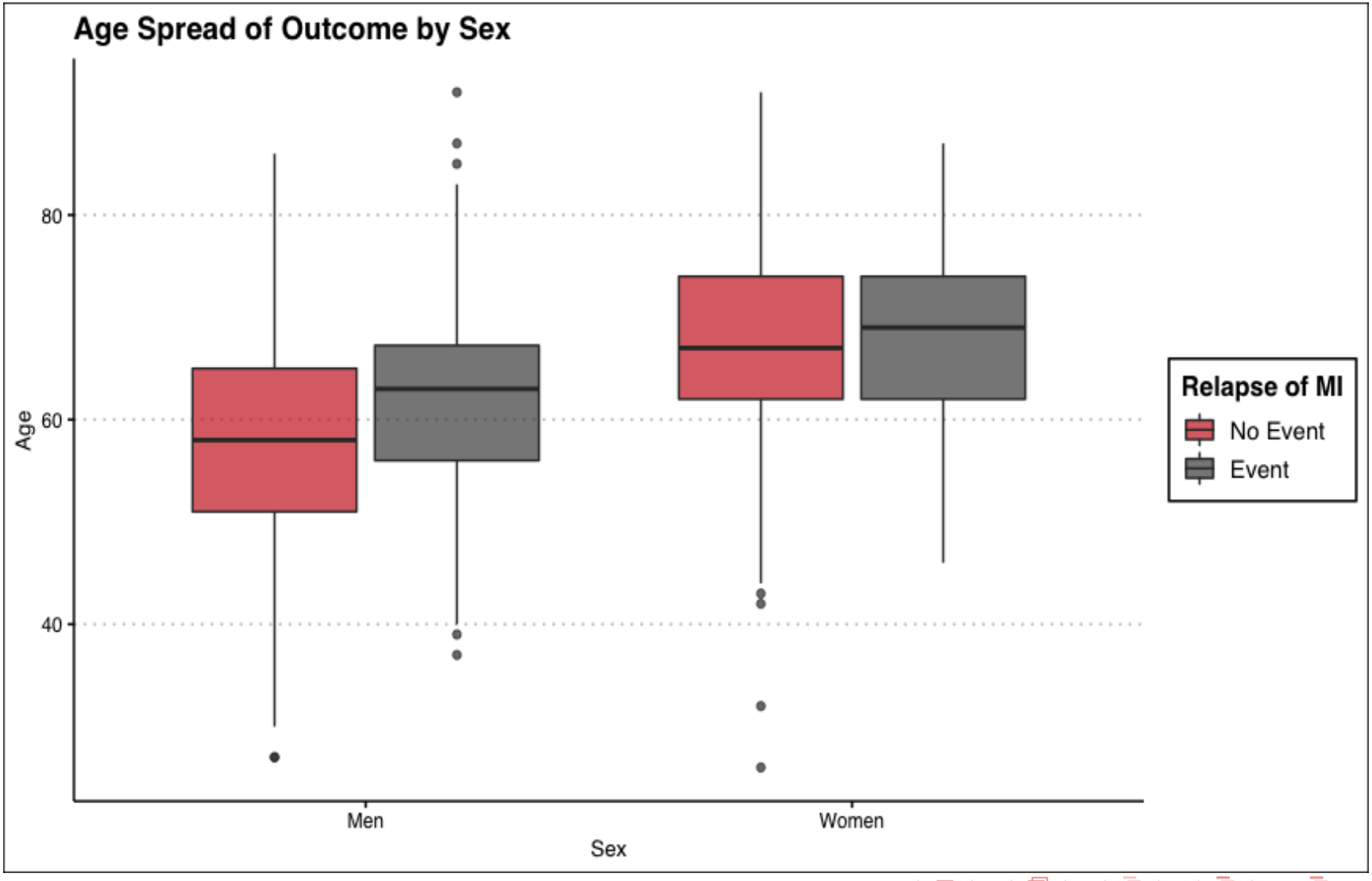
Empower providers with more information about risks and benefits associated with MI and pain treatments.

# The Data

- Collected at Krasnoyarsk Interdistrict Clinical Hospital № 20 from 1992-1995.
- 1700 Total Patients in the Data
- 111 Covariates.
- 12 Complications.
- 12 Continuous Variables.
- 21 Categorical Variables.
- 78 Binary Variables.

