Improving Emergency Department Nurse Triage via Big Data Analytics

by

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Improving Emergency Department Nurse Triage via Big Data Analytics

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Background: In the United States, emergency department nurses triage approximately 145 million patients a year. Triage is the brief period of time where nurses assess and prioritize patients who have the most significant risk for morbidity and mortality. Typical or atypical patient presentation for acute coronary syndrome (ACS), or heart attack, is challenging for nurses to distinguish given the over 30 potential symptoms at triage. Machine learning algorithms using routinely collected objective data have potential to improve identification of a coronary event and to potentially eliminate known biases in the current triage system, thus improving patient outcomes.

Purpose: The purpose of this study was to develop and validate a predictive triage algorithm that can identifiy ACS that requires immediate treatment in patients presenting with suspected ACS. We aimed to: 1) assemble and annotate a large cohort of patients presenting to the emergency department for suspicion of ACS; 2) develop, validate and compare five machine learning algorithms to develop a sensitive and specific model to predict the outcome of ACS; and 3) compare the performance of our best two machine learning algortihms against routine emergency department triage practice (i.e., the Emergency Severity Index).

Methods: We conducted a retrospective observational cohort study of adult patients who were triaged at the emergency department for a suspected coronary event. We developed, validated and compared five machine learning algorithms (binary logistic regression, naïve Bayes, random forest, gradient boosting machine, and artificial neural network) using routinely collected data that could be available at triage. We used 10-fold cross validation to predict the outcome of ACS

and to identify the best two performing algorithms using the area under the receiver operating characteristic curve (AUC). We used lasso regularization to select a subset of input variables for the outcome of ACS. We then compared performance of our machine learning classifiers to the dichotomized assigned scores from the Emergency Severity Index to correctly classify the diagnosis of ACS as high acuity using the AUC. We used the Delong test to compare the AUC of our best performing machine learning algorithms to correctly assigned high acuity triage scores.

Results: Our sample included 1201 patients (mean age 65±14 years, 46% female, 89% white, 1% Hispanic) with 522 (43%) patients having a diagnosis of ACS. We identified a total of 243 input variables with a subset of 43 variables chosen using lasso regularization. Artifical neural network and binary logistic regression were the best performing algorithms using the subset of 43 input variables with the AUC of 0.78 [95% confidence interval (CI), 0.76–0.80] and 0.77 (95% CI, 0.75–0.79), respectively. Both algorithms outperformed the diachotomized ESI triage scores for placing ACS as high acuity with an AUC of 0.61 (95% CI, 0.60–0.63). There was a statistically significant difference in AUC between the best performing algorithm (artificial neural network) and the correctly assigned ESI triage scores ($p < 0.001$).

Conclusion: Our machine learning algorithms outperformed routine triage scores in identifying highest risk patients among those with suspected ACS using baseline triage data collected in the brief period of time to assess a patient at the emergency department to identify ACS. There was a 17% accuracy rate improvement when comparing the artifical neural network accuracy rate to the correctly assigned high acuity triage scores for the outcome of ACS in our hetereogenious patient population. The application of predictive algorithms could be translated into a clinical

decision support tool to enhance identification of patients with potential ACS, improving timely treatments, which could improve patient outcomes.

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List of Abbreviations

Acute coronary syndrome (ACS)

Emergency department (ED)

Emergency Severity Index (ESI)

Emergency Nurses Association (ENA)

American College of Emergency Physicians (ACEP)

Electronic health record (EHR)

Machine learning (ML)

Health Record Research Request (R3)

Area under the receiever operating charcterstic curve (AUC)

Acute myocardial infarction (AMI)

Systolic blood pressure (SBP)

ST-segment myocardial infarction (STEMI)

Non ST-segemnt myocardial infarction (NSTEMI)

Major adverse cardiac event (MACE)

Myocardial infarction (MI)

Heart rate (HR)

Electrocardigram (ECG)

Shortness of breath (SOB)

Percutaneous coronary intervention (PCI)

Negative predicitve value (NPV)

Positive predictive value (PPV)

Preface

I would like to thank all of my committee members from the bottom of my heart whose mentorship and guidance has made this dissertation study possible. Thank you to my dissertation chair, Dr. Salah Al-Zaiti, whose expertise and dedication guided me through this research study. Thank you to: Dr. Clifton Callaway, my Co-Sponsor for this study, who believed an emergency nurse could become a researcher and dedicating your endless knowledge and expertise in Emergency Medicine to keep this research clinically applicable; Dr. Ervin Sejdić for your interdisciplinary contribution to guide the methods of machine learning and your relentless push to make me a data science expert; Dr. Susan Sereika, for your individualized approach to my training in research and for your ongoing encouragement; and Dr. Marilyn Hravnak, for your guidance in clinical machine learning applications, career guidance and inspiring me to figure out what type of nursing scientist I want to be. I also want to recognize and thank the late Dr. Susan Cohen, for her mentorship and who believed that I could accomplish obtaining a PhD in Nursing in a 3-year timeline. A big thank you to Dr. Heidi Donovan who has supported me through this process and who has been my cheerleader when I needed it the most. I am forever thankful to my research students, Julissa Brown, Jennie Stemler, Caroline Sisson, Katie Choice, Alex Tolassi, Tiffany Okerman, Corbin Fry, and Brandi Leverknight, who supported this research.

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1.0 Introduction

The concept of triage originated on the battlefields under desperate conditions where demand outstripped resources. However, military and wartime triage of the past shows little resemblance to emergency department (ED) triage today. Fast forward three centuries, with the modern healthcare system relying on the hospital EDs to sort, assess, and critically appraise nearly 145 million patients a year to receive patient-centered care from nurses, physicians, and ancillary staff.[1] The ED is the entry point to the entire hospital system. Nurses serve as the gate keepers to every patient that seeks emergent care. Their critical triage assessment drives efficient delivery of care and optimizes allocation of limited resources under strict time constraints.[2,3] Today, the focus of ED nurse triage is to differentiate clinical conditions to prioritize those with the most significant risk of morbidity and mortality.

Currently, a majority of EDs across the United States use the Emergency Severity Index (ESI) triage tool.[4] This clinical tool, used by nurses at triage, is an ordinal five-level algorithm that categorizes patients into different levels, but does not risk stratify patients. The ESI has significant limitations including: 1) subjectivity;[2] 2) racial bias;[5-7] 3) poor relation to patient-centered outcomes; and 4) failure to differentiate acute patients (poor specificity).[8,9] As such, the ESI tool fails to identify patient-specific factors that are present at triage assessment that can accurately predict critical conditions requiring life-saving treatments.

Due to its time sensitive nature, complex symptomatology, and variable outcomes, acute coronary syndrome (ACS) will be used as an exemplary time-sensitive critical condition. Of the 800,000 new annual ACS cases in the United States, nurses fail to identify approximately 50% of

them during triage.[10,11] This suggests an urgent need to improve triage tools, specifically one that correctly identifies ACS early, which could reduce mortality by 10%–20%.[10,12]

By utilizing big data analytics, hidden patterns will be revealed from the complex interactions of patient factors at triage to quickly and accurately identify patients at risk for ACS. Data science approaches hold promise for creating sensitive and specific predictive models for nurse triage that are not easily modeled using basic statistical techniques. State-of-the-art machine learning techniques such as naive Bayes classification[13] will be used to develop a predictive model for patients at risk for ACS at nurse triage.

1.1 Specific Aims

This study aims to use big data analytics to identify subtle patterns in patient factors collected at ED nurse triage to develop an objective prediction algorithm, which will equip nurses with a robust tool to make real-time clinical triage decisions, thereby improving patient outcomes. **Our overall purpose is to develop and validate a predictive triage algorithm that can identify acute coronary syndrome that requires immediate treatments in patients presenting with suspected acute coronary syndrome.**

Specific Aim 1a: Assemble and annotate a large retrospective cohort of patients presenting with a variety of chief complaints/symptoms suggestive of possible ACS (e.g., chest pain/ tightness, dyspnea, palpitations, syncope/pre-syncope, nausea/vomiting, indigestion, etc.) from 17 different EDs from a single healthcare system. An automated chart inquiry to identify eligible patients will be conducted. According to preliminary inquiry performed by the Health Record Research Request (R3) office (communication with the director of R3, Dr. Jonathan Silverstein on

March 20, 2019), it is estimated that more than 100,000 patients met the inclusion criteria in 2018 alone, suggesting that creating a large representative cohort will be feasible. We then plan to have: 1) an independent reviewer manually annotates each patient chart to extract patient factors (chief complaints/symptoms, vital signs, past medical history, etc.) and 2) two independent Emergency Medicine physician reviewers define patient outcomes in the index hospitalization and 30-day follow-up. The primary outcome is ACS that requires immediate treatment defined in accordance with the American Heart Association (AHA) and American College of Cardiology (ACC) universal definition.[14-17]

Specific Aim 1b: Develop, validate, and compare machine learning algorithms to develop a sensitive and specific model to predict the primary outcome. First, we will randomly divide our cohort into 2/3 training set and a 1/3 holdout test set. Next, we will develop an algorithm using state-of-the-art machine learning concepts based on the output of ACS. Then, using a validation sample within the training set, we will validate and refine the performance of the most accurate model. To reduce the risk of overfitting, we will use the leave-one-out approach. We will also use ten-fold cross validation. These approaches provide a way to examine the bias-variance tradeoff (i.e., very precise versus very accurate) in the estimation of the error of our proposed approach.

Specific Aim 1c: Compare the performance of our final model against routine care (i.e., ESI score). We will compute the area under the receiver operating characteristic curve (AUC) of both our final predictive model and the ESI score for detecting the outcome of ACS. Both areas under the curve will be compared using nonparametric methods.[18]

1.2 Background, Significance, Innovation

1.2.1 Background Overview

According to the Emergency Nurses Association (ENA), the current emergency care environment is faced with increased patient volume and acuity, thus making it important to ensure nursing competencies in triage. This refers to a demonstrated ability to integrate knowledge, skills, abilities and judgement based on scientific knowledge and expectations for nursing practice.[19] Mis-triage or incorrect triage acuity level assignment can cause delays in treatment for the patients involved as well as other patients in need of care, ultimately compromising patient outcomes and possibly leading to mortality.[20,21] There are known inconsistencies in triage decisions that are not fully understood, thus affording an opportunity for nursing research.[20] Additionally, the ENA Crowding, Boarding and Patient Throughput Position Statement encourages research to find solutions for process improvement approaches in all phases of ED care.[22] The ENA and the American College of Emergency Physicians (ACEP) support continued research and investigation of further refining patient acuity assignment, especially for high-risk patients.[23] The triage nurse is commonly the first healthcare worker to see patients when they arrive to the ED. They are faced with multiple constraints including: 1) high patient volume; 2) excess ED occupancy; 3) in-patient bed unavailability; 4) multiple interruptions; and 5) lack of privacy.[24] It is crucial for triage nurses to be able to identify critical conditions quickly and accurately.

1.2.2 Significance

1.2.2.1 Overcrowding

Since 2007, the Institute of Medicine has recognized ED overcrowding in the United States as a public health concern.[25] The overcrowding strain placed on the ED continues to threaten patient safety, [26-28] and jeopardize national safety goals.[29] The ED phenomenon of overcrowding is not universally defined in the literature. It is measured by numerous tools, with no criterion standard to measure overcrowding. The ACEP task force developed the following definition of ED overcrowding:

A situation in which the identified need for emergency services outstrips available resources in the ED. This situation occurs in hospital EDs when there are more patients than staffed ED treatment beds and wait times exceed a reasonable period. Crowding typically involves patients being monitored in nontreatment areas (e.g., hallways) and awaiting ED treatment beds or inpatient beds. Crowding may also involve an inability to appropriately triage patients, with large numbers of patients in the ED waiting area of any triage assessment category.[30]

Generally, ED overcrowding occurs when demand of services outstrip available resources.[31] Unfortunately, overcrowding has been directly related to objective clinical endpoints, such as increased morbidities and mortality.[32] This phenomenon of ED overcrowding puts added pressure on triage to be highly accurate and efficient. If nurses do not identify patients with critical conditions, then further complications occur.

1.2.2.2 Emergency Severity Index

Emergency Severity Index score is used to triage the majority of patients in the ED.[4] It is an ordinal 5-level triage tool used to categorize patients based on resource utilization in the ED

and likelihood of admission.[2] Triage acuity levels range from one to five to help nurses assign different levels; level one, immediate lifesaving intervention is required; level two, patient is considered high risk/emergent; level three, urgent but stable and can safely wait in the waiting room; level four, nonurgent; level five, no ED resources needed.[2] It is not a risk stratification tool, but rather an easy tool that asks three questions: 1) "Is the patient dying?"; 2) "Can the patient wait in the waiting room?"; and 3) "What resources will the patient use?"[2] The tool takes into account vital signs and nurse's intuition, which affords the nurse the subjective leniency to increase the acuity score.

The Emergency Severity Index score has significant limitations. It has shown only suboptimal accuracy rates when acuity levels are assigned by the nurses compared to proper tool usage (59%-77%); with interrater reliability ranging widely from 62%-86%.[9,33-37] A critical appraisal of ESI score literature has revealed many limitations, including: 1) racial bias, with blacks experiencing under triage and longer wait times compared to whites;[5-7,38] 2) ESI scores are not patient outcome driven; they are only validated against predicting hospital admission (yes/no) and ED resources used;[2] 3) the ESI scores are highly subjective; different nurses can assign different scores based on their personal clinical judgement;[2] and 4) the ESI scores lack the ability to differentiate middle acuity patients with more than 50% of patients being classified as ESI score 3.[9,34] This failure means that ESI 3 patients are a heterogeneous collection of subgroups with different time-sensitive needs.

ESI score does not differentiate within each category. Within each ESI level, there is potential to have multiple patients with a variety of chief complaints. Comparing different chief complaints with the same ESI score can lead to situations where the nurse is comparing apples to

oranges. This makes it difficult for triage nurses to determine who is the highest priority at each level.

1.2.2.3 Acute Coronary Syndrome as a Target Critical Condition

Acute coronary syndrome is the ideal critical condition to use as an exemplar for developing a prediction algorithm for use in the ED. Acute coronary syndrome is one of the most time-sensitive diagnoses that must be quickly and accurately recognized as a medical emergency. Approximately one in five patients with ACS will die very early in the event.[10] Early diagnosis of ACS can reduce this mortality by 10%–20%.[10,12] Chest pain is frequently recognized as a sign of potential ACS and is the second leading reason to seek medical care in the ED, accounting for nearly 7 million visits yearly.[1,39] The ACS triage dilemma stems from the fact that the classic symptom of chest pain that radiates to the arm is only a minority of cases. ACS can present with typical and atypical symptomology,[16,39-42] making it difficult for nurses to identify ACS over 30 potential symptoms at triage.[11,38,40,43,44] Unfortunately, vulnerable populations, especially women,[45,46] racial minorities,[7,38] persons with diabetes, and older adults often do not present with chest pain.[7,11,38,44,47,48] These subgroups of patients often experience treatment delays, misdiagnoses, and have higher in-hospital mortality rates. As such, ACS is an ideal condition, to apply state-of-the-art machine learning methods[13] due to its complexity of clinical presentation, treatability, allowing early recognition by nurses to directly improve patient outcomes.

Nurses facilitate initiation of life-saving treatments, but only when symptoms are recognized as an emergency. ED nurses lead triage and directly influence patient-centered outcomes of ACS patients. Time to treatments is directly linked to rates of morbidity and mortality.[10,12,39,49] Perceived acuity level at triage is based on clinical knowledge and decision-making skills.[50] Unfortunately, multiple studies have shown that nurses' accuracy in identifying

patients with emergent symptoms of ACS can be as low as 54%.[11,38,44,48,50,51] Worse, nurses hold cultural biases and stereotypes that interfere with clinical decisions at triage.[52] Moreover, a recent study by Vigil et al. found that provider gender is associated with the acuity level assigned to a patient,[53] which undermines the reliability assessment that the ESI tool claims to have. The innovation of our predictive algorithm is the insertion of checks and balances to ensure true ACS cases are not overlooked.

1.2.2.4 Acute Coronary Syndrome Predictive Algorithm

An ACS predictive algorithm is a simple solution to a complex problem. With complexity of illness and ED visits increasing, the application of an ACS-specific predictive algorithm at triage will help to overcome the current knowledge gap of failure to identify ACS at triage through prediction of key patient factors readily available to the nurse. Triage will be simplified as the predictive algorithm could be incorporated into electronic health record (EHR) software, allowing nurses to expedite accurate care based on objective data and patient-centered outcomes. Initial steps to build a robust, valid algorithm requires diligent and properly adjudicated well-defined ACS-specific clinical outcomes. The proposed innovative study will be the first of its kind to combine the wealth of objective data at the initial medical encounter and reveal hidden patterns related to ACS-specific patient outcomes. Importantly, such refinement in care that is data driven will make triaging evidence-based, efficient, and will not increase nurse burden (in fact burden may decrease).

1.2.2.5 Predictive Algorithms in Healthcare Applications

Complex mathematical modeling is a robust approach to develop predictive algorithms in healthcare applications. Big data science is based on the discovery and communication of subtle

patterns in high-dimensional data.[54,55] Machine learning (ML) or complex mathematical modeling is a mechanism of an artificial intelligence system that can develop algorithms that modify themselves in response to patterns and make inferences when applied to new data.[54-56] Application of big data analytics has been successful to improve efficiency in various healthcare arenas.[49,54,57] Machine learning algorithms have been proven superior to standard clinical tools for predicting in-hospital sepsis and cardiac mortality.[58,59] Additionally, ML algorithms have been shown to be successful in predicting interventions needed to improve trauma patient outcomes,[60,61] and to improve triage prediction of respiratory problems in pediatric patients.[62]

1.2.3 Innovation

This innovative proposed project was designed to improve ED triage to be data and patient-centered outcome driven. This new approach to link initial EHR information with ACS-specific patient-centered outcomes will be on the forefront and contribute new knowledge discovery to nursing science. It will address the opportunity to improve nurse identification of ACS approximately 50% of the time during triage (aim 1b, 1c), thus decreasing unnecessary morbidity and mortality. Our strong, established interdisciplinary research team, with a track record of successfully working together, operates within a world-renowned healthcare system with access to 17 different EDs serving over 578,000 patients a year. This strongly established collaborative relationship between the University of Pittsburgh and UPMC offers a unique and ideal place to use patient EHR data and data science approaches to transform nursing clinical practice. The EDs that are part of UPMC range from quaternary academic centers to small rural community hospitals. This broad representation of different EDs across a large section of the Mid-Atlantic region of the United States strengthens the study by including different triage environments that nurses are

working in. This new knowledge discovery will: 1) close the gap on identifying potential ACS patients (aim1b, 1c); 2) ensure patients are prioritized properly upon arrival; and 3) inform clinical nursing practice to initiate cardiac specific protocols (e.g., obtain one time or serial electrocardiograms). This project serves as the launching point for the principal investigator to create a complex algorithm in the future that will manage the variety of pathology seen by ED nurses at triage.

1.3 Conceptual Framework

To understand the flow within the ED, a conceptual model for ED crowding was created to provide a practical framework to understand the dynamic nature of the ED environment. This framework can be applied to understand the operational elements that occur during an ED stay. It was created as an overarching systematic understanding of why the problem exists and used as a reliable method to understand, measure and monitor ED capacity.[63]

The hospital acute care system is a complex environment where sick patients seek medical treatment for various reasons. This conceptual model consists of three phases including: 1) input; 2) throughput; and 3) output. It is broadly used to define the current healthcare system to include any delivery system component that provides unscheduled care.[63] Figure 1 below identifies components of the healthcare system that contribute to, or affected by, ED crowding.[63]

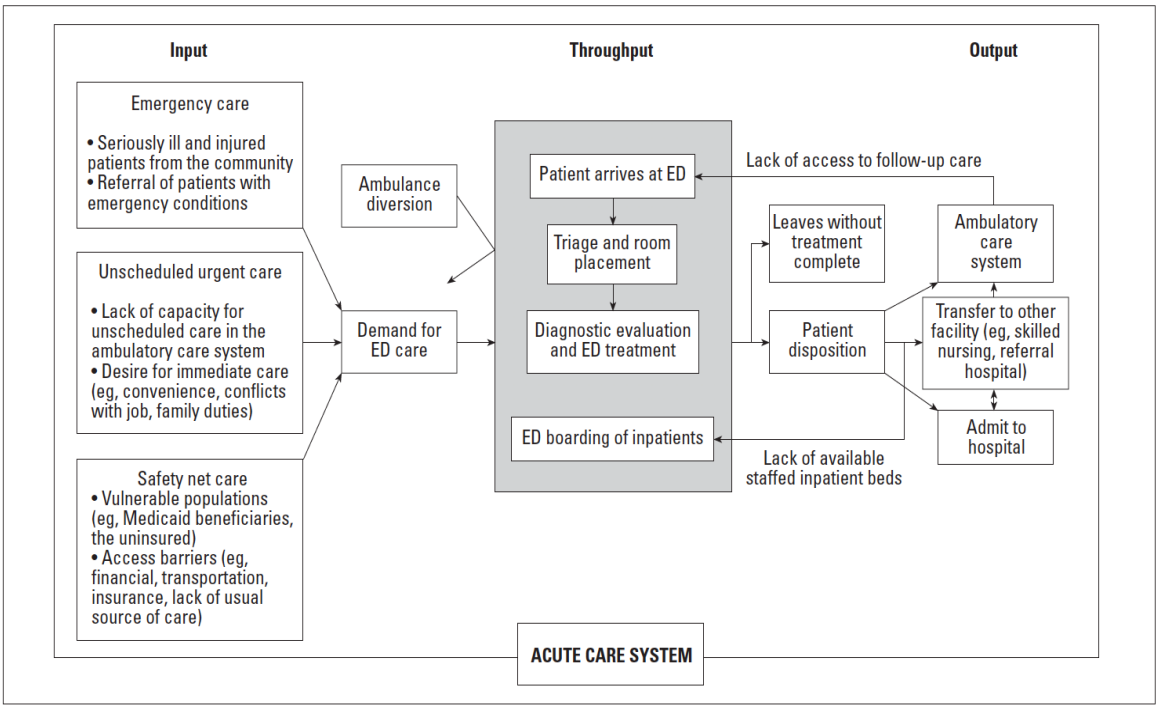

Figure 1: The Input, Throughput, and Output Conceptual Model for Emergency Department Flow

Note. ED = Emergency Department.

As the model shows, there is a number of reasons why a person will come to the ED on any given day. This study will focus on the first component of ED flow, when the patient arrives at the ED. Intake of patients is depicted as a small box shaded in gray, but the triage of patients is a complex process and when ED capacity reaches saturation, it is the triage nurse's duty to ask himself/herself the question: Does this patient condition need the last bed in the ED?[2] Too often nurses have multiple patients that need to be evaluated, but the limited ED capacity does not allow for immediate evaluation. Triage nurses are constantly reprioritizing and assessing the current status of every patient that presents to the ED. They are responsible for making critical decisions that will directly impact patient outcomes.

1.4 Preliminary Studies

1.4.1 The Correlation Between Patient Outcomes and the Initial Emergency Severity Index Triage Score in Patients with Suspected Acute Coronary Syndrome[1]

This retrospective correlational study was completed on the Electrocardiogram Methods for the Prompt Identification of Coronary Events study database to explore the association between initial emergency department nurse triage scores using the Emergency Severity Index. This study is proof of concept that the Emergency Severity Index scores in a cohort of prehospital patients that call 9-1-1 for chest pain or equivalent symptoms had a poor positive predictive value for high acuity patients that entered the emergency department. This adds to the existing literature that acute coronary syndrome is difficult to triage and unfortunately may be mis-triaged.

Background: The Emergency Severity Index is used to triage patients in most Emergency Departments across the United States. The Emergency Severity Index tool has significant limitations that make it difficult to accurately triage patients with suspected acute coronary syndrome.

Objective: We aimed to 1) evaluate the association between Emergency Severity Index score at initial triage and 30-day major adverse cardiac events in chest pain patients and then to 2)

[1] Portions of this preliminary study have been previously published as: Frisch, SO, Faramand, Z, Leverknight, B, Martin-Gill, C, Sereika, SM, Sejdić, E, Hravnak, M, Callaway, CW, & Al-Zaiti, S. 2020. The Association Between Patient Outcomes and the Initial Emergency Severity Index Triage Score in Patients with Suspected Acute Coronary Syndrome. Journal of Cardiovascular Nursing. In press. DOI: 10.1097/JCN.0000000000000644

compare the performance of the Emergency Severity Index score against other tools clinically validated to triage suspected ACS (i.e., HEART score).

Methods: This was a retrospective correlational study of patients from cohort one of the Electrocardiogram Methods for the Prompt Identification of Coronary Events study. We used Emergency Severity Index scores documented by triage nurses during routine care. We then computed a modified HEAR/T score based on patient History, ECG, Age, and Risk Factors (no Troponin). Major adverse cardiac event was defined as the incidence of acute coronary syndrome, in-hospital complications, or all-cause death.

Results: Our sample included 750 patients with an average age of 59 years, 43% female and 40% black. A total of 145 patients (19%) experienced major adverse cardiac events. The area under the receiver operating characteristic curve for Emergency Severity Index score for predicting major adverse cardiac events was 0.65, compared with 0.79 for the modified HEAR/T score. The positive predictive value of Emergency Severity Index scores of 1 and 2 for predicting major adverse cardiac events were low at 33% and 15%, respectively. Using the modified HEAR/T score, 181 of the 391 false positives (46%) and 16 of the 19 false negatives (84%) assigned by Emergency Severity Index could be reclassified correctly.

Conclusion: The Emergency Severity Index score is poorly associated with major adverse cardiac events within 30-days of the index hospitalization in patients with suspected acute coronary syndrome. Use of other validated clinical tools can improve upon the triage of patients with suspected acute coronary syndrome compared to the Emergency Severity Index score.

1.4.1.1 Implications to the Proposed Dissertation Study

This descriptive correlational secondary analysis reaffirmed findings that the Emergency Severity Index scores are poorly associated with acute coronary syndrome-specific outcomes with patients that present to the emergency department with chest pain.

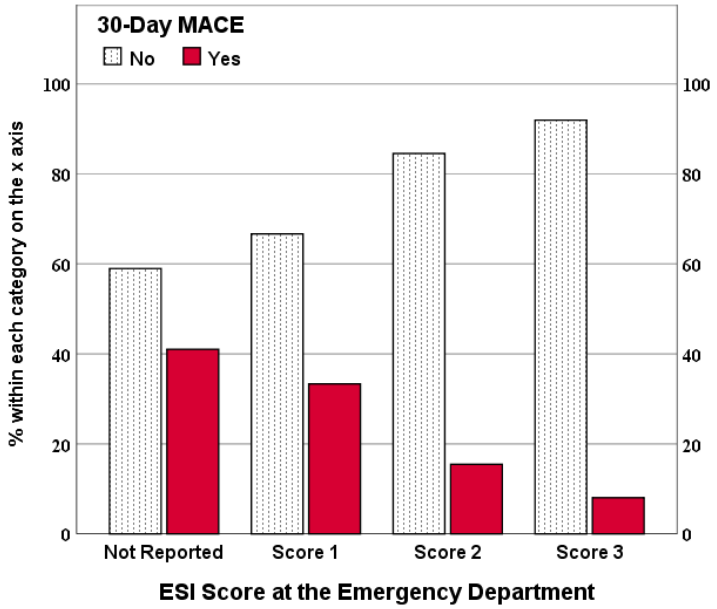

Figure 2: The Comparison of Emergency Severeity Index Scores at Emergency Department Nurse Triage with 30-day Major Adverse Cardiac Events

Note. ESI = Emergency Severity Index; MACE = major adverse cardiac events.

1.4.2 Emergency Department Triage Factors Predictive of Acute Coronary Syndrome[2]

This retrospective correlational study completed on cohort one of the Electrocardiogram Methods for the Prompt Identification of Coronary Events (EMPIRE) to identify key patient factors that could be available at initial nurse triage in the emergency department that are predictive of acute coronary syndrome. The current triage tool is a generalized tool that is applied to all patients. No specific acute coronary syndrome tool is used to help nurses identify patients with presentations that are suspicious for acute coronary syndrome. This study could help nurses to understand the complex presentation of acute coronary syndrome and what patient factors in tandem should be considered when triaging patients.

Background: The current emergency department nurse triage tool used has significant limitations including subjectivity, racial bias, poor relation to patient-centered outcomes, and a failure to differentiate acute patients. Nurses fail to identify acute coronary syndrome approximately 50% of time due to complex patient presentation, with over 30 potential presenting symptoms. This suggests an urgent need to improve triage tools, specifically ones that if it correctly identified acute coronary syndrome early could reduce mortality by 10%–20%.

Objective: The purpose of this study was to identify key patient factors available at initial emergency department presentation that are predictive of acute coronary syndrome in order to develop a novel cardiac triage tool to rapidly interpret clinical information.

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[2]Portions of this preliminary study have been previously published as: Frisch, SO, Brown, J, Faramand, Z, Stemler, J, Sejdić, E, Martin-Gill, C, Callaway, CW, Sereika, SM, & Al-Zaiti, S. 2020. Exploring the Complex Interactions of Baseline Patient Factors to Improve Nursing Triage of Acute Coronary Syndrome. Research in Nursing and Health. In press. **https://doi.org/10.1002/nur.22045**

Methods: This was a retrospective, correlational secondary analysis of the Electrocardiogram Methods for the Prompt Identification of Coronary Events study database that prospectively enrolled consecutive adult chest pain patients (N = 750) transported by emergency medical services in the city of Pittsburgh to a UPMC emergency department who received a 12-lead electrocardiogram in the prehospital setting. There were no restrictions to sex or race. Binary logistic regression was used to determine patient factors available at triage in a predictive model with the in-hospital diagnosis of acute coronary syndrome as the outcome.

Results: Participants were 57% male, 40% black, and an average age of 59 years. One hundred and fifteen patients (15.3%) were diagnosed with acute coronary syndrome. Older age, non-white race, and faster respiratory rate were independent predictors of acute coronary syndrome. There was an interaction between first emergency department heart rate and past medical history of type II diabetics in the context of ACS, with persons with type II diabetes who were taking insulin for better glycemic control manifesting faster heart rate that remained significant in the final model.

Conclusion: By identifying patient factors at emergency department nurse triage that could be predictive of acute coronary syndrome, accuracy rates of triage may improve, thus impacting patient outcomes. This information should be considered when triaging cardiac patients at initial presentation to the emergency department. Future studies are necessary to understand these data findings on a larger cohort of patients. This information has the potential to help develop a new cardiac triage tool to assist nurses in identifying acute coronary syndrome accurately.

1.4.2.1 Implications to the Proposed Dissertation Study

This preliminary, exploratory study led the principal investigator to consider the potential clustering of patient's factors that could affect the initial triage score that is assigned to patients

with a complex presentation suspicious of ACS. The discovery of multiple interaction terms in section 1.4.2 supports the use of machine learning approaches. Clinicians and nurses have a difficult time using different rules that are contingent on certain factors. This can be simplified by using potential machine learning techniques that will optimize the potential interactions between patient factors. It is evident that patient factors that present simultaneously could inform triage nurses to assign an accurate triage score.

1.4.3 Summary

1.4.3.1 Current Emergency Department Triage Shortfalls

The ESI tool is a standard general triage tool that is most used in the United States.[4] It is easy to use and asks three questions when the patients presents to the ED.[2] It has been established that the ESI tool has significant limitations including: racial bias, [5-7,38] not patient-specific outcome driven,[2] lack of specificity to ACS patients and being largely subjective.[2] The key stakeholders of Emergency Medicine practice, ACEP and the ENA, have both acknowledged the need to re-evaluate current triage practices, especially those in a high-risk population. Chest pain is the second leading reason to seek medical care in the ED, accounting for nearly seven million visits a year;[64] this does not, however, take into consideration a proven vulnerable population that may not present with chest pain (e.g., women, racial minorities, older adults, etc.).[7,45,47,48] Unfortunately, triage nurse are failing to identify acute coronary events at triage with an accuracy rate as low as 54%.[11,38,51] This failure to differentiate acute coronary events from the variety of patients presenting to the ED is a complex problem. The one size fits all chief complaint of chest pain that radiates down the left arm is long gone. Over 30 symptoms of acute coronary events have been identified in the literature that could potential raise concern for a triage nurse.[40,43,44] Time is of the

essence to equip triage nurses with a robust tool that could potentially assist in making real time clinical decisions to initiate critical treatments to decrease morbidity and mortality 10%–20%.[10,12] By improving recognition of acute coronary syndrome, patient outcomes will improve.

