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Effect Of In-Hospital Stroke Alert On Thrombolytic Therapy In Women

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EFFECT OF IN-HOSPITAL STROKE ALERT ON THROMBOLYTIC THERAPY IN WOMEN

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Date

PERMISSION

Title	Effect of In-Hospital Stroke Alert on Thrombolytic Therapy in Women
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Renee Colsch, Renee Colsch
April 17, 2019

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To my father Ralph Dale, angel who gave me wings.
To my mother Beverly, my mother-in-law Deb, my husband Chad,
and my children Cooper, Cameron, and Ryleigh.
You never gave up on me!

ABSTRACT

Background/Purpose. Stroke is the leading cause of disability in the United States. Women who have experienced a stroke have greater disability than men. Thrombolytic agents decrease adverse side effects of stroke by dissolving blood clots. Yet, women have 8% higher odds against being treated with a thrombolytic agent. Also, about 17% of stroke cases occur in-hospital. Therefore, the purpose of this study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition.

Methods. Guided by the Model for Nursing Effectiveness Research, a retrospective observational study of 149 women participants was completed for a 4 year period. Study measures based on empirical evidence included the primary independent variable of in-hospital stroke alert, and confounding variables (patient characteristics, clinical conditions, and context of care) that are conceptually related to the primary outcome of thrombolytic therapy and secondary outcome of discharge status. Analysis included regression models and propensity score matching to isolate the treatment (in-hospital stroke alert) and outcome (thrombolytic therapy) while controlling the effects of other influential variables.

Results. In-hospital stroke alert was activated in 46 of 149 or 30.9% women and 15 of 149 or 10.1% of women received thrombolytic therapy. In-hospital stroke alert was significant ($p < .001$) for women receiving thrombolytic therapy and significant to a home discharge status ($p = .014$). Age ($p < .001$), marital status ($p = .067$), ethnicity ($p < .001$), common ($p = <.001$) and unique symptoms ($p = .012$), stroke risk factors were present ($p <.001$), comorbid conditions

were present (p <.001), Time Last Known Well (the time that the patient was without stroke symptoms) (p = .041), diagnostic imaging (p <.001) were all significantly related to in-hospital stroke alert.

Discussion/Conclusions. Results from this study suggest that younger married women from non-Caucasian ethnic groups and women with risk factors or comorbid conditions are all at higher levels of late stroke symptom detection and no in-hospital stroke alert activation. Improved stroke detection in women with attention to barriers may improve in-hospital stroke alert activation and early treatment.

CHAPTER I

INTRODUCTION

Each year, almost 795,000 American people suffer stroke, a condition of clots occurring within the brain, that has a large impact on society (Benjamin et al., 2017; Mozaffarian et al., 2016). Furthermore, stroke is the fifth leading overall cause of death but the third cause of death for women, killing twice as many women as breast cancer every year (Benjamin et al., 2017; Mozaffarian et al., 2016). In addition, African-American women suffer from a significantly higher number of strokes than Caucasian women and stroke is a leading cause of death for Hispanic women (Benjamin et al., 2017; Mozaffarian et al., 2016). Stroke remains the leading cause of preventable disability in the United States (U.S.) (Benjamin et al., 2017; Mozaffarian et al., 2016). Each year 55,000 more women than men have a stroke, and their lives have a greater negative impact (Benjamin et al., 2017; Mozaffarian et al., 2016). Unique stroke symptoms in women are different from the common stroke symptoms (National Stroke Association, 2018). These unique stroke symptoms in women generate grave concern as these symptoms are often not recognized as a stroke and treatment is delayed (Berglund, Heikkilä, Bohm, Schenck-Gustafsson, & Euler, 2015; Dupre et al., 2014; Fothergill, Williams, Edwards, Russell, & Gompertz, 2013; Hodell et al., 2016; Lever et al., 2013; Madsen et al., 2016).

Thrombolytic therapy, the administration of drugs that dissolve blood clots, is crucial to decreased disability (Messé et al., 2016). Stroke cases receiving thrombolytic therapy have increased over the past few years. However, only 143,000 of the 795,000 average annual ischemic stroke cases receive the crucial thrombolytic therapy (Messé et al., 2016).

Early identification (the process of identifying stroke symptoms less than 3 hours of symptom onset) is crucial to timely thrombolytic treatment and better patient outcomes (Boden-Albala et al., 2015; Boehme et al., 2014; Hanselman, 2014; Powers et al., 2015; Sobolewski et al., 2015). Up to 135,150 (17%) of all stroke cases have symptom onset during an in-patient hospital stay for a separate condition (Cumbler, 2015; Messé et al., 2016). Patients who are hospitalized for cardiac disease or surgery are vulnerable to in-hospital stroke, a stroke occurring during a hospital stay in a patient originally admitted for another diagnosis, (Berglund et al., 2015; Boden-Albala et al., 2015; Hanselman, 2014; Park, Shin, Ro, Song, & Oh, 2013; Sobolewski et al., 2015).

The American Stroke Association (2019) recommends that every health care system has an organized protocol along with an acute stroke team that includes physicians, nurses, and laboratory/radiology personnel for the emergency evaluation of patients with suspected stroke (Powers et al., 2018). An organized stroke protocol may incorporate a stroke alert. Stroke alert is a system that activates a team of stroke experts who start stroke protocols when stroke symptoms are present. The strength of evidence for the effectiveness of stroke alert to accelerate evaluation and treatment of stroke is robust for use in the emergency department, which includes existing clinical practice guidelines (El Husseini & Goldstein, 2013; Meretoja et al., 2012; Meretoja et al., 2013; Middleton Grimley & Alexandrov, 2015). In-hospital stroke alert is the activation of stroke experts and protocols for a patient who has stroke symptoms during a hospital stay for a separate condition. The use of activating in-hospital stroke alert has shown to improve time to diagnosis and reduce symptom onset to thrombolytic treatment times (Cumbler, Zaemisch, Graves, Brega, and Jones, 2012; Meretoja et al., 2012; Meretoja et al., 2013). Delayed recognition, low adherence to stroke alert activation, and missed thrombolytic therapy treatment are the top contributors to poor in-hospital stroke outcomes. Given these contributors to poor in-hospital stroke outcomes, this study will identify opportunities for quality improvement of in-hospital stroke alert.

In this first chapter the problem, nature of the study, research questions and hypotheses, research aims, statement of purpose, theoretical and conceptual framework, operational definitions, assumptions, limitations, scope and delimitations, the significance of the study are discussed and a summary and transition concludes this chapter.

Problem Statement

As healthcare costs continue to increase, the quality of care in hospitals is increasingly linked to patient outcomes. In spite of intensive efforts in the past ten years to improve quality related outcomes in stroke patients, quality of care remains inadequate (Benjamin et al., 2017; Mozaffarian et al., 2016). Stroke cases, deaths, and cost continue to rise. The financial impact of stroke is profound, with an estimated direct and indirect cost of $184.1 billion annually by the year 2030 (Benjamin et al., 2017; Mozaffarian et al., 2016). When compared to the year of 2012, it is projected that there will be an additional 3.4 million U.S. adult stroke cases by the year 2030; women total 60% of all stroke deaths (Benjamin et al., 2017; Mozaffarian et al., 2016). Women have been found to have a worse functional recovery with greater long-term disability (Gall, Tran, Martin, Blizzard, and Srikanth, 2012). Stroke misdiagnosis has led to longer hospital stays, and woman have been found to have higher odds for less severe Emergency Severity Index and increased Modified Rankin Scale than men (Kes et al., 2016; Madsen et al., 2016; Park et al., 2013). The Emergency Severity Index is a five-level emergency department triage algorithm with 1 being the most urgent to 5 being the least urgent. The

Modified Rankin Scale is a tool that measures the degree of disability as either no disability to severe disability or death (Qin, Titler, Shever, & Kim, 2008).

Current data about in-hospital stroke alert is minimal. Current guidelines on the application of in-hospital stroke alert are variable; are often less than optimal; are matched toward the multidisciplinary emergency room roles, and are not specific to women (El Husseini & Goldstein, 2013; Meretoja et al., 2012; Meretoja et al., 2013; Middleton, Grimley, & Alexandrov, 2015). Gaps exist in the published literature and knowledge on criteria specific to in-hospital stroke alert for women and means to increase the frequency of thrombolytic therapy and thus decrease disability and cost. Analysis of the relationship between covariate/confounders and in-hospital stroke alert and subsequent thrombolytic therapy in women are necessary before decision makers can make more informed choices regarding deploying policy changes, best practice processes, and creating more practice models that affect the context of in-hospital care and treatment.

Nature of Study

More information is needed on the application and the frequency of receiving thrombolytic therapy in women who have in-hospital stroke alert. Therefore, a retrospective, descriptive observational propensity score designed study with a sample comprised of all stroke hospitalizations in an upper Midwestern hospital between May 2014 to May 2018 was completed, using a secondary administrative data source. First-time and repeat hospitalizations of stroke patients aged 18 years and older were identified using the International Statistical Classification of Diseases 10 (ICD) and ICD-9-CM codes and based on inclusion/exclusion criteria. Data elements also included part of the in-patient hospital admission and discharge summaries including diagnoses, comorbidities, risk factors, symptoms, demographic data, stroke assessment tools, diagnostics, treatment, and time. More details of the methodology are discussed in further detail in chapter three.

Statement of Purpose

The primary purpose of this descriptive quantitative study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition. This study estimated propensity scores to reduce the confounding covariates bias and examine the effects of in-hospital stroke alert. A propensity score analysis assumes that the treatment assignment is strongly ignorable if it is independent of the outcome after controlling for the observed confounders (Heinze and Jüni, 2011). The study also identified the factors that either facilitated or hindered an in-hospital stroke alert activation. Factors included patient characteristics, clinical conditions and context of care. In addition, the secondary endpoints of this study compared and contrasted the receipt of thrombolytic therapy and discharge status in women who had in-hospital stroke alert activation or no in-hospital stroke alert.

Research Objectives and Aims

This study focused on investigating the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition. The primary outcome for this study was whether the stroke patient received thrombolytic therapy or not. The secondary outcome was discharge status.

Specific Aims

The outcomes for this study will be achieved by examining the following specific aims:

Aim 1. Determine the frequency of women receiving thrombolytic therapy after receiving in-hospital stroke alert during hospitalization for a separate condition.

Aim 2. Match women who receive an in-hospital stroke alert activation to women with no in-hospital stroke alert.

Aim 3. Compare the effects and associated variables of an in-hospital stroke alert activation to no in-hospital stroke alert on outcomes in women admitted to the hospital for a separate condition.

Significance

This study is significant because it strengthens and builds criteria specific to stroke in women, in-hospital stroke alert activation, and timely diagnosis. The criterion from this study could contribute to the Agency for Healthcare Research and Quality (2018) initiative to increase knowledge of contributing factors that trigger diagnostic failure and aid in improving diagnosis.

As healthcare costs continue to increase, quality of care in hospitals is increasingly linked to patient outcomes. In spite of intensive efforts in the past ten years to improve quality related outcomes in stroke patients, quality of care remains inadequate (Benjamin et al., 2017; Mozaffarian et al., 2016). Stroke is projected to cost up to $184.1 billion annually by the year 2030 (Benjamin et al., 2017; Mozaffarian et al., 2016). When compared to the year of 2012, it is projected that there will be an additional 3.4 million U.S. adult stroke cases by the year 2030 (Benjamin et al., 2017; Mozaffarian et al., 2016). Each year, about 55,000 more women than men have a stroke, and women have greater disability than men do (Benjamin et al., 2017; Mozaffarian et al., 2016). In addition, women total 60% of all stroke deaths (Benjamin et al., 2017; Mozaffarian et al., 2016). Also, up to 17% of all stroke cases have symptom onset during an in-patient hospital stay with the cardiovascular wards (45%) and perioperative period (60%) being most common for an in-hospital stroke to occur (Cumbler, 2015; Kassardjian et al., 2017; Messé et al., 2016).

Increasing the number of women, who have experienced a stroke, who receive thrombolytic therapy could improve outcomes and lower cost. The National Quality Forum, the Joint Commission, and the Centers for Medicare and Medicaid Services (2018) all endorse the stroke core measure Thrombolytic Therapy. However, the stroke core measure standards are specific to patients who arrive at the emergency room with stroke symptoms and matched toward the emergency room provider roles. Stroke patients who receive thrombolytic therapy within 3 hours of symptom onset are almost three times more likely to recover with little or no disability (Benjamin et al., 2017; Mozaffarian et al., 2016).

Theoretical and Conceptual Framework

This study was guided by the Model for Nursing Effectiveness Research. Descriptive observational research studies are designed to describe the participants in an accurate way (George, 2011). A positivist tradition was used since it stresses the importance of doing quantitative research to get an overview of society as a whole (George, 2011). Positivist research looks at trends, relationships, and patterns between two or more variables rather than individuals (George, 2011). Effectiveness research uses comparative methods and tests treatments or interventions. It provides the knowledge and evidence of the success, harm, and benefits of a treatment or intervention (Hirsch, 2014). Effectiveness research can inform health-care clinical decision making (Hirsch, 2014). The Model for Nursing Effectiveness Research utilizes the propensity score method to determine the risk of treatment to the outcome (Qin et al., 2008; Shever et al., 2008). From a descriptive observational positivist theoretical perspective, the Model for Nursing Effectiveness Research supported this study's objectives and aims. Existing data can be directly measured to determine the impact of patient characteristics; clinical conditions; the context of care; and in-hospital stroke alert treatment has on administering the outcome of thrombolytic therapy in women. The selection of variables for this study was guided by the Model for Nursing Effectiveness Research as well as the principal investigator, committee advisory members and collaborators clinical knowledge, and empirical evidence. The Model for Nursing Effectiveness Research and theoretical basis for this study is discussed in further detail in chapter two. *Please see appendix A for the signed consent form for use of the Model for Nursing Effectiveness Research.*

Concept Definitions

Definitions for the major concepts within the Model for Nursing Effectiveness Research and operational definitions for variables that are reiterated in the text are provided here. Operational definitions for selected variables are as follows:.