Actual Hospital in Russia

# Exploratory Data Analysis



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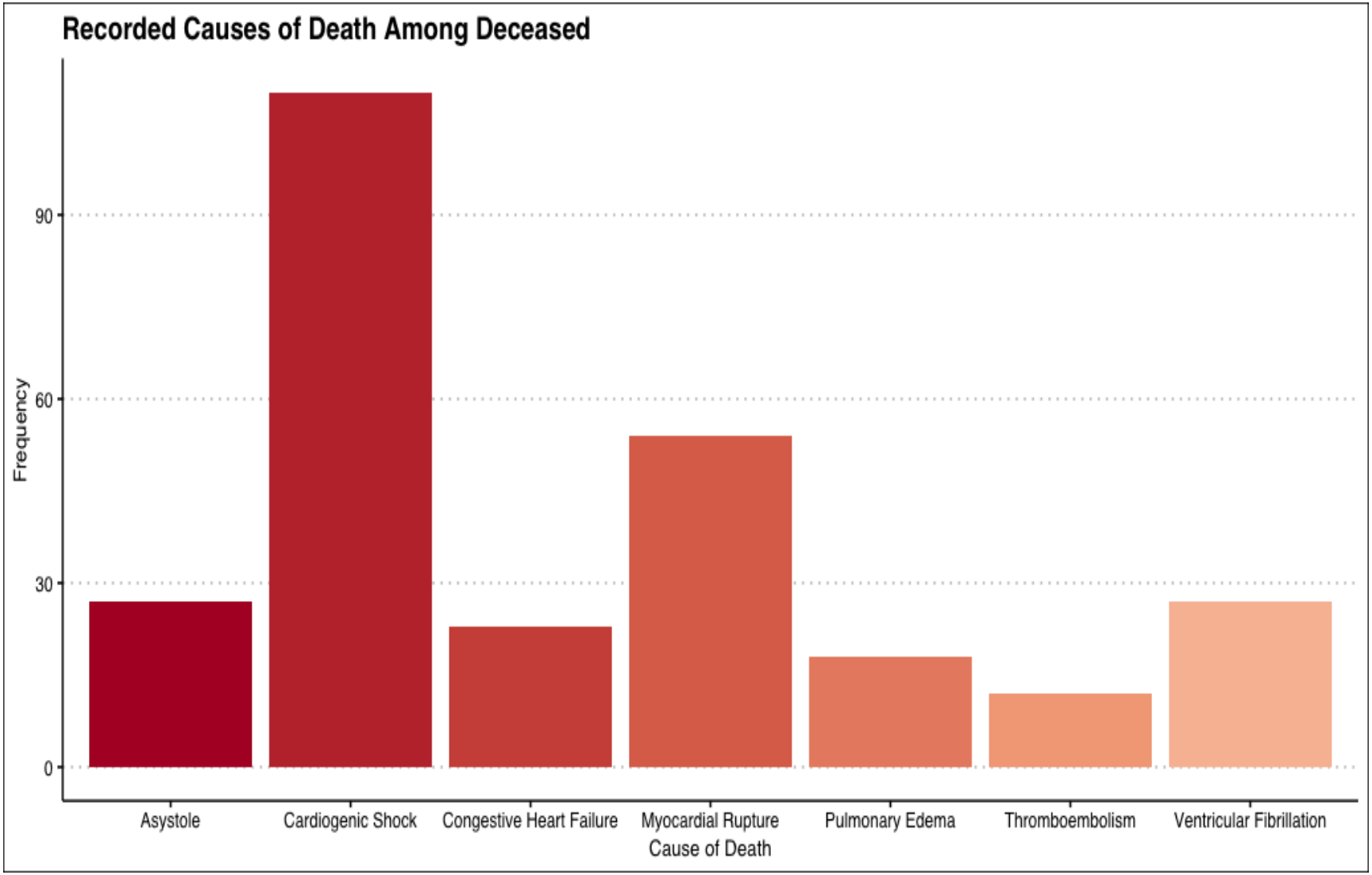