1.5 Research Design and Methods

1.5.1 Study Design

The proposed project will be a retrospective, correlational, descriptive cohort study of patients who present to the ED with symptomology suggestive of ACS. For the year of 2018, all patient charts who have any of the following presenting symptoms to the ED will be included (see Table 1).[10,12,15,16,39-42] Next, from that a cohort, a random sample of 1200 patients from 2018 will be selected (see Figure 3). This final large cohort of ED patients across an academic medical center will serve as the platform to apply supervised ML algorithms to identify patients with ACS. Our innovation will link patient factors present at the initial triage encounter with in-hospital clinical outcomes. The principal investigator will manage, review annotation, perform quality checks on every twentieth patient, to ensure high-quality, expert reviewed robust clinical database construction.

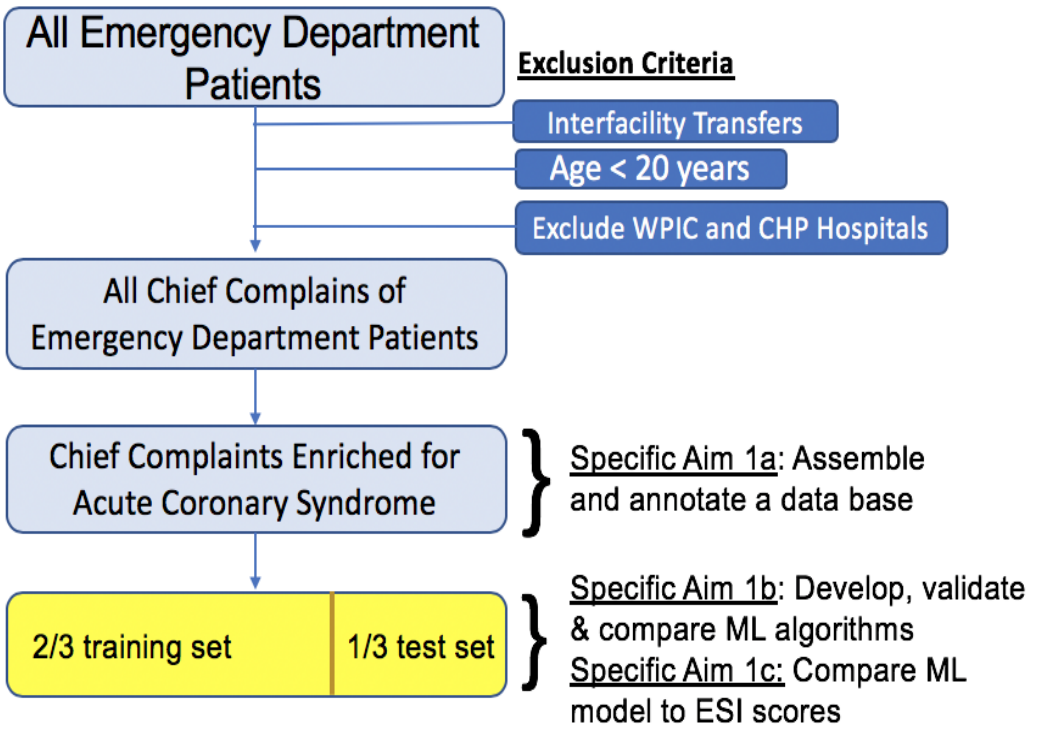


Figure 3: Study Design

Note. ML = machine learning; ESI = emergency severity index; WPIC = UPMC Western Psychiatric Institute and Clinic; CHP = UPMC Children's Hospital of Pittsburgh.

Table 1: Potenial Chief Complaint(s) and Symptom(s) of Patients Suspicious of Acute Coronary Syndrome

Typical Acute Coronary Syndrome Symptoms	Atypical Acute Coronary Syndrome Symptoms
• Chest pain • Chest heaviness • Chest discomfort/ burning • Chest pressure • Chest tightness • Chest squeezing • Chest pain that radiate to arm • Chest pain that radiated to the neck/jaw/back/abdomen • Dyspnea • Shortness of breath • Syncope • Presyncope/ near passing out • Palpitations	• Nausea • Vomiting • Indigestion • Abdominal pain • Sternal pain • Jaw/neck pain • Cough • Fever • Epigastric pain • Arm pain/ discomfort • Unexplained fatigue • Chest wall tenderness • Ear discomfort • Retrospective pressure/ heaviness/ burning • Pleuritic pain

1.5.2 Study Setting

The proposed study will be conducted at UPMC. All 17 hospitals share a single log-in electronic medical system (i.e., UPMC-Cerner), which will facilitate easy access for collecting the required patient factors. Our team has permanent access to this electronic medical system through an existing research collaboration agreement between the University of Pittsburgh and UPMC, which share a successful track record of collaboration. The School of Nursing and Department of Emergency Medicine have conducted several studies together,[49,65-69] with many still ongoing. The UPMC Health Record Research Request (R3) collaboration with University of Pittsburgh and UPMC has ensured that the proposed study cohort will be easily extracted from over 578,000 ED visits in 2018, with over 100,000 patients meeting study criteria as of November 2018. To reduce

the rate of false negative results, repeat ED visits and re-hospitalizations within 30 days of the indexed encounter will be reviewed. Unexplained sudden death will be considered positive for the primary outcomes.

1.5.3 Study Sample

1.5.3.1 Subject Inclusion, Exclusion and Data Collection Protocol

Patients meeting the following inclusion criteria will be included: 1) 20 years of age or older;[10,70] 2) present to the ED with symptoms suggestive of acute coronary syndrome (see Table 1).[10,14,42,49,71-73] There will be no sex or race restriction. Patients will be included regardless of mode of transportation to the ED. Inter-facility transfers from a non-UPMC facility ED or in-patient hospitalization will be excluded. Children and teens are less likely to have ACS-related chest pain and will not be included.[74]

Data collection will take place by extracting information from the electronic health record (EHR). Patient factors (independent variables) will be collected from an a priori list of variables. This list of patient factors is based off expert consensus opinion of the Department of Emergency Medicine Research group of what information could be available to the triage nurse upon initial encounter referencing the EHR. Fidelity of study procedures will be ensured in several ways including: 1) the principal investigator will train all research assistants in two hour didactic sessions on how to navigate, collect, and document extracted data from the EHR; 2) the principal investigator will be responsible for assisting research assistants in collection, management, and verification of extracted data; 3) research assistants will have access to data extraction reference sheet in training sessions and as a guide when collecting data; and 4) the principal investigator

will perform quality checks on every twentieth patient and five percent of all patients will be randomly selected to evaluate completeness and accuracy of data.

1.5.3.2 Sample Size Justification

Machine learning methods ideally require a balanced distribution for the outcome of interest of the sample. With a retrospective analysis of EHR data, a stratified random sample from UPMC-Cerner can easily be generated. In order to correct for the potential imbalance of positive outcomes of ACS, ICD-10 codes for ACS during the hospital admission will be used as strata in a stratified random selection from the EHR. We will select four non-ACS patients for each one ACS patient. This will increase the prevalence of ACS in the sample compared to the general population. This sample will enable the training, validation and testing sets to be both sensitive and specific to patient factors that lead to the outcome of ACS. Prospective testing of this predictive algorithm in the future will take place on a significantly bigger scale, e.g., 50,000 patient charts, and is beyond the scope of this project. The goal of the final algorithm will be to have a sensitivity of 90 percent and a specificity of 90 percent. With a predicted stratified prevalence of 20 percent, and precision set to 0.04 with 95 percent confidence intervals, the suggested total sample size is 1201 participants. Due to this project being a pilot study, a sample size of 1200 patients have been selected. These data will be divided randomly into 800 patients for training and 400 patients for testing.

1.5.4 Variables

1.5.4.1 Defining Patient Factors (Predictive Independent Variables)

Standard patient charting in UPMC-Cerner is by exception only. This means that the nurse only documents abnormal findings, if it is not charted, it is presumed to be normal.[75] Based on an extensive literature review, we have identified the following patient factors (see Figure 4) that are typically present at initial triage. The following variables according to the ACC[14,16,42,76] initial assessment requirements will be analyzed and included in the development of a supervised ML algorithm: 1) demographics (e.g., age, sex, race, ethnicity); 2) chief complaint(s)/symptom(s) (see Table 1);

Patient Factors: Independent Variables
1. Demographics (age, sex, race, ethnicity) 2. Chief compliant(s)/symptom(s) 3. Vital signs (e.g. temperature, heart rate, systolic & diastolic blood pressure, respiratory rate, pulse oximetry, pain score) 4. Patient self-reported past medical history & past medical history listed in the EHR 5. Patient self-reported home medications & home medications listed in the EHR 6. First in-hospital ECG 7. Pre-hospital data 8. Mode of Transportation

Figure 4: Patient Factors

Note. EHR = electronic health record; ECG = electrocardiogram.

3) vital signs [temperature, heart rate, systolic and diastolic blood pressure, heart rate, pulse oximetry, respiratory rate, pain score (visual analog, verbal numerical rating scale, verbal description scale)]; 4) patient self-report past medical history and chart past medical history (e.g., diabetes mellitus, previous heart attack, etc.); 5) self-reported home medications and home medications listed in the EHR: anti-dysrhythmics (e.g., Amiodarone, Metoprolol, etc.), statins (e.g., Simvastatin, etc.), nitrates (e.g., nitroglycerin, etc.), anti-platelet (e.g., Plavix, aspirin, etc.), anticoagulants (e.g., Eliquis, Coumadin, etc.), diabetic mellitus medications (e.g., metformin, insulin, etc.), oral contraception,[77] analgesics (e.g., Percocet, etc.), anti-hypertensives (e.g., Norvasc, etc.), anti-depressants,[78] and psychiatric medications;[79] and 6) first in-hospital ECG characteristics will be collected, including: automated computer generated ECG interpretation, and date and time of the ECG.[14,16,67] Clinical presentation factors will also be collected including: height and weight; and date and time of symptom onset. When possible, the prehospital data will be included as it is available at triage, which includes the following: initial and final pre-hospital vital signs, pre-hospital treatments, pre-hospital ECG, and pre-hospital chief complaint(s)/symptom(s). Mode of arrival to the hospital will also be considered, including private vehicle, ambulance (basic versus advance life support), wheelchair van, and helicopter transport.

1.5.4.2 Defining Acute Coronary Syndrome (Primary Outcome Variable)

The primary outcome is ACS defined as the presence of critical coronary occlusion (CCO) requiring immediate treatment defined in accordance with the AHA/ACC universal definition.[15,16,40,67] The presence of ACS will be manually annotated by two independent Emergency Medicine physician reviewers who will use patient's EHR from the ED, the index hospital admission, or 30-day follow-up to the index hospitalization. Patients meeting one of the following criteria will be considered positive for ACS: 1) clinical evidence of anginal symptoms

with a detectable rise and fall of cardiac troponin (cTn) with at least 1 value > 99th percentile; 2) ECG evidence of acute myocardial ischemia (diagnostic ST elevation or depression in two contiguous leads); 3) positive tracer uptake on single photo emission computed tomography (SPECT) scan; 4) positive coronary angiography demonstrating intracoronary thrombus and narrowing > 70%; or 5) positive electrocardiogram stress test demonstrating localized abnormal wall motion and hypokinesis. To reduce rate of false negative results, repeat ED visits and re-hospitalizations within 30 days from the indexed encounter will be reviewed. Unexplained sudden death will be considered positive for the primary outcome. The principal investigator and physician reviewers will have access to 30-day follow-up in UPMC-Cerner and Epic Electronic Health Records within the UPMC network. Death will be obtained from one of the following sources: 1) R3 will tabulate 30-day death follow-up for each patient in the study cohort; 2) the Center for Disease Control and Prevention national death index database; 3) internet searches of obituary records; and 4) Pennsylvania vital status records. In Pennsylvania, public reporting of death is required for survivors to receive death benefits, increasing reliability of reporting.

1.5.5 Methods

1.5.5.1 Development of Research Database (Specific Aim 1a)

We will assemble and annotate a large retrospective cohort of ED patients presenting with a variety of symptoms suggestive of possible ACS (e.g., chest pain/tightness, dyspnea, palpitations, syncope/pre-syncope, nausea/vomiting, indigestion, etc.) from 17 EDs. After extensive literature review, a list of typical and atypical symptoms suggestive of possible ACS was compiled with consensus from expert opinion of the Department of Emergency Medicine Research group. To assemble a large retrospective cohort of ED patients from UPMC's network, a query is

made to UPMC Health Record Research Request (R3) office. Aggregated patient data are readily available directly from the R3 office. Patients less than 20 years of age or from Western Psychiatric Institute and Clinic of UPMC or UPMC Children's Hospital of Pittsburgh will be excluded. R3 staff will generate a cohort of patients from a specific chief complaint listed from Table 1, who present to any one of the 17 UPMC EDs that have a centralized electronic charting system via UPMC-Cerner.

To generate this first patient cohort, fuzzy method search[80] against actual chief complaints will be utilized. Specifically, Levenstein distance,[81] use of lowercase search, and string length sorting will help to adjust for potential misspellings of all chief complaints, to best match the search for each specific chief complaint. This new cohort of patients, inclusive of all chief complaints will be pared down to the calendar year of 2018. From the date restriction, patients will then be randomly selected to generate the final cohort of patients. Once the final cohort is assembled, patients will be assigned a unique linkage study ID on a UPMC password-protected server. Only the principal investigator and key personnel will have access to the linkage list, which is stored in a sub-folder with separate password access. In Step 1, an independent reviewer (research assistant) will manually annotate each patient chart to extract important patient factors (section 1.4.4.1). From our past experience with similar patient databases, it takes approximately 30 minutes to annotate all patient factors for one chart.[68] We estimate that (N = 1200) charts will take a total of 600 hours of time to complete. Quality checks of data extraction will take place with every twentieth patient by the principal investigator to ensure accuracy of data. In Step 2, two independent Emergency Medicine physicians will adjudicate patient outcomes in the index hospitalization and 30-day follow-up (section 1.4.4.2). The principal investigator and physicians will have full access to inpatient and outpatient records under UPMC's network. To **guarantee**

accuracy, validity and reproducibility, the dataset will be: 1) divided between two independent Emergency Medicine physician reviewers; 2) discrepancies of outcomes between physician reviewers be adjudicated by a third physician. From our past experience, it takes approximately 15 minutes per chart to annotate the outcomes.[68] It will take approximately 600 hours to annotate all patient outcomes for this study. The Department of Emergency Medicine (EM) under Dr. Callaway will be responsible for providing EM physician reviewers for this study.

1.5.5.2 Develop a Specific Machine Learning Model (Specific Aim 1b)

We will develop, validate, and compare machine learning algorithms to develop a sensitive and specific machine learning (ML) model to generate the primary outcome of ACS. We are building a supervised machine that given a certain set of inputs (i.e., patient factors at triage) will produce a certain desired output (i.e., ACS) by finding patterns in data and learning from it. This model building (see Figure 5) is rooted in traditional ML methodology.[56] We will randomly divide our large patient cohort into 2/3 training set and 1/3 validation set.

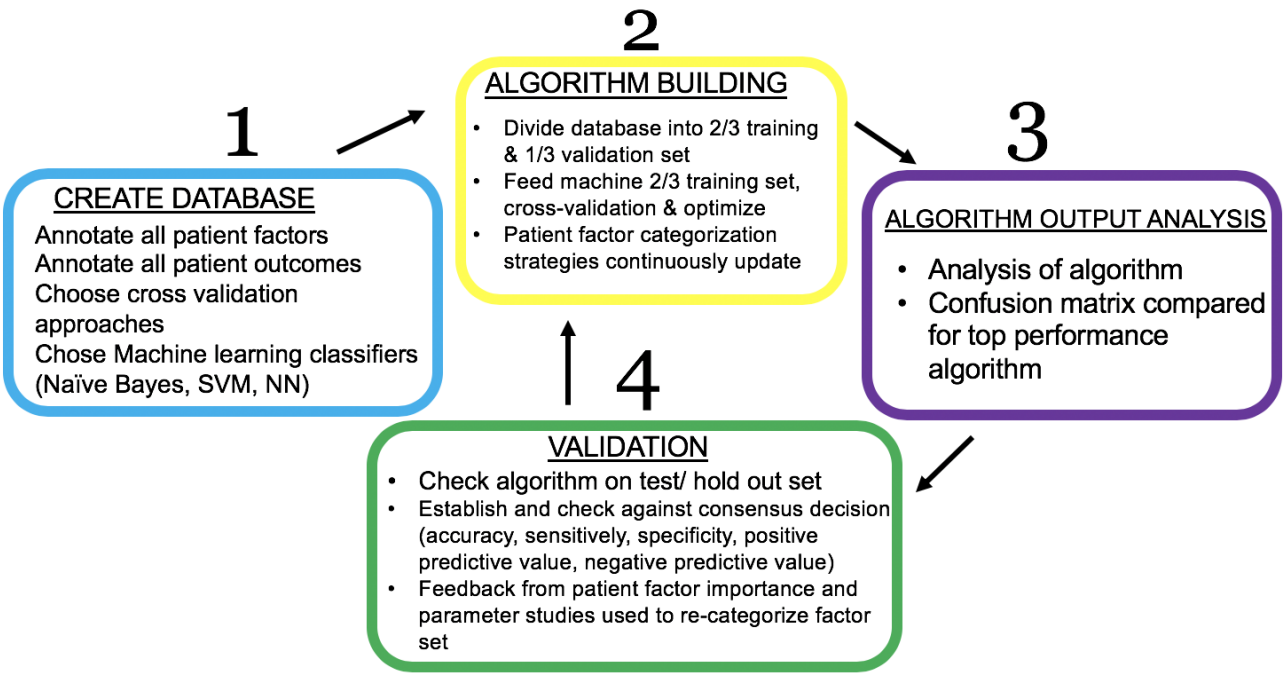


Figure 5: Machine Learning Process for Building a Predictive Model

Note. SVM = support vector machine; NN = neural network.

1.5.5.2.1 Specific Steps of Machine Building

STEP 1: We will establish the primary outcome of ACS as listed in section 1.4.4.2. This step is needed to establish ground truth identification of all myocardial ischemia in patients. This will serve as the gold standard outcome compared to current practice accuracy of the ESI score documented in the patients' charts. STEP 2: For each patient, a list of all independent variables (see Figure 4) from the first patient triage encounter will be extracted. Also, the primary outcome of ACS will be extracted from the patient chart. STEP 3: Based on the ESI score from step 1, and the independent variables for each patient and their respective primary outcomes, these data will be entered into a supervised machine learning algorithm based on the state-of-the-art machine

learning concepts whose output will be assigned based on the emergency severity index score from one to five. Specifically, we will use the naïve Bayes classifier machine learning approach (see Figure 6), which learns from probability distributions of input data.[13]

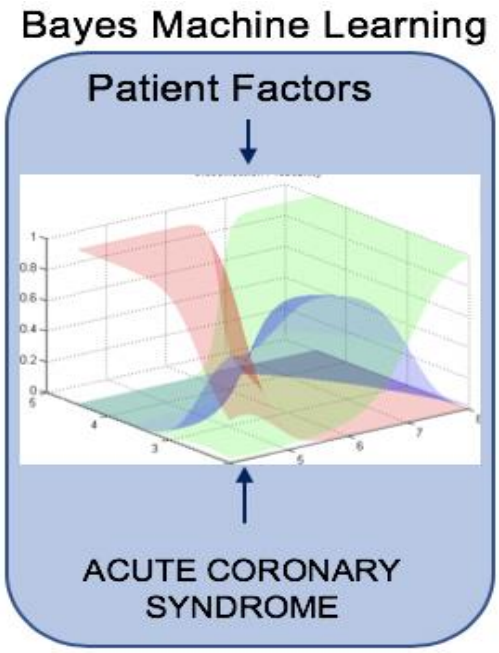


Figure 6: Bayes Machine Learning to Develop a Predictive Model for Acute Coronary Syndrome

At the first layer, we will focus on extracting the coarse details, i.e. details that will provide us with the understanding of patient factors that are important. At the second stage, we will focus on extracting details that will provide us with the understanding of ACS. STEP 4: To understand the accuracy of the developed ACS analysis algorithm in Step 3, we will now test the predictive algorithm on the holdout set. We will begin by calculating a confusion matrix (an approach in ML to describe the performance of an algorithm especially used when dealing with classification of more than two items).[56] The confusion matrix will be calculated by comparing the algorithm's output with scores from STEP 1. The confusion matrix will then be used to calculate true negatives,

false negatives, true positives and false positives and lastly sensitivity and specificity values for the algorithm. Specifically, the receiver operator characteristic (ROC) curve will be used to evaluate the specificity of algorithms without sacrificing sensitivity. We aim to maximize sensitivity with a value greater than or equal to 80%, with a specificity value of greater than or equal to 50%. Each ML algorithm will be compared based on these preset goals. These values will be initially calculated using the leave-one-out approach (the most exhaustive and computationally extensive cross-validation approach), but we will then repeat the analysis with 10-fold cross-validation. These two approaches provide a way to examine the bias-variance tradeoff (i.e., very precise vs. very accurate) in the estimation of our proposed approach's error. To accommodate the unexpected problem that the Bayes algorithm (STEP 3) cannot differentiate ACS, we will use non-Bayes learning approaches[56] (e.g. neutral networks[82] and support vector machines).[83] The principal investigator will be supervised and work collaboratively with Dr. Sejdić to develop and compare algorithms to ensure successful completion of aim 1b, and 1c.

1.5.5.2.2 Expected Outcome

The benchmark for success of specific aim 1b will be a creation of a ML algorithm to accurately predict ACS. Specifically, we will: 1) develop a ML algorithm that can correctly predict patients that will develop ACS from the list of patient factors from triage, identify when no ACS is present (with over 90% accuracy compared to the gold standard of ACS). This outcome will establish the evidence that patient factors can predict ACS and advanced analytics are capable of forming a robust and reliable predictive model that can be translated quickly to nursing practice to

assist in making real time clinical triage decisions, initiating care, thus improving patient outcomes.

1.5.5.3 Compare the Performance of the Final Model (Specific Aim 1c)

Comparison between the final ML model and routine care using the ESI score will be evaluated. All patients will be divided into their corresponding group of ESI scores from one to five. The final ML model will also be divided into quintiles. These will correspond to the one to five levels of the ESI tool. Descriptive statistics will be used to summarize the agreement between the groupings. Sensitivity and specificity at each ESI level for each technique (ML versus ESI) will be compared. The ROC curve will be produced for each technique and the area under the curve will be estimated.[18] For each ML technique used, the ROC curve will be compared to that of the ESI score. First, the five-level ESI scores that were assigned by the registered nurse upon initial ED encounter will be used to predict the outcome of ACS. This ROC curve from the ESI scores predicting the outcome of ACS will be compared to the ML approaches.

1.5.6 Measures

All measurements of independent (e.g. patient factors) and dependent variable (e.g. ACS) have been presented in Table 2.

Table 2: Measurement of Independent and Dependent Variables

Variables	Level of Measurement	Measures	Descriptive Statistics
INDEPENDENT VARIABLES			
chief compliant/ symptoms	nominal	narrative note; self-report	frequency/percentage of chief compliants
demographics (sex, race, ethnicity)	nominal	self-report; from EHR	frequency/percentage of demographics
age	ratio	self-report; from EHR	frequency/ percentage, mean, median, SD,mode, range, minimum, maximum, IQR
temperature	interval	Celsius	mean, median, SD, range, mimimum, maximum, IQR
blood pressure	ratio	mmHg	frequency, mean, median, SD, mode, range, minimum, maximum, IQR
pulse oximetry	ratio	% of oxygen saturation	frequency, mean, median, SD, mode, range, minimum, maximum, IQR
respiratory rate	ratio	breathes per minute	frequency, mean, median, SD,vmode, range, minimum, maximum, IQR
pain	ratio	verbal numeratical rating scale (0-10), visual analog scale (0-10)	frequency, mean, median, SD, mode, IQR
past medical history	nominal	self-report; from EHR	frequency/percentages of all illnesses
home medications	nominal	self-report; from EHR	frequency/percentage of each type of medication
ECG automated interpretation	nominal	machine interpretation of ECG	frequency/percentage of each ECG catergory: NSR, ST, SB, AFIB, 1DAVB, 2DAVB,
time of ECG	ratio	hours of the day (military time)	mean, median, IQR, SD
time of arrival to ED	ratio	hours of the day (military time)	frequency/percentage of each timeframe; nursing shifts, days, evenings, nights
mode of arrival	nominal	self-report; witnessed: private vehicle, ambulance, wheel chair van, helicopter	frequency/percentage of each mode of transportation
DEPENDENT VARIABLES			
critical coronary occlusion (5 outcomes)	nominal	clinical presentation	frequncy/percentage
1) clinical presentation	nominal	cardiac troponin (cTn) with at least 1 value > 99th%; ng/mL	frequncy/percentage
2) ECG evidence of acute myocardial ischemia	nominal	which contigous leads have ST elevation, ST depression	frequency
3) postitive single photo emission computed tomography	nominal	positive SPECT =tracer uptake detected by gamma rays	frequncy/percentage
4) coronary angiogram	nominal	presence of an intracoronary thrombus	frequncy/percentage
4a) from angio: percentage of occlusion	ratio	percentage of occlusion	mean, median, SD, range, mimimum, maximum, IQR
4b) from angio: site of lesion	nominal	where occlusion takes place: LAD, RCA, circumflex	frequncy/percentage
5) positive ECG stress test	nominal	stress ECG is different than baseline ECG	frequncy/percentage
5a) From stress ECG: changes present	nominal	ischemia: ST elevation, ST depression: baseline at a point 0.04 seconds after the J-point is at least 0.1 mV in a limb lead or 0.2 mV in a precordial lead	frequncy/percentage

Note: ECG = electrocardiogram; EHR = electronic health record; NSR = normal sinus rhythm; ST = sinus tachycardia; SB = sinus bradycardia; AFIB = atrial fibrillation; 1DAVB = 1st degree atrial ventricular block; 2DAVB = 2nd degree atrial ventricular block; ED = emergency department; SD = standard deviation; IQR = interquartile range; LAD =left anterior descending; RCA = right coronary artery; SPECT = single proton emission tomography.

1.5.7 Data Analysis Plan

1.5.7.1 Descriptive Statistics

Prior to any inferential analyses, we will perform detailed descriptive and exploratory analysis of each variable, yielding standard descriptive summaries (see Table 2). Means, medians and modes will be calculated for each variables as appropriate. Standard deviations, variances, interquartile range and ranges will be calculated as needed for each independent variable. Frequencies and percentages will be calculated for categorical dependent variables. Mean, median, interquartile range, standard deviation, variance will be calculated for the dependent variable of coronary angiography results.

1.5.7.2 Data Screening Procedures

Statistical assumptions for the planned analysis will be checked for violations (e.g., independence, no or little multicollinearity, linearity of the independent variables to the log odds) prior to performing the analysis. Frequencies of variables will be examined to check for outliers; minimums, maximums and percentiles will also help to determine outliers. Graphical techniques will be applied to identified data anomalies. The characteristics of distributions will be examined for kurtosis and skewness. Normality will be checked appropriately and adjusted for statistical analyses. Univariate outliers for continuous variables will be screened using Z scores. Multivariate outliers with be screened using Malhalanobis distance. Bivariate correlations and variance inflation factors will be used to assess for multicollinearity.

1.5.7.2.1 Screening for Outliers

All variables will be examined for univariate outliers. The detection of outliers is essential to ensure reliable and generalizable descriptive and test statistics. Univariate and multivariate outliers will be investigated. Graphical assistance (i.e., histograms, box plots, scatterplots) will be used to identify outliers from the observed data distribution. Z scores and Malhalanobis distance will also be examined to determine outliers. In categorical analysis, close attention will be given to frequencies and percentage of predictors and dependent variables that are lower than the general population. Upon discovery of outliers, data will be reexamined to ensure proper documentation from the EHR. Score alteration methods will be utilized to winsorize outliers. Transformation of data will be completed as needed. All alterations and transformations will be reported accordingly.

1.5.7.2.2 Missing Data

Thorough exploratory analyses will be conducted on the data extracted from the EHR. Standard patient charting in UPMC-Cerner is by exception only. This means that the nurse only documents abnormal findings, if it is not charted, it is presumed to be normal.[75] We anticipate the missing data will be random. From our past experience, we estimate that missing data will be 3%-5%.[68] Missing data patterns will be determined to ensure randomness in origin. Univariate and multivariate missing data distribution on independent variable(s) will be examined. Data will be examined for both missing completely at random and missing at random. Nonignorable and not missing at random data patterns will be reported and adjustment in analyses will occur. In cases

where greater than 30 percent of patient factors are missing, those cases will be eliminated from the dataset.

1.5.7.2.3 Checking for Underlying Assumptions

Due to the complex nature of statistical analyses anticipated with this dataset, theoretically driven underlying assumptions will be checked. We anticipate using binary logistic regression to accomplish specific aim 1b in addition to developing machine learning predictive algorithms. The relationship between patient factors and ACS will be examined. The dependent variable of interest is ACS, which is a yes/no binary outcomes. In order to maintain robust binary logistic regression, the following assumptions need to be assessed: 1) observations are independent; 2) no serious multicollinearity; 3) presence of no multivariate outliers; and 4) linearity of independent variables to the logit of the probability of ACS. Independence will be screened within the dataset by using graphical analyses. Duplicate cases will be closely reviewed. Repeat visits within 30 days of the initial hospital visit will be screened for reason to seek medical care and potentially eliminated due to repeated chief compliant. Each person will be included only once. The magnitude of skewness and kurtosis for each continuous type variable will be considered for transformed as needed. Multicollinearity will be checked by measuring tolerance and variance inflation factors. Tolerance values less than 0.3 will be investigated further for large standard errors. Variance inflation factors measures greater than 10 is an indication for serious multicollinearity and will be examined closely. If multicollinearity is present, clinical relevance of patient factors based on research literature will drive variable elimination or the combination of factors. With the anticipated sample size, small category and

cell sizes will be closely examined. In cases of sparse categories, patient factors may be collapsed or eliminated due to clinical relevance. Outliers will be examined closely. Linearity to the logit between variables will be investigated with bivariate scatterplots. Nonlinearity will be diagnosed from residual plots of studentized residuals versus predicted values. If nonlinear relationship is discovered, transformations may be completed to enhance linearity. After transformation, appropriate regression analyses will follow.

1.5.7.2.4 Transformation of Data

Data transformation will be considered when normal distribution is not present. Direction of the skewness will be determined to best identify a strategy to change the data to reflect the variable. Constants may be added to the original distribution if values are less than one. Logarithmic, square root, or inverse may be utilized. After conclusion of data transformation, all assumptions will be re-evaluated. Score alteration methods will be utilized to winsorize outliers. Transformation of data will be completed as needed. All score alterations and data transformations will be reported accordingly.