Operational Definitions

Stroke alert - a call system that activates a team of stroke experts who implement stroke protocols. For example, the nurse recognizes stroke symptoms in a patient and activates the stroke alert which alerts a neurologist, stroke certified nurse, and diagnostic personnel to the patient for further assessment and evaluation of stroke.

In-hospital stroke alert– a stroke alert that is activated during a patient's hospital stay on a medical or surgical floor, not an emergency department stroke alert. In-hospital stroke alert will be measured dichotomously as either no (0) or yes (1) an in-hospital stroke alert was activated during hospitalization for a separate condition.

Common stroke symptoms – most often occurring subjective and objective signs that are not usual for that individual and are suggestive of an ischemic stroke. Common stroke symptoms will be measured dichotomously as either no (0) common stroke symptoms were present at the time of admission or yes (1) common stroke symptoms were present at the time of admission (National Stroke Association, 2018).

Unique stroke symptoms – subjective and objective symptoms or signs that are unusual for that individual, regardless of the presence of common stroke symptoms. Unique stroke symptoms will be measured dichotomously as either no (0) unique stroke symptoms are present at the time of admission or yes (1) unique stroke symptoms are present at the time of admission (National Stroke Association, 2018).

Thrombolytic therapy - the administration of intravenous drugs that dissolve or break down blood clots known as thrombolysis. Thrombolytic therapy will be measured dichotomously as yes (1) or no (0) the patient did not receive thrombolytic therapy.

Assumptions

The ontological assumption of this study was that the use of in-hospital stroke alert can be observed and measured; that there is one defined reality for these constructs and if measured, will be readily visible to all who observe it (George, 2011). The epistemological assumption of this study was that the acquisition of knowledge of stroke and the use of in-hospital stroke alert is an objective process, one that can be measured, and that measured and objective report is reliable and useful knowledge (George, 2011). The methodological assumption of this study followed the quantitative Model for Nursing Effectiveness Research propensity score design which assumes through propensity scores the treatment (in-hospital stroke alert) will be strongly ignorable if it is independent of the outcome after controlling for the observed covariates. Therefore, the difference in outcomes (thrombolytic therapy and discharge status) between patients who received in-hospital stroke alert and those who did not is an unbiased estimate of in-hospital stroke alert treatment effect (George, 2011; Shever et al., 2008).

Limitations

This study had several limitations:

1. **Descriptive retrospective design.** The descriptive retrospective design presents limitations to the inferences that can be drawn from the study findings.

2. **Sample and sampling method.** The sample was largely homogenous (91% Caucasian, n = 136; 4% African American, n = 6; 1 % Native American, n = 1; 3% Alaskan Native, n = 5; and, 1% Middle Eastern American, n = 1) and may not represent the diversity of women who have an in-hospital stroke. Crucial variables for this study were only available for a 4 year time period and the fact that this in-hospital stroke population has a small incidence may have served to limit the number of women for this study.
3. **Missing variables.** The original study plan included collecting the National Institutes of Health Stroke Scale, a tool to objectively quantify the impairment caused by a stroke and the pre and post Modified Rankin Scale, a tool that measures the degree of disability at the time a stroke occurred and the degree of disability 90 days after a stroke occurred. These factors were not recorded within the Epic electronic medical record that was available to the medical centers informatics specialist team.
4. **External validity, or generalizability**. This study was only conducted at a single Midwestern urban hospital site and therefore, limits study findings and conclusions from this single sample population to the population at large.

Scope and Delimitations

This study was limited to one upper Midwestern hospital for the period of May 2014 to May 2018. This hospital is a comprehensive stroke center offering emergency care, inpatient, inpatient rehabilitation, peer visitor program, and patient outcomes and education. Eligible patients were women 18 years of age or older, who were diagnosed with ischemic stroke, first-time and repeat stroke diagnoses, during hospitalization for a separate condition. Patient records were excluded if patients were less than 18 years of age; cases had missing data; ischemic stroke was the primary diagnosis; stroke diagnosis was not obtained during an in-patient hospitalization for a separate condition; male gender, stroke diagnosis was only a hemorrhagic stroke; and if stroke diagnosis was greater than 4 years.

CHAPTER II

LITERATURE REVIEW

The purpose of this study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition. Specific Aims to address this purpose were to:

Aim 1. Determine the frequency of women receiving thrombolytic therapy after receiving in-hospital stroke alert during hospitalization for a separate condition.

Aim 2. Match women who receive an in-hospital stroke alert activation to women with no in-hospital stroke alert.

Aim 3. Compare the effects and associated variables of an in-hospital stroke alert activation to no in-hospital stroke alert on outcomes in women admitted to the hospital for a separate condition.

This chapter provides an overview of the present literature on stroke related to women, including patient outcomes, statistical facts, treatment, differences in gender symptoms, differences in stroke onset, and stroke alert. Specifically, unique stroke symptoms in women, quality of care and outcomes in women, thrombolytic therapy and in-hospital stroke alert will be discussed. Evidence-based practice and effectiveness research along with the theoretical and conceptual models for this study is discussed.

Stroke

Cerebrovascular disorders is an umbrella term that represents the functional abnormality to the central nervous system that occurs when the normal blood supply to the brain is disrupted (Capriotti & Frizzell, 2016). Cerebrovascular attack is the medical term for stroke (Capriotti & Frizzell, 2016). Cerebrovascular attacks or Strokes are divided into two major categories: ischemic (85%) and hemorrhagic (15%) (Capriotti & Frizzell, 2016). Although ischemic and hemorrhage strokes have some similarities, there are significant differences in etiology, pathophysiology, risk factors, clinical manifestations, and treatment (Capriotti & Frizzell, 2016). “An ischemic stroke occurs when a blood vessel that provides perfusion to the brain becomes blocked by a either a thrombolytic or embolic clot; thrombolytic clot is caused by a blood clot that develops inside the brain blood vessels; embolic stroke can be either caused by a blood clot or plaque debris that develops elsewhere in the body and then travels through the bloodstream to one of the brain blood vessels” (Capriotti & Frizzell, 2016, p. 753). There are two types of blood clots that can cause a thrombotic stroke: large vessel thrombosis or small vessel disease (Capriotti & Frizzell, 2016). A large vessel thrombosis is a clot in the brain’s large vessels and is the most common form of a thrombotic stroke (Capriotti & Frizzell, 2016). Small vessel disease is known as a lacunar stroke and occurs when blood flow is blocked in one of the small arterial vessels in the brain (Capriotti, & Frizzell, 2016). When an acute ischemic stroke occurs either a platelet or fibrin clot occludes the normal cerebral blood perfusion. The clot distally blocks blood flow to the surrounding brain tissue (Capriotti, & Frizzell, 2016). This surrounding tissue is referred to as the penumbra (Capriotti, & Frizzell, 2016). The penumbra area is brain or cerebral tissue that survives for a short period on collateral blood supply (Capriotti, & Frizzell, 2016). For the purpose of this study, the focus was only ischemic strokes.

Modifiable and non-modifiable risk factors for ischemic stroke have been identified and include: high blood pressure; smoking; diabetes; high cholesterol; physical inactivity and obesity; carotid or other artery disease; transient ischemic attacks; atrial fibrillation or other heart disease; certain blood disorders; excessive alcohol intake; illegal drug use; sleep apnea; increasing age; gender; heredity and race; and prior stroke (American Stroke Association [ASA], 2019a; Capriotti & Frizzell, 2016). About 15% of all embolic strokes occur in individuals with atrial fibrillation. High cholesterol is a common risk factor for large vessel strokes and lacunar strokes are closely linked to high blood pressure (ASA, 2019a).

Clinical manifestations are the subjective and objective signs and symptoms observed by medical professionals and reported by the patient or caregiver (Capriotti & Frizzell, 2016). Nationally accepted and published stroke symptoms are recognized with the letters “FAST:” “f” for face drooping, “a” for arm weakness, “s” for speech difficulty, and “t” for time to call 911 (ASA, 2019b). Additional common symptoms of stroke include sudden “(1) Numbness or weakness of face, arm or leg, especially on one side of the body, (2) Confusion, trouble speaking, or understanding, (3) Trouble seeing in one or both eyes, (4) Trouble walking, dizziness, loss of balance or coordination, and (5) Severe headache with no known cause” (ASA, 2019b para 3). In addition, The National Stroke Association (2017) recognizes the following 11 unique stroke symptoms in women: (1) loss of consciousness or fainting, (2) general weakness, (3) difficulty breathing or shortness of breath, (4) confusion, unresponsiveness or disorientation, (5) sudden behavioral change, (6) agitation, (7) hallucination, (8) nausea or vomiting, (9) pain, (10) seizures, and (11) hiccups (National Stroke Association, 2018).

The only U.S. Food and Drug Administration approved treatment for ischemic strokes is intravenous tissue plasminogen activator within 3 hours of the time of symptom onset (Powers et al., 2015). Tissue plasminogen activator is the most commonly utilized drug for thrombolytic therapy; thrombolytic therapy is the administration of medications called lytics or “clot busters” to dissolve blood clots that have suddenly blocked major arteries or veins and pose potentially serious or life-threatening implications (Powers et al., 2015). To be effective, thrombolytic therapy must be initiated as soon as possible, before permanent damage has occurred (Powers et al., 2015). Thrombolytic therapy is currently the best solution to dissolve fibrin bonds in a clot and recover the penumbra tissue and lessen potential complications of an ischemic stroke (Hanselman, 2014; Powers et al., 2015).

Literature Search Strategy

A computerized search of the University of North Dakota library databases, in both the Chester Fritz Library and Harley E. French Library of the Health Sciences databases, was completed to identify articles focusing on the concepts of stroke, women, thrombolytic therapy, in-hospital, stroke alert, and outcomes. Searches were initially set to recognize studies from the years 2012 to 2017 for current research; then a broader comprehensive search was completed to examine seminal work.

The review was conducted with electronic EBSCO databases, mostly utilizing health sciences databases including PubMed, CINAHL, ERIC, MEDLINE, PsycINFO, and Google Scholar**.** Key terms utilized in this search to identify relevant literature include text words, title, abstract and medical subject headings (MeSH). Searches included the terms “stroke or cerebral vascular attack.” These terms were combined using ‘‘AND’’ individually with each of the following: “gender” “difference” “sex” “symptom” “women” “female” “diagnosis” “assessment” “prehospital” “emergency” “unique” “non-traditional” “unique” “individual” “presentation” “recognition” “quality” “outcomes” “thrombolytic therapy” “tissue plasminogen activator (tPA)” "code stroke" "stroke code" "stroke alert" "in-patient" "in-hospital." A total of 27 appropriate articles were selected based on relevance to the study purpose for review and are summarized in tables 2, 3 and 4.

Stroke in Women

In the United States, one in five women will have a stroke in their lifetime (Centers for Disease Control and Prevention [CDC], 2019). Stroke is the third leading cause of death for women, killing twice as many women than breast cancer (CDC, 2019). Six out of ten individuals who die from a stroke are women, mainly attributed to women living longer than men; and because stroke increases with age. According to the Centers for Disease Control (2018), "not all women are equally affected by stroke" (para 8); the percentage of women who suffer a stroke aged 45 years and younger is increasing; younger women have greater unique symptoms than older women, when compared to women aged 46 years and older. When comparing African-American women to Caucasian women, the risk of stroke is nearly twice as likely; this is primarily attributed to the increased risk of having high blood pressure, increased weight, and diabetes (CDC, 2019).

Unique Stroke Symptoms in Women

Unique stroke symptoms in women generate grave concern as these symptoms are often not recognized as a stroke and the treatment is delayed (Berglund et al., 2015; Dupre et al., 2014; Fothergill, Williams, Edwards, Russell, & Gompertz, 2013; Hodell et al., 2016; Lever et al., 2013; Madsen et al., 2016). In addition, in general women delay seeking treatment for stroke symptoms up to three times longer than men (Kes, 2016; Madsen et al., 2016; Park et al., 2013). The National Stroke Association (2017) recognizes 11 symptoms as unique symptoms of stroke in women. However, current studies vary in terminology and symptoms for describing unique stroke symptoms in women (Colsch & Lindseth, 2018; National Stroke Association, 2018). This unstandardized terminology limits the ability to compare and generalize conclusions from and between each study. Lack of detail to unique stroke symptoms in women terminology, symptom recognition, diagnosis, and early treatment is a disservice to women.

Evidence indicates that a percentage of stroke patients' are initially misdiagnosed due to either unique symptoms or stroke mimics (nonvascular conditions that present with stroke-like symptoms) (Madsen et al., 2016). In a study by Fothergill et al. (2013), 16 out of 295 stroke cases were missed; these cases did not receive a timely definitive stroke diagnosis. In another study by Madsen et al. (2016), stroke identification failure was greater among younger patients and patients experiencing a decreased level of consciousness; altered mental status was the most common diagnosis among the missed stroke cases. Similarly, stroke identification failure occurred in 94 cases ($N = 2528$) whose brain imaging later revealed acute stroke (Dupre et al., 2014). Diagnosis was either altered mental status, syncope, hypertensive emergency, systemic infection, or suspected acute coronary syndrome (Dupre et al., 2014). In addition, 29 out of 189 patients (15.3%) were not identified as having a stroke when first admitted to the hospital; 4% of missed stroke cases presented with common stroke symptoms and 64% of the missed cases presented with unique stroke symptoms: de-generalized weakness, altered mental status, altered gait, and dizziness (Lever et al., 2013).