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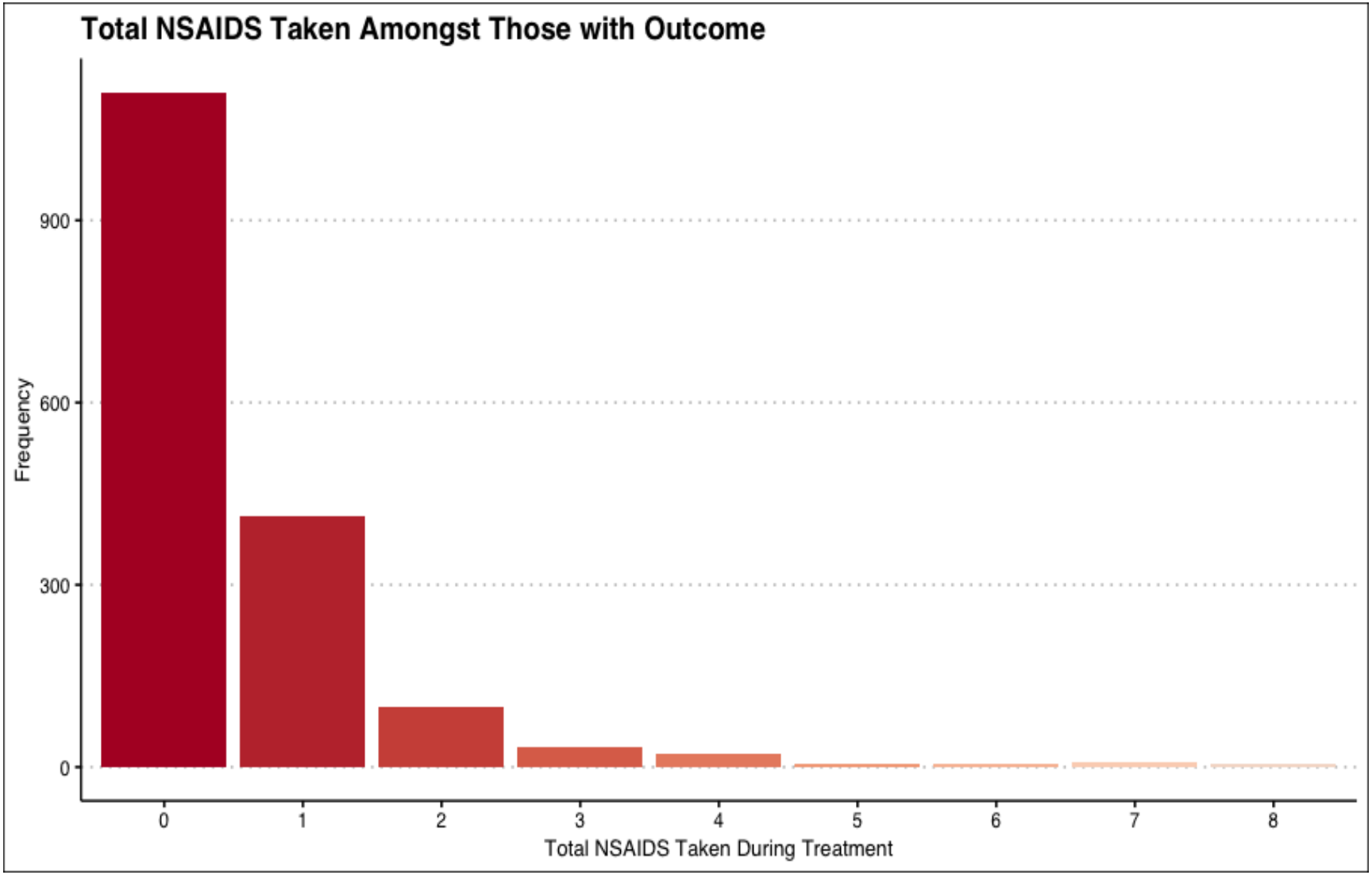