1.5.7.3 Data Analytics Procedures

Data analysis will be conducted using MATLAB®, R Studio, Python and/or IBM® SPSS® and customized ML algorithms developed by iMED lab under the direction of Dr. Sejdić. Prior to any inferential analyses, we will perform detailed descriptive and exploratory analysis of each variable, yielding standard descriptive summaries (e.g., means, standard deviations, percentages, and ranges). Please refer to descriptive statistics (section 1.4.7.1) and data screening for a detailed

plan for data screening procedures. The association of key independent variables and the outcome variables with extraneous covariates will be investigated to determine the need for covariate adjustment. Biological variables such as sex[47,48,73] and race[5,6] will be considered in all analyses. Once data are cleaned and ready for analyses, the robust dataset will be imported into the machine learning software of choice. Under the direction and guidance of Dr. Sejdić, state-of-the-art machine learning techniques will be performed. Machine learning algorithms used for medical translation are robust to missing data.[84] Naïve Bayes classifier assumes that the input variables or features are conditionally independent given a specific classification, for example, ACS versus not ACS, and uses maximization of likelihood to classify the outcome of interest. We have chosen naïve Bayes classifier because it optimizes model development over the entire dimensionality of data and is capable of learning even in the presence of some missing values. Further, naïve Bayes classifier is stable, and its classification result is not significantly changed due to noise that may be present in the data.

1.6 Potential Limitations and Alternative Approaches

We anticipate specific aim 1a to be the most time consuming. The primary aim data annotation will be on a strict timeframe under the direction of the principal investigator with supervision by mentors, Dr. Al-Zaiti, Dr. Callaway, Dr. Sejdić, Dr. Sereika and Dr. Hravnak. The sample population for this study is from one healthcare system in the Mid-Atlantic region and may have limited diversity. In the unlikely event that the predictive algorithm does not indicate patient factors that relate to ACS, we will include patient information from the first hour (60 minutes) of each patient ED visit. Time of ED visit starts at time of ED registration. This includes but may not

be limited to vital signs, laboratory tests, and treatments completed within this timeframe. The additional independent variables collected within the first hour of the ED stay will then be added to the algorithm and build a final parsimonious model. Follow-up outcomes will only be limited to within UPMC-Cerner and Epic (outpatient). Per R3 office, 72% of patients in UPMC Network follow-up within the system.

1.7 Study Timeline

Table 3: Study Timeline

STUDY TIMELINE

	Summer Semester 2019	Fall Semester 2019	Spring Semester 2020
STUDY TIMELINE			
Comprehensive Exams	Scheduled for 4/22/19		
IRB Approval for Dissertation	Completed		
Specific Aim 1a: Assemble and annotate a large retrospective cohort of 1,200 patients presenting with a variety of symptoms suggestive of possible ACS.			
Specific Aim 1b: Develop, validate, and compare machine learning algorithms to develop a sensitive and specific predictive algorithm model to predict the probability of the primary outcome.			
Specific Aim 1c: Compare the performance of our final algorithm against routine care (ESI score).			
Dissertation Manuscript & Presentation Preparation			
Dissertation Defense			
Dissemination of Results			

1.8 Protection of Human Subjects

1.8.1 Human Subjects Involvement, Characteristics and Design

Proposed involvement. This is not a clinical trial, but is a retrospective correlational study using data from an electronic health record of patients from the calendar year 2018. R3 office will only collect data from specific demographic and clinical data domains. R3 routinely acts as an Honest Broker and keeps the patients' linkage list which are de-identified by unique study ID. The extraction of additional electronic health record data not previously collected by the Honest Broker will be data mined on an as needed basis by the principal investigator's research team. These data (e.g., height, weight, laboratory tests, procedure notes, clinical notes and progress note data) will be obtained through manual annotation. Each patient will have a unique study ID linking these additional data to the same patients' previously collected data and will reside on a password protected secure server.

Characteristics of the subject population. The patient population of the study is consistent with that of a Mid-Atlantic regional healthcare system over the retrospective review period of 1/1/2018–12/31/2018. The racial, gender and ethnic characteristics of the participant population reflects the same population.

Inclusion criteria: Entry criteria were patients presenting to any UPMC affiliated ED that has EHR access via UPMC-Cerner and is 20 years of age or older that has symptoms suggestive of ACS, including but not limited to: chest pain/tightness, dyspnea, palpitations, syncope/pre-syncope, nausea/vomiting, indigestion, etc.

Exclusion criteria: Any patients presenting to the following hospitals will be excluded: UPMC Children's Hospital of Pittsburgh and UPMC Western Psychiatric Hospital. Interfacility patient transfers from outside a UPMC facility will be excluded.

Inclusion of special classes: No special classes of patient in the retrospective study interval (i.e., women of child-bearing age, pregnant women, prisoners and institutionalized individual) were excluded. Children were not included, as participants entry criterion was set at ≥ 20 years of age. No patients age < 18 years of age will be included in the retrospective chart review from 1/1/2018- 12/31/2018.

1.8.2 Source of Data

Description of Data

All UPMC Hospitals linked with an EHR known as UPMC-Cerner will be utilized to extract data from patients. Additionally, UPMC EPIC Electronic Medical Records is the outpatient medical records and are also linked to all UPMC affiliated outpatient facilities. All patient factors and outcomes are located within UPMC-Cerner and UPMC EPIC Medical Records.

Data Access

Data are stored on institutional shared drives on password protected servers behind firewalls. After a patient is included in the final cohort, the first step is to assign a unique study ID and de-identify the patient. The unique study ID will be used in the database were all patient factors and outcomes will be documented. The extraction of additional EHR data not previously collected by the Honest Broker will be data mined on an as needed basis by the prinipal investigator's research team. These data (e.g., height, weight, laboratory tests, procedure notes, clinical notes and progress note data) will be obtained through manual annotation, each patient will have a

unique study ID linking these additional data to the same patients' previously collected data and will reside on the same secure server. Only key personnel will have access to these linkage lists, which are stored in a sub-folder with separate password access. Identifiable data are kept in a separate folder from de-identified data to prevent co-mingling with other administrative records, and there are no general administrative records kept on our research servers. Access to any data is limited to only those necessary to complete the proposal aims. Training for these individuals includes completion of Collaboration Institutional Training Initiative (CITI) training in the responsible conduct of human subject's research.

We maintain advance electronic security to control and audit data access, including unique user identification with personal authentication at login, automatic log-off, data encryption for any transmission of identifiable data audit controls capable of generating audit reports for all individuals instances of data access.

1.8.3 Potential Risks and Adequate Protection Against Risk

Recruitment and Informed Consent

All medical data will be collected from routine medical care. The proposed study will include only access and extracting these patient data after 30 days of medical care completion and patient discharge. Accordingly, the proposed study is considered a retrospective correlational study, does not change patient care and includes minimal risk; therefore, it will be done under a waiver of informed consent. A study institutional review board (IRB) will need approval from the University of Pittsburgh (UPitt) to conduct this data collection.

Justification for Waiver of Informed Consent

This is a retrospective chart review of routine medical care. Informed consent should be waived

for all data collection because: 1) no protected health information will be recorded; 2) no identifiers will be recorded; 3) it would not have been possible to collect data on the full patient census and meet the aims of the study; and 4) patient were discharged between one to one and a half years prior to the data collection.

Protections Against Risk

Every effort will be made to protect patient confidentiality. All data and records obtained from the subjects will be maintained in strict confidence and will be restricted to research study personnel. Electronic data will be stored on a secure, password-protected computers that reside within the University of Pittsburgh School of Nursing firewalls. Computer security procedures will limit access to study personnel with appropriate user identification and password combinations. Furthermore, secure access will be structured in such a way that reach researcher will gain access only to the portions of the database required for his/her work. For example, bio-engineering collaborators will access only have access only to the de-identified database after unique study ID and will never be granted access to the linkage lists or other clinical data. No study files contain medical record numbers or other protected health Information, only assigned study IDs as identifiers. Moreover, all study personnel will complete both the NIH online tutorial, "Human Participants Protection Education for Research Teams" and the Collaborative Institutional Training Initiative (CITI) course as required by the UPitt HRPO IRB. Patient information will not be reused or disclosed to any other person or entity (other than investigators and research staff specified in this proposal), expect as required by law, for authorization oversight for the research study, or for other research for which the UPitt HRPO IRB has granted a waiver of written HIPPA authorization (45 CFR 164.512(i)(2)(ii)(A)(3).

1.8.4 Potential Benefits of the Proposed Research to Human Subjects

There will be no direct benefit to the subjects because all data will be retrospectively analyzed after all subjects are discharged from the hospital. However, the knowledge gained from the study likely will lead to improved ED nurse triage among patients with ACS. In fact, the substantial benefit to future patients outweighs the minimum risk of potential breach of confidentiality among study participants, which is very unlikely to occur.

1.8.4.1 Importance of the Knowledge to be Gained

Current ED triage has many limitations. Nurses fail to identify ACS approximately half the time at the time of triage. By using a retrospective chart review to data identify informative factors from the initial triage encounter, hidden patterns detected by machine learning algorithms may lead to robust clinical tools. The final machine learning model will be an objective data-driven prediction of who will develop coronary occlusion. These tools will inform nurses on how to make real time clinical triage decisions, identify patients at the time of triage to accurately initiated time sensitive treatments.

1.8.5 Data and Safety Monitoring Plan

This proposal is a retrospective correlational study that does not change patient care and involves minimal risk. Data safety monitoring will be overseen by the University of Pittsburgh Department School of Nursing, which has biweekly meetings to oversee the progress of all the mentor's ongoing studies. The principal investigator, who has no financial interests in the outcome of the study, already participates in these meetings.

The principal investigator and Co-investigators (Dr. Al-Zaiti and Dr. Callaway) will be responsible for the ongoing evaluation of the progress of the research study. They will ensure that no patient personal health information has entered the study database. During monthly meetings, Drs. Al-Zaiti and Callaway will review progression of the study, data integrity, and preliminary results when available. Any breaches in data safety will be investigated and reported to the IRB. Routine quality checks will occur with every twentieth patient. The principal investigator is responsible for all quality checks and reporting back findings to Dr. Al-Zaiti and Dr. Callaway.

To summarize and reiterate: There is no risk of physical harm to the patient by being in the study. The only risk to the patient would be a remote breach of confidentiality. However, we have minimized the opportunity for that to occur by collecting only one identifier--the medical record number--for linkage code purposes only, and even that is available only to the Honest Broker and principal investigator. Once the clinical data elements were collected, they are maintained in a research file identified only by study ID.

2.0 Changes to the Proposed Project

2.1 Research Design and Methods

2.1.1 Defining Variables

2.1.1.1 Primary Dependent Variable: Acute Coronary Syndrome

The outcomes for ACS will include myocardial injury, unstable angina and myocardial infarction as indicated in the fourth universal definition of myocardial infarction.[85] Myocardial injury is defined as the elevation of at least one cardiac troponin values (cTn) with at least one value above the 99th percentile of the upper reference limit; acute myocardial injury occurs when there is a rise and fall of cTn values.[85] Unstable angina is defined as patients with ischemic symptoms at rest or with minor exercise with no evidence of acute myocardial necrosis; troponin laboratory values are in normal range or may be mildly elevated due to other chronic causes.[17,85] The following criteria increased the likelihood of but were not mandatory for the diagnosis of unstable angina: typical angina pectoris at rest; worsening of a previously stable angina; cardiac stress test showing myocardial ischemia; coronary angiography revealing a diameter stenosis of at least 70%; fractional flow reserve documenting functional significance of a coronary lesion and sudden cardiac death or myocardial infarction occurred during 30-day follow-up.

Myocardial infarction is defined as having clinical evidence of acute myocardial ischemia and with detection of a rise and/or fall of troponin values with at least one value above the 99th percentile upper range limit and at least one of the following: 1) symptoms of myocardial ischemia; 2) new ischemia or presumed to be new ECG changes; 3) development of pathological Q waves;

4) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemia etiology; and 5) identification of a coronary thrombus by angiography or autopsy.[85]

2.1.2 Methods

2.1.2.1 Development of Research Database (Specific Aim 1a)

A retrospective observational cohort design was used to assemble patients from 2018 with help from UPMC Health Record Research Request (R3) at the University of Pittsburgh. All unique patients were identified who were greater than or equal to 20 years old and had one of the following inclusion criteria: 1) symptomology at ED presentation suggestive of an ACS event (see Table 1); 2) cardiac troponin (cTn) laboratory value; or 3) cardiac procedure codes [e.g., single-photon emission computerized tomography (SPECT) scan with exercise stress test, SPECT scan with drug induced stress test, and coronary angiogram]. We strived to have a balanced dataset with equal representation of the three inclusion criteria of patients who had a position clinical diagnosis for ACS versus patients who were negative for the outcome of ACS.

2.1.2.2 Develop a Specific Machine Learning Model (Specific Aim 1b)

We developed and validated multiple state-of-the-art machine learning algorithms using the leave-one-out approach with repeated analysis with 10-fold stratified cross-validation. We used the following machine learning classifiers for the outcome of ACS: 1) binary logistic regression;[86] 2) naïve Bayes;[13] 3) random forest;[87,88] 4) gradient boosting machine;[89] and 5) artificial neutral networks.[90] Each machine learning model will attempt to maximize sensitivity (> 80%) while keeping specificity at a moderate level (50%). All model comparisons will be

graphically displayed with the area under the receiver operating characteristic curve plotted on one figure. Next, least absolute shrinkage and selection operator (LASSO) regression[91] was utilized to help reduce over-fitting and to selected a subset of patient factors. This technique will inform which patient factors have the highest likelihood to predict the outcome of ACS in the final model, thus reducing the dimensionality of these data and potentially improving the interpretability of the results.[92] We then compared all five predictive machine learning algorithms using the subset of selected patient factors by comparing their performance by the area under the receiver operating characteristic curve.

2.1.2.3 Compare the Performance of the Final Model (Specific Aim 1c)

To determine the final parsimonious predictive machine learning algorithm for the outcome of ACS, the best two algorithms will be tuned to maximize sensitivity and to maintain specificity at a moderate level. Techniques such as lasso regression, leave-one-out approach, out-of-bag estimation, and 10-fold stratified cross-validation were utilized to avoid both under-fitting and over-fitting. The best predictive machine learning algorithm will then be compared to routine care (i.e., Emergency Severity Index) of assigned acuity scores for placing the outcome of ACS as high acuity.

3.0 DISSERTATION MANUSCRIPT 1: "Integrative Review of Tools and Strategies to Improve Emergency Department Cardiac Triage"

3.1 Abstract

Introduction: Emergency department (ED) nurses annually triage over 7 million patients with chest pain, making this complaint the second leading cause of emergency visits in the United States. Prompt identification of patients with acute coronary events significantly improves outcomes. However, patients with symptomatic coronary disease present with a wide array of symptomatology, making it difficult for clinicians to accurately triage this population. The purpose of this integrative review is to critically synthesize literature on cardiac triage tools, instruments, and clinical decision aids intended for use in the ED and to summarize their predictive metrics.

Methods: Using a thorough list of MESH terminologies, we searched PubMed, CINAHL and Google Scholar databases to identify original peer-reviewed articles pertaining to cardiac triage between 2009 and 2019. We supplemented the primary search by hand searches, and by using other search engine features like *cited by* and *similar articles*.

Results: We screened 1801 potential articles of which 20 were included in this review. We identified a total of 18 tools from 9 countries that were tested against predicting coronary events in the ED. Conceptually, these tools fit into one of the following clinical purposes: standard general triage tools currently used in practice to triage general ED patients (n = 6); tools specifically designed to detect potential acute coronary syndrome (n = 9); tools to stratify risk of mortality among patients with acute coronary syndrome (n = 3); and decision tools to improve 10-minute

door-to-electrocardiogram time (n = 2). Accuracy, sensitivity, and specificity of the tools ranged from 44%–83%, 7%–100%, and 14%–99%, respectively.

Conclusion: Many tools and instruments could be used by nurses at ED triage to identify patients with symptomatic coronary disease. The accuracy of these tools is highly variable and are designed to detect different patient outcomes. Future research should focus on prospective validation of these tools and on determining how they would fit into ED workflow to improve patient outcomes.

Keywords: Emergency department, cardiac triage, acute coronary syndrome, acute myocardial infarction

3.2 Introduction

Emergency nurses are usually the first healthcare worker in the Emergency Department (ED) to assess and prioritize patient acuity upon arrival to the hospital. Nurses strive to get the right patient to the right resources at the right time. All patients are undifferentiated upon arrival to the ED, meaning nurses must use both subjective and objective data to assess patients to determine who is at greatest risk for instability or even increased mortality. Nurses make triage decisions based on knowledge, intuition and past experiences.[93,94] Currently, typical nurse triage in North America is a three to five minute assessment asking specific questions based on the patients' chief complaint(s),[95] vital signs and pain rating,[94-97] symptomatology,[2,93,98] and past medical history.[93,96] Even when EDs implement 'push to fill' or 'immediate bedding' approaches, where patients are placed in available ED treatment areas without a formal triage screening, nurses are usually the first to assess the patients in an ED patient treatment area.

Chest pain is the second most common chief complaint among patients seeking care in the ED in the United States each year, accounting for nearly 7 million cases.[99] Chest pain may indicate that a patient has acute coronary syndrome (ACS). Other patient chief complaints or symptoms (e.g., shortness of breath or fatigue) also may indicate ACS. Because initiating time-dependent life-saving interventions can reduce morbidity and mortality from ACS, triage should rapidly identify potential ACS with few errors.[10] Due to the complex presenting symptomatology of potential ACS patients,[10,12] nurses have a difficult time triaging this population[11] with a current accuracy rate of 54%[11] and a sensitivity ranging from 7% to 100%.[100,101] There is not a universally accepted cardiac triage tool used in practice in the ED. Most of the current cardiac tools actually focus on decision support for physicians to decide about admission or further testing after ACS is suspected. Such widely used and accepted tools include: 1) HEART (History, Electrocardiogram, Age, Risk factors, and Troponin) score,[102,103] 2) TIMI (Thrombolysis in Myocardial Infarction) score,[104,105] 3) GRACE (Global Registry of Acute Coronary Events) score,[106] and 4) FRISC (Fast Revascularization in Instability on Coronary Disease) score.[107] However, these tools predict disposition (i.e., decision to admit, discharge or transfer a patient) after the ED evaluation instead of assessing pre-test probability of ACS upon initial triage encounter. Therefore, these tools do not address how nurses decide on the urgency of evaluation upon initial ED encounter. We performed this timely integrative review to determine what tools, instruments and clinical decision aids have been previously validated for the task of predicting potential ACS at the initial ED triage assessment.

3.3 Method

3.3.1 Search Strategies

We searched PubMed, Cumulative Index for Nursing and Allied Health Literature (CINAHL) and Google Scholar electronic databases to identify key articles pertaining to cardiac triage tools, instruments and clinical decision aids that can be used at ED arrival to the hospital. We used the following Medical Subject Headings (MESH) search terms used alone and in combination with "AND" and "OR": cardiac triage, triage, acute coronary syndrome, emergency department, chest pain. We used the *cited by* and *similar articles* features in PubMed and reference lists from reviewed articles to identify additional articles.

3.3.2 Inclusion and Exclusion Criteria

We included original peer-reviewed research articles on the topic of interest, published between 2009 and 2019 and available in English. Search limits included: human, peer-reviewed journal articles, English language, and adult. We included only tools, instruments and clinical decision aids designed to be used at the initial nurse-patient encounter in the ED. We excluded articles that required laboratory testing because the length of time to obtain results is not practical during initial nurse triage assessment. We excluded articles that only performed predictive analysis to identify ACS at triage due to the lack of a developed predictive system.

3.3.3 Data Extraction and Synthesis

We reviewed articles using the matrix method,[108] in which we sorted each in a table using ascending chronological order and the following eight domains: journal/author identification, purpose, design, sample, variables, results, limitations, and implications for future research. Result details included, when available, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the area under the curve of the receiver operating characteristic (ROC) curve. We also collected the specific outcomes for each study [i.e., ACS, non-ST-segment elevated myocardial infarction (NSTEMI), ST-segment elevated myocardial infarction (STEMI), etc.]. One author (SOF) created detailed descriptions of each study. After review of all articles, two authors (SOF and SS) categorized all articles into common themes based on conceptual purpose.

3.4 Results

As shown in Figure 7, our search yielded 1,801 articles. After removal of duplicate articles and adding eight articles identified by hand-search, a total of 1,467 records remained. All of these citations were reviewed by one author (SOF) to confirm relevance, leaving 48 studies. We excluded all other records because they failed to relate to clinical relevance of cardiac triage tools, including instruments and decision aid tools that were not intended to be used at initial ED triage encounter. After review of the full-length papers for these studies, we identified and included 20 articles that met search criteria.

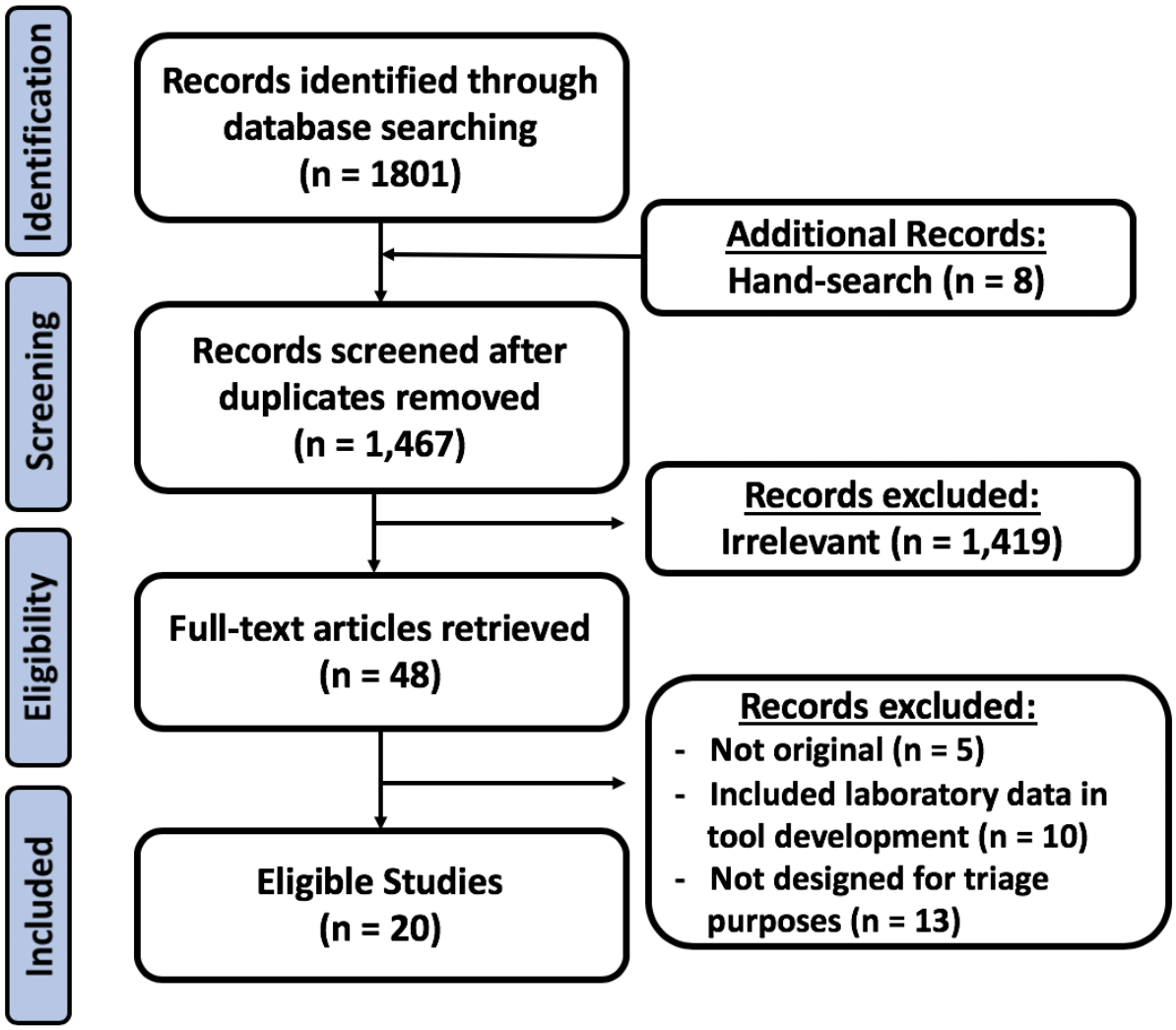


Figure 7: Preferred Reporting Items for Systemetic Review and Meta-Analysis (PRISMA) Flow Diagram of Included Articles

There are a total of 18 tools from nine countries used to triage patients with cardiac complaints at the ED. Conceptually, these tools fit into one of the following clinical purposes: standard general triage tools currently used in ED practice (n = 6); tools specifically designed to detect potential ACS or major adverse cardiac events (n = 9); tools to stratify risk of mortality among patients with ACS (n = 3); and decision tools to improve 10-minute door-to-electrocardiogram (ECG) time (n = 2). These tools are summarized in Table 4.

There were four standard, five-level triage tools there were validated against predicting ACS in the ED. Overall, the accuracy rate of these standard instruments ranged from 44.6%–83%.[11,21,109-112] The Canadian Triage System and Emergency Severity Index were each evaluated by a single study and both had an accuracy of approximately 50%. The Australian Triage Scale was also evaluated by a single study but had a much higher accuracy of around 80%. The Manchester Triage System was the only tool that was evaluated by multiple studies, which showed wide variability in predictive accuracy, ranging from 45%[110] to 83%.[111] This later scale was the only one of which sensitivity and specificity were reported, with corresponding values of 44.6% and 91.3%, respectively.[110]

There was a total of 9 tools that were specifically designed for detecting ACS or major adverse cardiac events. These tools included a wide range of variables such as: age, sex, past medical history, symptoms, pain severity, vital signs (e.g., heart rate and systolic blood pressure), and recent medications taken. Overall, the classification performance (area under the ROC curve) of these tools ranged from a low of 0.57 for Modified-Goldman Risk Score to a high of 0.78 for the HE-MACS (History and ECG-Manchester ACS).[100,113-116] There was a wide range of sensitivities and specificities reported, ranging from 7%–99% and 14%–99%, respectively.[47,100,113,114,116,117]

There was a total of 3 tools to stratify risk of mortality among patients with ACS at the ED. These tools mainly shared various combinations of the following predictive variables: age, body mass index, vital signs (e.g., heart rate and systolic blood pressure), Killip classification, ECG findings, past medical history (e.g., smoking status, history of myocardial infarction or percutaneous cardiac intervention) and cardiac arrest upon presentation. Overall, the classification

performance of these tools ranged from 0.72 for Canada ACS Risk Score to 0.82 for ProACS Risk Score.[118-120]

Finally, there were two decision aid tools that aimed to improve 10-minute door-to-electrocardiogram time. The sensitivity and specificity of these tools to identify acute myocardial infarction (AMI) patients for immediate ECG were 92%–100% and 20%–76%, respectively.[121,122]

Table 4: Characteristics of Included Articles

NAME OF TOOL	DESCRIPTION OF TOOL	MAIN FINDINGS OF VALIDATION STUDY	SENSITIVITY/ SPECIFICITY OF TOOL
CANADIAN TRIAGE SYSTEM	Five level triage tool: - Level I = resuscitation - Level II = emergency assessment - Level III = urgent - Level IV = less urgent - Level V = non-urgent	Atzema et al. (2009)[21]: - High acuity levels I & II had 50% accuracy for STEMI detection - 43.7% of all STEMI were assigned low acuity level scores of III to V	--
MANCHESTER TRIAGE SYSTEM	Five level triage tool: - Level 1 = Red (immediate), target time to be seen 0 minutes - Level 2 = orange (very urgent), target time to be seen 10 minutes - Level 3 = yellow (urgent), target time to be seen 30 minutes	Nishi et al. (2018)[22]: - High acuity levels 1 & 2 had 44.6% accuracy for AMI detection - 55% of all AMI were assigned low acuity level scores of 3 to 5 Providência et al. (2010)[23]: - High acuity levels 1 & 2 had 83% accuracy for STEMI and 77% for NSTEMI detection - 78% of STEMI patients with low acuity scores has atypical presentations (absence of chest pain)	Sensitivity = 44.6% Specificity = 91.3% --

	- Level 4 = green (standard), target time to be seen 90 minutes - Level 5 = blue (non-urgent), target time to be seen 120 minutes	Leite et al. (2015)[24]: - High acuity levels 1 & 2 had an overall accuracy of 77% for ACS detection - Rate of ACS in levels 1 to 5 was 100%, 16%, 4%, 3%, and 0% respectively	--
AUSTRALIAN TRIAGE SCALE	Five level triage tool: - Level 1 = immediate life threatening, target time to triage 0 minutes - Level 2 = imminently life threatening, target time to triage 10 minutes - Level 3 = potentially life-threatening, target time to triage 30 minutes - Level 4 = potentially serious, target time to triage 60 minutes - Level 5 = less urgent, target time to triage 120 minutes	Ryan et al. (2016)[25]: - High acuity levels 1 & 2 had 80% accuracy for AMI detection - Low acuity patients were older, more likely to be female, more likely to present without chest pain, and less likely to have a cardiac history	--

EMERGENCY SEVERITY INDEX	Five level triage tool: - Level 1 = immediate life-saving intervention is required - Level 2 = high risk/emergent - Level 3 = urgent but stable - Level 4 = non-urgent - Level 5 = no ED resources needed	Sanders and DeVon (2016)[11]: - High acuity levels 1 & 2 had 54% accuracy for AMI detection - Emergency nurse age was a significant predictor of accuracy in triage	--
HE–MACS (HISTORY & ECG–MANCHESTER ACS)	Divides patients into 4 risk groups based on age, sex, symptoms, smoking status, and SBP: - very low risk (possible immediate 'rule out'); - low risk (suitable for ambulatory care); - moderate risk (suitable for care in the ED) - high risk (potentially 'rule in' ACS)	Alghamdi et al. (2018)[26]: - Overall accuracy (AUROC) was 0.78 for AMI and 0.73 for ACS	Sensitivity = 98.9% Specificity = 13.9%

MODIFIED-GOLDMAN RISK SCORE	Computes a risk score based on: 1) typical new-onset chest pain at rest, 2) pain the same as previous MI, 3) pain not relieved by nitrites within 15 minutes, 4) pain last > 60 minutes, 5) pain occurring with increasing frequency, 6) hypotension (SBP<100), 7) acute SOB, 8) pain within 6 weeks of a MI or revascularization	Carlton, E, Khattab, A, & Greaves, K. (2015)[27]: - Overall accuracy (AUROC) was 0.65 for 30-day MACE by physicians and 0.57 by nurses	Sensitivity = 63%–73.9% Specificity = 45%–49.8%
MODIFIED HEAR/T SCORE	Computes a risk score by assigning 0–2 points for each of the following: - H = history - E = ECG - A = age - R = risk factors - T = troponin not included	Stopyra et al. (2018)[30]: - NPV of 98% & PPV of 15.1% for 30-day MACE	Sensitivity = 94.1% Specificity = 36.5%
ACT INTERVENTION	An education-focused and triage decision-making prompt to improve ED nurses' cardiac triage decisions for women with MI	Arslanian-Engorn, et al. (2010)[49]: - 87% of the nurses indicated that they intended to use the information presented to change their cardiac triage decision-making practices	--

FRONT DOOR SCORE	Computes a risk score based on age, past medical history, coronary risk factors, recent aspirin use, ST-segment elevation or depression	Ho, J, and Suen, L. (2013)[37]: - Accuracy rate of 84% for detecting patients with acute MI - High inter-rater agreement between physician and nurse users	--
TRIAGE FLOWCHART	A five-step triage flowchart designed to rule out ACS based on age, sex, CV risk factors, and chest pain characteristics	López et al. (2011)[12]: - Overall accuracy (AUROC) was 0.76 for ACS classification	Sensitivity = 7% Specificity = 99%
13–ITEM ACS CHECKLIST	Evaluates the presence of 13 suspicious symptoms for ACS: chest pain, pressure, or discomfort; arm, shoulder, or upper back pain; shortness of breath; palpitation; sweating; fatigue; lightheadedness; nausea; and indigestion	DeVon et al. (2014)[31]: - Highest sensitivity ranged from 63%–72% for chest pain, pressure, or discomfort - Rule in men ruled with ACS were more likely to report chest pain, less likely to report back pain, SOB & unusual fatigue - Rule in women with ACS were nearly 2x more likely to have should and arm pain	Female Sensitivity = 66% Female specificity = 64%–78% Male sensitivity = 63%–72% Male specificity = 70%–78%

		- Specificity > 60% was observed for arm, shoulder, or upper back pain; palpitation, sweating, & indigestion	
A RISK SCORING SYSTEM TO PREDICT ATYPICAL SYMPTOM PRESENTATION	Computes a risk score based on atypical symptomatology among those older than 75; female gender; diabetics; history of AMI; and absence of hyperlipidemia	Li, PW, Yu, D. (2017)[28]: - Overall accuracy (AUROC) was 0.74 for detecting AMI. - This model is based on atypical AMI presentation and could promote recognition of those who have atypical presenting symptomology	--
ACS TRIAGE MODEL	Computes a risk score based on chest pain complaints with or without proximal radiation, age, sex, symptoms of shock (e.g., diaphoresis), and symptoms of acute heart failure (e.g., SOB)	Tsai, K, Lin, RF, Lee, C, & Li, A. (2018)[29]: - Overall accuracy (AUROC) was 0.73 for detecting ACS - This model had better performance when compared to the chest pain, the Zarich, the flowchart and the HBI models	Sensitivity = 93.39% Specificity = 15.4%
CANADA ACS RISK SCORE	Ordinal score from 0–4 based on age ≥ 75 years, Killip classification > 1, SBP < 100 mmHg, and HR > 100 beats/ minute	Huynh et al. (2013)[32]: - Overall accuracy (AUROC) was 0.74–0.79 for in-hospital mortality in STEMI and 0.73–0.79 in NSTE-ACS	--

		- Overall accuracy (AUROC) was 0.72–0.79 for 5-year mortality in STEMI and 0.73–0.77 in NSTE-ACS	
SCAMI RISK SCORE	Computes a risk score based on age, BMI, SBP, ST depression, Killip classification, cardiac arrest, smoking status, and history of MI or PCI	Song et al. (2019)[33]: - Overall accuracy (AUROC) was 0.77 for in-hospital mortality	--
ProACS RISK SCORE	Computes a risk score based on age, SBP, Killip classification, and ST elevation	Timóteo et al. (2017)[34]: - Overall accuracy (AUROC) was 0.82 for in-hospital mortality	--
CHARACTERIZING PRESENTING SYMPTOMS OF STEMI BY AGE AND GENDER	A decision rule using age and chief complaint data to identify the subgroup of pts who should receive an immediate ECG	Glickman et al. (2012)[36]: - NPV of 100% for obtaining an ECG on STEMI patients within 10 minutes of presentation	Sensitivity = 91.9% Specificity = 76.2%
ACS APPLICATION (ACSAP)	An application that predicts which patients require an ECG within 10 minutes based on age, sex, chest pain characteristics, and history of coronary artery disease or diabetes mellitus	O'Donnell et al. (2019)[35]: - All patients with STEMI and NSTEMI received an ECG at triage in the appropriate time of < 10 minutes	ACS and non-ACS patients: sensitivity = 100% Specificity = 20%

Note. ACS = acute cornary syndrome; AMI = acute myocardial infarction; STEMI = ST-segment myocardial infarction; NSTEMI = non ST-segment myocardial infarction; ED = emergency department; AUROC = area under the receiver operating characteristic curve; SBP = systolic blood pressure; MACE = major adverse cardiac event; SOB = shortness of breath; MI = myocardial infarction; ECG = electrocardiogram; NPV = negative predictive value; CV = cardiovascular disease; HBI = heart broken index; HR = heart rate; PCI = percutaneous coronary intervention.