Gender Differences

In a study by Kes (2016) of 396 stroke patients, the younger patients (n =24) presented more often with a headache, seizure, and recovered better than older patients; older patients had greater heart conditions, smoking prevalence and went to rehabilitation treatment more often than the younger patients. Also, women had higher odds of hypertension, chronic heart failure and atrial fibrillation than men (Kes, 2016). Similarly, 103 (22%) of the 465 strokes cases were misdiagnosed; 37% of these were posterior strokes, and 16% were anterior strokes (Arch, 2016). Symptoms associated with greater odds of a missed stroke diagnosis included nausea/vomiting, dizziness, and a positive stroke history (Arch, 2016). Evidence suggests that gender influences stroke risk/incidence, diagnosis, symptoms, treatment, and outcomes (Gibson, 2013). The influence of gender on stroke can result from a combination of factors, including sex hormone exposure (e.g. estrogen replacement), and cultural and social factors (Gibson, 2013).

Stroke Diagnosis

In a qualitative study that explored the factors that either facilitated or hampered the identification of stroke, nurses' stroke expertise skills had a decisive effect on the identification of stroke (Berglund et al., 2015). Another qualitative study that sought to understand the barriers to recognizing stroke found that diversity within stroke symptoms, linguistics, alcohol and drug use, lack of hospital-physician educational feedback all contributed to obstacles in stroke diagnosis (Hodell et al., 2016).

Combined studies have highlighted the difference in stroke symptoms among gender, and acknowledge there is a low recognition of unique stroke symptoms in women . In addition, more women are initially misdiagnosed on presentation (Berglund et al., 2015; Colsch & Lindseth, 2018; Dupre et al., 2014; Fothergill et al., 2013; Hodell et al., 2016; Kes, 2016; Lever et al., 2013; Madsen et al., 2016; Park et al., 2013). However, data are lacking regarding the effect unique stroke symptoms in women has on in-hospital stroke alert activation. *Please see table 1 for the stroke and women review of the literature.*

Table 1. Review of the Literature, Stroke in Women

Gender Differences and Stroke in Women				
Author (Year)	**Purpose**	**Design**	**Sample**	**Findings**
Fothergill (2013)	"Investigated whether ROSIER stroke assessment tool use by ambulance clinicians can improve stroke recognition."	Research educational article	*N* = 311	47% (*n* =147) were women. 177 patients received a diagnosis of stroke and 118 received a diagnosis of non-stroke. 16 total missed were actual stroke.
Madsen (2016)	"Determine clinical predictors of missed AIS, and to report tissue plasminogen eligibility (tPA) among those with missed strokes."	Retrospective data review	*N* = 2027	14.0% (*n* =283) stroke cases missed in the ED. Race, gender, and stroke subtypes were similar between missed diagnoses. Length of stay was longer in those with a missed diagnosis (5 vs. 3 days, $p < 0.0001$). Younger age (OR 0.94, 95% CI 0.89 - 0.98) and decreased level of consciousness (OR 3.58, 95% CI 2.63 - 4.87) had higher odds of missed stroke diagnosis. Altered mental status was the most common diagnosis among those with missed acute stroke cases. Only 1.1% of those with a missed stroke diagnosis were eligible for tPA.
Dupre et al. (2014)	"The converse of the ''stroke mimic'' is a presentation suggestive of another condition, which actually represents stroke. These would be ''stroke chameleons.'' The recognition of a chameleon as stroke has implications for therapy and quality of care."	Retrospective chart review	*N* = 2528	94 cases were identified as chameleons (stroke mimic) when brain imaging revealed an acute stroke. Common chameleons were initially diagnosed as altered mental status (7%), syncope (4%), hypertensive emergency (8%), systemic infection (1%), and suspected acute coronary syndrome (1%).

Table 1. cont.

Gender Differences and Stroke in Women				
Author (Year)	**Purpose**	**Design**	**Sample**	**Findings**
Lever (2013)	"To establish whether there was an association between symptom presentation and diagnostic accuracy and to identify the type and frequency of nontraditional symptoms that resulted in a missed diagnosis in the emergency department."	Retrospective chart review	*N* =189	Diagnosis of suspected stroke missed (15.3%) who presented to the emergency department. ($p < 0.0001$) symptom presentation and diagnostic accuracy. patients presenting "traditional" or common symptoms = 4% missed. nontraditional or unique symptoms = 64% missed (odds ratio, 43.4; 95% confidence interval, 15.0 - 125.4). Unique symptoms: generalized weakness, altered mental status, altered gait, and dizziness.
Berglund et. al. (2015)	"To explore the factors that facilitate or hamper identification of stroke in emergency calls concerning patients with stroke who have fallen or been in a lying position."	Qualitative interpretive phenomenology study	*N* = 29	Nurses' expertise skills was only theme found to have a decisive effect on the identification of stroke
Hodell (2016)	"To systematically understand the challenges and barriers faced by paramedics in recognizing stroke presentations in the field."	Qualitative study	*N* = 28	Barriers to stroke included diversity of stroke presentations, linguistic diversity, and exam confounded by alcohol and or drug use. Lack of educational feedback from hospital staff and physicians and continuing medical education on stroke had major deterrents to enhancing diagnostic acumen.
Kes (2016)	"Determine age and gender impact on stroke patients"	Prospective	*N* = 396	Younger patients (*n* =24) recovered better; onset presented with headache, and seizure. Older patients went to secondary treatment more often; showed greater heart conditions and smoking prevalence. Women more prone to hypertension, chronic heart failure and atrial fibrillation. Men had carotid disease and more often smokers; higher alcohol intake than women.

Table 1. cont.

Gender Differences and Stroke in Women				
Author (Year)	**Purpose**	**Design**	**Sample**	**Findings**
Arch (2016)	"Examine the diagnosis of acute ischemic stroke in the emergency department of an academic teaching hospital and a large community hospital."	Retrospective chart review	*N* = 465	280 patients from academic hospital and 185 patients from community hospital. 103 (22%) strokes misdiagnosed at the combined centers 33% of these missed cases presented within the 3-hour time window for tPA. Symptoms associated with greater odds of missed stroke diagnosis: nausea/vomiting, dizziness a positive stroke history. 37% posterior strokes were initially misdiagnosed compared with 16% of anterior strokes (P<0.001).
Gibson (2013)	"Discuss the various pathologic mechanisms of ischemic stroke that may differ according to gender and compares how intrinsic and hormonal mechanisms may account for such gender differences"	Literature review		Evidence suggests that gender influences stroke including stroke risk/incidence, diagnosis, symptoms, treatment and outcomes. Sex differences in stroke probably result from a combination of factors, including sex chromosomes, effects of sex hormone exposure throughout the lifespan, and cultural and social factors.

Stroke Quality of Care and Outcomes for Women

Quality of Care

The Institute of Medicine (2001) defines the quality of care as "the degree to which health for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge" (p.1). Quality of care falls within the following six domains; (1) safe; (2) effective; (3) patient-centered; (4) timely; (5) efficient; and (6) equitable (AHRQ, 2018; Mitchell, 2018).

There are currently ten national core stroke measures for quality and safety measuring, and reporting (The Joint Commission, 2019). According to the Joint Commission (2019), "core measures serve as a standardized assessment measure for care given in specific areas" (The Joint Commission, 2019, para 1). Core measures have been widely disseminated. However, variation exists among the application and use of the core evidence-based processes of care across hospitals. Variations have been attributed to differences in guideline familiarity, training, tools, leadership, and organizational support (Masica, Richter, Convery, & Haydar, 2009). Core stroke measures have been developed in collaboration with the American Heart Association/American Stroke Association, Brain Attack Coalition for use by Disease-Specific Care-certified primary stroke centers. The National Quality Forum, the Joint Commission, and the Centers for Medicare and Medicaid Services (2018) all endorse the stroke core measure number 4- Thrombolytic Therapy defined as "acute ischemic stroke patients who arrive at this hospital within 2 hours of time last known well and for whom IV thrombolytic therapy was initiated at this hospital within 3 hours of time last known well" (The Joint Commission, 2019, para 9). This thrombolytic therapy stroke core measure standards are specific to patients who arrive at the emergency room with stroke symptoms and matched toward the emergency room provider roles.

Lack of standards specific to in-hospital patient-centered care, women and the multidisciplinary roles limits the quality of care, outcomes, and the ability to apply core measures to patients who have a stroke during a hospitalization for a separate condition.

Outcomes

According to the 2014 Quality of Care by Race/Ethnicity and Sex in the *Get With The Guidelines*–Stroke Program, women scored between 0.4–1.6 percent lower than men in 6 of the 7 key achievement measures for the *Get With The Guidelines* targets (Mozaffarian et al., 2016). In a prospective study by Park, Shin, Ro, Song, and Oh (2013) with 6635 stoke patients, the hospital mortality rate was higher in women (3.9%) than in men (2.9%); and disability was higher in women (67.8%) than in men (65.1%). Similarly, a study of 1272 stroke patients (567 women and 705 men), women had greater stroke severity at discharge (National Institute of Health Stroke Score: men 7, women 5) ($p < 0.001$); and women had worse outcomes (Modified Rankin Scale score >3: men 37%, women 44%) ($p = 0.030$) (Santalucia et al., 2013). Also, another outcome factor is the divide between a patient's financial status and stroke outcomes. In a large sample study ($N = 775{,}905$) patients from low-income groups had decreased thrombolytic therapy on the first admission day, and lower use of key stroke procedures compared to the high-income groups (Agarwal, Menon, & Jaber, 2015).

Evidence has demonstrated that response time to stroke symptoms, adherence to quality processes of care, treatment rates, and overall outcomes were lower for in-hospital strokes when compared to patients who had a stroke in the community and were treated by emergency services (Cumbler et al., 2015). Overall, patients who had a stroke during an in-hospital stay experienced more severe strokes, received less process-based quality measures, fared worse in outcomes (Cumbler et al., 2015). Patients with a higher mortality rate were less likely ($p < 0.0001$) to be discharged home in comparison to patients who had a community onset stroke (Cumbler et al., 2015). In a systematic literature review, overall women had a worse functional recovery with a greater long-term disability (Gall, Tran, Martin, Blizzard, & Srikanth, 2012). However, variability and confidence differed among these studies (Gall, Tran, Martin, Blizzard, & Srikanth, 2012). In a more recent literature review from Girijala, Sohrabji, and Bush, (2017) data was found to be consistent among the studies in that women faced greater rates of stroke at older ages and worse outcomes. However, data lacked in specifically identifying symptoms only women or men experienced, and if presentation times following a stroke were different among women and men (Girijala et al., 2017).

Overall, studies have concluded that misdiagnosis has led to longer hospital stays, and woman have been found to have higher odds for less severe Emergency Severity Index and increased Modified Rankin Scale than men (Kes, 2016; Madsen et al., 2016; Park et al., 2013); women fare worse in multiple quality of care domains in stroke measures, and have poorer outcomes than men; women experience more severe strokes, have longer hospital stays, and have a higher stroke related mortality and disability rate (Agarwal, Menon & Jaber, 2015; Cumbler et al., 2015; Gall et al., 2012; Girijala et al., 2017; Mozaffarian et al., 2016). *Please see table 2 for the stroke quality of care and outcomes for women review of the literature.*

Table 2. Review of the Literature, Stroke Quality of Care and Outcomes for Women

Author (Year)	Purpose	Design	Sample	Findings
Stroke Quality of Care and Outcomes				
Park (2013)	"To investigate the effect of gender difference on the accessibility to emergency care, hospital mortality and disability in acute stroke care."	Prospective and multicenter observational study	$N = 6635$	Time from symptom onset to emergency department arrival to computed tomography or magnetic resonance imaging scan was significantly longer in women. Hospital mortality rate was higher in women (3.9%) than in men (2.9%) ($p = .03$). The increased disability was significantly higher in women (67.8%) than in men (65.1%) ($p = .02$).
Cumbler (2015)	"Identify quality improvement opportunities for the in-hospital stroke gap"	Literature review		Evidence demonstrates that risk factors, mimics, and etiology for in-hospital stroke are different than for those in the community. Response times, adherence to quality processes of care, and treatment rates demonstrates a quality gap for in-hospital strokes. Outcomes for in-hospital stroke are uniformly observed to be worse than strokes in the community.
Gall (2012)	"Explore sex differences in (1) functional outcomes, also known as "activity limitations" and historically as "disability"; (2) handicap, also known as "restriction of participation"; and (3) quality of life."	Literature review		Women had worse functional outcomes, greater handicap, and poorer quality of life indicators than men in the long term after stroke. A lack of consistency in the selection of covariates among studies found along with a small number of purpose-designed studies.

Table 2. cont.