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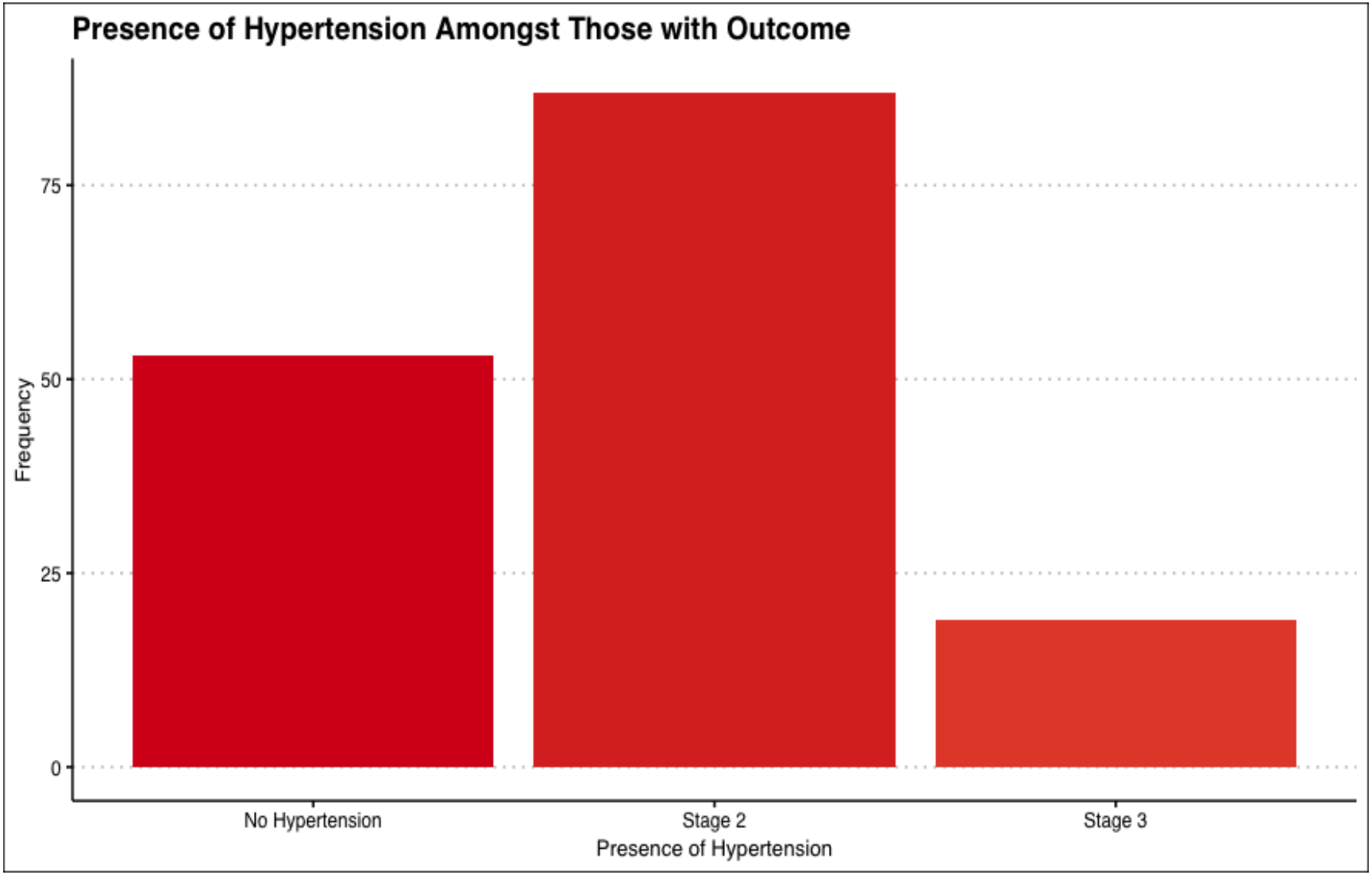


A Key Problem: Missing Data

# Data Wrangling

- Four covariates with more than 50% of the data missing. (Removed)
- Turned select categorical variables into binary variables using thresholds.
- Remaining categorical variables turned into dummy variables.
- Employed Multiple Imputation with Chained Equations (MICE) to impute missing data.
  - $\rightarrow$ Assumes data is missing at random (MAR).
  - $\rightarrow$ Robust method that imputes missing data in a dataset through an iterative series of predictive models.
  - $\rightarrow$ Iterations should be run until it appears that convergence has been met.
  - $\rightarrow$ Computationally expensive.

# Model Selection

- Model Type: Logistic regression with relapse of MI as the outcome.

  $\rightarrow$ Step-wise Selection

  $\rightarrow$ Started with an empty model and full model in stats::step()

  $\rightarrow$ Only kept covariates that were significant ($\alpha = 0.05$)