3.5 Discussion

The purpose of our integrative review is to identify data supporting use of tools, instruments and decision aids at initial ED encounter to triage patients with suspicion for ACS. There is a wide variety of instrument, tools and decision aid tools that have been developed for use at the ED. Many studies focused on one cardiac outcome, which limits the generalizability of the findings. Outcomes of interest across all 20 studies included ACS, AMI, 30-day ACS, 30-day major adverse cardiac events, STEMI, NSTEMI, unstable angina and mortality. This variety of outcomes may represent the lack of agreement among clinicians in defining what represents an ACS outcome. Five tools were tested prospectively with only one study being multi-center;[47] two tools focused on differentiating chest pain patients,[100,114] DeVon et al. validated a 13-item symptoms checklist,[47] Li and Yu evaluated atypical symptom presentation[115] and O'Donnell et al. developed an application to reduce the time to obtain a 12-lead ECG.[121]

The prevalence of ACS varied across studies, ranging from 1.3%–41%.[43,47,100,110,112,116,121] Potential patients with ACS can present with over 30 potential symptoms,[14,44] making it difficult for emergency nurses to accurately recognized ACS. It is well known that some patient subgroups such as women,[38] racial minorities,[5] diabetics and elderly patients[48] are more likely to present with symptoms other than chest pain. There were a number of studies that only risk stratified chest pain patients.[43,100,110,112-114,117] The data on these tools is therefore limited. Approximately 28%–46% of patients in this review did not present with a chief complaint of chest pain.[111,121,122] Tsai et al. was the only study that focused on atypical presentation of AMI in a Chinese population.[116]

The standard five-level general triage tools are widely accepted and almost universally used across the globe in ED nursing practice. The Emergency Severity Index tool is widely used in the United States.[4] According to Sanders and DeVon (2016) only 54% of patients who went on to have AMI were given an appropriate ESI score at the time of ED triage. This accuracy rate is concerning because accurate triage acuity level can help expedite treatments and interventions for patients at high-risk for instability and how quickly a healthcare provider evaluates that patient. Previous studies have also found low triage accuracy.[44,48,97,123] These inaccurate triage levels could lead to delay in care and may negatively affect patient outcomes.

3.5.1 Standard Tools for General Triage at the Emergency Department

Since the early 1990s, all global five-level triage systems to assess ED acuity derived from original work of FitzGerald,[124] resulting in the Manchester Triage System,[125] the Canadian Triage and Acuity System,[126] the Emergency Severity Index[2] and the Australian Triage Scale.[127] These categorical five-level scales take into account patient vital signs as well as a patient's chief complaint(s) and past medical history. Universally, because of the similar origin of these scales, level 1 (red) and level 2 (orange) are both considered high-risk patients. Level 3 (yellow) is considered middle acuity and level 4 (green) and level 5 (blue) are considered low acuity. The studies to follow deem level 1 (red) and level 2 (orange) to be the correct acuity for patients with symptoms suspicious of ACS or AMI.

Nishi et al. (2018) in Brazil, Providência et al. (2010) in Portugal evaluated the Manchester Triage System, Ryan et al. (2016) in Australia evaluated the Australian Triage Scale, Atzema et al. (2009) in Canada evaluated the Canadian Triage and Acuity Scale and Sanders and DeVon (2016) in the United Stated evaluated the Emergency Severity Index tool for the outcome of AMI.

Overall accuracy varied from 44%–83% (see Table 4). Providência et al. found that 50% of ACS patients with high acuity triage levels presented with less typical symptoms (i.e., no chest pain).[111] Also, both STEMI (22%) and NSTEMI (78%) patients were given inaccurate triage acuity with 14 patients having atypical presentations (i.e., no chest pain). Leite et al. found that all STEMI patients were given appropriate triage levels with one NSTEMI patient given inaccurately low triage (i.e., level 4).[112] Atzema et al. (2009) reported only 56.2% of STEMI patients received appropriate triage levels.[109] Elderly patients were more often incorrectly triaged (> 20%)[21,110] and were less likely to receive a high acuity triage level or to present with chest pain.[21,111] Sanders and DeVon (2016) did not find age to be a predictor of accurate triage rating with 54% of patients having accurate triage acuity.

3.5.2 Tools Geared Toward Detecting Potential Acute Coronary Syndrome

Suspected ACS patients benefit from accurate assessment and prioritization of prompt treatment in both the pre-hospital and ED settings. Early identification of a potential ACS event could reduce mortality 10%–20%.[10,12] Several studies focused on improving cardiac triage decisions by following American Heart Association (AHA) and American College of Cardiology (ACC) guidelines,[128] to help risk stratify patients what present with chest pain in the pre-hospital[117] and ED[43,100,113,114] settings. Other researchers have developed and validated tools and checklists that include symptoms other than chest pain.[47,115,116] All of these studies strive to improve cardiac triage for the outcomes of ACS, AMI, and 30-day major adverse cardiac events.

Arslanian-Engoren et al. (2010) tested the aid to cardiac triage intervention. This educational intervention includes review of clinical presentation of women with AMI, gender disparities in the cardiac triage decisions of emergency nurses, practice guidelines from the AHA

and ACC, and a triage decision aid prompt. The aid improved cardiac triage decisions by the majority of nurses at a 3-month follow-up.[128] Stopyra et al. (2018), Carlton et al. (2016) and Alghamdi et al. (2018) tested a simple triage tool to risk stratify chest pain patients without laboratory testing at the ED or by paramedics, using the outcome of 30-day major adverse cardiac event or ACS.[113,114,117] Each study tool included similar variables including past medical history, age, sex and symptomology of patients at presentation. Carlton et al. and Alghamdi et al. both used systolic blood pressure as a variable, while Stopyra et al. and Alghamdi et al. used ECG findings in their tools. Every study used the troponin laboratory value to validate each tool. All of these tools focus on 'rule out' of their outcome of interest, which means that the negative predictive value (NPV) or the ability to predict a patient without ACS (i.e., low-risk patients who could be discharged home) is high, ranging from 89.6% to 100%.

López et al. (2011) also validated a five-level triage flowchart ('rule out') for ACS using the variables of age, sex, past medical history (e.g., coronary heart disease and diabetes) and quality of chest pain. This flowchart had 100% specificity. The Front Door Score[43] is another triage tool that was simplified from the TIMI risk score[104] by removing the laboratory troponin value to be able to predict unstable angina or NSTEMI patients from an undifferentiated population of chest pain patients. This tool also used age, past medical history, and ECG findings in addition to aspirin use, and at least two anginal events in 24 hours as variables. Although it was not as specific as the TIMI risk score, it did perform better than the standard five-level triage scale used in Hong Kong. The authors recommended that this tool should be used in combination with nursing judgment to improve chest pain triage accuracy.

Li and Yu (2017), Tsai et al. (2018), and DeVon et al. (2014) included symptoms other than chest pain to risk stratify patients with AMI, and ACS.[47,115,116] Li and Yu focused on the

Chinese population to develop and validate a risk score only for atypical symptoms because this population less often endorses typical symptoms.[129] The variables in their tool included age, sex, past medical history of diabetes, previous AMI and absence of hyperlipidemia. The area under the ROC curve was 0.74. Tsai et al. also considered features of the presenting symptoms in their ACS triage model. The following variables were included, in order of importance: chest pain, age, sex, proximal radiation pain, shock and acute heart failure. Using a threshold set at 2.5, the ACS triage model[116] performed better than the flowchart[100] with sensitivities of 99.39% to 93.18%, respectively.

DeVon et al. used a 13-item symptom checklist at the ED to statistically test for the outcome of ACS between men and women.[47] Symptoms of chest pain, chest discomfort and chest pressure had the highest sensitivity for ACS in both men and women, which was similar to the Tsai et al. study.[116] In the DeVon et al. study, symptoms of shoulder pain, sweating, palpitations, upper back pain, arm pain and indigestion had higher specificities (> 60%), while Tsai et al. found sweating symptoms to be a predictor of ACS.[116] In women, shoulder pain (OR = 2.53, 95% CI, 1.29–4.96) and arm pain (OR= 2.15, 95% CI, 0.30–0.79) were predictive of ACS, but these symptoms were not predictive for men. Moreover, shortness of breath was predictive of non-ACS outcome in men (OR= 0.49, 95% CI, 0.30–0.79), but was not related to ACS in women. This differed from the Tsai study, in which shortness of breath and difficulty breathing increased likelihood of ACS.[116]

3.5.3 Tools to Stratify Mortality Risk Among Patients with Acute Coronary Syndrome

Simple and easy to implement tools designed for wide use among clinicians both in the pre-hospital setting and upon arrival to the ED for predicting mortality include the Canada Acute

Coronary Risk Score,[118] the Portuguese Registry on Acute Coronary Syndromes[120] and the China Acute Myocardial Infarction- NSTEMI risk score.[119] Variables common to all of these risk scores are age, systolic blood pressure, and Killip classification. The Chinese AMI-NSTEMI risk score is the most complicated risk score with nine total variables (see Table 4). The Portuguese ACS risk score and the Canada ACS risk score each have five variables. The area under the ROC curve for the Portuguese ACS risk score and the Chinese AMI-NSTEMI risk score were 0.815, and 0.7819, respectively. The Canada ACS risk score had an area under the ROC curve of ≥ 0.75 in most validation cohorts, with an NPV for a score ≥ 1 of 0.98 (95% CI, 0.97–0.99) for in-hospital mortality. Each risk score had slightly less discrimination power compared to the well-established GRACE risk score using area under the ROC curve. Despite this, the GRACE risk score is limited by requiring laboratory values and cannot be used at first medical contact. All authors agreed that the ability to easily use their risk scores at first medical contact had merit to risk stratify potential ACS patients early.

3.5.4 Decision Tools to Improve 10-minute Door-to-Electrocardiogram Time

The 12-lead ECG is considered an important diagnostic tool that is easily used at triage. For patients with suspected ACS, ED care across the globe sets a goal to obtain and have a physician examine the ECG within 10 minutes of arrival.[10,130] Delays in care results from a lack of recognition of who needs this rapid ECG screening. Glickman et al. (2012) aimed to develop and validate a simple prioritization rule by using different combinations of age and clinical chief complaints to determine need for an ECG.[122] O'Donnell et al. (2019) also aimed to improve ECG screening by prospectively using an application with the following weighted variables: age, sex, past medical history of coronary artery disease or diabetes mellitus, symptoms onset, and intensity

and nature of symptoms.[101] Each study obtained sensitivites > 90% with a 50.6% specificity in the O'Donnell study. Both studies noted that approximately 30% of patients did not present with a chief complaint of chest pain. The second most frequent chief complaint in both studies, in the absence of chest pain was shortness of breath.

3.5.5 Limitations

We found limitations in the available data of our integrative review. All studies were cross sectional in nature. Many studies had different outcomes of interest and these outcomes were not consistently defined across all studies. In some cases, the outcome of interest was not clearly defined. Several of the tools were developed using different methodology, which also made it difficult to compare studies. Specifically, Tsai et al. used cluster analysis and stepwise logistic regression, but did not mention checking interaction terms within the model.[116] A universal limitation pertinent to integrative reviews includes challenges associated with search term limitations and this leading to bias when reporting findings.

3.6 Clinical Implications

Emergency department triage is a difficult task because numerous diagnoses can present with similar symptomatology. Patients with potential ACS are a population that needs to be identified rapidly in order to expedite appropriate clinical treatments and interventions. Nurses should be aware of potential tools, instruments and clinical decision aids that are available to potentially improve accuracy of ACS triage. Due to the variability of tools and presentation,

integrating these tools in real time may prove difficult to perform in a busy ED, the place where a support tool may be most impactful.

3.7 Conclusion

There was a wide variability in the predictive accuracy in the variety of tools, instruments, and decision aid tools designed to improve cardiac triage at the ED. Such wide variability is probably due to different outcome definitions of cardiac events, differences in methodologies used to develop these tools, as well as differences in selection of input predictors during instrument derivation and development. Of utmost importance is that most of these tools are not currently being used in practice. The widely used Emergency Severity Index tool in the US has an accuracy rate of approximately 50%. Future research should focus on prospective validation of these tools and on determining how they would fit into ED workflow to improve patient outcomes.

4.0 DISSERTATION MANUSCRIPT 2: "Comparing Predictive Machine Learning Algorithms for Optimizing Nursing Triage of Acute Coronary Syndrome at the Emergency Department"

4.1 Abstract

Background: Acute coronary syndrome (ACS) accounts for nearly 1.5 million hospitalizations and has a cost burden of $85 billion each year in the United States. Current emergency department triage tools have difficulty differentiating patients with suspected ACS from those with no ACS because similar symptoms can vary in etiology. Machine learning algorithms show promise to differentiate etiology in a heterogeneous patient population of potential patients with ACS.

Methods: We performed an observational retrospective cohort study to develop and compare five predictive machine learning algorithms (binary logistic regression, naïve Bayes, random forest, gradient boosting machine, and artificial neural network) using 10-fold stratified cross-validation for the outcome of acute coronary syndrome.

Results: In our sample of 1201 patients (mean [standard deviation] 65 [14] years; 46% female, 89% white; 1% Hispanic), we identified a total of 243 input variables that are specific to triaging a patient with suspected ACS and could be available during emergency department triage. A positive ACS outcome was identified in 522 (43%) patients. We developed and compared different machine learning algorithms to predict ACS using all available input variables and using a subset of 43 selected input variables chosen by using lasso regularization. Artificial neural network classifier was the best performing algorithm using the subset of 43 variables with an area under the receiver operating characteristic curve of 0.78 (95% confidence interval: 0.76–0.80) followed

by binary logistic regression = 0.77 (0.75–0.79); naïve Bayes = 0.76 (0.73–0.79); random forest = 0.75 (0.73–0.77); and gradient boosting machine = 0.75 (0.73–0.77). The algorithms did not perform as well when all 243 variables were considered.

Conclusion: All five predictive machine learning algorithms show good discrimination abilities for predicting ACS using routinely collected data that could be available at emergency department triage. Artificial neural network classifier and other predictive algorithms could be translated into a clinical decision support tool to assist triage nurses to identify patients with potential ACS with an acceptable degree of clinical accuracy and thereby improve patient outcomes.

Keywords: machine learning, predictive algorithms, acute coronary syndrome, emergency department, triage

4.2 Introduction

Coronary heart disease is the leading cause of death worldwide, accounting for seven million (11.2%) of all deaths annually.[131] Globally, up to two-thirds of patients who die with coronary heart disease do so before reaching a hospital.[131] Heart disease is the most common cause of death in the United States.[132] Acute coronary syndrome (ACS) is an overarching term used for unstable angina, myocardial injury and myocardial infarction.[85,133] Many patients who may have ACS seek care at the emergency department (ED) for various cardiovascular complaints, including chest pain, which is the second most common chief complaint of all patients evaluated at the ED.[99] However, chest pain is not very specific to ACS, and there is significant variation in how patients with ACS present. Patients often present with less frequent symptoms (e.g., shortness of breath,

weakness, fatigue), which overlap with diseases of a non-cardiac etiology,[41,44,99] such as pulmonary embolism.

It is well known that patient presentation for a possible ACS event varies by sex and race/ethnicity.[5,38,44,134] Several studies report the incidence of classic symptoms (e.g., chest pain, severe dyspnea, syncope/presyncope, or palpitations)[40,135] during an acute myocardial event to be as low as 27%.[44,48,101] Patients presenting with non-classic symptoms at the ED may be assigned an inaccurate triage acuity which may cause delays in treatment. Emergency department nurses lead triage and directly influence patient-centered outcomes of ACS patients. Time to treatments is directly linked to rates of ACS mortality and morbidity.[133] Across the globe, five-level triage systems, which are standard triage tools and used for all patients who arrive at the ED have difficulty distinguishing those patients with likely ACS events. These triage systems are highly subjective, and acuity levels can change based on nurse judgement. Currently, in the United States, several studies show the accuracy of nurse-assigned triage level to be as low as 54%, and the inability of the emergency nurse to consistently identify impending ACS.[11,51,97] Similarly, Canadian and European triage systems are only about 50% accurate in identifying patients with acute myocardial infarction.[109,110,136] The complexity of predicting whether or not a patient is having a potential ACS event is difficult due to limited information on presentation and the time constraint of the triage assessment. By utilizing information that is readily available in the electronic health record (EHR) combined with new information routinely obtained at the ED encounter, there is potential to improve accuracy of ACS event triage, by utilizing predictive machine learning algorithms.

Machine learning algorithms can identify subtle patterns in highly dimensional medical data[54] by learning a task and improving from experience without being explicitly programmed.

Many models have been successful at improving efficiency and accuracy in various healthcare arenas.[57,137,138] Supervised machine learning infers a function that maps the input variables with provided labels. This process involves fitting (or training) statistical models to capture inherent patterns of data and making predictions on previously unseen data of similar distribution. One advantage of machine learning modeling is the ability to explore non-linear relationships between input variables and outcomes which may account for higher order interactions to make individualized outcome predictions. This non-linear relationship may lead to exploration of the classes of the outcome variable that are likely linearly separable in the N-dimension.

With the rapid growth of EHR data within hospital systems nationwide, numerous prediction algorithms have leveraged vast EHR data to achieve significant improvements.[139-141] Previous studies have used a variety of popular machines such as gradient boosting machine (GBM),[89] classification and regression trees,[88] random forest (RF),[87] deep neural network,[142] and support vector machine[143] for the following outcomes: 1) 1-year mortality after hospital discharge for ACS patients,[141] 2) ACS patients requiring revascularization,[144] 3) predicting hospital admission at the ED,[145] and 4) the redistribution of ED triage acuity for a critical care outcome.[34] To date, there is no research on the machine learning application to predict ACS in all patients who potentially could have the diagnosis upon arrival to the ED and the immediate triage period. With complexity of illness and ED visits increasing, an ACS-specific predictive algorithm at triage could help to overcome the current knowledge gap of failure to identify ACS at ED triage. Ideally, the ACS-specific predictive algorithms would not require direct human calculation and would run in the background of the EHR system to automatically update a patient's prediction as new information is entered or is readily available in the system to support the nurse at the time of triage decision making. The appropriate triage process of patients with potential ACS could improve

accuracy, initiate time sensitive treatments and therefore could improve patient outcomes. The purpose of this study is to compare the area under the receiver operating characteristic curve (AUC), sensitivity and specificity of five machine learning algorithms in a real-world dataset of ED patients with a suspicion of ACS to predict its definitive occurrence.

4.3 Data and Methods

4.3.1 Study Setting and Sample

This is an observational retrospective cohort study design (see Figure 8). Patients who sought emergency care between January 1st and December 31st of 2018 in one of the EDs in our regional healthcare system that utilize Cerner© (North Kansas City, MO) electronic charting system and the Emergency Severity Index for triage were eligible for the study. Of the 40 system wide hospitals, the included 17 EDs represent rural, community, and two academic level one trauma center settings. All EDs have the ability to transfer a patient to a full-service operating room and/or primary percutaneous coronary intervention treatment location. Those treated at two specialty hospitals (UPMC Children's Hospital of Pittsburgh and UPMC Western Psychiatric Hospital) were excluded from the study. To determine the sample, we first identified all unique patients equal to or greater than 20 years of age who sought emergent care at the ED. With assistance from Office of Health Record Research Request, a random subset of patients were identified who met at least one of the following inclusion criteria: 1) symptomology at ED presentation suggestive of an ACS event (see Table 7); 2) cardiac troponin (cTn) laboratory value; or 3) cardiac procedure codes [e.g., single-photon emission computerized tomography (SPECT)

scan with exercise stress test, SPECT scan with drug induced stress test, and coronary angiogram]. Next, patients were included from each of the above categories to allow for equal representation of inclusion criteria. We selected this cohort approach to enrich our sample for ACS events.

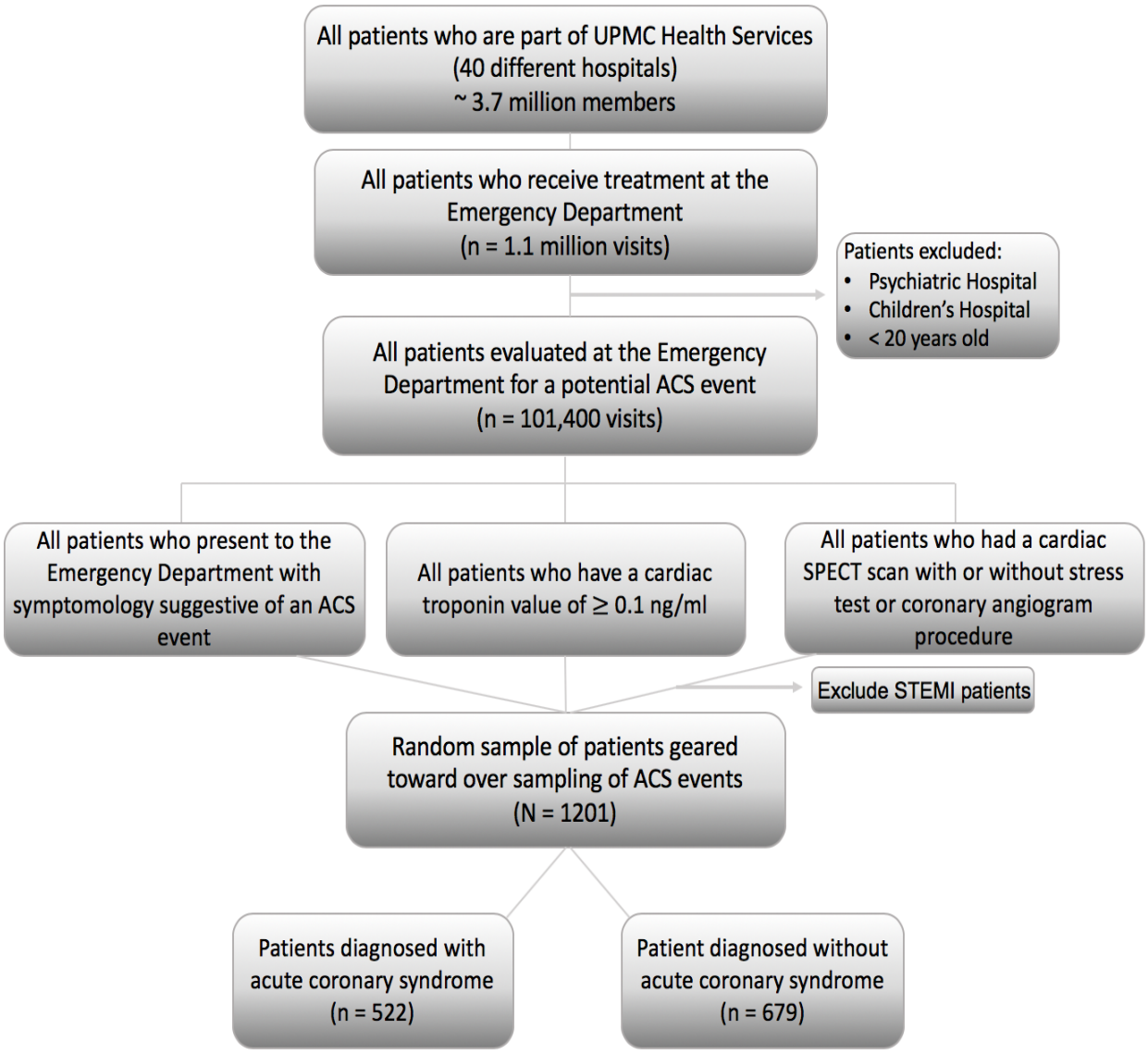


Figure 8: Flow Diagram of Study Sample

Note. ACS = acute coronary syndrome; SPECT = single-photon emission computerized tomography; STEMI = ST-segment elevation myocardial infarction.

Trained independent reviewers abstracted data from the EHRs of patients included in the study. We excluded from subsequent analysis patients who were a trauma alert or a stroke alert. We also excluded patients who had an ST-segment elevation myocardial infarction (STEMI) on the first 12-lead electrocardiogram (ECG), since their ensuing triage is completely driven completely by the single ECG definitive diagnosis rather than the more diffuse clinical presentation that we sought to study. STEMI was identified based on the following criteria: 1) ST-elevation in two contiguous leads ≥ 1 mm; 2) horizontal or down sloping ST-depression ≥ 0.5mm in two contiguous leads; and/or 3) T-wave inversion > 1 mm in two contiguous leads.[85] All 12-lead ECGs suspicious of ischemic changes were reviewed by a board certified Emergency Medicine physician to determine presence of a STEMI.

4.3.2 Data Collection

The Human Resource Protection Office (institutional review board) of the University of Pittsburgh approved collection of our dataset with a waiver of informed consent. Patients were automatically screened and identified using a dedicated service for coordinating studies using EHR research (i.e., Office of Health Record Research Request). After eligible patients were identified by our Office of Health Record Research Request, research assistants manually extracted pertinent clinical data from the pre-hospital and in-patient medical records using Cerner©. An expert user of the electronic record (SOF) trained each research assistant on data collection. Research assistants used an author developed data collection protocol and instrument with well-defined variables. Basic demographic and clinical characteristics for each patient were collected per an *a priori* data coding scheme which is described in detail in the data dictionary (see Appendix A).

4.3.3 Input Variables

As shown in Table 5 (detail in Appendix A) we collected 243 variables for each subject of the types and number (k) as follows:

Demographics (k=4): Demographic information collected at triage or available from the EHR at the time of patient encounter included age, sex, ethnicity, and race. The race variable was recorded as a tertiary split (e.g., white, black/African American, and other). Ethnicity was recorded as Hispanic and non-Hispanic.

Triage evaluation (k=239): Triage evaluation included variables routinely collected at triage and documented in the EHR or available data from the EHR at the time of the patient encounter, including body mass index (k=1), mode of arrival (k=1), prehospital variables (k=27), triage vital signs (k=7), chief complaint(s)/symptomology (k=32), duration of symptoms (k=8), past medical history/past surgical history (k=57), known family history (k=21), automatic 12-lead electrocardiogram features (k=23) and current home medications (k=62).

Table 5: Input Variables for the Acute Coronary Syndrome Prediction Model

DATA TYPE	INPUT VARIABLES
CONTINUOUS (9)	age, body mass index, temperature, heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate, oxygen saturation, pain rating
CATEGORICAL (234)	sex, race, ethnicity, mode of transportation, past medical history, past surgical history, known past family medical history, known past family surgical history, chief complaints, symptoms, current home medications, emergency department automatic computer generated 12-lead electrocardiogram features, 12-lead electrocardiogram done at

	triage, duration of symptoms, patient transported by emergency medical services, prehospital chief complaint, prehospital dispatch level, prehospital automatic computer generated 12-lead electrocardiogram features

4.3.4 Outcome Variable

ACS is the overarching term used for unstable angina, myocardial injury and myocardial infarction.[85,133] We considered three outcomes as diagnostic of ACS: unstable angina, myocardial injury and myocardial infarction. Unstable angina is defined as patients with ischemic symptoms at rest or with minor exercise with no evidence of acute myocardial necrosis; troponin laboratory values are in normal range or may be mildly elevated due to other chronic causes.[17,85] Acute myocardial injury is defined as the rise and fall of an elevated cardiac troponin (cTn) with at least one value above the 99th percentile upper reference limit.[85] Myocardial infarction is defined as myocardial injury with clinical evidence of acute myocardial ischemia and with detection of a rise and/or fall of cardiac troponin (cTn) values with at least one value above the 99th percentile upper range and at least one of the following: 1) symptoms of myocardial ischemia; 2) new ischemia or presumed to be new ECG changes; 3) development of pathological Q waves; 4) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemia etiology; and 5) identification of a coronary thrombus by angiography or autopsy.[85] Two board certified Emergency Medicine physicians first independently reviewed the outcome variable data for each case, and adjudicated the outcome as ACS positive if any of the criteria for unstable angina, myocardial injury, or myocardial infarction as defined above were

found, and ACS negative if none of the criteria were found. Any cases of disagreement in outcome between the two reviewers were then reviewed by a third board certified Emergency Medicine physician, and the majority label was assigned to that case.

4.3.5 Dataset Preparation

For each patient visit, we collected the 243 input variables (Appendix A). Symptoms were divided into more and less frequent categories shown in Table 7, and the one output variable (confirmed clinical diagnosis of ACS) was dichotomized to yes or no. We collected study data from the EHR and managed data using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at the University of Pittsburgh.[146,147] REDCap is a secure, web-based software platform design to support data capture for research studies, providing: 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources. All subsequent processing used custom programs in Python. Before model development, we converted categorical input variables into numerical values using the label or one-hot encoding method,[148] as appropriate. Missing data was examined for patterns. The imputation method for missing continuous data was to replace with the average of the available data for that variable. All outlier values of continuous input variables were checked for accuracy in the EHR.