Stroke Quality of Care and Outcomes				
Author (Year)	**Purpose**	**Design**	**Sample**	**Findings**
Girijala (2017)	"Explore the differential physiology, epidemiology, and clinical presentation of stroke between men and women, as well as the current status of laboratory and clinical data"	Literature review		Data consistent in that women face greater rates of stroke at older ages and worse outcomes. Data lacks in the identification of how men and women present differently following a stroke, both with regards to symptoms and signs as well as to presentation times.
Agarwal (2015)	"Analyze the impact of socioeconomic status on in-hospital outcomes, cost of hospitalization, and resource use after acute ischemic stroke"	Retrospective nationwide in-patient sample database	*N* = 775,905	Patients from lower-income quartiles had decreased reperfusion on the first admission day, compared with patients from higher-income quartiles. The cost of hospitalization of patients from higher-income quartiles was significantly higher than that of patients from lowest-income quartiles, lower use of key procedures among patients from lowest-income quartile.
Santalucia (2013)	"Evaluate for sex differences in clinical presentation, severity of stroke and outcome"	Retrospective	*N* = 1272	Women with stroke had worse functional prognosis measured by modified Rankin Scale score (MRS $\geq$ 3)

Thrombolytic Therapy and Stroke alert

Thrombolytic Therapy

Early identification (the process of identifying stroke symptoms less than 3 to 4.5 hours of symptom onset) is crucial to timely thrombolytic treatment and better patient outcomes (Boden-Albala et al., 2015; Boehme et al., 2014; Hanselman, 2014; Powers et al., 2015; Sobolewski et al., 2015). Research by Sandercock et al., (2012) and Wahlgren et al. (2008) found patients treated at 3 to 4.5 hours (30.6%) to only 3 hours (31.5%) had similar amount of unfavorable events; and long-term functional outcomes equalized among both groups (Hanselman, 2014). However, it was found that patients who were treated at 4.5 to 6 hours (47.3%) did have unfavorable events with the likelihood of intracranial hemorrhage increasing when thrombolytic therapy is administered after 3 hours of onset (Hanselman, 2014). Research by Sobolewski et al. (2015) supported the previous studies in their findings that the value of thrombolytic therapy did not lessen when administered at 3 to 4.5 hours (n = 132), compared to the 3 hours (n =271) timeframe; mortality and favorable outcomes did not differ between groups. One study by Boehme et al. (2014) found that African American women with an admission National Institute of Health Stroke Score less than seven were at lower odds (OR 0.66) of receiving thrombolytic therapy than the other race-gender groups.

Only one out of four stroke patients seek treatment within the recommended time frame (CDC, 2019). In a randomized study of 1193 stroke patients, 40-50% of the participants arrived at the hospital for treatment at less than 3 hours of symptom onset (Boden-Albala et al., 2015). Of these participants, 4.3% were treated with thrombolytic therapy (Boden-Albala et al., 2015).

Studies illustrate that stroke is often misdiagnosed initially for a different diagnosis with brain imaging revealing acute stroke further in the hospital stay (Berglund et al., 2015; Dupre et al., 2014; Fothergill et al., 2013; Hodell et al., 2016; Kes, 2016; Lever et al., 2013; Madsen et al., 2016; Park et al., 2013). Misdiagnosis of stroke can delay thrombolytic therapy. In a multidisciplinary team (medical, nursing and allied health professionals) a face-to-face survey study (*N* = 96) identified that stroke symptom knowledge was 92% accuracy for naming ≥ 3 stroke symptoms. However, these symptoms identified only reflected the publically advertised FAST (Face, Arm, Speech, Time); and 49% of the multidisciplinary team were aware of thrombolytic therapy and 48% of the multidisciplinary team could identify the crucial timeframe for which thrombolytic therapy must be administered for an acute ischemic stroke (Mellon, Hasan, Lee, Williams, & Hickey, 2015).

Stroke alert

Current acute stroke thrombolytic therapy can only aid patients within the first 3 to 4.5 hours of stroke onset (Healthy people.gov, 2019; Powers et al., 2017). The use of activating emergency and in-hospital stroke alert have shown to improve time to diagnosis and reduce thrombolytic treatment times (Meretoja et al., 2012). In a study by Candelaresi et al. (2017) a high urgency stroke alert protocol decreased the median door to thrombolytic therapy (103 min to 37 min with the stroke alert ($p < 0.001$) and decreased the median onset-to-treatment time (177 min to 114 min with the new stroke alert ($p < 0.001$). Similarly, another study that initiated a stroke alert found that the rate of thrombolytic therapy among ischemic stroke patients increased from 33.3% to 59.2% ($p = 0.0001$) (Kim et al., 2015). In a study found that stroke alert improved the use of thrombolytic therapy with a decreased median door-to-needle time (88 to 51 min, $p = 0.001$), and stroke alert patients had better outcomes at discharge (Modified Rankin Score 49.5 vs. 39.6%, $p = 0.11$) (Chen et al., 2014). Another study by Kalnins et al. (2017), a structured quality improvement program was applied and cause and effect stroke alert delay drivers were identified as: (1) definition of stroke was not clear; (2) confusion about when to call a stroke alert; (3) measurement for last known well or door time was not clear; (4) variation on symptoms is confusing; (5) not clear who should activate the stroke alert; and (6) unclear about roles and responsibilities. Following the quality improvement intervention, the stroke alert to computed tomography time decreased to a mean of fewer than 14 minutes (Kalnins et al., 2017).

In-hospital stroke alert. Studies on emergency stroke alert are robust. However, studies that specifically focus on in-hospital stroke alert are minimal. In a prospective thrombotic therapy registry study by Meretoja et al. (2012) 94% ($N = 1860$) of patients with in-hospital stroke ($n = 59$) had longer delays compared to patients arriving 30–150 minutes from symptom onset. In a prospective interventional study by Kassardjian et al., (2017), an in-hospital stroke alert algorithm was developed and implemented in the cardiovascular and perioperative units. In-hospital strokes were more commonly found on cardiovascular wards (45%) and during the perioperative period (60%). Following the in-hospital stroke alert intervention and educational initiative, a decrease in all median timed outcome measures was observed; stroke assessment fell from 600 to 160 minutes; and time to computed tomographic scan dropped from 925 to 348.5 minutes (Kassardjian et al., 2017). Similarly, in another study the post-intervention median in-hospital stroke alert-to-computed tomography time decreased to 29.5 minutes from 69.0 minutes pre-intervention time ($p = 0.0001$) (Cumbler et al., 2012). In a chart review by El Husseini and Goldstein (2013), in-hospital stroke alert ($N = 93$) was compared to emergency stroke alerts ($N = 204$). In-hospital stroke alerts were found to be less likely to have thrombolytic treatment (OR, 0.27; 95% CI) with altered mental status (48%) being the main contributor for not initiating immediate neurologic care (El Husseini & Goldstein, 2013).

Similarly, in a literature review by Cumbler et al. (2015) evidence indicates that a quality gap exists for in-hospital stroke; in-hospital strokes have increased delay time for evaluation and treatment. In 2015, Cumbler in collaboration with the National Stroke Association created an in-hospital stroke alert protocol for individual medical centers to modify based on their needs and resources. *The National Stroke Association in-hospital stroke alert protocol is presented in Figure 1. Please see Table 3 for the thrombolytic therapy and stroke alert review of the literature. An example of this study's participating medical center's in-hospital stroke alert protocol is illustrated in appendix B.*

Figure 1. In-Hospital Stroke Alert Protocol: Pocket Card for Stroke Response Team Member

National STROKE Association

In-Hospital Stroke Alert Protocol

Pocket Card for Stroke Response Team Members

****GOAL: CT performed within 25 minutes from symptom onset!!!****

1. Stroke Alert initiated by calling *(number)*.
2. Primary RN records time of symptom onset if witnessed or time patient was last known without deficit.
3. Primary RN assesses ABCs and vital signs and records current vital signs.
4. Provide oxygen to O_2 saturation $\geq$ 92%.
5. Primary RN notifies charge RN and remains at patient's bedside.
6. Primary RN obtains finger stick blood sugar.
7. Charge RN assists with equipment collection and coordination of who will transfer patient to CT and notifies patient's primary physician of patient's status change.
8. Primary RN ensures patient has minimum 20 gauge AC IV.
9. Primary RN draws blood for testing *(color)* top, *(color)* top with gel, and *(color)* top. If female patient of childbearing age, also draw a *(color)* top.
10. Stroke Response Team responds within 15 minutes.
11. Stroke Response Team performs rapid patient assessment including NIHSS.
12. *(individual)* orders stat labs (CBC, Chem-7, PT/INR, PTT, troponin, and HCG if age appropriate), and stat non-contrast brain CT.
13. Clerk sends stat CT request and enters stat orders.
14. Primary RN prepares to accompany patient emergently to CT (with portable oxygen and cardiac monitor).
15. *(individual)* calls CT tech at *(number)* with notification that stroke patient is en route.
16. *(individuals)* transfer patient to CT *(location)* immediately after notifying CT tech.
17. Stroke Response Team communicates assessment with neurology or designee and evaluates inclusion and exclusion criteria for IV tPA and determines if patient is candidate for treatment (refer to institution's inclusion/exclusion criteria).
    - If IV thrombolysis is to be given, Stroke Response Team member notifies *(individual) (number)*.
    - Send thrombolytic orders to pharmacy STAT and send runner for drug if needed.
    - Primary RN establishes patient's weight.
    - Stroke Response Team or designee will assist with tPA administration.
    - If IA/mechanical thrombolysis is indicated, activate endovascular team *(number)*.
18. A member of the Stroke Team and the *(individual)* will remain at patient bedside until patient is transferred to the ICU or endovascular suite.
19. Once IV tPA is started, monitor vitals and neurological assessment every 15 minutes for two hours, then every 30 minutes for 6 hours, then hourly.
20. Stroke Response Team will document in-hospital response evaluation form.

Note: "In-hospital stroke alert protocol card was designed to be individualized to meet the needs and resources of the individual hospital. Depending on delays identified, the order of the protocol may be modified" (Cumbler, E. (2015). In-hospital ischemic stroke. *The Neurohospitalist*, *5*(3), 173)

Table 3. Review of the Literature, Thrombolytic Therapy and Stroke alert

Thrombolytic Therapy and In-hospital Stroke alert				
Author (Year)	**Purpose**	**Design**	**Sample**	**Findings**
Hanselman (2014)	"Examine the central body of research related to the timing of t-PA and makes recommendations for eligible candidates based on this literature"	Literature review		Compared outcomes of patients treated with t-PA in 3-hour window with those treated from 4.5 to 6 hours post onset of symptom – found that likelihood of intracranial hemorrhage increases when t-PA is administered after 3 hours of onset, but long-term functional outcomes appear to equalize among those with early and late t-PA administrations
Sobelewski (2015)	"Assess the long-term outcome and complication rate of i.v. thrombolysis performed in the extended 'time window'"	Retrospective chart review	$N = 403$	Effectiveness of t-PA not lessoned; mortality and favorable outcomes did not differ) when administered at 3 to 4.5 (25% n =132) hours when compared to only 3 hour time frame (75% n = 271) patients treated at 3 to 4.5 hours of stroke favorable with mortality not vary.
Boden-Albala (2015)	"Compared Stroke Warning Information and Faster Treatment (SWIFT) as an interactive intervention (II) with enhanced educational (EE) materials on recurrent stroke arrival times"	randomized controlled trial	$N = 1193$	Assessed differences in arriving to emergency department <3 hours, prepost intervention arrival <3 hours – Prepost 49% increase in the proportion arriving <3 hours ($p = 0.001$), had greater stroke knowledge at 1 month (odds ratio =1.63; 1.23–2.15). II had higher preparedness capacity at 1 month (odds ratio = 3.36; 1.86, 6.10) and 12 months (odds ratio = 7.64; 2.49, 23.49).
Kassardjian (2017)	"Evaluate an in-hospital code stroke algorithm and educational program aimed at reducing the response times for inpatient stroke"	Educational intervention	$N = 218$	In-patient code stroke algorithm was developed. In-patient strokes were more common on cardiovascular wards (45% of cases) and occurred mainly during the perioperative period (60% of cases). After in-patient code stroke intervention and educational initiative, decrease in all median timed outcome measures: assessment fell from 600 to 160 minutes; time to computed tomographic scan fell from 925 348.5 minutes.

Table 3. cont.

Thrombolytic Therapy and In-hospital Stroke alert				
Author (Year)	**Purpose**	**Design**	**Sample**	**Findings**
Mellon (2015)	"Assess the knowledge of stroke symptoms, acute treatments, and hospital protocols among hospital staff for treatment of stroke"	Cross-sectional face-to-face survey	$N = 96$	Stroke Awareness Questionnaire adapted survey was conducted among hospital ward staff members - 81% surveyed was clinical staff (medical, nursing, allied health professionals). 92% could name ≥3 stroke symptoms. 49% of staff were aware of thrombolysis treatment, and 48% could identify the time window for thrombolysis administration, 52% of staff on general wards were aware of an in-hospital stroke protocol.
Meretoja (2012)	"Analyze the effect of interventions aimed to reduce treatment delays in our single-center observational series"	Prospective Helsinki Stroke Thrombolysis Registry	$N = 1{,}860$	Patients treated with tPA – 31% ischemic stroke patients - 94% were treated within 60 minutes from arrival. Patients with in-hospital stroke or arriving very soon from symptom onset had longer delays because there was no time to prepare for their arrival.
Candelaresi et al., (2017)	"Assess the timing of thrombolysis "	Prospective	$N = 400$	Thrombolysis decreased from 103 min to 92 min and to 37 min with the new Stroke Code ($p < 0.001$) median onset-to-treatment time decreased from 177 min to 155 min to 114 min with the new Stroke Code ($p < 0.001$ and $p = 0.005$, respectively)
Kim (2015)	"Analyze the long-term yield and efficiency of a code stroke program"	Prospective single-center registry	$N = 791$	626 (79.1%) stroke code activations were positive for a stroke, with 461 (58.3%) ischemic strokes and 165 (20.9%) hemorrhagic strokes. The rate of thrombolytic therapy among ischemic stroke patients increased from 33.3% to 59.2% (p for trend = 0.0001).

Table 3. cont.