# Model Selection

## Start

111 Covariates

## Pre ICU

88 Covariates

## After step-wise selection

24 Covariates

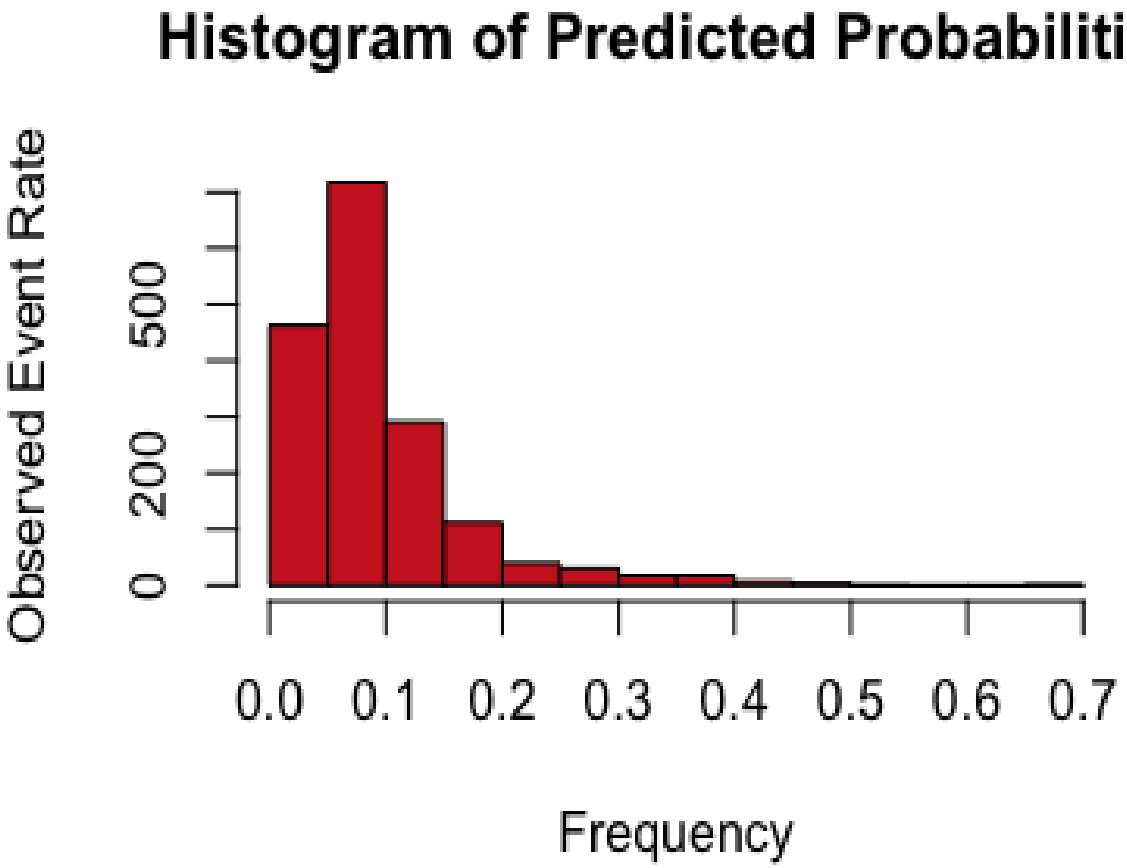
## After test for significance

9 Covariates

# Baseline Model

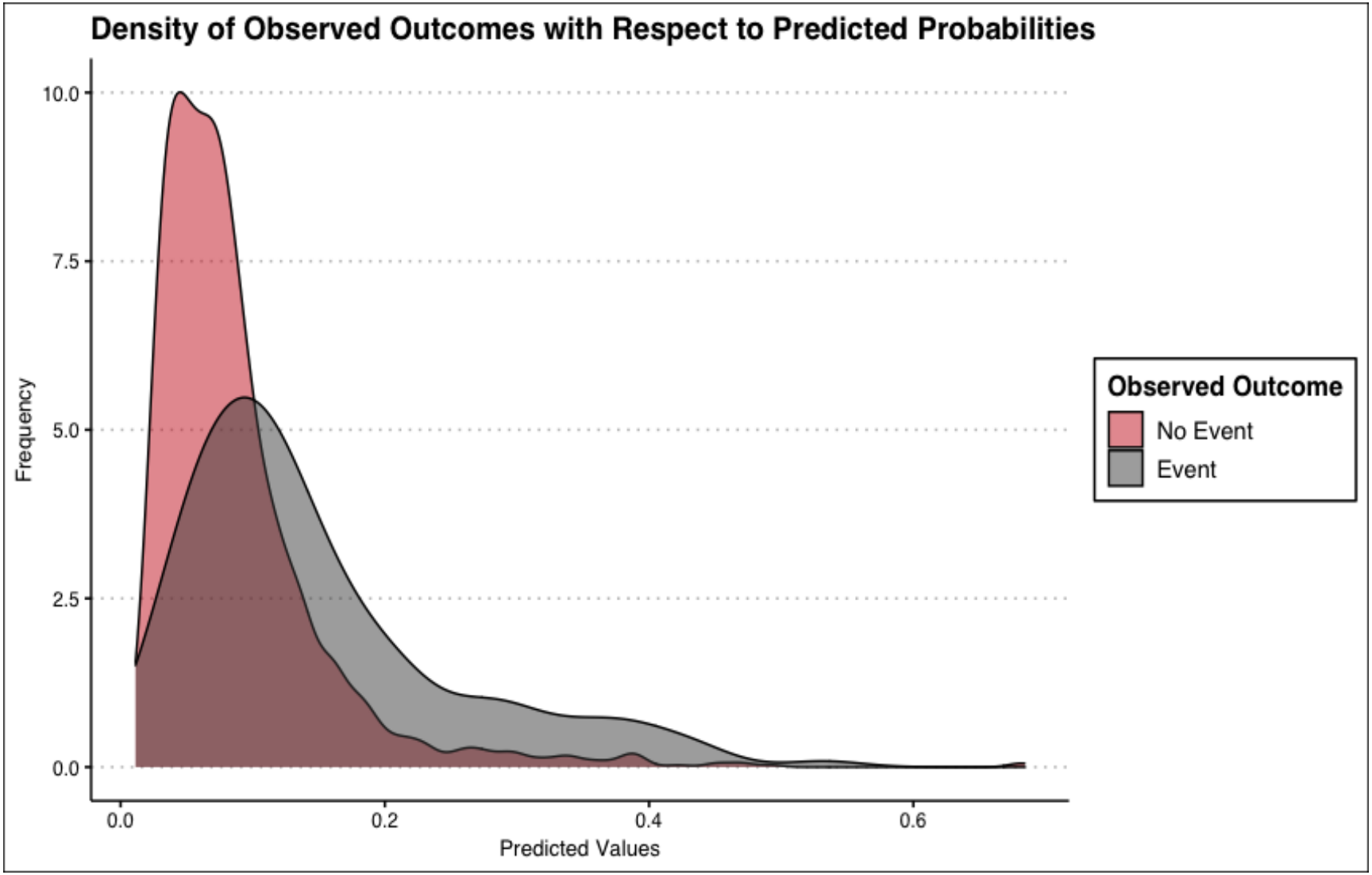
| Variable | Coefficient | P-Value |
|---|---|---|
| Pain Relapse | 1.066 | 0.000 |
| No angina pectoris | -0.626 | 0.002 |
| Increased Sodium | 1.346 | 0.001 |
| Age | 0.021 | 0.007 |
| Incomplete RBBB | 1.406 | 0.002 |
| Ventricular tachycardia at admission | 1.932 | 0.01 |
| Lidocaine EMT | -0.594 | 0.002 |
| Opioids EMT | 0.460 | 0.015 |
| White Blood Cell | 0.047 | 0.041 |