4.3.6 Supervised Machine Learning Algorithms

After an extensive literature review of predictive machine learning algorithms that were being used on multidimensional EHR data for various outcomes, and given our past experience with using predictive algorithms for the outcome of ACS,[149] the following algorithms were used to predict the outcome of ACS.

4.3.6.1 Binary Logistic Regression

Binary logistic regression (LR) is a classifier method for a binary outcome that finds a monotonous differentiable function (i.e., Sigmoid) to associate the true label of the classification task to the prediction of the logit-transformed linear regression model.[86] It correlates a set of independent variables to the probability of the outcome of interest which can be helpful for development of clinical decision support.

4.3.6.2 Naïve Bayes

The naïve Bayes (NB) classifier approach learns from the probability distributions of all the input variables based on Bayes rule and assumes that the presence of a particular input variable is a class that is unrelated to the presence of any other input variable, and thus, all of these input variables contribute to the outcome independently in the predictive model.[13]

4.3.6.3 Random Forest

Random forest (RF) is an ensemble supervised machine learning algorithm that is composed of a multitude of decision trees.[87,88] This algorithm applies the general techniques of boot-strapping aggregating and random selection of input variables to construct the collection of

decision trees with controlled variance. The final output of a RF model is the mode of the classes of individual trees. There are many hyperparameters that need to be tuned for random forest to be precise. In our study, we selected "max_depth," "n_estimators", and "random_state". We used 100 trees as our "max_depth" parameter with the final output as a majority vote.

4.3.6.4 Gradient Boosting Machine

Gradient boosting machines (GBM) utilize the general gradient descent boosting paradigm to which a model is built and then generates a fitting model to the residual and then combines both models.[89] Models continue to generate sequentially in the presence of residuals. The final predictive model is the result of several models being generated until residual is eliminated.

4.3.6.5 Artificial Neural Network

Artificial neural networks (ANN) were inspired by biological neural networks to extract the relevant features from the input data and perform pattern recognition task by learning from examples without defining the rules used to perform that task.[90] The hidden layers within an ANN can be used for complex pattern recognition tasks. We used single layer architecture, with exploration of both two and three hidden layers with backpropagation.

4.3.7 Input Variable Selection

To further fine-tune the algorithms, we used lasso regularization[92] with 10-fold stratified cross validation to reduce the dataset dimensionality. All five machine learning classifiers were evaluated again using only a subset of input variables that were selected by lasso regularization. This input variable selection optimizes input variable selection by L1 norm which shrinks

coefficient values of all input variables, and then eliminates the input variable that have a coefficient of zero.

4.3.8 Model Construction

We used the dataset with all available input variables and the subset of input variables selected using lasso regularization as the platform to apply all five supervised machine learning algorithms. We used the Python library 'Sklearn' to apply the machine learning algorithms.[150] We used a randomly stratified 10-fold cross-validation to assess model performance, which is a widely used and a preferred method of validation.[151] We only used primary data (i.e., no data transformation techniques were performed) to simplify application of algorithms into clinical environments. Ten subsets were constructed by randomly dividing the overall dataset and each subset had a hold-out set that was used as a test set and the remaining subsets were used as the training sets. We report the performance of our models as the average across all of the ten testing sets. Hyperparameters for each model were optimized by maximizing the average validation of the area under the receiver operating characteristic curve (AUC) across all ten validation sets.

Step one of our comparison of all algorithms was completed on all available input variables. Next, a subset of input variables was selected using lasso regularization from all of the available input variables. Finally, all algorithms were developed and compared using the subset of selected input variables. The steps in the proposed approach are shown in Figure 9.

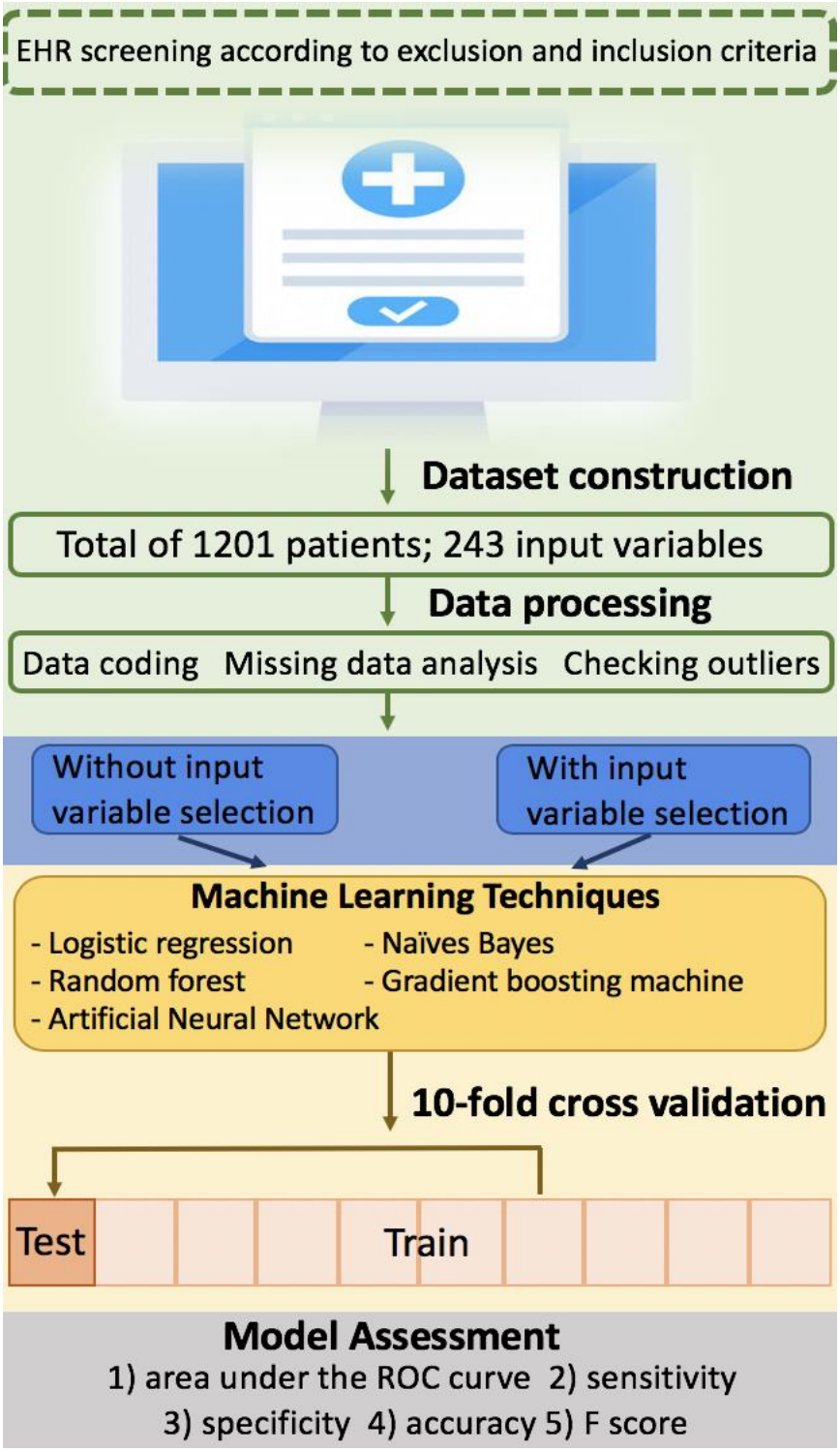
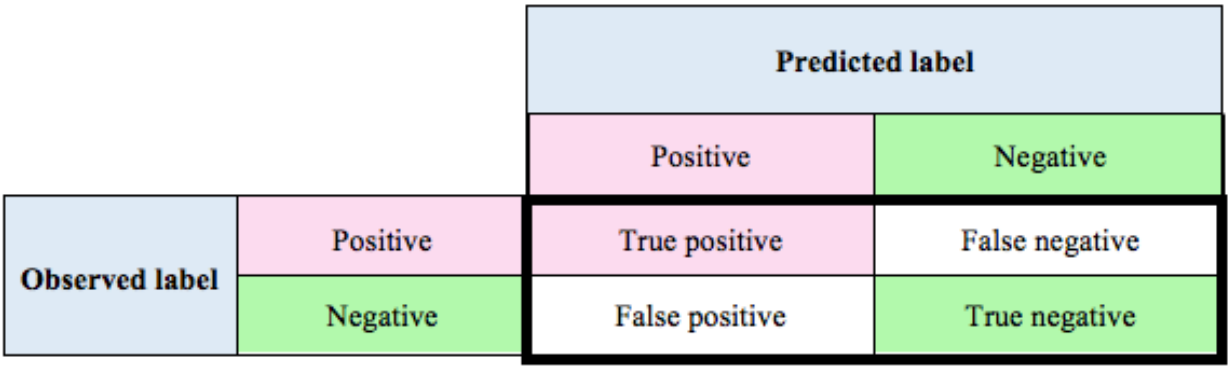


Figure 9: Flow Chart of Proposed Method

Note. EHR = electronic health record; ROC = receiver operating characteristic curve.

4.3.9 Model Assessment

Predictive model performance was evaluated between real and predicted classification for the outcome of ACS using the following metrics: discriminative ability based on AUC, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and F score. In order to determine the performance metrics based on the confusion matrix (see Figure 10), we first adjusted the hyperparameters for each algorithm to optimize the AUC. We then set thresholds that were determined a priori to maintain specificity greater to or equal to 50% while optimizing the sensitivity greater to or equal to 80%. True positives (TP) reflect when both the observed label and the predicted label match to be a true positive outcome. When the observed and predicted label are both negative, the outcome is a true negative (TN). When the observed label is positive and the predicted label is negative, this is a false negative (FN) outcome. False positive (FP) outcome is when the observed label is negative, and the predicted label is positive. The sensitivity indicates the rate of ACS samples that are correctly predicted as ACS and is defined by the following formula: sensitivity = $\frac{TP}{TP+FN}$. The specificity indicates the rate of non-ACS samples that are correctly predicted as non-ACS and is defined by the following formula: specificity = $\frac{TN}{TN+FP}$. Positive predictive value (PPV) is defined as: $PPV = \frac{TP}{TP+FP}$. Negative predictive value (NPV) is defined as: NPV = $\frac{TN}{TN+FN}$. Accuracy is the rate of how often the classifier is correct and is defined by the following formula: accuracy = $\frac{TP+TN}{TP+TN+FP+FN}$. F score is a measure of a classifier's accuracy. It consider both relevant measures of precision (PPV) and recall (sensitivity) and is defined as: F score = $2\ \frac{precision \times recall}{precision + recall}$.



True positive is the number of correct predictions that an instance is positive.

True negative is the number of correct predictions that an instance is negative.

False positive is the number of incorrect predictions that an instance is negative.

False negative is the number of incorrect predictions that an instance is positive.

Accuracy is calculated as the number of all correct predictions (true positive + true negative) divided by the total number of the dataset.

Figure 10: Confusion Matrix

4.3.10 Statistical Analysis

Descriptive data were presented as mean ± standard deviation for continuous input variables. Categorical input variables were presented as frequencies and percentages. To evaluate the relation between the continuous input variable differences between the ACS positive and negative cohorts, we used an independent two sample t-test. We perform the Chi-squared test of independence for categorical input variables and the Fisher's exact test when categorical input variables had expected cell values of < 5. Statistical significance was set to $p < 0.05$. Data were processed and analyzed using IBM® SPSS® software version 26 (IBM Corp., Armonk, NY).

4.4 Results

4.4.1 Descriptive Statistics

As seen in Table 6, our study sample included 1201 patients (mean [standard deviation] age 65 [14] years; 46% female; 89% white; 1% Hispanic). Over 60% of patients were walk-in patients to the ED. A total of 522 (43%) patients had the clinical outcome of ACS. Summary statistics describing patient characteristics between ACS and non-ACS groups are also in Table 6. The differences between the groups on demographics were that the ACS group was significantly older and more likely to be male. There was also a difference between the mode of transportation to the ED between ACS and non-ACS groups. The Emergency Severity Index was used to assign acuity levels to patients, with 56% being assigned a level 2 score. Acuity levels based on the ESI between positive ACS and negative ACS patients were significantly different, $p < 0.001$. In terms of first ED vital signs, the ACS positive patients had a significantly higher heart rate, and higher respiratory rate than the ACS negative group, but there were no differences in blood pressure.

Table 6: Summary of the Characteristics of the Patients With and Without Acute Coronary Syndrome

Patient characteristic	All Patients (N=1201)	Acute Coronary Syndrome	
		ACS n = 522 (43%)	No ACS n= 679 (57%)
Demographics			
Age (years, mean ± standard deviation)*	65 ± 14	68 ± 13	62 ± 14
Sex (male)*	654 (54%)	316 (61%)	333 (49%)
Ethnicity [n (%)]			
Hispanic	16 (1%)	4 (1%)	11 (2%)
Race [n (%)]			
White	1080 (89%)	475 (91%)	595 (88%)
Black/African American	115 (10%)	42 (8%)	72 (11%)
Other	17 (1%)	5 (1%)	12 (2%)
Mode of Transportation to Emergency Department [n (%)]*			
Walk-in	759 (62%)	297 (57%)	462 (68%)
EMS	421 (35%)	211 (40%)	201 (29%)
Wheel car van	30 (3%)	14 (3%)	16 (2%)
Emergency Department First Vital Signs			
Temperature	36.6 ± 0.5	36.8 ± 0.5	36.8 ± 0.4
Heart Rate (beats per minute)*	86 ± 23	88 ± 26	84 ± 19
Systolic Blood Pressure (mmHg)	146 ± 29	147 ± 32	145 ± 25
Respiratory rate (respirations per minute)*	19 ± 5	20 ± 6	19 ± 3
Oxygen Saturation (%)*	96 ± 5	96 ± 5	96 ± 4
Pain rating	4 ± 3	4 ± 3	4 ± 3
Emergency Severity Index scores*			
Not documented	109 (9%)	67 (13%)	42 (6%)
Level 1	74 (6%)	46 (9%)	28 (4%)
Level 2	677 (56%)	313 (60%)	364 (54%)
Level 3	336 (28%)	93 (18%)	243 (36%)
Level 4	4 (< 1%)	2 (< 1%)	2 (<1%)
Level 5	1 (< 1%)	1 (<1%)	--

Note. ACS = acute coronary syndrome; EMS = emergency medical services. The asterisk (*) indicates that the variable difference between acute coronary syndrome group and non-acute coronary syndrome group is statistically significant with a p-value < 0.05.

As seen in Table 7, there were differences between chief complaints/symptoms between ACS and non-ACS groups, with the ACS group having a higher frequency of shortness of breath symptomology. Symptom of headache and flu-like symptoms had higher frequency in ACS negative patients. The following chief complaints/symptoms did not have a statistical difference between with ACS and non-ACS with the Fisher exact test being calculated as follows: ear pain/discomfort (p=0.314), chest tenderness (p=0.395) and chest soreness and implantable cardioverter defibrillator (ICD) firing, both had a p-value of 1.0.

There was less than 1% missing data on all data. Missing data was completely missing at random. We imputed missing data on continuous data with the average of all the available data for that variable.

Table 7: Frequent and Less Frequent Chief Complaint(s)/Symptom(s) of Patients at the Emergency Department for the Potenial Outcome of Acute Coronary Syndrome

INPUT VARIABLES	ALL PATIENTS (N=1201) [N(%)]	ACUTE CORONARY SYNDROME	
		ACS (n = 522, 43%) [n(%)]	No ACS (n = 679, 57%) [n(%)]
FREQUENT CHIEF COMPLAINT(S)/SYMPTOMS			
CHEST PAIN	684 (57%)	304 (58%)	380 (56%)
SHORTNESS OF BREATH*	650 (54%)	316 (61%)	334 (49%)
PAIN RADIATES TO ANOTHER BODY PART	323 (27%)	144 (28%)	179 (26%)
SYNCOPE/DIZZINESS	288 (24%)	117 (22%)	171 (25%)
CHEST PRESSURE	241 (20%)	111 (21%)	130 (19%)
DIAPHORESIS/SWEATING	210 (18%)	103 (20%)	107 (16%)

CHEST TIGHTNESS	142 (12%)	68 (13%)	74 (11%)
PALPITATIONS (I.E., HEART RACING)	129 (11%)	61 (12%)	68 (10%)
CHEST HEAVINESS	100 (8%)	46 (9%)	54 (8%)
LESS FREQUENT CHIEF COMPLAINT(S)/SYMPTOM(S)			
COUGH	205 (17%)	92 (18%)	113 (17%)
NAUSEA ONLY	194 (16%)	90 (17%)	104 (15%)
GENERALIZED WEAKNESS	170 (14%)	78 (15%)	92 (14%)
ARM PAIN	161 (13%)	81 (16%)	80 (12%)
BACK PAIN	127 (11%)	49 (9%)	78 (12%)
ABDOMINAL PAIN	119 (10%)	42 (8%)	77 (11%)
FATIGUE	119 (10%)	56 (11%)	63 (9%)
INDIGESTION	108 (9%)	45 (9%)	63 (9%)
NAUSEA AND VOMITING	96 (8%)	47 (9%)	49 (7%)
HEADACHE*	72 (6%)	19 (4%)	53 (8%)
NECK PAIN	63 (5%)	34 (7%)	29 (4%)
SHOULDER PAIN	62 (5%)	27 (5%)	35 (5%)
FEVER	58 (5%)	32 (6%)	26 (4%)
JAW PAIN	54 (5%)	25 (5%)	29 (4%)
FLU-LIKE SYMPTOMS*	49 (4%)	12 (2%)	37 (5%)
ANXIETY/ PANIC ATTACK	45 (4%)	18 (3%)	27 (4%)
NUMBNESS/TINGLING IN HAND/ARM	44 (4%)	22 (4%)	22 (3%)
ALTERED MENTAL STATUS/ALTERED LEVEL OF CONSCIOUSNESS*	17 (1%)	12 (2%)	5 (1%)
VOMITING ONLY	15 (1%)	7 (1%)	8 (1%)
EAR PAIN/ DISCOMFORT	9 (1%)	2 (< 1%)	7 (1%)

CHEST SORENESS	8 (1%)	3 (1%)	5 (1%)
ICD FIRING	6 (1%)	3 (1%)	3 (< 1%)
CHEST TENDERNESS	5 (< 1%)	1 (< 1%)	4 (1%)

Note. ACS = acute coronary syndrome; ICD = implantable cardiovascular defibrillator. The asterisk (*) indicates that the variable difference between acute coronary syndrome group and non-acute coronary syndrome group is statistically significant with a p-value < 0.05.

4.4.2 Input Variable Selection

Of the 243 input variables, Figure 11 presents the 43 most important variables selected by lasso regularization in descending order. A total of 200 input variables were eliminated due to the lasso regularization model shrinking the coefficients to a zero value for the predictive value for the outcome of ACS. Input variables of ED ECG ST-segment elevation, past medical history of peripheral vascular disease and 12-lead ECG completed at triage ranked the highest to increase the likelihood for the outcome of ACS, while no documented family past medical history, taking irritable bowel medication and ED 12-lead ECG reading of normal sinus rhythm all decreased the likelihood for ACS.

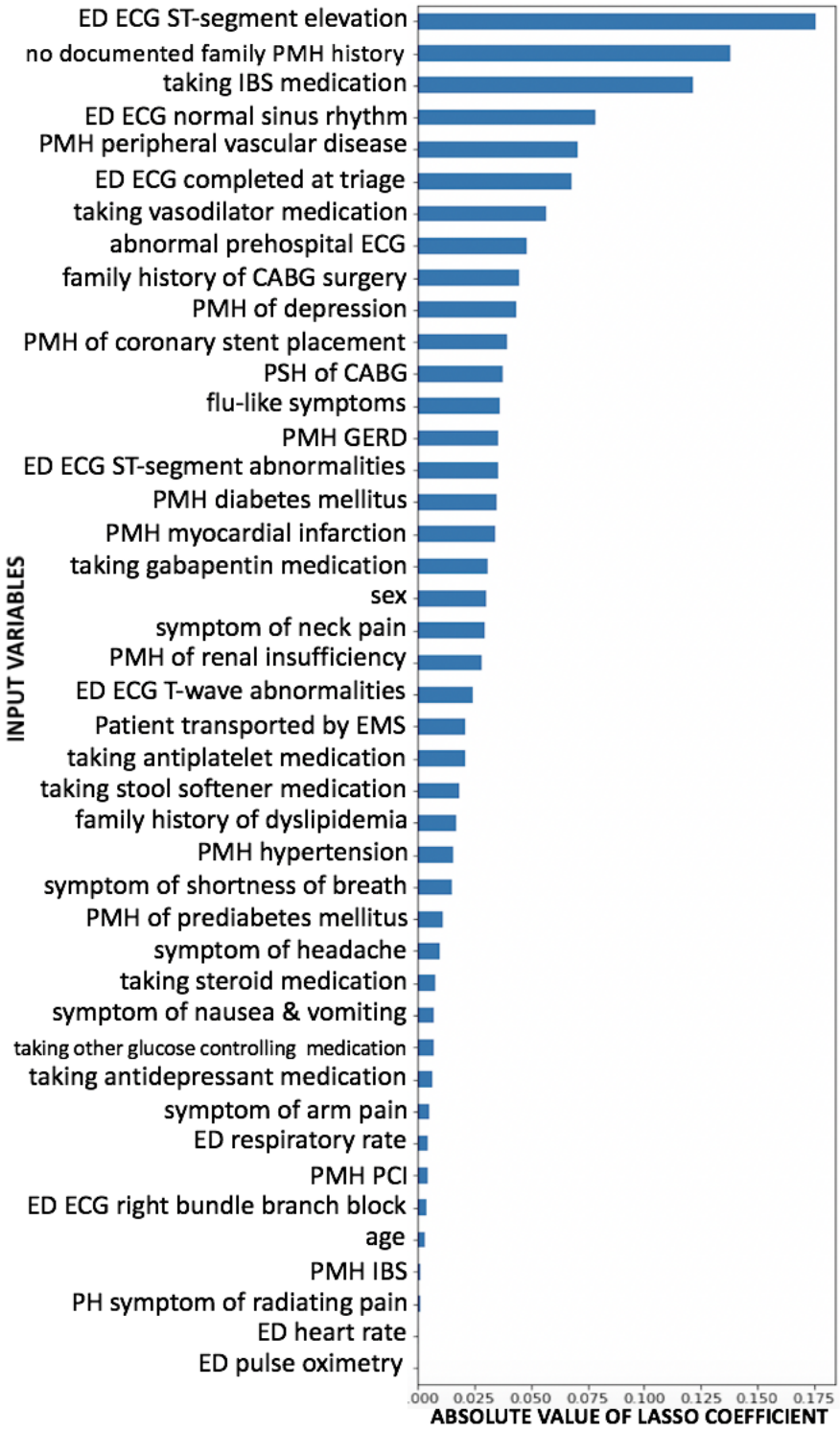


Figure 11: Variable Selection Using Lasso Regularization with Cross Validation for Predicting the Outcome of Acute Coronary Syndrome

Note. ED = emergency department; ECG = electrocardiogram; PMH = past medical history; PSH = past surgical history; GERD = gastroesophageal reflux disease; PH = prehospital; CABG

= coronary artery bypass graft surgery; IBS = irritable bowel syndrome; PCI = percutaneous coronary intervention; EMS = emergency medical services.

4.4.3 Model Performance

We compared five machine learning algorithm classifiers using the 43 selected variables and all available input variables for the outcome of ACS. Figures 12A and 12B display the AUC curve for the five machine learning algorithms with all input variables and with input variable selection, respectively. As shown, the AUC results for all the algorithms improved when the subset of selected input variables were considered (AUC minimum 0.75 and maximum 0.78) than when all the input variables were utilized (AUC minimum 0.72 and maximum 0.74). Table 8 summarized metric outcomes for all algorithms using all available variables. The best performing algorithm when all available variables were included was the LR classifier with an AUC of 0.74 [95% confidence interval (CI), 0.72–0.76]. All machine learning classifiers had similar performance with RF classifier having the highest sensitivity at 79%, accuracy at 64%, and lowest misclassification rate at 35%, while the GBM classifier having the highest specificity at 54%.

After creating a subset of selected variables from lasso regularization and rerunning all classifiers, model performance improved for all five algorithms (see Table 9). The best performing algorithm for the subset of input variables was ANN classifier with an AUC of 0.79 (95% CI, 0.76–0.80). LR, NB and ANN classifiers produced models with similar performance. LR and ANN classifiers had the highest sensitivity at approximately 86%, highest accuracy rate at 67%, and the lowest misclassification rate at 33%. The GBM classifier had the highest specificity at 58%. Both NB and GMB classifiers had comparable accuracy rate and F scores to LR and ANN classifiers.

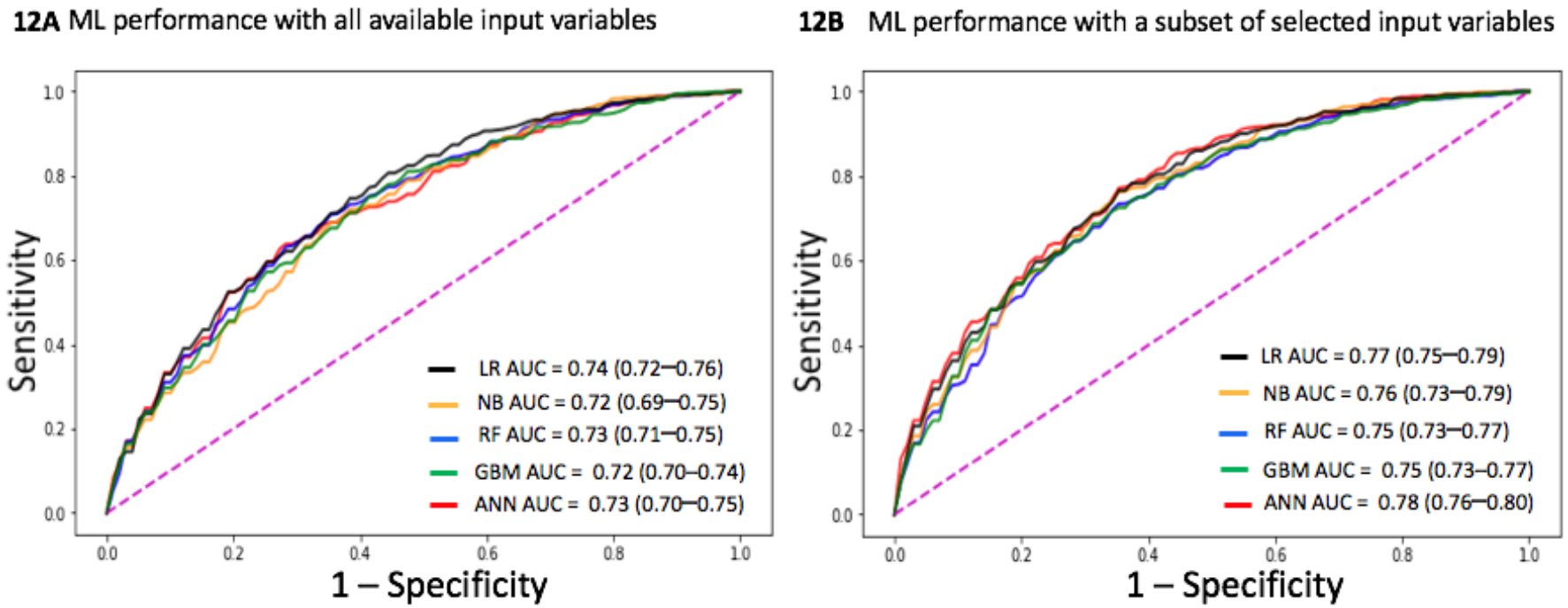


Figure 12: Comparison of Predictive Machine Learning Algorithms Performance on All Available Input Variables (12A) Versus a Subset of Selected Input Variables (12B) Using the Area Under the Receiver Operating Characteristic Curve

Note. ML = machine learning; LR = logistic regression; NB = naïve Bayes; RF = random forest; GBM = gradient boosting machine; ANN = artificial neural network; AUC = area under the receiver operating characteristic curve. 95% confidence intervals are reported in parentheses. The diagonal dotted line represents a non-discriminatory test.

Table 8: Comparison of Predictive Machine Learning Model Performance Without Input Variable Selection

	LOGISTIC REGRESSION (LR)	NAÏVE BAYES (NB)	RANDOM FOREST (RF)	GRADIENT BOOSTING MACHINE (GBM)	ARTIFICAL NEURAL NETWORK (ANN)
AUC (95% CI)	0.74 (0.72, 0.76)	0.73 (0.69, 0.75)	0.73 (0.71, 0.75)	0.72 (0.70, 0.74)	0.73 (0.70, 0.75)
SENSITVITY (95% CI)	74.33% (71.67, 76. 97)	76.82% (72.55, 81.07)	79.69% (76.13, 83.26)	74.71% (70.22, 79.19)	75.86% (72.87, 78.85)
SPECIFICITY (95% CI)	54.05% (49.96, 58.11)	54.64%(51.916, 58.13)	52.58% (49.90, 55.24)	54.93% (52.30, 57.55)	54.05% (50.60, 57.47)
PPV	0.73	0.75	0.77	0.74	0.74
NPP	0.55	0.57	0.56	0.56	0.56
ACCURACY (%)	62.86%	64.28%	64.36%	63.53%	63.53%
F SCORE	0.63	0.64	0.64	0.64	0.64
MISCLASSIFICATION RATE (%)	37.14%	35.80%	35.14%	36.47%	36.39%

Note. AUC = area under the receiver operating characteristic curve;; PPV = positive predictive value; NPP = negative predictive value; CI = confidence interval.

Table 9: Comparison of Predictive Machine Learning Model Performace With Input Variable Selection

	LOGISTIC REGRESSION (LR)	NAÏVE BAYES (NB)	RANDOM FOREST (RF)	GRADIENT BOOSTING MACHINE (GBM)	ARTIFICAL NEURAL NETWORK (ANN)
AUC (95% CI)	0.77 (0.75, 0.79)	0.76 (0.73, 0.79)	0.75 (0.73, 0.77)	0.75 (0.73, 0.77)	0.78 (0.76, 0.80)
SENSITVITY (95% CI)	84.67% (81.40, 87.92)	82.18% (78.69, 85.65)	78.16% (74.56, 81.74)	72.99% (69.28, 76.69)	86.78% (83.91, 89.63)
SPECIFICITY (95% CI)	53.46% (51.07, 55.83)	54.34% (50.10, 58.57)	54.64% (51.15, 58.12)	58.17% (54.09, 62.23)	51.40% (49.45, 53.34)
PPV	0.82	0.80	0.78	0.72	0.83
NPP	0.58	0.58	0.59	0.55	0.58
ACCURACY (%)	67.05%	66.44%	62.62%	66.86%	67.78%
F SCORE	0.67	0.66	0.62	0.67	0.67
MISCLASSIFICATION RATE (%)	32.97%	33.56%	33.14%	37.39%	33.22%

Note. AUC = area under the receiver operating characteristic curve; PPV = positive predictive value; NPP = negative predictive value; CI = confidence interval.

4.5 Discussion

Using routinely collected data that could be available at ED triage, all five supervised machine learning algorithms for the outcome of ACS have good discriminative value with an AUCs ranging from 0.72 to 0.74 when all available input variables are used, and improving to an AUC of 0.75 to 0.78 when a subset of most important variables are used. Of the five proposed models, the ANN classifier was the best performing model with input variable selection for the outcome of ACS with an AUC of 0.78. When considering the metrics of sensitivity and specificity, the LR, NB, RF and ANN predictive algorithms all show promise for identifying ACS and could be translated into a clinical decision support tool to effectively triage patients who present with symptoms and a clinical assessment that may be suggestive of ACS.

To optimize predictive machine learning algorithms for the clinical outcome of ACS, we created a balanced dataset as a platform to apply predictive machine learning algorithms to avoid random under-sampling which can falsely improve performance gains.[56] We used lasso regularization to select a subset of input variables to determine an optimal dataset. When comparing different model performance (see Figure 12A and 12B), using a subset of selected input variables, all models' AUC and sensitivity improves compared to using all available input variables in the dataset. The specificity, accuracy rate and misclassification improved as well by using the selected input variables for a majority of algorithms.