Thrombolytic Therapy and In-hospital Stroke alert				
Author (Year)	**Purpose**	**Design**	**Sample**	**Findings**
El Husseini (2013)	"Hypothesized that the yield of code stroke evaluations would be lower in hospitalized than in ED patients, and sought to identify potential targets for quality improvement efforts"	Retrospective chart review	*N* = 294	A total of 93 in-hospital and 204 ED code strokes - Compared with ED patients, hospitalized patients were less likely to have had a stroke/transient ischemic attack (26.8% vs 51.4%; *p* = .0001) and less likely to have been treated with a thrombolytic agent (odds ratio, 0.27; 95% confidence interval, 0.07-0.97: *p* = 5.03). Conditions not necessitating immediate neurologic care accounted for 63.4% of in-hospital strokes, compared with 31.3% of ED code strokes (*p* = .0001). ''Altered mental status'' was the sole presenting symptom in 48% of the hospitalized patients, compared with only 10% of ED patients (*p* = .0001), and was the only clinical feature independently associated with a stroke mimic in the hospitalized patients (odds ratio, 63.52; 95% confidence interval, 7.37-547.69; *p* = .0002).
Chen (2014)	" To investigate the impact of stroke code on thrombolysis"	Retrospective data review	*N* = 5957	1301 (21.8%) stroke patients arrived to emergency department within 3 h of stroke onset and 307 (5.2%) received IV-tPA. Stroke code improved the efficiency of IV-tPA administration; the median door-to-needle time decreased (88 to 51 min, *p* = 0.001) and stroke code patients had more patients with good outcome (modified Rankin Scale #2) at discharge (49.5 vs. 39.6%, *p* = 0.11), with no difference in symptomatic hemorrhage events or in-hospital mortality.

Table 3. cont.

Thrombolytic Therapy and In-hospital Stroke alert				
Author (Year)	**Purpose**	**Design**	**Sample**	**Findings**
Kalnins (2017)	"To decrease time for non-pre-notified stroke code patients from a baseline mean of 20 minutes to one less than 15 minutes during an 18-week period by applying quality improvement methods in the context of a structured QI program"	QI project		A structured quality improvement program was applied and cause and effect of stroke code delay drivers were identified as: e.g Methods – definition of stroke not clear; Confusion about when to call a stroke code; Measurement not clearly (e.g. door time); People - Variation on symptoms; Not clear who should activate the stroke code; Unclear roles and responsibilities; Stroke code team arrival times vary; Delays in neurologic assessment. After intervention the stroke code to CT time for non-pre-notified stroke code patients decreased to a mean of less than 14 minutes.
Boehme (2014)	"Determine the association of race and gender on initial stroke severity, thrombolysis and functional outcome after acute ischemic stroke"	Retrospective data from identified Prospective stroke registries	$N = 4925$ Women $n = 2346$	White women had the highest median NIHSS on admission (8) with White men had the lowest median NIHSS on admission (6). A smaller percentage of Black women than White women were treated with tPA (27.6% vs. 36.6%, $p < 0.0001$), partially due to a greater proportion of White women presenting within 3 hours (51% vs. 45.5%, $p = 0.0005$). Black women with a NIHSS on admission of less than 7 were at lower odds of receiving tPA than the other race gender groups, even after adjusting for arriving within 3 hours and admission glucose (OR 0.66, 95% CI 0.44-0.99, $p = 0.0433$).

Table 3. cont.

Thrombolytic Therapy and In-hospital Stroke alert				
Author (Year)	**Purpose**	**Design**	**Sample**	**Findings**
Cumbler (2012)	"To reduce time to evaluation for strokes occurring in patients already hospitalized, through systematic analysis of current processes and application of standardized quality improvement methodology"	Prospective interventional		Pre-intervention median inpatient stroke alert-to-CT time was 69.0 minutes, Post-intervention median inpatient stroke alert-to-CT time was 29.5 minutes ($p < 0.0001$).

Key initiatives of Healthy People.gov 2020 (2019) and American Stroke Association: Target Stroke include improving quality care and patient outcomes by reducing the amount of time to within 3 hours of symptom onset so eligible stroke patients can be treated with a thrombolytic agent (Mozaffarian et al., 2016). The Agency for Healthcare Research and Quality (2018) initiative includes increasing knowledge of contributing factors that trigger diagnostic failure and that aid in improving diagnosis. To meet the stroke measure thrombolytic therapy and improve stroke patient quality of care and outcomes, the development and activation of in-hospital stroke alert that is specific and sensitive to the hospital floor units, multidisciplinary team, unique stroke symptoms in women , race, and gender are required. Furthermore, studies conclude that thrombolytic therapy can safely be administered to eligible candidates up to 4.5 hours of symptom onset (Boden-Albala et al., 2015; Boehme et al., 2014; Hanselman, 2014; Powers et al., 2015; Sobolewski et al., 2015). Low symptom recognition, seeking treatment late, and misdiagnosis of stroke all contribute to delayed thrombolytic therapy (Boden-Albala et al., 2015; CDC, 2019; Mellon et al., 2015). Stroke alert when streamlined can lead to early assessment; increase the administration of thrombolytic therapy; quicker stroke interventions; and contribute to better patient outcomes (Candelaresi et al., 2017; Chen et al., 2014; El Husseini & Goldstein, 2013; Kalnins et al., 2017; Kassardjian et al., 2017; Kim et al., 2015; Meretoja et al., 2012). Therefore, in consideration of previous work, the purpose of this study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes as uniquely manifested in women admitted to the hospital for a separate condition.

Theoretical Perspective

Epistemological beliefs of this study were grounded in a descriptive observational positivism perspective, which emphasizes that the social world exists externally to the researcher; therefore, its properties can be measured directly through observation (George, 2011). Positivism argues that: (1) reality consists of what is available to the senses; (2) inquiry should be based upon scientific observational empirical inquiry; and (3) the natural and human sciences share common logical and methodological principles, dealing with facts and not with values (George, 2011). The purpose of this descriptive observational study was to provide a picture of a phenomenon as it naturally occurs. Descriptive observational studies collect data without changing the environment (George, 2011). Descriptive observational studies can demonstrate associations between things in the world around you (George, 2011). Multiple research methods including descriptive observational studies have been proven to achieve effectiveness research (Hirsch, 2014). Therefore, from a descriptive observational positivism perspective, this study observed the impact patient characteristics; clinical conditions; the context of care; treatments; and specifically the effectiveness of an in-hospital code stroke activation on delivering the outcome of thrombolytic therapy in women as it naturally occurred in existing data.

Conceptual Framework

This descriptive observational study was guided by the Model for Nursing Effectiveness Research developed by Shever et al., (2008). This model was influenced by Titler, Dochterman, and Reed's (2004) Effectiveness Research Model and is similar to the Outcomes Conceptual Model by Kane (1997; 2006). Effectiveness science is comparative research that identifies what health interventions such as treatment protocols work best for improving health outcomes and cost (Potempa, Daly, & Titler, 2012). The Model for Nursing Effectiveness Research Using Propensity Scores is a comparative effective science research method that reduces bias and observational study causal effect to determine the risk of treatment to the outcome (Qin et al., 2008; Shever et al., 2008).

The activation of emergency and in-hospital stroke alert has shown to improve time to stroke diagnosis and treatment (Candelaresi et al., 2017; Cumbler et al., 2012; Kalnins et al., 2017; Kassardjian et al., 2017; Kim et al., 2015; Meretoja et al., 2012). However, gaps exist in evidence regarding stroke as manifested in women, criteria specific to in-hospital stroke alert for women and means to increase the frequency of thrombolytic therapy for women who have an in-hospital stroke. Therefore the purpose of this study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate.

Effectiveness Science

In recent years, effectiveness science and research have been receiving increasing attention within the various healthcare setting (Potempa, Daly, & Titler, 2012). The United States population, in general, has poorer health outcomes and higher health risk factors when compared to other developed countries (Organization for economic co-operation and development, 2016). A large need exists to inform decisions, increase value and improve our nation's health system. Comparative effectiveness and cost-effectiveness research have the potential to transform health care delivery systems and thus improving patient outcomes (Hirsch, 2014). Effectiveness research develops knowledge and provides the evidence on the effectiveness, harm, and benefits of a treatment which then can inform health-care decision making (Hirsch, 2014). The Institute of Medicine (2009) defines comparative effectiveness research as “the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care” (Sox and Greenfield, 2009). Specifically, comparative effectiveness research is “a translational science that has been defined as the conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat, and monitor health conditions in real-world settings” (U.S. Department of Health and Human Services, 2009). Effectiveness research has the potential for researchers conducting studies to generate new evidence (Hirsch, 2014). Defining characteristics of comparative effectiveness research include the following:

- “It is conducted in settings similar to those in which the intervention will be used in practice.
- It employs methods and data sources appropriate for the decision of interest.
- It includes measures of outcomes that are important to patients, both benefits and harms.
- It directly informs a specific clinical decision from the patient perspective or a policy decision from the population perspective.
- It compares at least two alternative interventions.
- It describes results at the population and subgroup level” (IOM, 2009 as cited in Titler, and Pressler, 2011 p. 76).

According to Potempa, Daly, and Titler, (2012) effectiveness science and research are “essential to improving quality and cost of healthcare” (p. 1). Effectiveness research uses comparison and context of care testing to determine the best treatments or interventions for a given population and environmental setting (Potempa, Daly, & Titler, 2012). Effectiveness research provides the evidence, for informed decision making within health care systems, which will improve healthcare delivery, quality and outcomes at the individual and population level (Potempa, Daly, & Titler, 2012).

Studies by Shever et al. (2008) and Titler et al. (2008) both used a model that examined factors (patient characteristics, clinical conditions, nursing unit context of care variables, medical treatments, pharmaceutical treatments, and nursing treatments) that contributed to adverse incidents of hospitalized older adults. These studies together demonstrate the importance of a unified nursing effectiveness research approach, practice, and multidisciplinary partnering has on addressing evidence-based practice and quality of care measures.

Therefore, effectiveness research can study nursing interventions on patient outcomes that are achieved under ordinary practice circumstances for typical patients. By determining the impact an intervention or treatment has on the quality of patient care, patient outcomes, and financial costs, effectiveness research in nursing can enhance evidence-based practice, clinical decision-making, reinforce and promote excellence in patient-centered care, and build the clinical bridge between research and practice.

Outcomes Conceptual Model

According to Kane (2006) "outcomes suggest to an investigator where to look for more information about the process of care" (p. 6). Kane (2006) explains that the basic model for analyzing outcomes of care is the same no matter the research method of choice; "outcomes will always = f (baseline, patient clinical characteristics, patient demographics/psychosocial characteristics, treatment, setting)" (p. 9). Treatments are classified under the Donabedian (1966) taxonomy and consist of doing the appropriate thing and doing it well (Kane, 2006). "The goal of outcomes research is to establish what treatment is appropriate for a given situation by isolating the effects of treatment from the effects of the factors that influence outcomes" (Kane, 2006 p. 12). Understanding how current structure and processes within a system function and where the need exists for change can improve the likelihood of achieving desired outcomes (Kane, 1997).

This Outcomes Conceptual Model by Kane (1997; 2006) provides the foundation for the Model for Nursing Effectiveness Research developed by Shever et al., (2008). Therefore, the Outcomes Conceptual Model provides specific details of how a treatment (in-hospital stroke alert) influences outcomes (thrombolytic therapy) for defined subgroups of patients (women) and how special analysis such as a propensity score method must be conducted to eliminate the effects of the confounding variables that influence outcomes.

Effectiveness Research Model

According to Titler, Dochterman et al. (2004) outcomes are the result of interventions as experienced by the recipient of the intervention (i.e. change in function or physiological parameter) or by some broader measure related to the impact of the intervention, such as readmission to the hospital or length of stay. Titler et al. with Shever as a co-investor (2006), examined the relationships between nursing interventions and several outcome measures for three different patient populations funded by the National Institute of Nursing Research. It was one of the first studies to conduct nursing outcome effectiveness research using existing data from that several electronic data repositories. Another study by Titler et al. (2008), a retrospective exploratory study using electronic clinical data repositories was conducted to "determine the impact of patient characteristics, clinical conditions, hospital unit characteristics, and health care interventions on hospital cost of patients with heart failure" (para 1). A cost model was tested using generalized estimating equations analysis resulting in variability within hospital costs for heart failure patients 60 years of age and older (Titler et al., 2008). In addition, numerous studies conducted by Titler et al. (2008), using the effectiveness model have been used to identify nursing interventions that are associated with a higher incidence of good or poor patient outcomes such as cost, and longer hospital stays (Titler et al., 2005; Titler et al., 2006; Titler et al., 2007; Titler et al., 2008).