# Baseline Model Evaluation




Model Weakness: Hesitant to predict high probabilities of the outcome (low discriminatory capabilities).

# Baseline Model Evaluation



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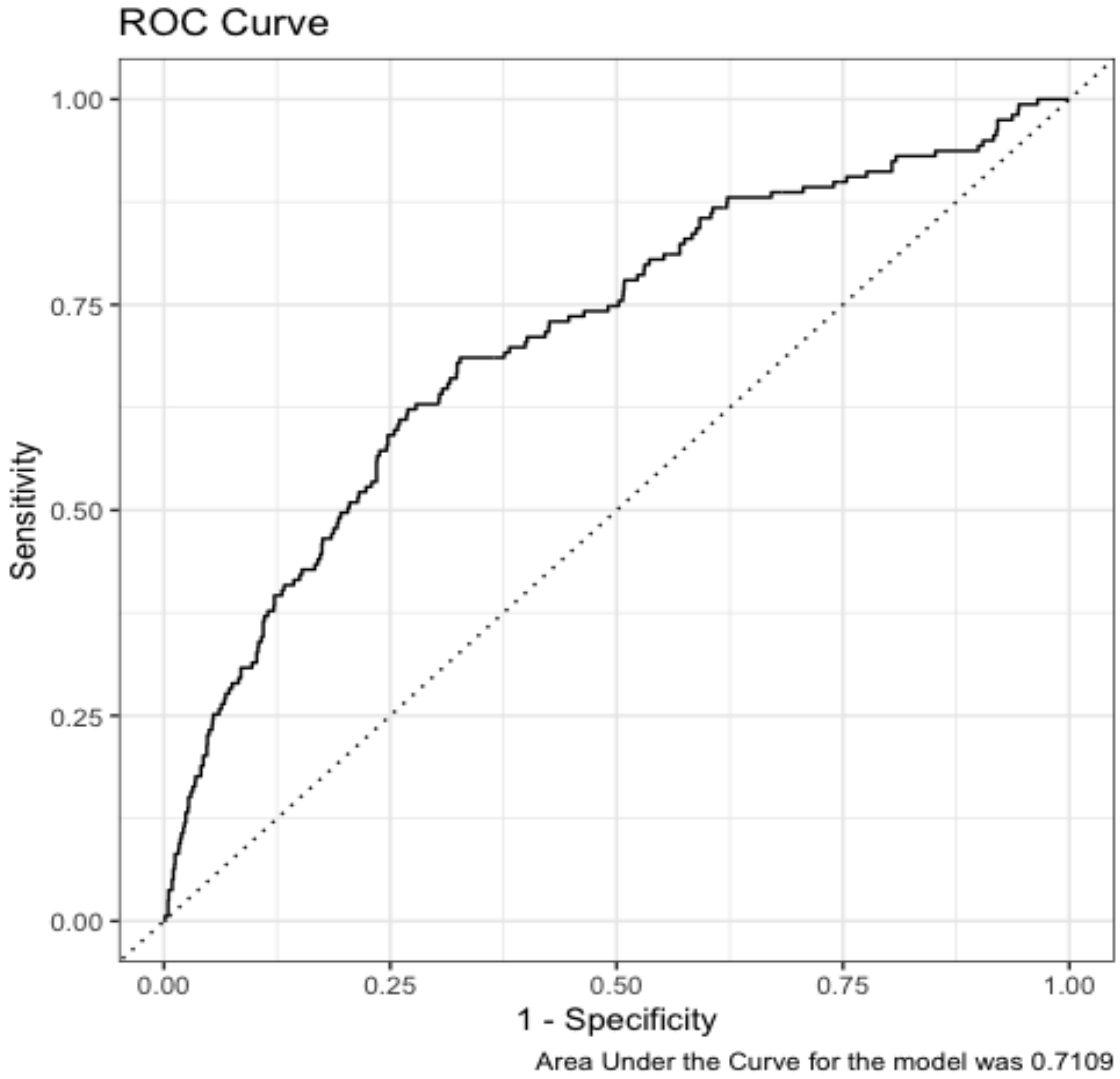
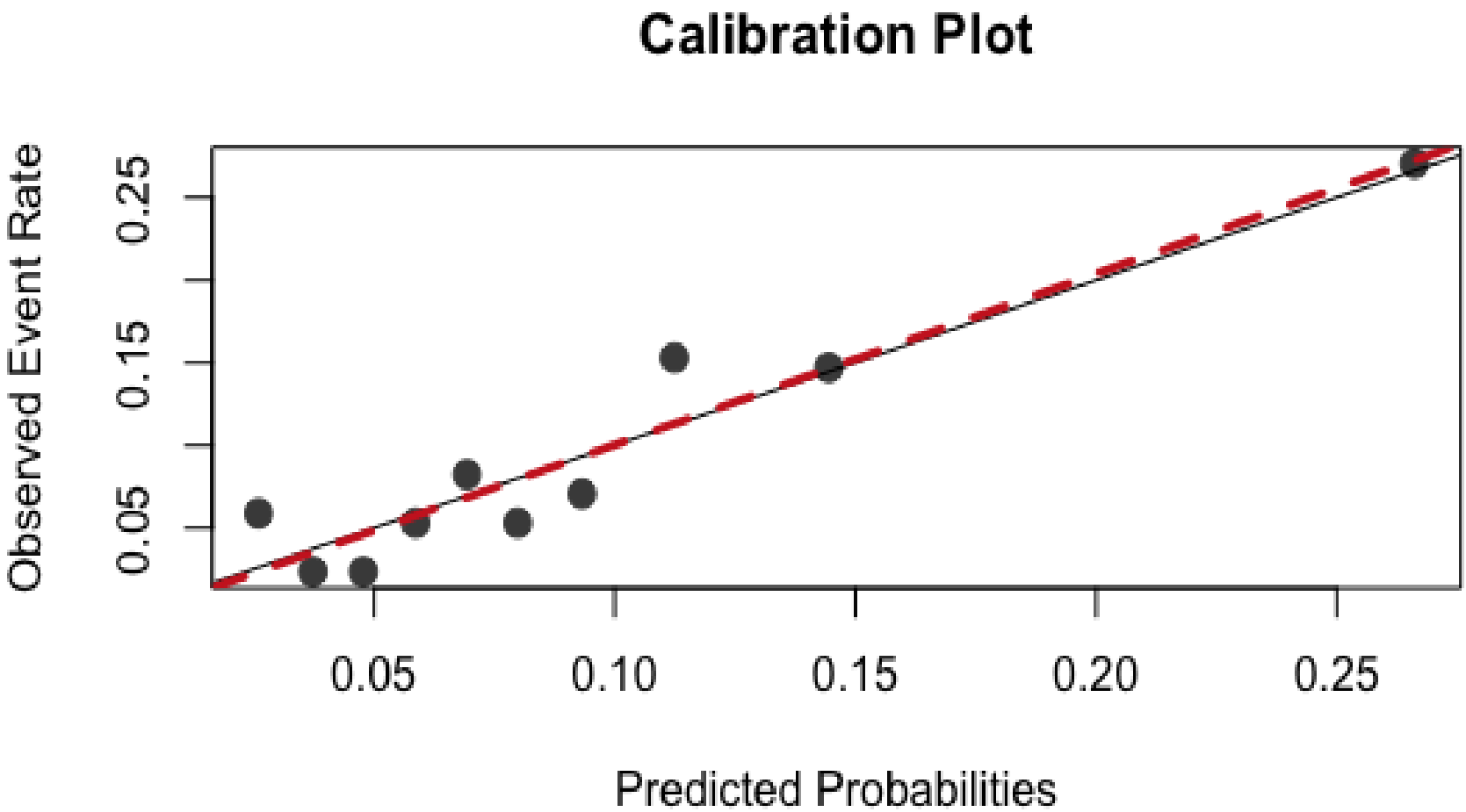