Other studies have used machine learning algorithms for predicting outcomes of major adverse cardiac events, ACS, ACS requiring revascularization, and acute myocardial infarction (AMI). Hu et al. (2019) used EHR data to predict the outcome of major adverse cardiac events

using the machine learning algorithms of support vector machine, classification and regression trees, binary logistic regression and the ACS risk stratification tool GRACE (Global Registry of Acute Coronary Events).[152] Both Dempster-Shafer Theory[153,154] and Rough Set Theory[155] were utilized to explore an ensemble approach to generate a comprehensive predictive model which yielded an AUC of 0.715. Their ensemble modeling approach has shown potential to combine established risk scores and EHR data to predict and warn clinicians of which patients may develop major adverse cardiac events during hospitalization. Their model could help drive protocols and treatment strategies for those at significant risk. VanHouten et al. (2014) compared performance of machine learning algorithms for the outcome of ACS using a real-world clinical dataset based on only structured input variables from the EHR to develop a physician clinical support tool.[140] They collected input data from the entire ED visit as their model was intended to help physicians risk stratify patients near the end of their visit. Random forest predictive model performed the best with an AUC of 0.849 which outperformed elastic net (AUC=0.818), ridge regression (AUC=0.810), modified TIMI[156] (Thrombolysis in myocardial infarction; AUC=0.745) and GRACE risk score (AUC=0.623). Their algorithm development has future implications to be translated into a physician clinical support tool to help improve stratification of patients are risk for ACS at the ED.

Noh et al. (2019) compared two different machine learning algorithms to predict ACS requiring revascularization in patients who presented with angina-like symptoms.[144] Support vector machine with mean imputation had the best prediction with an AUC of 0.86. The authors explored different models using a reduced dataset (i.e., eliminating missing data/listwise deletion) versus a dataset with mean imputation of missing data. Support vector machine using the reduced dataset yielded results of no misclassification of patients with ACS, which is clinically relevant

when physicians are making a decision about who needs to be revascularized. It should be noted that this lack of misclassification did not apply to the mean imputation model. Finally, Than et al. (2019) used a large international sample of patients who presented to the ED with suspected AMI as a platform to develop a novel tool using GBM classifier to predict the likelihood of a diagnosis of a type 1 AMI.[157] The myocardial-ischemic-injury-index (M^3) algorithm generates a value from 0 to 100 by taking age, sex, paired cardiac troponin I concentrations and rate of change in troponin concentration into account. The M^3 model had an AUC of 0.963 (95% CI, 0.957–0.968) in patients who had a diagnosis of type 1 AMI versus those that did not. Their model provides an individualized and objective assessment to predict the likelihood of AMI, which can be used by physicians to identify patients who could benefit from early clinical decision for treatment.

All of the prior studies demonstrate that machine learning algorithms shows promise for improving current risk stratification scores with information that is readily available in the EHR. All of these prior algorithms use laboratory test values, which are typically not available at ED triage. Our triage predictive algorithms are unique in that they do not include laboratory values and only include variables that should or could be considered by a triage nurse evaluating a patient for suspected ACS. To our knowledge, this is the first study to use a real-world heterogeneous dataset limited to data available upon initial assessment of all patients who present to the ED to predict ACS. Our predictive machine learning algorithms have potential to be used in the future as an integral part of ED triage as a clinical decision support tool that would assist nurses in determining who is at greatest risk for ACS. We observed a difference in the Emergency Severity Index scores assigned between ACS and non-ACS groups, but 56% of patients receiving a high acuity score of level 2. This same categorization of both ACS and non-ACS patients does not help differentiate which patient should be evaluated for possible ACS first. Our algorithm improves

accuracy by 25% compared to the 54% current ED accuracy rate[11] for assigning ACS as a high acuity level using the Emergency Severity Index. Our novel algorithm can predict ACS and has the potential to expedite treatments to patients who may have otherwise been mis-triaged and therefore may improve patient outcomes.

Limitations

This study has several limitations, one of which is the lack of racial and ethnic diversity in the sample. There is a low proportion of non-whites and Hispanics compared to general United States population. This sample is representative of our Mid-Atlantic region healthcare system. Validation of our algorithms in more than one regional healthcare system would be of benefit. However, our sample did include a diverse representation care facilities: academic, level one trauma, community and rural hospitals all using the same EHR charting system. Another potential limitation is lack of external validation of our algorithms. Future research should include an external independent test dataset to improve reliability of models.

4.6 Conclusion

This study demonstrates that a variety of machine learning algorithms are beneficial in predicting the outcome of ACS, with the ANN model being the best. These results using machine learning algorithms that use routinely collected data limited to the time of ED triage have great potential to improve identification of patients with suspicion of ACS. These predictive algorithms could be translated into a robust clinical decision tool to equip ED nurses in making real-time clinical triage decisions, thereby improving patient outcomes.

5.0 DISSERTATION MANUSCIPRT 3: "Machine Learning-Based Algorithms Outperform the Emergency Severity Index for Assigning High Acuity Scores for the Outcome of Acute Coronary Syndrome at the Emergency Department

5.1 Abstract

Introduction: Current triage systems have difficulty accurately differentiating acute coronary syndrome (ACS) cases. We used machine learning algorithms to predict ACS based on emergency department (ED) triage assessment data.

Methods: This was a retrospective cohort study of adult patients who were triaged at the ED for a suspected coronary event. With a subset of 43 routinely collected input variables, two machine learning algorithms (binary logistic regression and artificial neural network) were compared for their prediction of ACS. ED triage nurses use the Emergency Severity Index (ESI) to assign acuity scores, where scores of < 3 are deemed high acuity, and scores ≥ 3 are middle/low acuity. The correct ESI acuity score for ACS is high acuity (ESI < 3). We compared performance of binary logistic regression and artificial neural network machine learning classifiers to the ESI assigned scores to accurately classify the diagnosis of ACS as high acuity, using the area under the receiver operating characteristic curve (AUC), sensitivity, and specificity. We compared the performance of the best performing machine learning classifier and ESI using the Delong test and the McNemar's test.

Results: Our sample included 1201 patients (mean age 65±14 years, 46% female, 89% white, 1% Hispanic) of whom 522 (43%) had a diagnosis of ACS. In our dataset, ESI was accurate for placing ACS as high acuity score at triage (ESI < 3) and had an AUC of 0.61 (95% CI, 0.60–0.63),

sensitivity of 89.66 (95% CI, 84.63–94.65), and specificity of 22.09 (95% CI, 10.95–33.29). Artificial neural network was the best performing machine learning algorithm with an AUC of 0.78 (95% CI, 0.76–0.80), sensitivity of 86.78 (95 % CI, 83.91–89.63), and specificity of 51.40 (95% CI, 49.45–53.34). The artificial neural network AUC was higher than the ESI AUC ($p < 0.001$) and the proportion of ACS cases accurately classified by the dichotomized ESI score was lower than that for the artificial neural network classifier ($p < 0.001$).

Conclusion: Using routine triage data, machine learning predictive algorithms demonstrated superior performance compared to nurse assigned ESI scores, improving accuracy rate by 17% for the correct assignment of high acuity for patients with ACS in our heterogeneous patient sample. The application of machine learning algorithms may enhance nurses' triage decision making, improving timeliness of ACS evaluation and care, which could improve patient outcomes.

Keywords: triage, emergency department, machine learning, emergency severity index, acute coronary syndrome

5.2 Introduction

Emergency department (ED) visits in the United States have increased over 50% during the past twenty years, with over 145 million visits in 2019.[1] ED triage influences ED throughput, and is the first opportunity to promptly identify high-risk patients and efficiently assess and prioritize those with the most significant risk for morbidity and mortality.[63] Nurses typically assign triage acuity levels based on their own clinical judgment and intuition,[50,158] aiming to optimize allocation of resources and decrease waiting times based on the severity of the medical condition. Among various triage tools, the Emergency Severity index (ESI) is widely used in the United

States.[4] ED nurses use ESI to categorize patients' acuity into five levels based on the resource utilization and likelihood of admission.[2] The ESI tool is not a diagnostic tool, but rather a tool nurses use to make sure high priority patients (i.e., high acuity) are efficiently evaluated by a physician or advance practice provider. The ESI heavily relies on clinical judgement, often leading to inaccuracy and misclassification,[34,159] high inter-rater variability,[8] and suboptimal predictive ability.[4,9,34,36,160] The ESI has particular difficulty differentiating between levels 2 and 3.[161,162] Triage requires assessing and prioritizing a patient under a significant time constraint, and technological advances for analyzing electronic health data could improve triage efficiency and reliability. Machine learning algorithms have the potential to improve efficiency and assist nurses in processing multidimensional data.

Machine learning approaches account for high-order, non-linear interactions between variables, are able to handle extensive data, and may gain more stable prediction than clinical judgement.[56,148] In the past few years, studies have tested several machine learning-based prediction models to improve the triage process to predict proxies for acuity such as critical outcomes [e.g., admission to the intensive care unit,[163] mortality,[9,34] hospitalization,[145,164] diagnosis of acute coronary syndrome (ACS),[149] and disposition of patients with asthma and chronic obstructive pulmonary disease].[165] Machine learning models often outperform current clinical risk tools.[166] A machine learning predictive model may improve proper identification of patients at greatest risk of morbidity and mortality and would be superior to a non-systematic experienced-based assessment.[34,167]

Acute coronary syndrome is a medical condition with complex symptomatology and variable outcomes, for which diagnosis and treatment are time sensitive. The current rate for the widely used ESI, to accurately assign ACS as high acuity (ESI < 3) is approximately 54%.[7,11,38,44,51]

Our previous research revealed an accuracy rate of 38% in patients with chest pain who called an emergency number to activate emergency medical services, who had a final diagnosis of ACS during hospitalization and were assigned high acuity ESI scores at initial nurse triage.[167] This gap indicates an opportunity to improve triage tools, specifically ones that correctly identify ACS early, which could lead to initiation of time sensitive treatments, and potentially reduce mortality by 10%–20%.[10,12,40] Predictive machine learning algorithms have not been previously used and could be an easy solution to the difficulty recognizing an ACS event at triage. To address this gap, our current study aims to develop and compare machine learning predictive models using the routinely available clinical data available at triage to predict the outcome of ACS and to compare these models to current routine care, the assigned ESI scores documented at triage.

5.3 Methods

5.3.1 Dataset

This was an observational retrospective cohort study of patients seeking emergency care in one of our seventeen EDs within our healthcare system that use the same electronic charting system (Cerner©, Kansas City, MO). The Human Resource Protection Office (institutional review board) of the University of Pittsburgh granted a waiver of consent and approved this study. We included patients presenting between January 1st and December 31st of 2018 and excluded patients who were treated in our system's pediatric and psychiatric hospitals. All EDs use the ESI as an ED triage tool. Our diverse regional healthcare system includes a combination of rural, community, academic and two level-one trauma centers.

We first identified all unique patients, greater than or equal to 20 years old who presented to the ED seeking emergent care. Next, we identified a random subset of patients who met at least one of the following inclusion criteria: 1) had symptom(s) that are suspicious for a coronary event; 2) had a cardiac troponin (cTn) laboratory value ≥ 0.1ng/ml; or 3) had a cardiac procedure during the index hospitalization [e.g., single-photon emission computerized tomography (SPECT) scan with or without exercise stress test, SPECT scan with drug induced stress test, or coronary angiogram]. Next, we selected an equal numbers of patients from each of the preselected groups to ensure patient selection was distributed equally.

Before selecting equal numbers from each inclusion criteria, we excluded patients being evaluated for stroke or trauma or who had an ST-segment elevation myocardial infarction (STEMI) on the first 12-lead electrocardiogram (ECG) because their ED triage assessment is typically focused on the diagnostic criteria of the ECG and less focused on the clinical presentation. Those patients who had an initial ECG suspicious for ischemic changes were reviewed by a board certified Emergency Medicine physician and were excluded based on the following STEMI criteria: 1) ST-elevation in two contiguous leads ≥ 1 mm; 2) horizontal or down sloping ST-depression ≥ 0.5mm in two contiguous leads; and/or 3) T-wave inversion > 1 mm in two contiguous leads.[85] We created a final sample of 1201 patients based on sample size calculations to optimize sensitivity and specificity with precision set to 0.04 with 95% confidence.

5.3.2 Data Collection

The University of Pittsburgh, Office of Health Record Research Request conducted searches of the electronic health records (EHR) to identify our cohort. The Office of Health Record Research Request manages the UPMC data warehouse and assists with screening and identifying

patients within the EHR. An experienced user of the EHR trained independent reviewers on data collection, and these reviewers extracted clinical information from the pre-hospital and in-hospital EHRs. Reviewers used a standard author-developed data collection tool with well-described, a priori defined variables which are described in detail in the data dictionary (see Appendix A). Reviewers entered study data from the EHR into online survey developed using the REDCap electronic data capture system hosted at the University of Pittsburgh.[146,147]

5.3.3 Input Variables

We collected clinical data that could be available at ED triage from the EHR (for a complete list of variables see Appendix A). We collected patient demographics such as age, sex, ethnicity (Hispanic, non-Hispanic), and race (e.g., white, black/African American, or other). Additional input variable data included the following: mode of arrival, prehospital information, triage vital signs, chief complaint(s), symptomology, past medical history, past surgical history, automatic computer generated 12-lead ECG features and current home medications. We used the automatic computer-generated interpretations for 12-lead ECG variables. These interpretations print at the top of the 12-lead ECG report for each patient.

We utilized least absolute shrinkage and selection operator (lasso) regularization[92] with 10-fold cross validation to reduce dataset dimensionality of our dataset. This technique uses an L1 penalty which shrinks some coefficients to zero and thus omitting the corresponding variable from the model in order to reduce the sum of the squared errors within the model. This procedure ensures the selection of the most significant input variables to be included in the model. A subset of 43 variables were selected to be used as input variable for the machine learning algorithms. Input

variable data were checked for missing data patterns. Continuous input variables had missing data replaced with the mean of that variable for all other cases.

5.3.4 Routine Triage Tool is the Emergency Severity Index

The ESI tool is widely used and accepted in the United States.[4] ESI is a standard five-level triage tool to categorize patient acuity based on expected resource utilization and likelihood of admission.[2] Application of the ESI tool comprises asking three questions: 1) Is the patient dying?; 2) Can the patient wait for treatment?; and 3) How many resources will the patient use during their ED visit?[2] Levels range from one to five with the following general descriptions: level 1-requires immediate life-saving interventions; level 2-patient is considered high-risk and requires emergent treatment; level 3-patient is urgent, but can safely wait in the waiting room; level 4-nonurgent; and level 5-does not require any ED resources. Application of the ESI can consider vital signs and nursing intuition to increase an acuity level. Interpretation of ESI is as follows: level 1 and level 2 patients are high acuity, level 3 is middle acuity, and levels 4 and 5 are low acuity.[2]

For this study, we dichotomized ESI scores 1 and 2 as high acuity and ESI scores 3, 4 and 5 as middle/low acuity. While level three patients are not high acuity they typically need numerous ED resources and significant amount of time to reach an ED disposition (i.e., decision to be admitted or discharged home).[93]

5.3.5 Adjudication of Primary Study Outcome

For our study, we defined ACS as the conglomerate outcome of having one of the following, being diagnostic for ACS: unstable angina, myocardial injury, and myocardial

infarction.[85,133] We defined unstable angina as ischemic symptoms at rest, or with minor exercise, with no evidence of acute myocardial necrosis, and troponin laboratory values in normal range or mildly elevated due to other chronic causes.[17,85] We defined acute myocardial injury as the rise and fall of an elevated cardiac troponin (cTn) with at least one value above the 99th percentile upper reference limit.[85] We defined myocardial infarction as the detection of a rise and/or fall of cTn values with at least one value above the 99th percentile upper range limit and at least one of the following: 1) symptoms of myocardial ischemia; 2) new ischemia or presumed to be new ECG changes; 3) development of pathological Q waves; 4) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemia etiology; and 5) identification of a coronary thrombus by angiography or autopsy.[85] Two board certified Emergency Medicine physicians, blinded to the study outcome, reviewed each patient's EHR and assigned the outcome variable as ACS positive if any of the criteria for unstable angina, acute myocardial injury, or myocardial infarction as defined above were met and ACS negative if the criteria were not found. In cases where there was a discrepancy in the outcome between the two physician reviewers, a third board certificated Emergency Medicine physician reviewed the case and the majority label was chosen as the designated outcome.

5.3.6 Dataset Processing

Data cleaning: Patients age 20-100 years were included. All records were checked for erroneous values, with all outliers checked and unreasonable values removed. ED vital signs were limited to the following: heart rate < 250 beats/minute, systolic blood pressure < 275 mmHg, diastolic blood pressure < 160 mmHg, respiratory rate < 42, and oxygen saturation $\leq$ 100%.

Data encoding: All categorical input variables were encoded as numerical values using the label or one hot encoding method,[148] as needed. We used mean imputation methods for missing data on continuous input variables.[168]

5.3.7 Machine Learning Algorithm Fitting and Evaluation

Predictive machine learning algorithms [binary logistic regression (LR) and artificial neural network (ANN)] utilized a subset of 43 selected input variables to fit models using stratified 10-fold cross validation.[151] Hyperparameters for each model were optimized to maximize the area under the receiver operating characteristic curve (AUC) across ten validation and test sets.[169] All machine learning algorithms and ESI's AUC were programmed using Python (Version 3.8.1) and the 'Sklearn' open source library.

5.3.8 Statistical Analysis

The AUC, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), F score and accuracy for the dichotomized ESI score were calculated for the outcome of ACS. To determine the performance metrics for each algorithm, we first optimized the AUC by adjusting the hyperparameters for the individual predictive algorithms for the outcome of ACS. We then set thresholds of sensitivity greater to or equal to 80% with a specificity of greater than or equal to 50% to optimize each predictive algorithm. The best performing machine learning predictive model was defined as having the highest AUC.

We summarize descriptive data as mean ± standard deviation (SD) for continuous input variables and as frequencies and percentages for categorical input variables. Data were screened

for missingness patterns and extraneous outliers. We used independent samples t-test to compare the relation between the continuous variables' differences between ACS and non-ACS groups. The Chi-squared test for independence was performed to compare categorical input variables for the outcome of ACS. Statistical significance is set to $p < 0.05$. The AUC curves were compared between the best machine learning classifier and the assigned ESI score to identify ACS as high acuity using the Delong test.[18] The McNemar's test[170] was also calculated comparing the proportion of correctly classified ACS cases between accurately assigned high acuity ESI scores and the best performing machine learning classifier. IBM® SPSS® software version 26 was used to process and analyze these data.

5.4 Results

5.4.1 Descriptive Statistics

Our study sample included 1201 patients (mean [standard deviation] age 65 [14]; 46% female; 89% white; 1% Hispanic). Over 60% of patients were walk-in patients to the ED. We observed a total of 522 (43%) patients with the clinical outcome of ACS. Summary statistics describing the characteristics of patients in the study, overall and by ACS status, are presented in Table 6. There were demographics differences between ACS positive and ACS negative patients with ACS positive patients being on average significantly older and less likely to be female. There were significant differences between the ACS group and the non-ACS group with regard to the mode of transportation ($p < 0.001$).

There were less than 1% missing data in the entire dataset; missing data patterns were examined and a subset of missing data from input variables appear to be unpredictable and completely missing at random. We imputed values for continuous variables by using the mean of available data for the total sample. Mean imputation method is widely accepted[168] and was used due to the small amount of missing data.

5.4.2 Selected Input Variables

Figure 11 displays the 43 input variables that were selected using lasso regularization with 10-fold cross validation in descending order of their lasso coefficient. The following input variables decrease the model's probability of predicting ACS, in descending order: no documented family history, patient taking IBS medication, ED ECG is normal sinus rhythm, past medical history of depression, having flu-like symptoms, past medical history of gastroesophageal reflux disease, patient taking gabapentin medication, female sex, patient taking stool softener medication, symptom of headache, and patient taking antidepressant medication. The following top five input variables increase the model's probability of predicting ACS: ED ECG with ST-segment elevation, past medical history of peripheral vascular disease, ECG completed at ED triage assessment, patient taking vasodilator medication, and abnormal prehospital ECG.

Table 10 displays characteristics and the distribution of the subset of 43 selected input variables for ACS and non-ACS groups. The ACS group was older and had a higher proportion of males. The ACS group had a higher average heart and respiratory rates than the non-ACS group. There were no differences between the ACS group and the non-ACS group for the following input variables: past medical history of coronary artery stent placement, past medical history of

gastroesophageal reflux disease, symptoms of neck pain, nausea and vomiting, arm pain, and prehospital symptom of radiating pain.

Table 10: Patient Characteristcs and Distribution of Selected Input Variables in Descending Order from the Lasso Regularization Model for the Outcome of Acute Coronary Syndrome

SELECTED INPUT VARIABLE	ALL PATIENTS (N = 1201) MEAN ± SD OR N (%)	ACUTE CORONARY SYNDROME	
		Yes n = 522 (43%) mean ± SD or n (%)	No n= 679 (57%) mean ± SD or n (%)
ED ECG WITH ST-SEGMENT ELEVATION*	12 (1)	10 (2)	2 (< 1)
NO DOCUMENTED FAMILY PMH*	558 (46)	176 (34)	382 (56)
TAKING IBS MEDICATION*	16 (1)	1 (< 1)	15 (2)
ED ECG WITH NORMAL SINUS RHYTHM*	773 (64)	288 (55)	485 (71)
PAST MEDICAL HISTORY OF PERIPHERAL VASCULAR DISEASE*	167 (14)	102 (20)	65 (10)
ED ECG DONE AT TRIAGE*	557 (46)	290 (56)	267 (39)
TAKING VASODILATOR MEDICATION*	224 (19)	138 (27)	86 (13)
ABNORMAL PREHOSPITAL ECG*	21 (2)	15 (3)	6 (1)
FAMILY HISTORY OF CABG SURGERY*	38 (3)	25 (5)	13 (2)
PAST MEDICAL HISTORY OF DEPRESSION*	176 (15)	57 (11)	119 (18)
PAST MEDICAL HISTORY OF CORONARY ARTERY STENT PLACEMENT	182 (15)	118 (23)	64 (9)
PAST SURGICAL HISTORY OF CABG SURGERY*	130 (11)	86 (17)	44 (7)

FLU-LIKE SYMPTOMS*	49 (4)	13 (3)	36 (5)
PAST MEDICAL HISTORY OF GASTROESOPHAGEAL REFLUX DISEASE	516 (43)	209 (40)	307 (45)
ED ECG WITH ST-SEGMENT ABNORMALITIES*	152 (13)	88 (17)	64 (9)
PAST MEDICAL HISTORY OF DIABETES MELLITUS*	413 (34)	230 (44)	346 (51)
PAST MEDICAL HISTORY OF MYOCARDIAL INFARCTION*	266 (22)	162 (31)	104 (15)
TAKING GABAPENTIN MEDICATION*	163 (14)	55 (11)	108 (16)
SEX (MALE AS REFERENCE GROUP)*	649 (54)	316 (61)	333 (49)
SYMPTOM OF NECK PAIN	63 (5)	34 (7)	29 (4)
PAST MEDICAL HISTORY OF RENAL INSUFFICIENCY*	137 (11)	83 (16)	54 (8)
ED ECG WITH T WAVE ABNORMALITIES*	182 (15)	102 (20)	80 (12)
PATIENT TRANPORTED TO HOSPITAL BY EMS*	370 (31)	193 (37)	177 (26)
TAKING ANTIPLATLET MEDICATION*	162 (14)	100 (19)	62 (9)
TAKING STOOL SOFTENER MEDICATION*	59 (5)	16 (3)	43 (6)
FAMILY PMH OF DYSLIPIDEMIA*	19 (2)	14 (3)	5 (1)
PAST MEDICAL HISTORY OF HYPERTENSION*	876 (73)	422 (81)	454 (67)
SYMPTOM OF SHORTNESS OF BREATH*	650 (54)	315 (60)	335 (49)
PAST MEDICAL HISTORY OF PRE-DIABETES MELLITUS*	25 (2)	16 (3)	9 (1)
SYMPTOM OF HEADACHE*	72 (6)	19 (4)	52 (8)
TAKING CORTICOSTERIOD MEDICATION*	140 (12)	73 (14)	67 (10)
SYMPTOM OF NAUSEA AND VOMITING	96 (8)	46 (9)	50 (7)

TAKING OTHER GLUCOSE MEDICATION*	155 (13)	91 (17)	64 (9)
TAKING ANTIDEPRESSANT MEDICATION*	377 (31)	145 (28)	232 (34)
SYMPTOM OF ARM PAIN	161 (13)	81 (16)	80 (12)
ED RESPIRATORY RATE (RESPIRATIONS PER MINUTE)*	19 ± 5	20 ± 6	19 ± 3
PAST MEDICAL HISTORY OF PERCUTANEUOS CORONARY INTERVENTION*	328 (27)	191 (37)	137 (20)
ED ECG WITH RIGHT BUNDLE BRANCH BLOCK*	109 (9)	60 (12)	49 (7)
AGE*	65 ± 14	68 ± 13	62 ± 14
PAST MEDICAL HISTORY OF IBS*	28 (2)	6 (1)	22 (3)
PREHOSPITAL SYMPTOM OF RADIATING PAIN	19 (2)	13 (3)	6 (1)
ED HEART RATE (BEATS PER MINUTE)*	86 ± 13	88 ± 26	84 ± 19
ED OXYGEN SATURDATION (%)*	96 ± 5	96 ± 5	96 ± 4

Note. IBS = irritable bowel syndrome; PMH = past medical history; CABG = coronary artery bypass graft surgery; ED = emergency department; ECG = electrocardiogram; EMS = emergency medical services; SD = standard deviation. An asterisk (*) indicates that the difference between acute coronary syndrome group and non-acute coronary syndrome group for a particular input variable is statistically significant with p-value < 0.05.

5.4.3 Emergency Severity Index Assigned Scores

Overall, the distribution of patients in levels one to five for ESI were: 74 (16%) for ESI score 1, 677 (56%) for ESI score 2, 336 (28%) for ESI score 3, 4 (< 1%) for ESI score 4 and 1 (< 1%) for ESI score 5. We combined patients assigned an ESI score of 4 and ESI score 5 with patients assigned an ESI score 3 in subsequent analysis due to the low frequencies for ESI score of 4 and ESI score 5. The ESI scores were missing in 109 (9%) subjects in our sample. Our analysis showed

that these patients were not missing at random based on their association with the outcome of ACS and we included them in analysis and labeled as the ESI subgroup of "undocumented." Figure 13 compares the distribution of ACS cases to each ESI triage score. A majority of ACS cases were assigned an ESI score of 2 (56%), while 18% were assigned a middle acuity of ESI score 3. As shown in Figure 13, 62% of patients with an ESI score of 1 had ACS, compared with 46% for ESI score 2 and 28% for ESI score 3. Conversely, 52% of all patients assigned an ESI score of 1 and 2 did not have ACS.

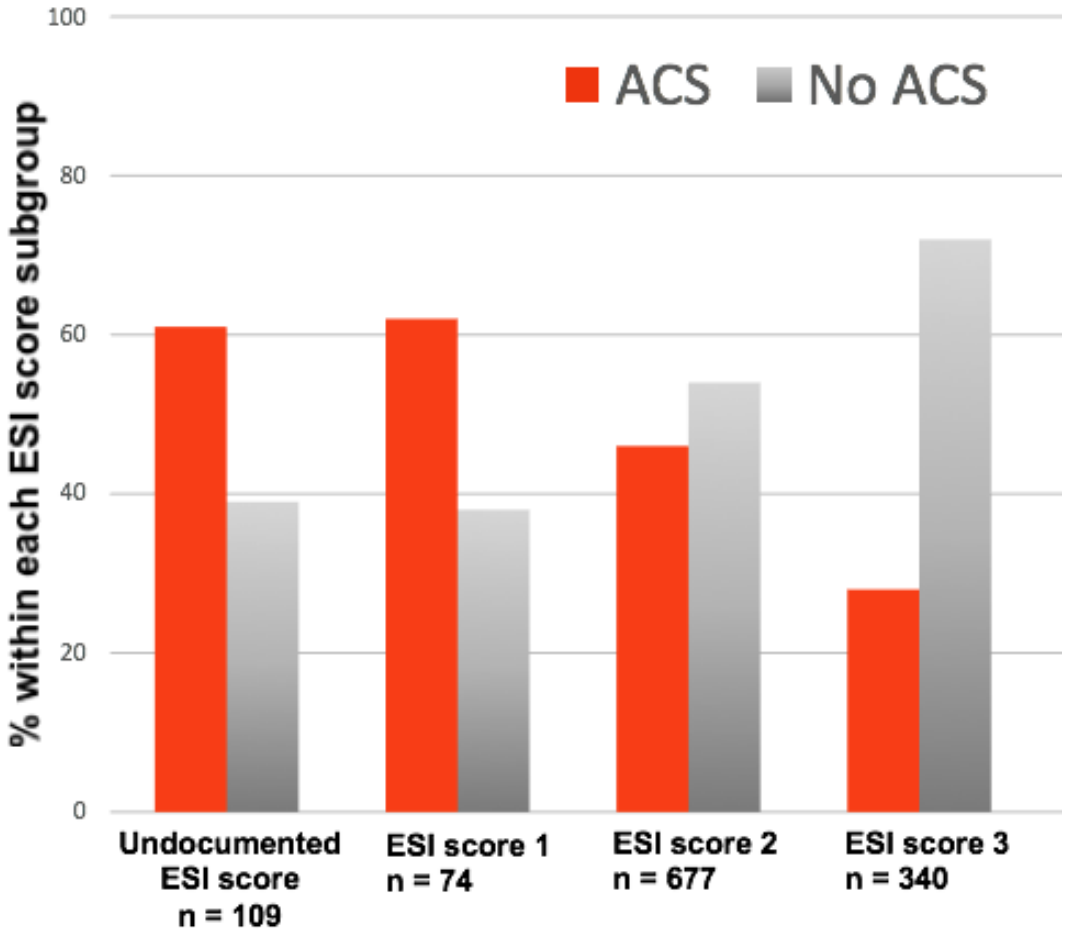


Figure 13: Distribution of Emergency Severity Index Scores for the Outcome of Acute Coronary Syndrome

5.4.4 Machine Learning Algorithm Evaluation

As shown in Figure 14, the ANN classifier performed the best with an AUC of 0.78 (95% CI, 0.76–0.80). Compared to the LR classifier, the ANN classifier has a higher sensitivity with the LR model having the highest specificity. Both machine learning classifiers have similar values for the PPV, NPV, accuracy, F score, and misclassification rate. Tables 11 summarizes the performance metrics for the two machine learning algorithms and ESI documented scores for placing ACS in high acuity.