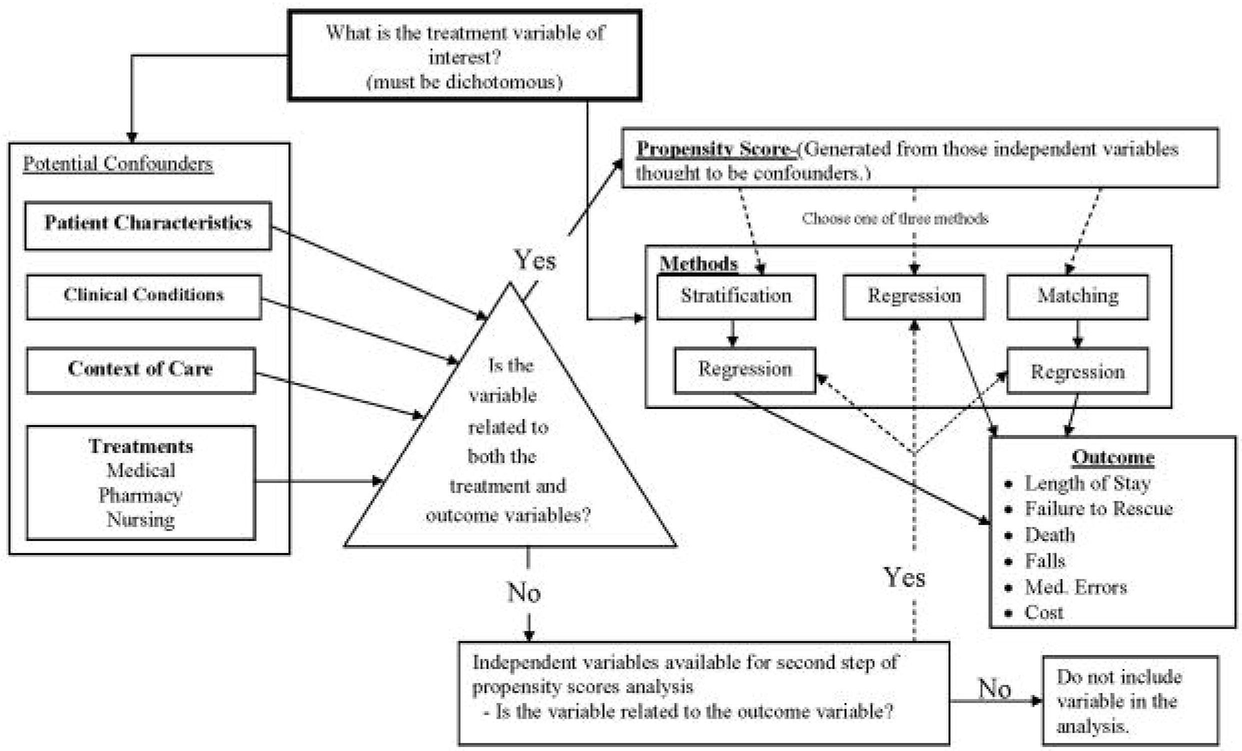
Since the development of the Effectiveness Research Model, it has been tested in multiple studies (Simpson et al., 2010; Smaldone, Tsimicalis, & Stone, 2011; Sox, 2010). In one study by Titler, Shever, Kanak, Picone, and Qin (2011) the model was tested to evaluate factors that explain falls of hospitalized older adults. A sample of 10,187 hospitalizations was included in this study along with nursing interventions as a variable associated with falls. This study found that registered nurse skill mix was significantly and inversely associated with falling while hospitalized; the odds of falling decreased 18.8% for each 10% increase in RN skill mix (Titler et al., 2011). Since the Effectiveness Research Model (Titler et al., 2004) provides the foundation for the Model for Nursing Effectiveness Research developed by Shever et al. (2008) it guides this study by identifying nursing interventions such as in-hospital stroke alert activation and the patient outcomes associated with thrombolytic therapy.

Model for Nursing Effectiveness Research

Shever et al. (2008), with Titler as a co-investigator, designed the Model for Nursing Effectiveness Research Using Propensity Scores for their study that determined the cost of nursing surveillance for older hospitalized adults at risk for falling. The cost of nursing surveillance study was an observational study that used existing data from one hospital data repository (Shever et al., 2008). The nursing treatment was surveillance, and the outcome variable was the total hospital cost associated with surveillance (Shever et al., 2008). Shever et al. (2008) used a propensity score method and generalized estimating equations. Findings concluded that the median cost was different ($p = 0.050$) for patients who received high versus low surveillance.

This Model for Nursing Effectiveness Research utilizes the propensity score method to determine the risk of treatment to the outcome (Qin et al., 2008; Shever et al., 2008). The propensity score method has become a powerful technique to reduce bias and study causal effects in observational non-experimental studies (Heinze & Jüni, 2011; Qin et al., 2008; Shever et al., 2008). The use of regression adjustment for propensity scores in observational studies reduces bias and makes a causal inference (Heinze & Jüni, 2011). The propensity score analysis assumes that the treatment assignment is strongly ignorable if it is independent of the outcome after controlling for the observed confounders (Heinze & Jüni, 2011). A propensity score is the probability that a patient received treatment (in-hospital stroke alert) given all the observed covariates and confounders (Heinze & Jüni, 2011; Qin et al., 2008; Shever et al., 2008). It is a conditional probability of receiving treatment and thus always has a value between 0 and 1 (Heinze & Jüni, 2011; Qin et al., 2008; Shever et al., 2008). The larger a propensity score, the more likely a patient was to receive the specified treatment (Heinze & Jüni, 2011; Qin et al., 2008; Shever et al., 2008). By including potential treatment confounders in the propensity score, treatment bias will be greatly reduced or removed (Heinze & Jüni, 2011; Qin et al., 2008; Shever et al., 2008). A recent study used propensity score methods to match cases of ischemic stroke patients who had thrombolysis to the control cases to a 1:2 ratio by demographical and clinical covariates (Muruet et al., 2018). Kaplan–Meier estimates, and Cox proportional hazard was used to determine the primary outcome; concluding that thrombolysis is associated with improved long-term survival and functional status (Muruet, Rudd, Wolfe, & Douiri, 2018). Therefore, the propensity score method for this study can ensure that the results associated with in-hospital stroke alert are the accurate effects of in-hospital stroke alert on administration of thrombolytic therapy and not a product of the confounding variables.

Figure 2. Model for Nursing Effectiveness Research Using Propensity Scores



Shever, L. L., Titler, M. G., Kerr, P., Qin, R., Kim, T., & Picone, D. M. (2008). The effect of high nursing surveillance on hospital cost. *Journal of Nursing Scholarship*, *40*(2), 161-169.
Permission to reprint granted 11.21.17

Variable selection for this study was guided by this Model for Nursing Effectiveness Research, in addition to clinical knowledge and empirical evidence from literature review. Variables were validated by the principal investigator's collaborators; which consists of an expert neurologist and research coordinator. The dichotomous treatment variable was in-hospital stroke alert. Designating the treatment or intervention as a dichotomous variable treats the dose of treatment as equal for those who received interventions at least once during a specified period (Reed et al., 2007).

The primary independent treatment variable for this study was in-hospital stroke alert. Potential confounding variables included patient characteristics (age, marital status, ethnicity, and admission hospital floor); clinical conditions (stroke risk factors, comorbid conditions, primary medical diagnosis, common and unique stroke symptoms); and the context of care (Time Last Known Well, Emergency Severity Index, diagnostic imaging, number of hospital units/floors, unit stroke alert occurred, delay time, and average nurse-patient ratio). The endpoints were the primary dependent outcome variable of thrombolytic therapy and the secondary outcome of discharge status. *The complete model illustrating variables and steps for a propensity score analysis is presented in Figure 2.*

Summary

Although stroke research associated with women has increased in the recent years, much remains unknown regarding strategies specific to in-hospital stroke alert activation in women. Current studies confirm the difference in stroke among gender and the significance of stroke alert on outcomes. Women who have experienced a stroke are more likely to be misdiagnosed and, also fare worse in stroke outcomes compared to men. Although the activation of emergency and in-hospital stroke alert has shown to improve time to stroke diagnosis and treatment, gaps exist in evidence regarding criteria specific to in-hospital stroke alert for women and means to increase the frequency of thrombolytic therapy. Therefore the purpose of this study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition. *Tables 1, 2 and 3 summarize the 27 articles selected for this studies review of the literature.*

CHAPTER III

METHODOLOGY

The purpose of this study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition. Specific Aims to address this purpose were to:

Aim 1. Determine the frequency of women receiving thrombolytic therapy after receiving in-hospital stroke alert during hospitalization for a separate condition.

Aim 2. Match women who receive an in-hospital stroke alert activation to women with no in-hospital stroke alert.

Aim 3. Compare the effects and associated variables of an in-hospital stroke alert activation to no in-hospital stroke alert on outcomes in women admitted to the hospital for a separate condition.

Included in this chapter are descriptions of the study design, setting, sample, data sources, data collection, study measures and analysis.

Study Design

A retrospective descriptive propensity score design was used to determine the frequency of receiving thrombolytic therapy in women who have in-hospital stroke alert during hospitalization for a separate condition. The use of propensity scores in observational studies reduces bias and makes a causal inference by controlling for observed confounders (Heinze & Jüni, 2011). There are current gaps in criteria specific to in-hospital stroke alert for women; thus limiting the use of thrombolytic therapy which has the potential to decrease disability and cost.

Study Setting

The setting for this study was a 556 bed non-profit medical center within a major metropolitan service area in the upper Midwest. In 2014, this upper Midwest hospital was awarded certification as a Comprehensive Stroke Center by Det Norske Veritas® Healthcare (DNVGLHealthcare, 2018). Certification as a Comprehensive Stroke Center is recognition that this medical center can offer the highest level of treatment and care available for stroke patients, including advanced neuro-interventional radiology, neurosurgery, and neuro-critical care services. This comprehensive Stroke Center has been conducting stroke alert for 10 years, providing an integrated and comprehensive approach to stroke care from diagnosis, treatment and rehabilitation while offering evidence-based, best-of-practice acute care, and rehabilitation (DNVGLHealthcare, 2018).

Data Sources

Data for the period of May 2014 to May 2018, was extracted using the hospital's Clinical Research Informatics and Analytics team. This team is composed of staff with expertise in health informatics, project management, data extraction and report writing, and statistics. This team provided comprehensive research support services related to research data access, use, and disclosure. Data extracted by the informatics team was from the Epic Systems Corporation electronic medical record and was de-identified. Data included elements that were part of the in-patient hospital admission and discharge summaries including diagnoses, comorbidities, risk factors, symptoms, demographic data, stroke assessment tools, diagnostics, treatment, and time.

Sample

A Midwestern hospital for this study, serves over 200,000 patients annually with roughly 12,000 of the patients being stroke hospitalizations; 53% Caucasian, 17.8% Asian, 15.2% African American. About 21.2% of the study's population lived below the poverty line. Based on a recent publication from this hospital, the anticipated study's population would be about 60% women with a median age of 78 years. The ethnic composition of this sample would be 60% Caucasians, 15% Asian, and 10% African American (Brown, Luby, Shah, Giannakidis, & Latour, 2015).

A sample was obtained from patient records that met the inclusion criteria. The initial plan was for stratified random sampling by dividing groups of women into quarters for 10 years (16 groups) and according to in-hospital stroke alert or no in-hospital stroke alert for a total of 32 groups. Subsamples would then have been randomly selected from each strata. Due to the fact that this population has a small incidence and crucial variables were only available for the past 4 years, difficulties were encountered extracting a large enough sample size to meet the estimated effect size. A sample size of 114 participants, 46 from per group, was required to provide 80% power to detect a 20% difference in a mean outcome score with an effect size of 0.84 (Faul, Erdfelder, Buchner, & Lang, 2009).

Sample size estimation was completed for a bivariate correlation and logistic regression using a z-statistic to approximate the t-statistic (Faul et al., 2009). Therefore, stratification was eliminated and a convenience sample was obtained from patient records that met the inclusion criteria. In-addition, coding for stroke alert included rapid response because coding specific to stroke alert was not always initiated on every hospital floor up until the year 2016. Participants were eligible for study inclusion if they met the following criteria: Patient was greater than 18 years of age, female gender, was admitted to the participating medical center, and had a discharge diagnosis of ischemic stroke. Ischemic stroke diagnosis was confirmed by the principal investigator, attending neurologist, and by diagnostic testing between May 1, 2014 to May 31, 2018; including all ICD 10 - I63 or ICD 9 grouping codes (Cerebral infarction). In addition, the ischemic stroke was documented as a secondary or other diagnosis obtained during in-patient hospitalization for a separate condition. Patient records were excluded if they had requested their medical records not be used for research purposes, patients who were less than 18 years of age, male gender, had an admitting diagnosis of ischemic stroke, and patients whose ischemic stroke diagnosis was greater than 4 years, prior to the year 2014. Eligible records were included regardless of patient gender, ethnicity or national origin.

The initial sample extracted by the informatics specialist included 101 records from May 2014 through May 2018, 21 records from in-hospital stroke alert was activated during hospitalization group and 80 records from in-hospital stroke alert was not activated during hospitalization group. After aforementioned adjustment of the inclusion of rapid response, a final sample size of 149 women met inclusion criteria. Of the 149 women included in this study, 46 women had an in-hospital stroke alert activated during hospitalization and 103 women had no in-hospital stroke alert activated during hospitalization.

Data Collection

The initial patient medical records were extracted by the informatics team based on a diagnosis of ischemic stroke identified as ICD stroke codes ICD-10 (Oct. 2016 to present) and ICD-9 (2014-2016). Patient records that had a stroke diagnosis listed as the primary diagnosis were excluded. The remaining patient charts were scanned to ensure they met the remaining inclusion and exclusion criteria.

Individual-level retrospective demographic, clinical, and administrative data was used. Data for this research study was collected from patients records recorded in an electronic medical record system. Patient medical records are held in the Epic system-wide healthcare software. Epic software offers an integrated suite of healthcare software centered on a Caché database provided by InterSystems. The Epic's applications support functions related to patient care, including registration and scheduling; clinical systems for doctors, nurses, emergency personnel, and other care providers; systems for lab technologists, pharmacists, and radiologists; and billing systems for insurers (Epic, 2018). Permission was obtained from the organization's Institutional Review Board to use data from the medical records of patients who were diagnosed with ischemic stroke during hospitalization for a separate condition for the period specified. *See Appendix C for the participating hospital's Institutional Review Board signed approval letter.*

Study Measures

Patient Characteristics

Patient characteristics abstracted from the medical record included one continuous variable, age at the time of hospitalization, and three nominal (categorical) variables, marital status, ethnicity, and admission floor. The rationale for choosing these variables was based on the literature and the potential relationship of these variables to stroke risk, diagnosis, treatment, and outcomes. All data was abstracted at the individual patient level. *See operational and coding table 4 below for definitions and data sources.*

In-Hospital Stroke Alert

The primary variable of interest for this study was in-hospital stroke alert, which included the activation of stroke alert after nursing/physician/or medical personnel assessment reveals stroke symptoms. Stroke alert consists of a team of stroke experts (e.g., nurse, neurologist, diagnostics, lab, respiratory therapist) who emergently arrive to assess, diagnosis, and treat the stroke patient. In-hospital stroke alert was coded dichotomously as either no (0) or yes (1) an in-hospital stroke alert was activated during hospitalization for a separate condition.