# Baseline Model Evaluation

| Decile Group | Observed Event Rate | Predicted Mean Probabilities |
|---|---|---|
| 1 | 0.0588 | 0.0261 |
| 2 | 0.0235 | 0.0373 |
| 3 | 0.0235 | 0.0478 |
| 4 | 0.0529 | 0.0587 |
| 5 | 0.0824 | 0.0693 |
| 6 | 0.0529 | 0.0799 |
| 7 | 0.0706 | 0.0932 |
| 8 | 0.1529 | 0.1124 |
| 9 | 0.1471 | 0.1445 |
| 10 | 0.2706 | 0.2661 |

Our model is able to remain close to observed mean probabilities within each decile.

# Baseline Model Evaluation



# Treatments

Tested all treatments preformed in the ICU

| Treatment | Coefficient Estimate | P-Value |
|---|---|---|
| Fibrinolytic Therapy 1 | 0.160 | 0.838 |
| Fibrinolytic Therapy 2 | -0.436 | 0.415 |
| Fibrinolytic Therapy 3 | -12.95 | 0.985 |
| Fibrinolytic Therapy 4 | -0.136 | 0.916 |
| Fibrinolytic Therapy 5 | 1.049 | 0.347 |
| Fibrinolytic Therapy 6 | -13.628 | 0.988 |
| Liquid Nitrate | 0.213 | 0.387 |
| Opioid Day 1 | 0.221 | 0.236 |
| Opioid Day 2 | 0.321 | 0.268 |
| Opioid Day 3 | -0.029 | 0.939 |
| NSAIDs Day 1 | 0.095 | 0.628 |
| NSAIDs Day 2 | 0.206 | 0.467 |
| NSAIDs Day 3 | -0.173 | 0.630 |
| Lidocaine | -0.186 | 0.369 |
| Beta-Blockers | 0.162 | 0.552 |
| Calcium-Blockers | -0.177 | 0.342 |
| **Anticoagulants** | **0.501** | **0.026** |
| Acetylsalicylic Acid | 0.226 | 0.317 |
| Ticlid | 0.763 | 0.209 |
| Trental | -0.366 | 0.138 |

# Pain Treatments

| Treatment | Coefficient Estimate | P-Value | Odds Ratio |
|---|---|---|---|
| Opioid Day 1 | 0.221 | 0.236 | 1.247 |
| Opioid Day 2 | 0.321 | 0.268 | 1.379 |
| Opioid Day 3 | -0.029 | 0.939 | 0.971 |
| NSAIDs Day 1 | 0.095 | 0.628 | 1.099 |
| NSAIDs Day 2 | 0.206 | 0.467 | 1.229 |
| NSAIDs Day 3 | -0.173 | 0.630 | 0.841 |
| Lidocaine | -0.186 | 0.369 | 0.83 |

# Discussion

- No pain medications were predictive of MI relapse
- Inconsistent with longer term studies in literature
- Could be explained by short term use in the hospital

# Anticoagulants Treatments

| Treatment | Odds Ratio | P-Value | Confidence Interval |
|---|---|---|---|
| Anticoagulants | 1.65 | 0.026 | (0.99 , 2.72) |

The anticoagulant group are 1.65 more likely of a relapse in MI.

# Discussion

- Heparin significantly raised risk of MI relapse
- Not intuitive
- Other blood thinners were not significant

# Weaknesses and Limitations

- Sample is not representative of current US population.
  - $\rightarrow$ Data collected over two decades ago.
  - $\rightarrow$ Different culture facilitates different environmental conditions from $21^{st}$ century USA.
  - $\rightarrow$ Difficult to generalize findings.

- Computational limitations may have resulted in a biased imputation (via MICE).

- Model possesses low discriminatory capacity.

# Future Directions

- Further investigate anticoagulants
- Replicate study with US sample
- Evaluate risk of long-term prescription medications

# Questions