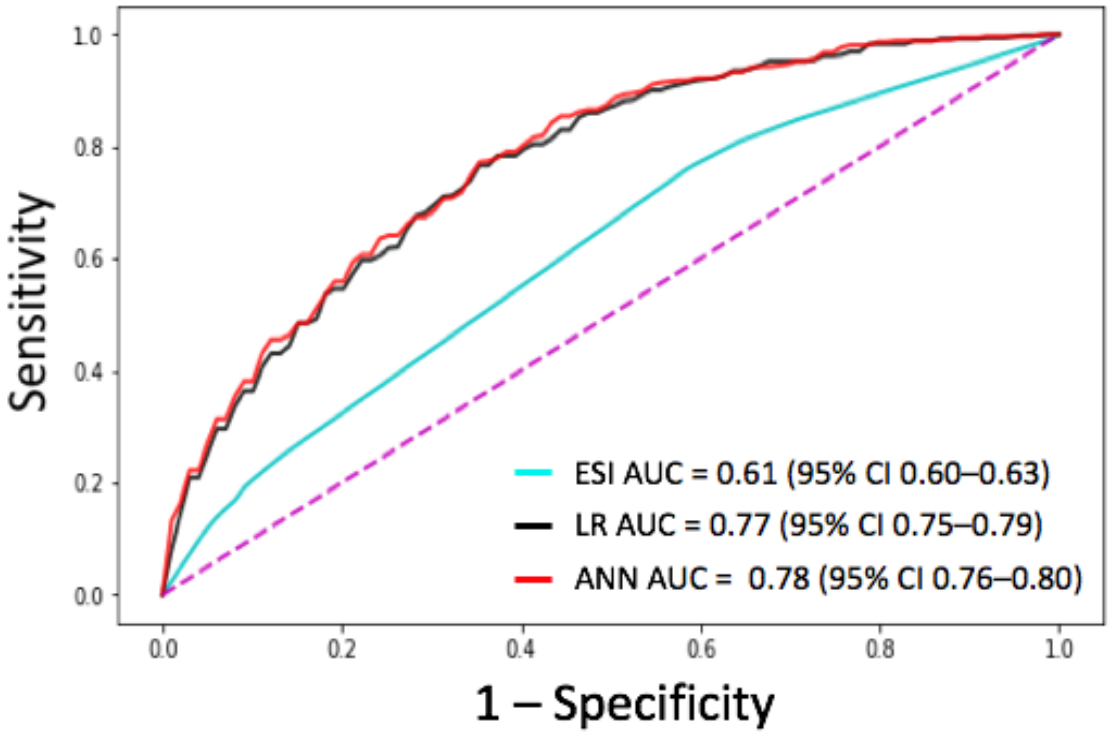


Figure 14: Comparison of the Area Under the Receiver Operating Characteristic Curve of the Machine Learning Algorithms Binary Logistic Regression (LR) and Artificial Neural network (ANN) for the Outcome of Acute Coronar Syndrome and the Emergency Severity Index (ESI) Dichotomized Assigned Scores (ESI < 3 vs. ESI ≥ 3) for Accurately Placing Acute Coronary Syndrome in the ESI High Acuity Category

Note. ESI = Emergency Severity Index; LR = logistic regression; ANN = artificial neural network; AUC = area under the receiver operating characteristic curve; CI = confidence interval. 95% confidence intervals are reported in parentheses. The diagonal dotted line represents a non-discriminatory test.

Table 11: Comparison of Performance Metrics of Machine Learning Classifiers for the Outcome of Acute Coronary Syndrome and the Emergency Severity Index Dichotomized Assigned Scores for Accurately Placing Acute Coronary Syndrome in the ESI High Acuity Category on the SubSet of 43 Selected Input Variables

	EMERGENCY SEVERITY INDEX (ESI)	BINARY LOGISTIC REGRESSION (LR)	ARTIFICAL NEURAL NETWORK (ANN)
AUC (95% CI)	0.61 (0.60, 0.63)	0.77 (0.75, 0.79)	0.78 (0.76, 0.80)
SENSITVITY (95% CI)	89.66% (84.63, 94.65)	84.67% (81.40, 87.92)	86.78% (83.91, 89.63)
SPECIFICITY (95% CI)	22.09% (10.95, 33.29)	53.46% (51.07, 55.83)	51.40% (49.45, 53.34)
PPV	0.47	0.82	0.83
NPP	0.72	0.58	0.58
ACCURACY (%)	51.46%	67.05%	67.78%
F SCORE	0.51	0.67	0.67
MISCLASSIFICATION RATE (%)	48.54%	32.97%	33.22%

Note: ESI = Emergency Severity Index; AUC = area under the receiver operating characteristic curve; CI = confidence interval; PPV = positive predictive value; NPV = negative predictive value.

5.4.5 Comparing Emergency Severity Index to the Best Performing Machine Learning Classifier

Figure 14 shows the comparison of the AUCs for the machine learning classifiers compared to ESI. We compared the AUC [18] for ESI accurately placing ACS in high acuity versus the best machine learning classifier (ANN), which is 0.61 versus 0.79 ($p < 0.001$). This means that the ANN model demonstrates a significantly higher AUC than ESI. An exact McNemar's test[170] determined that there was statistically significant difference in the proportion of ACS cases by the dichotomized ESI score for accurately placing ACS as high acuity when compared to the ANN machine learning classifier ($p < 0.001$).

5.5 Discussion

In this work, we compared predictive machine learning models using data that are routinely collected at triage assessment for the outcome of ACS to ESI scores placing the outcome of ACS in high acuity. We found that the ANN classifier (AUC = 0.78) had the best performance on our large retrospective dataset. Both LR and ANN classifiers demonstrated a superior performance at identifying ACS compared to documented ESI scores placing ACS as high acuity. The McNemar's test showed that there was a statistically significant difference in the proportion of ACS patients predicted by the dichotomized ESI score for accurately placing ACS as high acuity when compared to the ANN machine learning model.

The ESI tool was originally validated for the outcome of hospitalization, anticipated ED resource utilization and mortality within 30 and 60 days.[171,172] Although it was not developed to identify any specific medical diagnosis, it is intended to recognize critically ill patients needing time sensitive treatments. In our study, the ESI tool had difficulty differentiating the acuity in patients with suspected ACS (i.e., 56% of the sample had an ESI score of 2). It had poor classification performance in accurately placing the outcome ACS in the ESI high acuity category (AUC = 0.61, accuracy rate 51%). Importantly, there was an 17% increase in accuracy rate by using our ANN classifier.

Our ANN machine learning model has improved accuracy to detect patients with ACS and with the potential to initiate treatment more effectively. The current triage system does not differentiate specific clinical diagnoses that may be more complex (e.g., ACS, sepsis). The process of triage is highly subjective and is usually guided by nurses' intuition.[95,158] Several researchers found both individual and contextual factors influence ED triage decision-making.[173,174] Fry (2004) found that gathering sufficient patient information in a timely manner and having to quickly make a clinical decision were core elements of triage decisions. Specific routine questions are not asked for every patient, but rather symptomology/chief complaints or mechanism of injury may guide a nurse's line of questioning allowing them to understand a patient's risk for significant increase in morbidity and mortality.[175] By shifting triage assessments to include standard objective data, these data would be used as input variables for a predictive machine learning model. It is ideal to have the machine learning algorithms running in the background of an EHR system, which could serve as a check and balance for the triage data that the nurses collect. These objective machine learning algorithms could potentially remove known stereotypes[94,98,176] and racial biases[5-7] that influence triage decisions.

Input variables identified by our machine learning algorithm are not always explicitly asked by the nurse at triage. For example, nurses may not be aware of how clinically significant a patient taking irritable bowel syndrome medication or having symptoms of neck pain or radiating pain may be on predicting ACS. Complex patient presentations at triage are common, and nurses should be supported with clinical decision support tools that will consider all the input variables that are associated with an increased or decreased likelihood of identifying a patient with ACS. Many predictive machine learning algorithms have been developed to improve triage of different disease processes, but these do not include ACS models.

Machine learning algorithms are currently being explored in an attempt to navigate ED disease processes with heterogeneous presentations. The focus has been on early identification[137,177], disease management[61], and outcome prediction[34,164,165,178] with varying results. Triage improvements using machine learning approaches often are presented/interpreted as predicting a potential outcome so that an ED disposition (i.e., patient is admitted to the hospital or discharged home) can be made. For example, Goto et al. (2019) used machine learning-based predictions on a pediatric population to predict the outcome of admission to an intensive care unit (or in-hospital death) or hospitalization. The researchers used routinely available triage data as input variables, similar to our work, which included the following overlapping variables: age, sex, mode of transportation, ED vital signs, visit reason, and patient comorbidities. Additionally, they included ED visit information from the preceding 72 hours in their model. Their machine learning algorithms were superior to the conventional reference model of routine practice (i.e., ESI tool).

Similar research has been conducted in the adult population by Levin et al. (2018), Raita et al. (2019), and Kwon et al. (2018). Both Levin et al. and Raita et al. determined the distribution of ESI scores across a population by using machine learning models to correct under-triage and

over-triage for the outcomes of hospitalization and critical care. All machine learning models had superior performances compared to routine triage practice using the ESI tool. These researchers have shown the use of machine learning algorithms can improve accuracy for specific outcomes, but they also support additional benefits to ED triage.

ED triage is challenging because it requires astute assessment of both acquired and EHR data of patients under significant time constraint.[2,179] Predictive machine learning algorithms at ED triage could be helpful to find novel relationships not readily apparent to nurses[57] and may improve pace of evaluation and improve patient management.[180] Nurses' triage decisions are influenced by contextual factors but using predictive models that are translated into a clinical decision support tool, these factors may be eliminated. Predictive models can also improve triage because these models are scalable and can be customized to a healthcare system populations. This growing trend to develop predictive models that are specific to a healthcare system instead of a model that is generalizable to a population[55] should be considered. Ideally, predictive machine learning algorithms for ED triage would be translated into a clinical decision support tool that would run in the background of an EHR system and assist nurses in real time clinical decision-making. The algorithm would automatically retrieve and include patient data from past medical and surgical history and update automatically in real time as new information is entered into the system.

By combining technological advances, such as machine learning based clinical decision support tools, to ED nurses' practice, it is possible to capitalize on the vast data that are readily available within the EHR system, allowing for the potential to improve identification of patients with ACS. Machine learning models can identify high-risk conditions, such as ACS or sepsis,[181] by capturing data from available records or to prevent mis-triage by providing clinical decision

support in a heterogeneous patient population. Machine learning algorithms are indispensable and will be the next-generation assistive technology to further improve triage and advance clinical decision-making abilities with readily available data from the EHR.[166] Triage can become more efficient by equipping nurses with a robust clinical decision support tool that can easily calculate the patient probability of a potential diagnosis of ACS. As diagnostic accuracy improves, protocols for potential patients with ACS could be initiated, which may improve patient outcomes.

Strengths/Limitations

This study has several strengths. Our study design oversampled for the outcome of ACS [n=522 (43%)] to avoid the necessity of random under-sampling in an unbalanced dataset which can falsely improve performance gains.[56] By enriching our dataset for ACS cases, the predictive performance of our model has optimal stability. We also used stratified cross-validation to prevent overfitting. Recent research by our team (see section 4.0: Dissertation manuscript 2) explored several machine learning algorithm performances for the outcome of ACS to determine the best models to compare to routine practice (i.e., ESI tool) for this study. We also simplified our machine learning models by selecting input variables using lasso regularization, which improves predictive stability and reduces the chance of overfitting.[56] Finally, collecting data across a large regional hospital healthcare system strengthens this study because it represents the attributes of the patient population. Although it is limited to one healthcare system, with over a million ED visits a year, results may not be generalizable to other healthcare systems.

This study has a few limitations. Due to the retrospective design of our study, there is a possibility that not all past medical and surgical history, home medications, and symptomology were entered into the EHR and therefore these data may not have been collected. Future research could explore patient self-report mechanisms upon arrival to the ED to ensure proper data

collection. The selection of input variables could also be a potential limitation because of the tolerance value set for feature selection. Changing the tolerance value could result in selection of different input variables. Another potential limitation is the high acuity ESI scores assigned to patients could represent other non-ACS diagnosis that could warrant an assigned high acuity ESI score. Exploration of these non-ACS diagnoses is not within the scope of this study and should be evaluated in future research. Another limitation of our research is the difficulty to explain the prediction results in the machine learning based approaches because ANN are non-linear models and do not identify major input variables that influence the final model. Comparatively, the LR model is clinically interpretable and does identify input variables that have an increased likelihood for suspected patients with ACS. Lastly, there is a lack of external validation of our final model on a test set. Future research should further validate our final model on an independent test set.

5.6 Conclusion

We have demonstrated that predictive machine learning models that use routinely available input variable in the EHR have good discrimination value and increase accuracy by 17% compared to the assigned high ESI acuity scores for the clinical outcome of ACS in our study. These models outperform standard triage tools that are currently used in ED triage practice. Future research should focus on determining the best way to implement these machine learning algorithms into ED workflow as clinical decision support tools for identification of patients with ACS.

6.0 Summary, Discussion, Future Directions

6.1 Summary of Dissertation Study

This dissertation includes three complementary studies that progress from a discussion of the state of the current literature via an integrative review (Manuscript #1), to a data-based study to comparing the development, validation, and comparison of multiple predictive machine learning algorithms for the nurse triage of ACS (Manuscript #2), and finally comparison between the best performing machine learning classifier to routine care (i.e., using the Emergency Severity Index) for nurse-assigned high acuity triage scores of a clinical diagnosis of ACS (Manuscript #3). In this section, we summarize all three studies and their nursing implications. Finally, we discuss what future studies could be beneficial based on this dissertation study.

In Manuscript 1, we critically synthesized the literature on cardiac triage tools, instruments and clinical decision aids intended for ED triage use and summarized their accuracy. In this integrative review, we identified a total of 18 different tools from nine countries, that were designed for ED triage. The accuracy of these tools for triaging for suspected ACS ranged from 44%–83%. Several studies used different statistical techniques to develop their tools and instruments for a variety of outcomes. Another main finding from this study was that there is no universal outcome of interest for cardiac triage. The different outcomes across all studies included: final diagnosis during index admission (i.e., ACS, acute myocardial infarction, STEMI, NSTEMI, unstable angina), confirmed ACS with 30-days of presentation, major adverse cardiac events within 30 days of presentation, or all-cause mortality. This variation in outcomes may represent clinical variance for universally defining an outcome of interest for cardiac triage. Lastly, all

studies used different input variables or predictor variables in an attempt to improve cardiac ED triage. Comparing studies with different outcomes and different variables (i.e., predictor variables) proved to be difficult.

Most studies reviewed were cross-sectional, no studies addressed interaction terms when models were derived and developed, different methodologies were used, selection of input predictors varied, and a variation of the outcome variable was present. These tools may be difficult to implement at ED triage where time and information exchanged between nurse and patient is limited. This review of the literature informed this dissertation study of the current state of cardiac triage globally, and the need to universalize definitions and the approach to improve identification of patients with a suspected ACS event. Specifically, in the United States, ED triage practice does not use a specific cardiac triage tool in routine care. The Emergency Severity Index tool is widely used[4] with an accuracy rate of 54% for the outcome of acute myocardial infarction.[11] These concerning results suggest an urgent need to improve triage tools, specifically finding one that correctly identifies ACS early, which could reduce mortality by 10%–20%.[12,40,133]

In Manuscript 2, we performed an observational retrospective cohort study to develop and compare five different machine learning algorithms for the outcome of acute coronary syndrome. A sample of 1201 ED patients with suspicion for an ACS event, from one regional healthcare system, with 522 cases of ACS, served as a platform to run the following machine learning algorithms: logistic regression (LR), naïve Bayes (NB), random forest (RF), gradient boosting machine (GBM), and artificial neural network (ANN). We compared all algorithms performances using all available input variables (i.e., 243) and using a subset of selected input variables (i.e., 43) generated with lasso regularization.[92] Ten-fold cross validation was utilized to optimize model performance and minimize the risk of overfitting.[162]

The main finding from manuscript 2 was that, when using routinely collected data that could be available at ED triage, all machine learning algorithms for the outcome of ACS had good discriminative value using all available input variables with an area under the receiver operating characteristic curve (AUC) of 0.72–0.74. The best performing algorithm using all available input variables was the LR classifier with an AUC of 0.74 (95% confidence interval (CI), 0.72–0.76). All algorithms improved performance by using a subset of 43 selected input variables with their AUCs ranging from 0.75 to 0.78. ANN classifier had the best performance with an AUC of 0.78, (0.76–0.80) followed by LR (AUC = 0.77, 0.75–0.79), naïve Bayes (AUC = 0.76, 0.73–0.79); random forest (AUC = 0.75, 0.73–0.77); and gradient boosting machine (AUC = 0.75, 0.73–0.77).

Predictive machine learning algorithms show promise with good discriminative value to use routine data that could be available at ED triage to predict the diagnosis of ACS. Although ANN was the best performing algorithm, the performance of all algorithms was much higher compared to the current routine care as reported in the literature. By incorporating predictive algorithms into the electronic health record (EHR) and translating their utility into a clinical decision support tool, accuracy could improve, and triage time can be shortened. These refinements in the triage process could help initiate more timely treatments and could improve patient outcomes.

In Manuscript 3, we use the same retrospective observational cohort dataset of 1201 patients with ED visits. We focus on using routine data collected at triage, which is the short period of time after arrival to the hospital when a nurse typically collects relevant clinical data from a patient in a three to five minute assessment to determine the patient's risk for morbidity and mortality.[2,174] We aimed to compare our best performing machine learning algorithms (LR and ANN) to the established triage tool, the ESI tool, to accurately assign a high acuity triage score

(ESI < 3) to ACS. Based on the findings in manuscript 2, we used a subset of 43 input variables selected by lasso regularization[92] instead of all available input variables for the development of the machine learning algorithms.

The main finding of manuscript 3 was that both machine learning algorithms outperformed the ESI for correctly placing ACS as high acuity at triage. Further, there was a 17% increase in accuracy rate when comparing our data of nurses assigning high acuity triage scores to ACS patients versus using the ANN classifier to identify ACS. We used the AUC, sensitivity, and specificity to compare performance between the ESI scores and the machine learning classifiers. The ESI had an AUC of 0.61 (95% CI, 0.60–0.63), sensitivity of 89.66% (84.63–94.65), and specificity of 22.09% (10.95–33.29) of accurately placing ACS as high acuity. The best performing algorithm for the outcome of ACS was ANN with an AUC of 0.78 (0.76–0.80), sensitivity of 86.78% (83.91–89.63), and a specificity of 51.40% (49.45–53.34). The Delong's test showed a statistically significant difference between the AUC of the ESI to accurately assign ACS as high acuity compared to the ANN classifier ($p < 0.001$). The McNemar's test yielded a statistically significant difference in the proportion of ACS cases predicted by the ESI tool versus the ANN classifier. The ESI tool had difficulty differentiating ACS cases from non-ACS cases because a majority of patients were assigned an ESI score of 2.

Our machine learning algorithms have good discriminative value, outperforming the standard ESI triage tool for identifying and assigning high acuity triage scores to patients with potential ACS using routine data. The 17% increase in accuracy rate could help nurses identify patients with suspected ACS who may have been previously mis-triaged with the ESI tool. We have shown that predictive machine learning algorithms could be beneficial in triaging patients

and could be translated into a clinical decision support tool that will help nurses make real time triage decisions to initiate care, and thereby improve patient outcomes.

6.2 Discussion of Dissertation Study

ED triage is a challenging process that occurs once in a patient's visit to the hospital. This unique and fluid assessment must investigate a patient's condition by collecting subjective, objective, and psychological factors, in a short timeframe, to determine how sick a patient is.[182] With the standard practice of documenting all patient assessments in the EHR, there is opportunity to improve care. With the advent of the EHR, the ability to combine medical knowledge and technology has rapidly evolved. Leveraging this technology to improve patient care lies at the center of this work.

6.2.1 Triage in Our Current Healthcare System

Triage in the ED is a challenging task. Overcrowding in the ED environment has put added pressure on nurses who are trying to provide exceptional patient care.[183] The definition of patient "acuity" upon arrival to the ED lacks a universal definition. Acuity does not have a gold standard and several different proxies have been used to develop triage scales.[184] The most common proxies are hospital admission, ED resources utilization and mortality rate. Validation of triage tools are based on these general outcomes, but it has become a tool to identify certain diagnoses.

Nurses are typically the first healthcare worker a patient sees upon arrival to the ED. The triage decision making process usually takes place under considerable time pressure with a limited

amount of data.[96,185] Nurses make clinical decisions at triage based on many factors, including issues of other patients,[183] knowledge and experience,[96,186] work environment[174] and ethical considerations.[187] Nurses use a dual process theory of clinical decision making.[188] Part one relies on intuition, which is fast, highly automatic and is usually applied by experts,[189] and is encouraged and utilized by triage nurses.[2,94] We know that most errors classified as cognitive biases,[190] originate in part one because of the tendency for humans to have prejudice.[188] Part two serves as the analytical process which typically is slower, but reliable.[189] It may be difficult to use deliberate data analysis (i.e., part two) to make a decision at ED triage because it may be time consuming, and the triage process is expected to be completed in a very short period of time.[185] Triage scales, like the Emergency Severity Index, are intended to be used to generate data, form a clinical judgement and lastly a triage decision, which is believed to be most likely from the data analysis phase.[183,186] These triage scales, whether they are three, four or five level systems, are intended to improve triage, but they may be hindering the process. While use of the triage multilevel scales were meant to simplify and standardize the triage process, due to the evolution of medicine, they may not reflect the current need of our healthcare system.[184]

6.2.2 How Could We Improve Cardiac Triage?

From our integrative review, we have learned that many researchers have sought to develop and validate simple tools to improve ED cardiac triage. All authors acknowledge the complexity of this potential ACS population, their vulnerability to time sensitive interventions and the short comings of current practice. To date, no one has yet to leverage technological advances to create a clinical tool specifically for this vulnerable patient population.

The review revealed that a variety of outcomes were used across all studies, making it difficult to compare results. There were however commonalities between predictors (input variables) used in our study and those in previous studies on the topic. For example, while 57% of our patients had symptoms of chest pain, there were a few previous studies that only included patients with chest pain in their sample.[43,100,113,114,117] Other factors (i.e., input variables) present in our study were seen in other studies as well. The following predictors (in descending order of frequency of studies) were present: age,[43,100,113,115-119,121,122] shortness of breath, past medical history of diabetes mellitus, past medical history of myocardial infarction, past history of coronary artery bypass graft surgery, symptom of arm pain, past medical history of PCI, ST-segment elevation,[43,111,113] sex,[100,113] symptom of neck pain,[114,121] symptom of radiating pain,[113,116] heart rate,[100,118] symptom of nausea and vomiting[122] and past medical history of coronary stent placement.[43] This overlap in predictors/input variables demonstrates that this dissertation study is including key variables that have been supported in previous literature.

In completing the integrative review of the previous literature on cardiac triage tools, instruments and clinical decision aids intended for use in the ED, we identified several strategies that have been developed to improve cardiac triage. Unfortunately, there appears to be a lack of a universal outcome when developing these strategies with numerous outcome variables being used. The main finding of the review was that it was difficult to compare studies as there was significant variation in both predictors and outcome variables.

6.2.3 How Machine Learning Algorithms Improve Cardiac Triage

Predictive machine learning algorithms have been utilized in medicine in hopes of building statistical models from massive datasets to find unique and meaningful relationships that are not

readily apparent to humans.[57] ED triage is an important part of the hospital intake process and should be performed rapidly and effectively.[180] Machine learning algorithms have been used to improve general ED triage with hospitalization;[9,34,145,164,178] critical care;[9,34,164,165,178] and mortality,[9,34,164,165,178,191] used as outcomes to represent acuity.

Levin et al. (2018) aimed to improve redistribution of patient acuity levels into five levels, similar to the ESI tool and improve identification of clinical patient outcomes. Their electronic triage support system (e-triage) had equivalent or improved identification for critical care, emergency procedure, and inpatient hospitalization outcomes compared to the ESI triage tool with an AUC ranging from 0.73–0.92.[34] It also improved classification of ESI level 3 patients. Hong et al. (2018) sought to predict hospital admission with both patient history and triage information. Their best predictive machine learning model was gradient boosting machine on their full dataset, which was both triage and patient history information, with an AUC on the test set of 0.924. Goto et al. (2019) and Raita et al. (2019) conducted similar studies comparing machine learning algorithms to the conventional triage for the outcome of critical care and hospitalization, with Goto et al. focusing on a pediatric population. Raita et al. compared four machine learning algorithms performances to the ESI triage tool. All four algorithms outperformed the ESI tool for the outcome of critical care with deep neural network (AUC of 0.86, 95% CI, 0.85–0.87) versus the ESI tool (AUC of 0.74, 95% CI, 0.72–0.75).[164] Also, all four algorithms outperformed the ESI triage tool for the outcome of hospitalization. Goto et al. (2019) had similar results with all machine learning algorithms having higher discriminative ability compared to the ESI triage tool. The deep neural network [C-statistic of 0.85(95% CI, 0.78–0.91)] was not statistically different than the reference [C-statistic of 0.78 (95% CI, 0.71–0.85). Additionally, all machine learning algorithm for the outcome of hospitalization also outperformed the ESI triage model.

All the above-mentioned studies used predictive machine learning algorithms similar to our dissertation study. The following machines were used: logistic regression,[34,145] lasso regression,[164,165,178] random forest,[164,165,178] gradient boosting machine,[145,164,165,178,191] and deep neural networks.[145,164,178] Additionally, we used naïve Bayes (NB) classifier and artificial neural network (ANN) classifier with one hidden layer. We attempted to use deep neural network (i.e., more than one hidden layer), but with addition of two or three hidden layers, our model performance did not improve.

Although no predictive machine learning algorithms have specifically been applied to the triage of all potential patients with ACS, a few researchers have sought to compare predictive machine learning algorithms against routine practice in patients presenting with chest pain. We acknowledge that chest pain is a strong predictor of ACS, but only 57% of our sample in our dissertation study presented with symptoms of "chest pain". Iannattone et al. (2020) conducted a meta-analysis of machine learning algorithms that investigated the outcome of acute coronary syndrome up to January 2019. Upon further review, some studies used algorithms that included laboratory values as input variables, which are typically not available at ED triage. Once these articles were not considered due to the use of laboratory values, only three studies remained. These articles all used an ANN classifier for the outcome of ACS or acute myocardial infarction and only included patient who presented to the ED with chest pain.

Baxt and Skora (1996) used an ANN classifier compared a physician reviewer of the medical chart for the diagnosis of acute myocardial infarction in ED patients with chest pain. The ANN classifier outperformed the physician with an accuracy of 96.0% and 80.5% respectively.[192] Of the 20 variables used, there were nine variables in common compared to our dissertation study: age, sex, radiation of pain, symptoms of nausea and vomiting, symptom of shortness of breath,

past medical history of myocardial infarction, past medical history of diabetes mellitus, ST-segment elevation, and T-wave inversions. Green et al. (2005) compared LR and ANN classifier for the outcome of ACS, which was defined as acute myocardial infarction or unstable angina. Their ANN ensemble outperformed the LR classifier with an AUC of 0.78 (95% CI, 0.658–0.88) compared to 0.77 (95% CI, 0.654–0.880), which were statistically different.[193] A total of eleven input variables were used for their study with the following six variables being the same as our dissertation study: age, sex, past medical history of diabetes mellitus, past medical history of myocardial infarction, past medical history of PCI, and past CABG surgery.

Lastly, Harrison and Kennedy (2005) compared LR and ANN classifier for the outcome of ACS, which was defined as having a positive cardiac marker or having an acute myocardial infarction. The ANN classifier using different input variables performed equally to the LR classifier. While there was increase in performance with the AUC of 0.98, with the greatest number of input variables used, the authors stated that a more complex model would have to be justified[194] and ED clinicians would likely accept and use a simple model.[195] Of the 40 variables used, the following eight overlapped with our dissertation study: age, sex, ST-segment elevation, past medical history of diabetes mellitus, past medical history of myocardial infarction, past medical history of hypertension, symptom of nausea and vomiting, and symptom of shortness of breath.

Although, all the above-mentioned studies were similar to our research, they were different because they only included patients with chest pain in their studies. Including our dissertation study and the above three studies, that had the common goal of improving identification of patients with ACS at triage, there were only four common variables as follows: age, sex, past medical history of diabetes mellitus, and past medical history of myocardial infarction. This limited input variable overlap could be due to the different patient population between studies.

Prior research has identified that the use of predictive machine learning algorithms usually performs superior to routine practice. This dissertation study also supports those findings with our LR and ANN classifier outperforming the ESI triage scores that were documented by nurses upon the patient's arrival to the ED for placing ACS as high acuity. There still remains a paucity of literature that uses predictive machine learning algorithms to predict the outcome of ACS upon immediate arrival to the ED. This very short period of time to collect and process data could become more efficient by incorporating predictive models into the EHR and translating these data into a clinical decision support tool that could improve identification of patients with potential ACS, initiate time sensitive treatments, and thereby improving patient outcomes.

6.2.4 Strengths and Limitations

There are many strengthens to our study. This dissertation study has shown that predictive learning algorithms have great potential to be translated and incorporated into ED triage. Our study design and sample aimed to have a balanced dataset to avoid random under-sampling in an unbalanced dataset which can falsely improve performance gains.[56] We used stratified cross validation to prevent overfitting of these data. By using lasso regularization to select a subset of input variables, we have simplified our machine learning models, which may improve stability and reduces the chance of overfitting.[56] Finally, our dataset is collected across a large regional healthcare system of 17 different EDs, with over a million ED visits a year. These data may represent our regional healthcare system, but the results from our machine learning algorithms may not be generalizable to other healthcare systems.

Our study has a few limitations. Our predictive model would benefit from being externally validated on an independent test set to assess for overfitting of these data. Although we attempted

to minimize the risk for overfitting, by using 10-fold cross validation, out-of-bag estimation, and lasso regularization, there is a chance that we overfit our data. Another limitation is that the ESI tool was developed for a different purpose (i.e., assigning acuity to all patients). While collapsing ESI categories into high acuity (ESI < 3) and middle/low acuity (ESI ≥ 3) may not have been ideal. Another limitation is the difficulty to explain the prediction results of the ANN classifier because of the non-linearity of the algorithm and it does not identify major input variables that influence the final model. Comparatively, the LR classifier can be interpreted clinically and does identify input variables that have an increased likelihood for suspected patients with ACS. This inability to interpret the ANN classifier is known as the black box paradox and should be considered when planning for integration of predictive algorithms into clinical practice. Since the translation of predictive machine algorithms into practice is evolving, future studies should explore how these algorithms will be incorporated into ED care. Another limitation is that our study population was lacking in racial and ethnic diversity but was expected for the mid-Atlantic Western region. It would be beneficial in the future to collect data from more than one regional healthcare system. Additionally, due to the retrospective nature of our data collection with information that was not entered into the EHR, would not have been included.

6.3 Implications for Nursing Practice

The findings from the integrative review and the development of our machine learning algorithms for the outcome of ACS have implications for nursing practice. Given the findings from the integrative review, nurses should be aware of the available clinical support tools, instruments and decisions aids that have been developed and validated to improve cardiac triage. Nurses

working in the ED environment could implement these tools to see how they integrate with their patient intake process and ED flow. Every ED environment is unique, so there is potential that these tools may not be generalizable.

Machine learning algorithms have the potential to improve ED cardiac triage in two ways. Frist, it has potential to eliminate biases. We are well aware of the dual process that nurses use at triage to make real time clinical decisions.[188] Part one relies on intuition, and while this is a fast process, which is favorable for the triage process, it may have unconscious biases associated with it.[188,190] Unfortunately, it is well documented in the literature that nurses hold sex different behavioral beliefs patients presenting with symptoms suspicious of myocardial infarction.[196,197] Further, ED nurses are more likely to associate the signs and symptoms of younger male patients with myocardial infarction with a cardiac diagnosis when compared to the same aged woman with the exact same symptoms.[196] Some nurses in fact may hold cultural biases and stereotypes that may interfere with timely care of a potential ACS event.[97] By implementing a predictive algorithm for the outcome of ACS based on only objective data, there is great potential to eliminate known racial,[5-7,38] cultural, sex and stereotype biases that are present in the cardiac triage process. By eliminating these unfortunate short comings there could be significant improvement in patient outcomes.

The second way predictive machine learning algorithms could improve ED cardiac triage is in assisting nurses with data analysis. The second part of dual process that nurses use at triage serves as the analytical process, which typically is slow.[189] Predictive algorithms have the ability to process data and identifying subtle patterns in highly dimensional medical data[54] by learning a task and improving from experience without being explicitly programmed. This rapid interpretation of data could be helpful to nurses needing to make a timely decision at triage to

improve the current accuracy rate of identifying patients with emergent symptoms of ACS, which is only currently 56%.[11,44,51] These predictive algorithms could be translated to a clinical decision support tool, which will initiate time sensitive treatment, thereby improving patient outcomes.