Clinical Conditions

Multiple clinical conditions contribute to the risk, recognition, and severity of stroke (ASA, 2019a; Mozaffarian et al., 2016). The clinical conditions selected for this study included two dichotomous variables, common and unique stroke symptoms, and three nominal (categorical) variables, stroke risk factors, comorbid conditions and primary medical diagnosis. Risk factors directly related to an increased risk for stroke included high blood pressure, smoking, diabetes, high cholesterol, physical inactivity and obesity, carotid or other artery disease, transient ischemic attacks, atrial fibrillation or other heart disease, certain blood disorders, excessive alcohol intake, illegal drug use, sleep apnea, and prior stroke (ASA, 2019a; Capriotti & Frizzell, 2016). These variables were extracted from the patient's history in the electronic medical record.

Comorbid conditions. Clinical conditions were obtained from International Classification of Diseases ICD codes and were grouped categorically according to the 17 Charlson Comorbidity Index Categories: Myocardial Infarction; Congestive Heart Failure; Peripheral Vascular Disease; Cerebrovascular Disease; Dementia; Chronic Pulmonary Disease; Connective Tissue Disease- Rheumatic Disease; Peptic Ulcer Disease; Mild Liver Disease; Diabetes without Chronic Complications; Diabetes with Chronic Complications; Paraplegia and Hemiplegia; Renal Disease; Cancer; Moderate or Severe Liver Disease; Metastatic Carcinoma; HIV/AIDS (Lix et al., 2016). The Charlson Comorbidity Index is a method for categorizing comorbidities based on all the ICD–9–CM has been validated as a measure of mortality risk and burden of disease; it has been extensively used in research to address the confounding influence of comorbidities (Frenkel, Jongerius, Mandjes-van Uitert, Munster, & Rooij, 2014; Quan et al., 2011).

Primary medical diagnoses. Primary medical diagnoses were grouped categorically according the following human body systems: Diseases and Disorders of the Nervous System; Diseases and Disorders of the Ear, Nose, Mouth And Throat; Diseases and Disorders of the Respiratory System; Diseases and Disorders of the Circulatory System; Diseases and Disorders of the Digestive System; Diseases and Disorders of the Musculoskeletal System And Connective Tissue; Diseases and Disorders of the Endocrine, Nutritional And Metabolic System; Diseases and Disorders of the Kidney And Urinary Tract; Diseases and Disorders of the Female Reproductive System; Diseases and Disorders of the Blood and Blood Forming Organs and Immunological Disorders; Infectious and Parasitic disease and disorders; and Factors Influencing Health Status and Other Contacts with Health Services (Lix et al., 2016). These variable ICD codes were extracted from the patient electronic medical record.

Stroke symptoms. Stroke symptoms were categorized into common and/or unique symptom of stroke. Common stroke symptoms as recognized by the American Heart and Stroke Association (2017b) were coded dichotomously as either no (0) common stroke symptoms were present at the time of admission or yes (1) common stroke symptoms were present at the time of admission (National Stroke Association, 2018). Unique stroke symptoms were coded dichotomously as either no (0) unique stroke symptoms are present at the time of admission or yes (1) unique stroke symptoms are present at the time of admission (National Stroke Association, 2018).

Context of Care

Eight confounding variables related to thrombolytic therapy included the following measurements: 1) Stroke symptom recognition, 2) degree of patient condition urgency, 3) diagnostic imaging, 4) number of units, 5) unit of stroke alert, 6) average nurse-patient ratio, 7) diagnostic delay time and 8) stroke alert delay time. These variables were chosen based on evidence, expertise, availability, and the potential of these variables to affect stroke recognition, diagnosis, and treatment.

Time Last Known Well. The Time Last Known Well is defined by the Joint Commission National Quality Measures (2018) as "the time prior to hospital arrival at which the patient was last known to be without the signs and symptoms of the current stroke or at his or her baseline state of health" (The Joint Commission, 2018, para 1). The Time Last Known Well is documented when a stroke alert is activated. The Time Last Known is used in determining if the patient meets thrombolytic therapy inclusion or not (The Joint Commission, 2018). The rationale for including Time Last Known Well in this study was because documentation of Time Last Known Well is part of the American Stroke Association guidelines. The Time Last Known Well informs the benchmark times to diagnostics and treatment (Benjamin et al., 2017; Mozaffarian et al., 2016). The Time Last Known Well was extracted from the patient's electronic medical record. Consideration was made to the Time Last Known Well variable since not all patients had a Time Last Known Well documented because Time Last Known Well is part of the stroke alert documentation meaning it was only documented for women who had an in-hospital stroke alert activated.

Emergency Severity Index. The Emergency Severity Index is a five-level emergency department triage algorithm with 1 being the most urgent to 5 being the least urgent. This index is used to determine how emergent a current patient condition is when they arrive at the emergency department. It is a reliable and valid tool for triaging patients (Tanabe, Gimbel, Yarnold, Kyriacou, & Adams, 2004; Wuerz et al., 2001). The rationale for including the Emergency Severity Index in this study is because evidence has indicated that women have a higher odds for being rated as a less severe Emergency Severity Index when compared to men (Kes, 2016; Madsen et al., 2016; Park et al., 2013). The Emergency Severity Index score for each case was extracted from the patient's electronic medical record and was coded integrally 1 to 5 as urgent to non-urgent. Consideration was made to the Emergency Severity Index variable since not all patients had an Emergency Severity Index documented because not all patients were admitted through the emergency department.

Diagnostic imaging. Diagnostic imaging is key for accurately assessing a patient with an acute stroke. It expedites clinical decision making about administering thrombolytic therapy. According to the American Heart and Stroke Association 2018 guidelines, "centers should attempt to obtain a non-contrast head computed tomography within 20 minutes of arrival in ≥ 50% of stroke patients who may be candidates for IV tissue plasminogen activator or mechanical thrombectomy" (Powers et al., 2018, para 4). For this study diagnostic imaging included a computed tomography scan or magnetic resonance imaging to be completed within 45 minutes of a patient's Time Last Known Well, the time right before symptoms started. Diagnostic imaging was dichotomously measured as either yes or no computed tomography scan was completed within 45 minutes of last known well.

Hospital context of care. Variables directly related to hospital context of care included the number of units, average nurse-patient ratio, unit the stroke alert occurred, the delay time in diagnostics, and the delay time in stroke alert. The number of units the patient resided on during the course of their hospitalization and the unit in which the stroke alert occurred represents the possibility for decreased quality of care and outcomes. Multiple unit transfers have been shown in prior studies to affect the quality of care and outcomes (Solano et al., 2017). Hospital units were classified as critical care (e.g., intensive care unit), non-critical (e.g., medical), or emergency per the patient electronic medical record. Consideration was made to the unit the stroke alert occurred variable as this was only included in the yes in-hospital stroke alert was activated group of women, as this was not documented if no stroke alert was activated.

Delay time. In addition, the delay time in stroke diagnostics and time to a stroke alert represents variables for delayed thrombolytic therapy and reduced outcomes. Evidence suggests that low symptom recognition and misdiagnosis of stroke all contribute to delayed thrombolytic therapy and has led to longer hospital stays (Boden-Albala et al., 2015; CDC, 2019; Kes, 2016; Madsen et al., 2016; Mellon et al., 2015; Park et al., 2013). Delay time was measured as the time, in minutes, from when the patient was Last Known Well (without stroke symptoms) to the time of diagnostics and to the time of in-hospital stroke alert activation as recorded in the patient electronic medical record (Qin et al., 2008; Shever et al., 2008; Titler & Dochterman, 2004). Consideration was made to the delay time as these variables were only included in the yes in-hospital stroke alert was activated group of women, as these were not documented if no stroke alert was activated.

Outcomes

Thrombolytic therapy. The primary dependent outcome variable that was extracted from the electronic medical record was the measure of administering thrombolytic therapy. Thrombolytic therapy is a stroke core measure and remains the best treatment for acute ischemic stroke (Powers et al., 2018). According to the American Heart and Stroke Association 2018 guidelines, "the benefits of intravenous tissue plasminogen activator are time-dependent, and treatment for eligible patients should be initiated as quickly as possible (even for patients who may also be candidates for mechanical thrombectomy); thrombolytic therapy should be administered to all eligible acute stroke patients within 3 hours of time last known normal and to a more selective group of eligible acute stroke patients (based on ECASS III exclusion criteria) within 4.5 hours of last known normal. Centers should attempt to achieve door-to-needle times of < 60 minutes in ≥ 50% of stroke patients treated with thrombolytic therapy" (Powers et al., 2018 para 3). For this study, thrombolytic therapy was dichotomously measured as yes (1) or no

(0) the patient did not receive thrombolytic therapy. Contraindications to thrombolytic therapy were reviewed for patients who did not receive thrombolytic therapy and are discussed in chapter five.

Discharge status. The secondary outcome included discharge status. Discharge status was included in this study because discharge is an outcome indicator which suggests better outcome compared to poor outcome post stroke. For example a patient discharged to home has a better stroke outcome versus a patient who has expired. In addition, evidence suggests that gender influences stroke outcomes to include discharge status (Gibson, 2013). Therefore, for this study discharge status was categorically measured as discharged/transferred to skilled nursing facility, discharged/transferred to a long term care hospitals, discharged/transferred to intermediate care facility, discharged/transferred to another type of health care institution, discharged/transferred to an inpatient rehabilitation, discharged/transferred to home care, left against medical advice or discontinued care, hospice, or expired.

Coded Variables Planned for Data Entry and Analysis

Guided by the Model for Nursing Effectiveness Research, clinical knowledge and empirical evidence the independent variables that were extracted from the electronic medical record for this study included the primary independent treatment predictor of in-hospital stroke alert, and 17 additional confounding variables (patient characteristics, clinical conditions, context of care, and treatment variables) that are conceptually related to the primary dependent outcome variable of thrombolytic therapy and secondary outcome of discharge status (Shever, 2008). All variables were extracted for the key hospitalization at the individual patient level. *A complete list of variable operational definitions and coding is presented in table 4.*

Table 4. Operational Definitions and Coding

	Variable Category	Variable Name	Operational Definition	Value and Code
	Primary Treatment Predictor			
1	Independent	In-hospital stroke alert as recorded in the EMR	Activation of stroke alert after nursing/physician/or medical personnel assessment reveals stroke symptoms	Dichotomous No, in-hospital stroke alert was not activated during hospitalization = 0 Yes, in-hospital stroke alert was activated during hospitalization = 1
	Patient characteristics as recorded in the EMR	**Variable Name**	**Operational Definition**	**Value and Code**
1	Independent	Age	Age at time when patient was admitted to hospital	Continuous Measured in years
2	Independent	Marital status	Having or not having a husband or wife	Nominal(Categorical) Married = 1 Separated/divorced or single = 2 Widowed = 3
3	Independent	Ethnicity	The fact of belonging to a common national or cultural tradition	Nominal(Categorical) Caucasian = 1 African American = 2 Native American = 3 Alaskan Native = 4 Pacific Islander = 5 Middle Eastern American = 6
4	Independent	Admission floor	The floor from which the patient was admitted to within the hospital	Nominal (Categorical) Critical care = 1 Non-critical = 2 Surgical = 3 Emergency = 4
	Clinical conditions as recorded in the EMR			
1	Independent	Risk factors	Any attribute, characteristic or exposure of an individual that increases the likelihood of developing stroke. Modifiable risk factors for stroke per AHA (2017) will include: high blood pressure, smoking, diabetes, high cholesterol, physical inactivity and	Nominal (Categorical) Each stroke risk factor will be clustered and treated as Nominal (Categorical) variables High blood pressure = 1 Smoking = 2 Diabetes = 3 High cholesterol = 4 Physical inactivity = 5 Obesity = 6 Carotid or other artery disease = 7 Transient ischemic attack = 8

Table 4. cont.

	Variable Category	Variable Name	Operational Definition	Value and Code
	Clinical conditions as recorded in the EMR			
				Atrial fibrillation or other heart disease = 9 Certain blood disorders = 10 Excessive alcohol intake = 11 Illegal drug use = 12 Sleep apnea = 13 Prior stroke = 14
2	Independent	Comorbid conditions	Clinical conditions that exist before admission, are not related to the principal reason for hospitalization, and are likely to be significant factors influencing mortality and resource use. The Charlson Comorbidity Index Categories and the Associated ICD Codes will be used to cluster comorbid conditions (Lix et al., 2016)	Nominal (Categorical) Each comorbid condition will be clustered and treated as Nominal (Categorical) variables Myocardial Infarction = 1 Congestive Heart Failure = 2 Peripheral Vascular Disease =3 Cerebrovascular Disease = 4 Dementia = 5 Chronic Pulmonary Disease = 6 Connective Tissue Disease-Rheumatic Disease = 7 Peptic Ulcer Disease = 8 Mild Liver Disease = 9 Diabetes without Chronic Complications = 10 Diabetes with Chronic Complications = 11 Paraplegia and Hemiplegia = 12 Renal Disease = 13 Cancer = 14 Moderate or Severe Liver Disease = 15 Metastatic Carcinoma = 16 HIV/AIDS =17
3	Independent	Primary medical diagnoses	Primary medical diagnosis will be obtained from International Classification of Diseases ICD codes and will grouped according to diseases and disorders of each body system guided by ICD and Charlson Comorbidity Index Categories (Lix et al., 2016)	Nominal (Categorical) Each primary medical diagnosis will be clustered and treated as Nominal(Categorical) variables Diseases and Disorders of the Nervous System = 1 Diseases and Disorders of the Ear, Nose, Mouth And Throat = 2 Diseases and Disorders of the Respiratory System = 3 Diseases and Disorders of the Circulatory System = 4

Table 4. cont.