6.4 Future Research Direction

6.4.1 Implications for Future Research

Finally, this dissertation study has implications for future research. The findings of the integrative review of cardiac triage tools, instruments and decision aids suggest these tools should be prospectively tested in the ED environment. It is important to determine if these tools could be utilized in the dynamic ED setting. With the low accuracy rate for identifying patients with symptoms suggestive ACS, it may be vital to pilot these tools potentially in a high-fidelity simulation setting before implementation in the ED.

Future research should also address the future use of our predictive machine learning algorithm at ED triage. Our final predictive model for the outcome of ACS should be tested on an independent test set. This additional step of testing our final model would indicate potential issues of over-fitting on the training/validation data. It is normal to anticipate a decrease in performance during the testing phase of an algorithm, but there are no set parameters to establish how much of a decrease in performance is acceptable.[198] Evaluating an algorithm on an independent test set adds to the robustness of the algorithm because it demonstrates a lack of overfitting of the data. If there is improve, or a reduction in algorithm performance, and it is not statistically significant and fits within the variance of error on the training/validation set, this mean that the algorithm performs

well on unseen data and could be generalizable. If there is a reduction in performance that is statistically significant, this may mean the model overfit the data and the model should be reevaluated.

Testing our algorithm on data from a different healthcare system could strengthen the utility of our predictive algorithm. Future studies for algorithm development could also be expanded to all patients within a healthcare system that present to the ED with symptoms and presentations suspicious of ACS. Overall, this dissertation study has started to shed light on the importance that data science and big data analytics could play on improving ED triage of patients with a potential cardiac event.

6.5 Conclusion

This dissertation study provides a new perspective of how data science, big data analytics and leveraging EHR data could improve ED triage for the improved identification of patients with a potential diagnosis of ACS. We have shown that predictive machine learning algorithms perform superior to conventional triage practice, the ESI tool. In conclusion, I hope this study emphasizes the importance of removing known biases at ED triage. By developing an objective driven algorithm that can easily be translated into clinical practice, we can contribute to a *Culture of Health*,[199] which strives for health equity, which is free of discrimination.

Appendix A Data Dictionary for Dissertation Study

Input variable	Data type	Description	Outcome
Study ID	Integer	Unique number ID for all enrolled participants	1-1201
Race	Nominal	Race identified as per the patient as listed in the electronic health record	0 = white, 1= black/African American, 3 = other
Ethnicity	Categorical	Ethnicity identified per the patient as listed in the electronic health record, Hispanic or Latino	0 = no, 1 = yes
Sex	Nominal	Gender identified as per the patient	0 = male, 1= female, 2 = non-binary
Age	Integer	Age in number of years of the patient as listed in the electronic health record	
Body mass index	Integer	Body mass index is a person's weight in kilograms divided by the square of the height in meters as calculated by the height and weight listed in the electronic health record	
Transport	Nominal	Mode of transportation to the emergency department as listed in the electronic health record	1 = walk-in, 2 = emergency medical services, 3 = other
PAST MEDICAL/SURGICAL HISTORY			
History of hypertension	Categorical	Known Past medical history of hypertension listed in the electronic health record	0 = no, 1 = yes
History of diabetes mellitus	Categorical	Known past medical history of diabetes mellitus listed in the electronic health record	0 = no, 1 = Type I diabetes mellitus 2 = Type II diabetes mellitus
History of gastroesophageal reflux disease	Categorical	Known past medical history of gastroesophageal reflux	0 = no, 1 = yes

		disease listed in the electronic health record	
History of smoking	Nominal	Status of smoking listed in the electronic health record	0 = never, 1 = prior, 2 = current
History of heart failure	Categorical	Known past medical history of congestive heart failure listed in the electronic health record	0 = no, 1 = yes
History of atrial fibrillation	Categorical	Known past medical history of atrial fibrillation listed in the electronic health record	0 = no, 1 = yes
History of dyslipidemia	Categorical	Known past medical history of dyslipidemia listed in the electronic health record	0 = no, 1 = yes
History of coronary artery disease	Categorical	Known past medical history of coronary heart disease listed in the electronic health record	0 = no, 1 = yes
History of angina	Categorical	Known past medical history of angina listed in the electronic health record	0 = no, 1 = yes
History of myocardial infarction	Categorical	Known past medical history of myocardial infarction listed in the electronic health record	0 = no, 1 = yes
History of a percutaneous cardiac intervention	Categorical	Known past surgical history of a percutaneous cardiac intervention listed in the electronic health record	0 = no, 1 = yes
History of stent	Categorical	Known past surgical placement of coronary artery stenting listed in the electronic health record	0 = no, 1 = yes
History of coronary artery by-pass graft surgery	Categorical	Known surgical history of coronary artery by-pass graft surgery listed in the electronic health record	0 = no, 1 = yes
History of pacemaker	Categorical	Known past medical history of pacemaker/ICD placement listed in the electronic health record	0 = no, 1 = yes

History of ablation	Categorical	Known past surgical history of an ablation procedure listed in the electronic health record	0 = no, 1 = yes
History of peripheral artery disease	Categorical	Known past medical history of peripheral artery disease listed in the electronic health record	0 = no, 1 = yes
History of stroke	Categorical	Known past medical history of stroke listed in the electronic health record	0 = no, 1 = yes
Type of stroke	Nominal	Known past medical history of the type of stroke the participant had as listed in the electronic health record	0 = unknown, 1 = ischemic, 2 = hemorrhagic, 3 = other
History of COPD	Categorical	Known past medical history of chronic pulmonary obstructive disease listed in the electronic health record	0 = no, 1 = yes
History of chronic lung disease	Categorical	Known past medical history of chronic lung disease listed in the electronic health record	0 = no, 1 = yes
History of past drug abuse	Categorical	Known past medical history of illicit drug abuse listed in the electronic health record	0 = no, 1 = yes
History of current drug abuse	Categorical	Known current illicit drug abuse listed in the electronic health record	0 = no, 1 = yes
History of peripheral vascular disease	Categorical	Known past medical history of peripheral vascular disease listed in the electronic health record	0 = no, 1 = yes
History of renal insufficiency	Categorical	Known past medical history of renal insufficiency, chronic renal insufficiency, chronic kidney disease, chronic renal disease listed in the electronic health record	0 = no, 1 = yes

History of dialysis	Categorical	Known past medical history of participant being on dialysis listed in the electronic health record	0 = no, 1 = yes
History of transplant	Categorical	Known past surgical history of participant receiving a transplant listed in the electronic health record	0 = no, 1 = yes
History of pre-diabetes	Categorical	Known past medical history of pre-diabetes mellitus listed in the electronic health record	0 = no, 1 = yes
History of cancer	Categorical	Known past medical history of cancer listed in the electronic health record	0 = no, 1 = yes
History of breast cancer	Categorical	Known past medical history of breast cancer listed in the electronic health record	0 = no, 1 = yes
History of colon cancer	Categorical	Known past medical history of colon cancer listed in the electronic health record	0 = no, 1 = yes
History of skin/dermal cancer	Categorical	Known past medical history of skin/dermal cancer listed in the electronic health record	0 = no, 1 = yes
History of lung cancer	Categorical	Known past medical history of lung cancer listed in the electronic health record	0 = no, 1 = yes
History of lymphoma cancer	Categorical	Known past medical history of lymphoma cancer listed in the electronic health record	0 = no, 1 = yes
History of cervical/uterine cancer	Categorical	Known past medical history of cervical/uterine cancer listed in the electronic health record	0 = no, 1 = yes
History of prostate cancer	Categorical	Known past medical history of prostate cancer listed in the electronic health record	0 = no, 1 = yes

History of other cancer	Categorical	Known past medical history of other cancer listed in the electronic health record	0 = no, 1 = yes
History of transient ischemic attack	Categorical	Known past medical history of transient ischemic attack listed in the electronic health record	0 = no, 1 = yes
History of obstructive sleep apnea	Categorical	Known past medical history of obstructive sleep apnea listed in the electronic health record	0 = no, 1 = yes
History of hypothyroidism	Categorical	Known past medical history of hypothyroidism listed in the electronic health record	0 = no, 1 = yes
History of arthritis	Categorical	Known past medical history of arthritis listed in the electronic health record	0 = no, 1 = yes
History of pulmonary embolism	Categorical	Known past medical history of pulmonary embolism listed in the electronic health record	0 = no, 1 = yes
History of pulmonary hypertension	Categorical	Known past medical history of pulmonary hypertension listed in the electronic health record	0 = no, 1 = yes
History of cognitive impairment/Alzheimer disease	Categorical	Known past medical history of cognitive impairment/ Alzheimer disease listed in the electronic health record	0 = no, 1 = yes
History of bipolar	Categorical	Known past medical history of bipolar disorder listed in the electronic health record	0 = no, 1 = yes
History of irritable bowel syndrome	Categorical	Known past medical history of irritable bowel syndrome listed in the electronic health record	0 = no, 1 = yes
History of diverticulosis/ diverticulitis	Categorical	Known past medical history of diverticulosis/ diverticulitis listed in the electronic health record	0 = no, 1 = yes

History of gastric ulcer	Categorical	Known past medical history of gastric ulcer listed in the electronic health record	0 = no, 1 = yes
History of anxiety	Categorical	Known past medical history of anxiety listed in the electronic health record	0 = no, 1 = yes
History of depression	Categorical	Known past medical history of depression listed in the electronic health record	0 = no, 1 = yes
History of osteoporosis	Categorical	Known past medical history of osteoporosis listed in the electronic health record	0 = no, 1 = yes
History of back pain	Categorical	Known past medical history of back pain listed in the electronic health record	0 = no, 1 = yes
History of cardiomyopathy	Categorical	Known past medical history of cardiomyopathy listed in the electronic health record	0 = no, 1 = yes
History of kidney stone	Categorical	Known past medical history of kidney stone listed in the electronic health record	0 = no, 1 = yes
History of cholecystectomy	Categorical	Known past surgical history of cholecystectomy listed in the electronic health record	0 = no, 1 = yes
History of migraine	Categorical	Known past medical history of migraine listed in the electronic health record	0 = no, 1 = yes
History of cataracts	Categorical	Known past medical history of cataracts listed in the electronic health record	0 = no, 1 = yes
History of anemia	Categorical	Known past medical history of anemia listed in the electronic health record	0 = no, 1 = yes
KNOWN FAMILY PAST MEDICAL/SURGICAL HISTORY			

Family history of coronary artery disease	Categorical	Known past family medical history of coronary artery listed in the electronic health record	0 = no, 1 = yes
Family history of stroke	Categorical	Known past family medical history of stroke listed in the electronic health record	0 = no, 1 = yes
Family history of hypertension	Categorical	Known past family medical history of hypertension listed in the electronic health record	0 = no, 1 = yes
Family history of dyslipidemia	Categorical	Known past family medical history of dyslipidemia listed in the electronic health record	0 = no, 1 = yes
Family history of diabetes mellitus	Categorical	Known past family medical history of diabetes mellitus listed in the electronic health record	0 = no, 1 = yes
Family history of type of diabetes mellitus	Categorical	Known past family history of type I or type II diabetes mellitus listed in the electronic health record	0 = type I diabetes mellitus, 2 = type II diabetes mellitus
Family history of congestive heart failure	Categorical	Known past family medical history of congestive heart failure listed in the electronic health record	0 = no, 1 = yes
Family history of myocardial infarction	Categorical	Known past family medical history of myocardial infarction listed in the electronic health record	0 = no, 1 = yes
Family history of coronary artery by-pass graft surgery	Categorical	Known past family surgical history of coronary artery by-pass graft surgery listed in the electronic health record	0 = no, 1 = yes
Family history of chronic renal insufficiency	Categorical	Known past family medical history of renal insufficiency, chronic renal insufficiency,	0 = no, 1 = yes

		chronic kidney disease, chronic renal disease listed in the electronic health record	
Family history of chronic obstructive pulmonary disease	Categorical	Known past family medical history of chronic obstructive pulmonary disease listed in the electronic health record	0 = no, 1 = yes
Family history of chronic lung disease	Categorical	Known past family medical history of chronic lung disease listed in the electronic health record	0 = no, 1 = yes
Family history of peripheral vascular disease	Categorical	Known past family medical history of peripheral vascular disease listed in the electronic health record	0 = no, 1 = yes
Family history of cardiovascular disease	Categorical	Known past family medical history of cardiovascular disease listed in the electronic health record	0 = no, 1 = yes
Family history of other diseases	Categorical	Known past family medical history of other diseases listed in the electronic health record	0 = no, 1 = yes
Family history of cancer	Categorical	Known past family medical history of cancer listed in the electronic health record	0 = no, 1 = yes
Family history of unknown cancer	Categorical	Known past family medical history of unknown cancer listed in the electronic health record	0 = no, 1 = yes
Family history of breast cancer	Categorical	Known past family medical history of breast cancer listed in the electronic health record	0 = no, 1 = yes
Family history of colon cancer	Categorical	Known past family medical history of breast cancer listed in the electronic health record	0 = no, 1 = yes
Family history of lung cancer	Categorical	Known past family medical history of lung	0 = no, 1 = yes

		cancer listed in the electronic health record	
EMERGENCY DEPARTMENT 12-LEAD ELECTROCARDIOGRAM			
First 12-lead electrocardiogram completed within the first 10 minutes of arrival to the emergency department	Categorical	Difference in time from when the patient was registered in the emergency department until the time of the first 12-lead electrocardiogram was completed in minutes; did the patient receive their first 12-lead electrocardiogram within the first 10 minutes of their emergency department visit	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department was normal sinus rhythm	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as normal sinus at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department was sinus tachycardia	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as sinus tachycardia at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department was sinus bradycardia	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as sinus bradycardia at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department was left bundle branch block	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as left bundle branch block at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department was right bundle branch block	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as right bundle branch block at the emergency department	0 = no, 1 = yes

First 12-lead electrocardiogram at the emergency department was paced	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as being paced at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department was atrial fibrillation	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as atrial fibrillation at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department was atrial flutter	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as atrial flutter at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department was sinus arrhythmia	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as sinus arrhythmia at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department had ST-segment elevation	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as having the words "ST-segment elevation," appearing in the text of the report at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department had ST-segment depression	Categorical	First automatic 12-lead electrocardiogram result at the emergency department had the words "ST-segment depression" listed in the interpretation	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department was supraventricular tachycardia	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as supraventricular tachycardia at the emergency department	0 = no, 1 = yes

First 12-lead electrocardiogram at the emergency department was 1st degree atrioventricular heart block	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as 1st degree atrioventricular heart block at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department had premature ventricular complex	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as having premature ventricular complex at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department premature atrial complex	Categorical	First automatic interpretation of the 12-lead electrocardiogram was reported as having premature atrial complex at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department had t-wave inversion	Categorical	First automatic interpretation of the 12-lead electrocardiogram reports t-wave inversion at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department was T wave abnormalities	Categorical	First automatic interpretation of the 12-lead electrocardiogram reports T-wave abnormalities at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department had ST-segment abnormalities	Categorical	First automatic interpretation of the 12-lead electrocardiogram reports ST-segment abnormalities at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department other abnormalities noted	Categorical	First automatic interpretation of the 12-lead electrocardiogram reports other abnormalities noted at the emergency department First automatic	0 = no, 1 = yes

First 12-lead electrocardiogram at the emergency department had prolonged QT	Categorical	First automatic interpretation of the 12-lead electrocardiogram reports prolonged QT wave at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department had left ventricular hypertrophy	Categorical	First automatic interpretation of the 12-lead electrocardiogram reports left ventricular hypertrophy at the emergency department	0 = no, 1 = yes
First 12-lead electrocardiogram at the emergency department had atrial enlargement	Categorical	First automatic interpretation of the 12-lead electrocardiogram reports atrial enlargement at the emergency department	0 = no, 1 = yes
EMEGENCY DEPARTMENT VITAL SIGNS			
Emergency department first temperature	Integer	Emergency department first temperature value listed in the electronic health record	Recorded in Celsius
Emergency department first heart rate	Integer	Emergency department first heart rate value listed in the electronic health record	Recorded in beats per minute
Emergency department first systolic blood pressure	Integer	Emergency department first systolic blood pressure value listed in the electronic health record	Recorded in mmHg
Emergency department first diastolic blood pressure	integer	Emergency department first systolic blood pressure value listed in the electronic health record	Recorded in mmHg
Emergency department first respiratory rate	Integer	Emergency department first respiratory rate value listed in the electronic health record	Recorded in breaths per minute
Emergency department first oxygen saturation	Integer	Emergency department first oxygen saturation/ pulse oximetry value as listed in the electronic health record	Recorded in percentage of oxygen saturation

Emergency department first pain rating	Number	Emergency department first pain rating on a scale of 0 to 10	Recorded as the numerical pain scale 0 to 10
HOME MEDICATIONS			
Taking a beta blocker medication	Categorical	Patient is taking a beta blocker medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking metoprolol medication	Categorical	Patient is taking metoprolol medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking atenolol medication	Categorical	Patient is taking atenolol medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking propranolol medication	Categorical	Patient is taking propranolol medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking another kind of beta blocker medication	Categorical	Patient is taking another kind of beta blocker medication other than metoprolol, atenolol, or propranolol, according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking an ace inhibitor medication	Categorical	Patient is taking an ace inhibitor medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking lisinopril medication	Categorical	Patient is taking lisinopril medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking another kind of ace inhibitor medication	Categorical	Patient is taking another type of ace inhibitor medication, other than enalapril, lisinopril, or imidapril, according to self-report or listed in the electronic health record	0 = no, 1 = yes

Taking an angiotensin receptor blocker medication	Categorical	Patient is taking an angiotensin receptor blocker medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking losartan medication	Categorical	Patient is taking losartan medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking irbesartan medication	Categorical	Patient is taking irbesartan medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking valsartan medication	Categorical	Patient is taking valsartan medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking a calcium channel blocker medication	Categorical	Patient is taking a calcium channel blocker medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking amlodipine medication	Categorical	Patient is taking amlodipine medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking diltiazem medication	Categorical	Patient is taking diltiazem medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking nifedipine medication	Categorical	Patient is taking nifedipine medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking verapamil medication	Categorical	Patient is taking verapamil medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking vasodilator medication	Categorical	Patient is taking vasodilator medication according to self-report or listed in the electronic health record	0 = no, 1 = yes

Taking an antiarrhythmic medication	Categorical	Patient is taking an antiarrhythmic medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking amiodarone medication	Categorical	Patient is taking amiodarone medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking another type of antiarrhythmic medication	Categorical	Patient is taking another type of antiarrhythmic medication other than amiodarone, flecainide, procainamide, according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking aspirin medication	Categorical	Patient is taking aspirin medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking narcotic medication	Categorical	Patient is taking narcotic medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking fentanyl medication	Categorical	Patient is taking fentanyl medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking oxycodone medication	Categorical	Patient is taking oxycodone medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking hydrocodone medication	Categorical	Patient is taking hydrocodone medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking another narcotic medication	Categorical	Patient is taking another narcotic medication, other than fentanyl, morphine, dilaudid, oxycodone, or hydrocodone, according to	0 = no, 1 = yes

		self-report or listed in the electronic health record	
Taking insulin medication	Categorical	Patient is taking insulin medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking rapid acting insulin medication	Categorical	Patient is taking rapid acting insulin medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking short acting insulin medication	Categorical	Patient is taking short acting insulin medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking another glucose controlling medication	Categorical	Patient taking another type of glucose controlling medication other than insulin or metformin, according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking metformin medication	Categorical	Patient is taking metformin medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking anti-anxiety medication	Categorical	Patient is taking anti-anxiety medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking antidepressant medication	Categorical	Patient is taking antidepressant medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking statin medication	Categorical	Patient is taking a statin medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking an anticontraception medication	Categorical	Patient is taking an anticontraception medication according to	0 = no, 1 = yes

		self-report or listed in the electronic health record	
Taking an anticoagulant medication	Categorical	Patient is taking an anticoagulant medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking coumadin medication	Categorical	Patient is taking coumadin medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking Xarelto medication	Categorical	Patient is taking Xarelto medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking Eliquis medication	Categorical	Patient is taking Eliquis medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking another anticoagulant medication	Categorical	Patient taking another type of anticoagulant medication other than coumadin, heparin, Pradaxa, Xarelto, Eliquis, arixtra, or Savaysa®, according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking antiplatelet medication	Categorical	Patient is taking antiplatelet medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking diuretic medication	Categorical	Patient is taking antidiuretic medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking gastroesophageal reflux disease medication	Categorical	Patient is taking gastroesophageal reflux disease medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking muscle relaxant medication	Categorical	Patient is taking muscle relaxant medication	0 = no, 1 = yes

		according to self-report or listed in the electronic health record	
Taking gabapentin medication	Categorical	Patient is taking gabapentin medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking nonsteroidal anti-inflammatory medication	Categorical	Patient is taking nonsteroidal anti-inflammatory medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking Tylenol medication	Categorical	Patient is taking Tylenol medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking levothyroxine medication	Categorical	Patient is taking levothyroxine medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking antihistamine medication	Categorical	Patient is taking antihistamine medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking bronchodilator medication	Categorical	Patient is taking bronchodilator medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking benign prostate hypertrophy medication	Categorical	Patient is taking benign prostate hypertrophy medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking schizophrenia/bipolar medication	Categorical	Patient is taking medication for bipolar/schizophrenia disorder according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking antibiotic medication	Categorical	Patient is taking antibiotic medication according to	0 = no, 1 = yes

		self-report or listed in the electronic health record	
Taking anticonvulsant medication	Categorical	Patient is taking medication for a seizure disorder or anticonvulsant medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking medication for irritable bowel syndrome	Categorical	Patient is taking medication for irritable bowel syndrome according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking dopamine promotor medication	Categorical	Patient is taking medication for irritable bowel syndrome according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking corticosteroid medication	Categorical	Patient is taking corticosteroid medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking stool softener medication	Categorical	Patient is taking stool softener medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
Taking Zofran medication	Categorical	Patient is taking Zofran medication according to self-report or listed in the electronic health record	0 = no, 1 = yes
CHIEF COMPLAINT(S)/SYMPTOM(S)			
Chest pain	Categorical	Patient experiencing chest pain according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Radiating pain to a different body part	Categorical	Patient experiencing pain that radiates to a different body part according to self	0 = no, 1 = yes

		-report or listed in the electronic health record at time of emergency department triage assessment	
Chest tightness	Categorical	Patient experiencing chest tightness according to self -report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Chest pressure	Categorical	Patient experiencing chest pressure according to self -report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Chest soreness	Categorical	Patient experiencing chest soreness according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Chest heaviness	Categorical	Patient experiencing chest heaviness according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Chest tenderness	Categorical	Patient experiencing chest tenderness according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Shortness of breath/dyspnea	Categorical	Patient experiencing shortness of breath/dyspnea/difficulty breathing according to self-report or listed in the electronic health record at	0 = no, 1 = yes

		time of emergency department triage assessment	
Palpitations	Categorical	Patient experiencing chest tenderness according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Cough	Categorical	Patient experiencing cough according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Fever	Categorical	Patient reports having a fever according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Flu-like symptoms	Categorical	Patient experiencing flu-like symptoms according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Sweating/diaphoretic	Categorical	Patient experiencing sweating or being diaphoretic according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Syncope/passing out/dizziness	Categorical	Patient experiencing syncope or feeling like they were going to pass out or feeling dizzy according to self-report or listed in the electronic health record at time of	0 = no, 1 = yes

		emergency department triage assessment	
Indigestion/heart burn	Categorical	Patient experiencing indigestion/heart burn according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Nausea	Categorical	Patient experiencing nausea according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Vomiting	Categorical	Patient experiencing vomiting according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Nausea and vomiting	Categorical	Patient experiencing nausea and vomiting according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Fatigue/tiredness	Categorical	Patient experiencing fatigue/tiredness according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Generalized weakness/weakness	Categorical	Patient experiencing generalized weakness or weakness according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes

Anxiety/nervousness	Categorical	Patient experiencing anxiety or nervousness, or nurse reports patients appears nervous according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Implantable cardioverter defibrillator firing	Categorical	Patient experiencing their implantable cardioverter defibrillator firing according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Abdominal pain	Categorical	Patient experiencing abdominal pain according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Jaw pain	Categorical	Patient experiencing jaw pain according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Arm pain	Categorical	Patient experiencing arm pain according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Ear pain/discomfort	Categorical	Patient experiencing ear pain/discomfort according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes

Back pain	Categorical	Patient experiencing back pain according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Shoulder pain	Categorical	Patient experiencing shoulder pain according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Headache	Categorical	Patient experiencing a headache according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Neck pain	Categorical	Patient experiencing neck pain according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Numbness/tingling	Categorical	Patient experiencing numbness or tingling in any body part according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Other symptoms	Categorical	Patient experiencing other symptoms, excluding all above listed symptoms, according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Symptoms lasting longer than 24 hours	Categorical	Patient experiencing symptoms lasting longer	0 = no, 1 = yes

		than 24 hours according to self-report or listed in the electronic health record at time of emergency department triage assessment	
Symptoms lasting for 1 day	Categorical	Patient experiencing symptoms lasting for 1 day according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Symptoms lasting for 2 days	Categorical	Patient experiencing symptoms lasting for 2 days according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Symptoms lasting for 3 days	Categorical	Patient experiencing symptoms lasting for 3 days according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Symptoms lasting for 4 days	Categorical	Patient experiencing symptoms lasting for 4 days according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Symptoms lasting for 5 days or greater	Categorical	Patient experiencing symptoms lasting for 5 days or greater according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes

Symptoms lasting for weeks	Categorical	Patient experiencing symptoms lasting for weeks according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
Symptoms lasting for months	Categorical	Patient experiencing symptoms lasting for months according to self-report or listed in the electronic health record at time of emergency department triage assessment	0 = no, 1 = yes
PREHOSPITAL DATA			
Prehospital records from emergency medical services is part of the electronic health record	Categorical	Patient prehospital documentation is documented in the electronic health record	0 = no, 1 = yes
Prehospital symptom of chest pain	Categorical	Patient experiencing chest pain according to self-report or listed in the prehospital documentation as part of the electronic health record	0 = no, 1 = yes
Prehospital symptom of chest tightness	Categorical	Patient experiencing chest tightness according to self-report or listed in the prehospital documentation as part of the electronic health record	0 = no, 1 = yes
Prehospital symptom of shortness of breath/dyspnea	Categorical	Patient experiencing shortness of breath/dyspnea/difficulty breathing according to self-report or listed in the prehospital documentation as part of the electronic health record	0 = no, 1 = yes
Prehospital symptom of syncope/dizziness/passing out	Categorical	Patient experiencing sweating or feeling diaphoretic or feeling dizzy according to self-report or listed in the	0 = no, 1 = yes

		prehospital documentation as part of the electronic health record	
Prehospital radiating pain to another body part	Categorical	Patient experiencing pain that radiates to a different body part according to self -report or listed in the prehospital documentation as part of the electronic health record	0 = no, 1 = yes
Prehospital symptom of palpitation	Categorical	Patient experiencing palpitation according to self-report or listed in the prehospital documentation as part of the electronic health record	0 = no, 1 = yes
Prehospital symptom(s) of sweating/diaphoresis	Categorical	Patient experiencing sweating or feeling diaphoretic according to self-report or listed in the prehospital documentation as part of the electronic health record	0 = no, 1 = yes
Prehospital symptom(s) of syncope/passing out/dizzy	Categorical	Patient experiencing syncope or feeling like they were going to pass out or feeling dizzy according to self-report or listed in the prehospital documentation as part of the electronic health	0 = no, 1 = yes
Prehospital symptom of nausea	Categorical	Patient experiencing nausea according to self-report or listed in the prehospital documentation as part of the electronic health	0 = no, 1 = yes
Prehospital symptom of nausea and vomiting	Categorical	Patient experiencing nausea and vomiting according to self-report or listed in the prehospital documentation as part of the electronic health	0 = no, 1 = yes
Prehospital symptom of generalized weakness/weakness	Categorical	Patient experiencing generalized weakness/weakness	0 = no, 1 = yes

		according to self-report or listed in the prehospital documentation as part of the electronic health	
Prehospital symptom of abdominal pain	Categorical	Patient experiencing abdominal pain according to self-report or listed in the prehospital documentation as part of the electronic health	0 = no, 1 = yes
Prehospital symptom of arm pain	Categorical	Patient experiencing arm pain according to self-report or listed in the prehospital documentation as part of the electronic health	0 = no, 1 = yes
Prehospital symptom of back pain	Categorical	Patient experiencing back pain according to self-report or listed in the prehospital documentation as part of the electronic health	0 = no, 1 = yes
Prehospital symptom of another symptom/chief complaint	Categorical	Patient experiencing another symptom(s) other than the ones listed above according to self-report or listed in the prehospital documentation as part of the electronic health	0 = no, 1 = yes
Prehospital dispatch level of delta/priority 2	Categorical	Initial prehospital dispatch level for an ambulance response was delta/priority 2	0 = no, 1 = yes
Prehospital dispatch level of charlie	Categorical	Initial prehospital dispatch level for an ambulance response was charlie	0 = no, 1 = yes
Prehospital dispatch level of alpha	Categorical	Initial prehospital dispatch level for an ambulance response was alpha	0 = no, 1 = yes
Prehospital dispatch level of priority one/ES 1	Categorical	Initial prehospital dispatch level for an ambulance response was priority one/ ES 1	0 = no, 1 = yes
Prehospital dispatch level of other response code	Categorical	Initial prehospital dispatch level was one not listed as	0 = no, 1 = yes

		mentioned above for an ambulance response code	
Prehospital 12-lead electrocardiogram was normal sinus rhythm	Categorical	Prehospital automatic interpretation of the 12-lead electrocardiogram was reported as normal sinus rhythm	0 = no, 1 = yes
Prehospital 12-lead electrocardiogram was sinus tachycardia	Categorical	Prehospital automatic interpretation of the 12-lead electrocardiogram was reported as sinus tachycardia	0 = no, 1 = yes
Prehospital 12-lead electrocardiogram was atrial fibrillation	Categorical	Prehospital automatic interpretation of the 12-lead electrocardiogram was reported as atrial fibrillation	0 = no, 1 = yes
Prehospital 12-lead electrocardiogram was abnormal	Categorical	Prehospital automatic interpretation of the 12-lead electrocardiogram was reported as abnormal	0 = no, 1 = yes
OUTCOME VARIABLE			
Acute coronary syndrome	Categorical	Patient had a clinical diagnosis of acute coronary syndrome	0 = no, 1 = yes

Appendix B Dissertation Study Internal Review Board Approval

University of Pittsburgh
Institutional Review Board

Human Research Protection Office
3500 Fifth Avenue, Suite 106
Pittsburgh, PA 15213
Tel (412) 383-1480
www.hrpo@pitt.edu

APPROVAL OF SUBMISSION (Exempt)

IRB:	STUDY18110026
PI:	Stephanie Frisch
Title:	Improving Emergency Department Nurse Triage via Big Data Analytics
Funding:	None
Date:	April 10, 2019

On 4/10/2019, the Institutional Review Board reviewed and approved the above referenced application through the administrative review process. The study may begin as outlined in the University of Pittsburgh approved application and documents.

Approval Documentation

Review type:	Initial Study
Approval Date:	4/10/2019
Exempt Category:	(4) Secondary research on data or specimens (no consent required)
Determinations:	• Waiver of HIPAA authorization
Approved Documents:	• HRP-723 - WORKSHEET - Exemption_Secondary Data.Specimens_Version_0.01.docx • Improving Emergency Department Nurse Triage Spreadsheet

As the Principal Investigator, you are responsible for the conduct of the research and to ensure accurate documentation, protocol compliance, reporting of possibly study-related adverse events and unanticipated problems involving risk to participants or others. The HRPO Reportable Events policy, Chapter 17, is available at http://www.hrpo.pitt.edu/.

Research being conducted in an UPMC facility cannot begin until fiscal approval is received from the UPMC Office of Sponsored Programs and Research Support (OSPARS). Contact OSPARS@upmc.edu with questions.

If you have any questions, please contact the University of Pittsburgh IRB Coordinator, Deane Quillen.

Please take a moment to complete our Satisfaction Survey as we appreciate your feedback.

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