	Variable Category	Variable Name	Operational Definition	Value and Code
	Clinical conditions as recorded in the EMR			
				Diseases and Disorders of the Digestive System = 5 Diseases and Disorders of the Musculoskeletal System And Connective Tissue =6 Diseases and Disorders of the Endocrine, Nutritional And Metabolic System = 7 Diseases and Disorders of the Kidney And Urinary Tract = 8 Diseases and Disorders of the Female Reproductive System = 9 Diseases and Disorders of the Blood and Blood Forming Organs and Immunological Disorders = 10 Infectious and Parasitic DDs = 11 Factors Influencing Health Status and Other Contacts with Health Services =12
4	Independent	Common Stroke Symptoms	Common stroke symptoms will be defined as: (sudden) (a) numbness or weakness of face, arm or leg, especially on one side of the body; (b) confusion, trouble speaking, or understanding; (c) trouble seeing in one or both eyes; (d) trouble walking, dizziness, loss of balance or coordination; (e) severe headache with no known cause (National Stroke Association, 2018).	Dichotomous Each common stroke symptom will be treated as a dichotomous variable No common stroke symptoms are present at time of admission = 0 Yes common stroke symptoms are present at time of admission = 1
5	Independent	Unique Stroke Symptoms	Unique symptoms of stroke will be defined as symptoms that are new or different from common stroke symptoms (National Stroke Association, 2018).	Dichotomous Each unique stroke symptom will be treated as a dichotomous variable No unique stroke symptoms are present at time of admission = 0 Yes unique stroke symptoms are present at time of admission = 1

Table 4. cont.

	Variable Category	Variable Name	Operational Definition	Value and Code
	Context of Care			
1	Independent	Last known well	The time that the patient was last known well (without stroke symptoms)	Dichotomous No, last known well was documented during hospitalization = 0 Yes, last known well was documented during hospitalization = 1
2	Independent	Emergency Severity Index	A five-level ED triage algorithm with 1 (most urgent) to 5 (least urgent)	Ordinal (Integral) Most urgent = 1 Emergent = 2 Urgent = 3 Less urgent = 4 Nonurgent = 5
3	Independent	Diagnostic imaging	Computed tomographic scan (CT) or magnetic resonance imaging (MRI) completed within 45 minutes of last known well	Dichotomous No CT or MRI scan completed or the CT was not within 45 minutes of last known well = 0 Yes CT or MRI scan completed within 45 minutes of last known well = 1
4	Independent	Number of units	The patient resided during hospitalization - The sum of the number of units on which treatment was provided to an individual patient during the course of the hospital visit	Ordinal (Integral) 1 unit = 1 2 units = 2 3 units = 3 4 units = 4 >5 units = 5
5	Independent	Unit stroke alert occurred	Hospital units will be classified as critical care, non-critical, surgical or emergency	Nominal (Categorical) Critical care =1 Non-critical = 2 Surgical = 3 Emergency =4
6	Independent	Average nurse patient ratio	The number of patients cared for by one nurse per shift; this ratio will be expressed as the staffing assignment for RN FTE/patient or patients/RN FTE per shift for each hospital unit: critical care, non-critical, surgical and emergency	Ordinal (Integral) 1 patient= 1 2 patients = 2 3 patients = 3 4 patients = 4 5 patients = 5 6 patients = 6

Table 4. cont.

	Variable Category	**Variable Name**	**Operational Definition**	**Value and Code**
	Context of Care			
7	Independent	Diagnostic imaging delay time	The time from when the patient was last known well (without stroke symptoms) to time of computed tomographic scan or magnetic resonance imaging	Continuous Measured in hours
8	Independent	In-hospital stroke alert delay time	The time from when the patient was last known well (without stroke symptoms) to time the stroke alert - response team is activated	Continuous Measured in hours
	Outcome as recorded in the EMR			
1	Primary Dependent	Thrombolytic therapy	Thrombolytic therapy was administered during hospital stay	Dichotomous No IV thrombolytic therapy given = 0 Yes IV thrombolytic therapy given = 1
2	Secondary Independent	Discharge status	Discharge status was classified according to the Medicare Severity Diagnosis Related Groups (Medicare Reimbursement) (CMS, 2018)	Nominal (Categorical) Discharged to home/self-care = 1 Discharged/transferred to skilled nursing facility = 2 Discharged/transferred to a long term care hospitals = 3 Discharged/transferred to intermediate care facility =4 Discharged/transferred to another type of health care institution = 5 Discharged/transferred to an inpatient rehabilitation = 6 Discharged/transferred to home care = 7 Left against medical advice or discontinued care = 8 Hospice = 9 Expired = 10

Abbreviations: EMR, Electronic Medical Record; NHISS, National Institutes of Health Stroke Scale; LKW, Last Known Well; ESI, Emergency Severity Index; ED, Emergency department; MRS, Modified Rankin Scale; ICD, International Statistical Classification of Diseases and Related Health Problems; CT, computerized tomography

Independent Variables

There were a total of 17 independent variables which included four dichotomous, three continuous, seven nominal (categorical), and three ordinal (integral) variables. The primary predictive variable of interest was in-hospital stroke alert. Patient characteristics included age, marital status, ethnicity, and admission floor. Clinical conditions included risk factors, comorbid conditions, primary diagnosis, common stroke symptoms, and unique stroke symptoms. The context of care included Last Known Well time, Emergency Severity Index, diagnostic imaging, number of units, unit stroke alert occurred, average nurse-patient ratio, diagnostic and stroke diagnosis delay time.

Procedures

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice and applicable regulatory requirements. This study was conducted in accordance with the regulations of the United States Food and Drug Administration as described in 21 CFR 50 and 56, applicable laws and IRB requirements (U.S. Department of Health & Human Services [HHS], 2016). All participant information remained strictly confidential, and no patient identifiers were used. This study was approved by the participating medical center's Institutional Review Board and the University of North Dakota Institutional Review Board prior to data collection. *See Appendix B and C for Institutional Review Boards signed approval letters.*

Data were collected retrospectively, de-identified and coded by the dedicated medical center's informatics specialist. No personal protected health information was collected. No procedure, drug or therapy was applied to the participants. The de-identified coded hospital medical record data was transferred electronically from the medical center's informatics to the primary investigator's password protected personal computer in Microsoft Excel format using a secure system. The primary and co-investigators did not have access to participant personal identifying information at any time during the study. The coding key is maintained within the medical center's informatics specialist's password protected, locked secure excel spreadsheet and medical center computer. Data was then transferred by the principal investigator to a Statistical Package for the Social Science software, version 25 for further formatting, cleaning, merging, matching and analysis (Pallant, 2011). Variables, such as calculated times were transferred into Statistical Package for the Social Science software as appropriate.

Analysis

Steps in the analysis were conducted by the principal investigator under the guidance of the advisory committee members from the University of North Dakota, which included a biostatistician with experience and expertise in propensity score methods. The database was downloaded and constructed as described in procedures of this chapter. The overall purpose of this retrospective observational study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition. The primary outcome was whether the stroke patient received thrombolytic therapy or not. The secondary outcome included discharge status. Confounding variables were included to determine their effect on both the primary outcome of thrombolytic therapy and the treatment, in-hospital stroke alert.

As described in study measures, the following variables within the Excel spreadsheet had to be further formatted for Statistical Package for the Social Science software entry: The in-hospital stroke alert variables (n = 21) were combined with the rapid response variables (n = 25) and coded dichotomously to fit research model and regression analysis; primary diagnosis variables for propensity score matching were grouped according to diseases and disorders of each body system; discharge status was classified according to the Medicare Severity Diagnosis

Groups (CMS, 2018); stroke risk factors were coded according to the Modifiable risk factors for stroke per American Heart Association (2017) and further coded dichotomously for propensity score matching and regression analysis; comorbid conditions were categorized according to the Charlson Comorbidity Index Categories and further coded dichotomously for propensity score matching and regression analysis; Last Known Well was coded dichotomously and measured in hours; thrombolytic therapy was coded dichotomously; common and unique stroke symptoms were dichotomously coded according to documented admission status; diagnostics delay time was calculated by subtracting the time of computed tomographic scan or magnetic resonance imaging from the documented Last Known Well (without stroke symptoms) time; and stroke alert delay time was calculated by subtracting the time of stroke alert from the documented Last Known Well (without stroke symptoms) time. The outcome variables were further coded dichotomously for propensity score matching .

To realize the specific aims, the plans for analysis are described as follows:

Aim 1. Determine the frequency of receiving thrombolytic therapy in women who have in-hospital stroke alert during hospitalization for a separate condition. The analysis approach to achieve aim one was descriptive and involved examining frequencies and estimating propensity scores using regression models.

The first step in aim 1 was to run descriptive statistics on the main continuous variables (e.g., age, delay time). Frequencies statistics were run on the nominal (e.g., gender, ethnicity) and ordinal variables (e.g. Emergency Severity Index) (Creswell, 2013; Polit & Beck, 2016). Data were displayed per group along with the means and standard deviation results for each group, in-hospital code alert was activated during hospitalization and no in-hospital stroke alert was activated.

The second step in aim 1 and first step in estimating propensity score analysis involved assessment of the imbalance of the baseline demographics and other covariates between in-hospital stroke alert was activated and no in-hospital stroke alert was activated groups. An independent-samples t-test was completed on all covariates to assess the standardized difference (Qin et al., 2008).

The second step in the propensity score analysis was calculated by Binary Logistic regression. For this study logistic regression was completed because logistic regression model is used to predict the probability that an event occurs (Heinze & Jüni, 2011; Polit & Beck, 2016). Logistic regression can transform the probability of an event into its odds, the ratio of the probability of an event occurring to the probability of the event not occurring (Heinze & Jüni, 2011; Polit & Beck, 2016). Therefore logistic regression was the best fit for achieving this studies aim 1; determine the frequency of women receiving thrombolytic therapy after receiving in-hospital stroke alert during hospitalization for a separate condition (Heinze & Jüni, 2011; Polit & Beck, 2016).

The following assumptions for logistic regression were followed:

> ***Design***. <u>Assumption #1</u>: You have one dependent variable that is dichotomous. The dependent variable for this study was thrombolytic therapy which was dichotomously measured as yes (1) or no (0) the patient did not receive thrombolytic therapy. Contraindications to thrombolytic therapy were reviewed and discussed for patients who did not receive thrombolytic therapy.
>
> <u>Assumption #2</u>: You have one or more independent variables that are measured on either a continuous or nominal scale, ordinal level, it can still be entered in a binomial logistic regression, but it must be treated as either a continuous or nominal variable. 17 independent variables at the continuous, nominal and ordinal level were measured. Two of the independent variables, Emergency Severity Index and number of hospital units, measured at the ordinal integral level were transformed and treated at the nominal level for entry into the binomial logistic regression.
>
> <u>Assumption #3</u>: You should have an independence of observations, and the categories of the dichotomous dependent variable and all your nominal independent variables should be mutually exclusive and exhaustive. There was no relationship between the observations in each category of the dependent variable. Women were either "yes" or

“no” placed into the dependent dichotomous variable of thrombolytic therapy, they did not have both. There was no relationship between the observations in each category of the nominal independent variables and no relationship between the categories. Each nominal variable category covered all potential groups. The Durbin-Watson statistic of .324 indicated that there might be correlated errors meaning linear regression is not a suitable method of analysis. However, the test for analysis is logistic regression and independence of observations is largely a study design issue rather than something you can test for using Statistical Package for the Social Science software (Creswell, 2013; Polit & Beck, 2016; Tabachnick & Fidell, 2014). Therefore, each variable was reassessed for independence of observations and the decision was made that each variable was independent and was left within the study.

<u>Assumption #4</u>: You should have a bare minimum of 15 cases per independent variable. Every independent variable included into the regression model had a minimum of 46 cases.

Data. <u>Assumption #5:</u> There needs to be a linear relationship between the continuous independent variables and the logit transformation of the dependent variable (Box & Tidwell, 1962). Linearity of the continuous variable of age with respect to the logit of the dependent variable was assessed via the Box and Tidwell (1962) procedure. A Bonferroni correction was applied using all four terms in the model resulting in statistical significance being accepted when $p < .0125$ (Tabachnick & Fidell, 2014). Based on this assessment, the continuous independent variable ($p > .036$) was found to be linearly related to the logit of the dependent variable, thrombolytic therapy.

<u>Assumption #6</u>: Your data must not show multicollinearity. (Correlation coefficients and Tolerance/VIF values). Logistic regression procedures for categorical dependent variables do not have collinearity diagnostics. Therefore, the linear regression procedure was completed to check for multicollinearity. Dummy variables were manually created for all categorical independent variables in Statistical Package for the Social Science software in order to correctly run the linear regression procedure. Collinearity statistics in regression analysis concerns the relationships among the predictors, ignoring the dependent variable. Therefore, the dependent variable was not dummy coded. Results of correlation coefficients indicated that all the Tolerance values were much greater than 0.1 with only 2 variables slightly over 0.1 (the lowest range is 0.107 to 0.163). The VIF values were much less than 10 for most variables. However, 3 variables were found to be between the 5 to 10 (range 5.45 to 9.35). Therefore, I was fairly confident that there is no problem with collinearity in this particular data set.

<u>Assumption #7:</u> There should be no significant outliers, high leverage points or highly influential points (casewise diagnostics) (Creswell, 2013; Polit & Beck, 2016; Tabachnick & Fidell, 2014). There was three standardized residuals with values of 2.619, 2.719 and 3.470 standard deviations. Each case was manually inspected and no case was determined to be unusual. Casewise diagnostics was completed on a split file In-hospital Stroke Alert = In-hospital stroke alert was activated during hospitalization, and the casewise plot was not produced because no outliers were found. Therefore, the decision was made to keep each case in the analysis with consideration that further analysis was completed on a split file, matched groups. In addition, homoscedasticity was inspected to assess the variance of the errors (residuals). There was

homoscedasticity, as assessed by visual inspection of a plot of standardized residuals versus standardized predicted values. Furthermore, residuals were normally distributed as assessed by visual inspection of a normal probability plot.

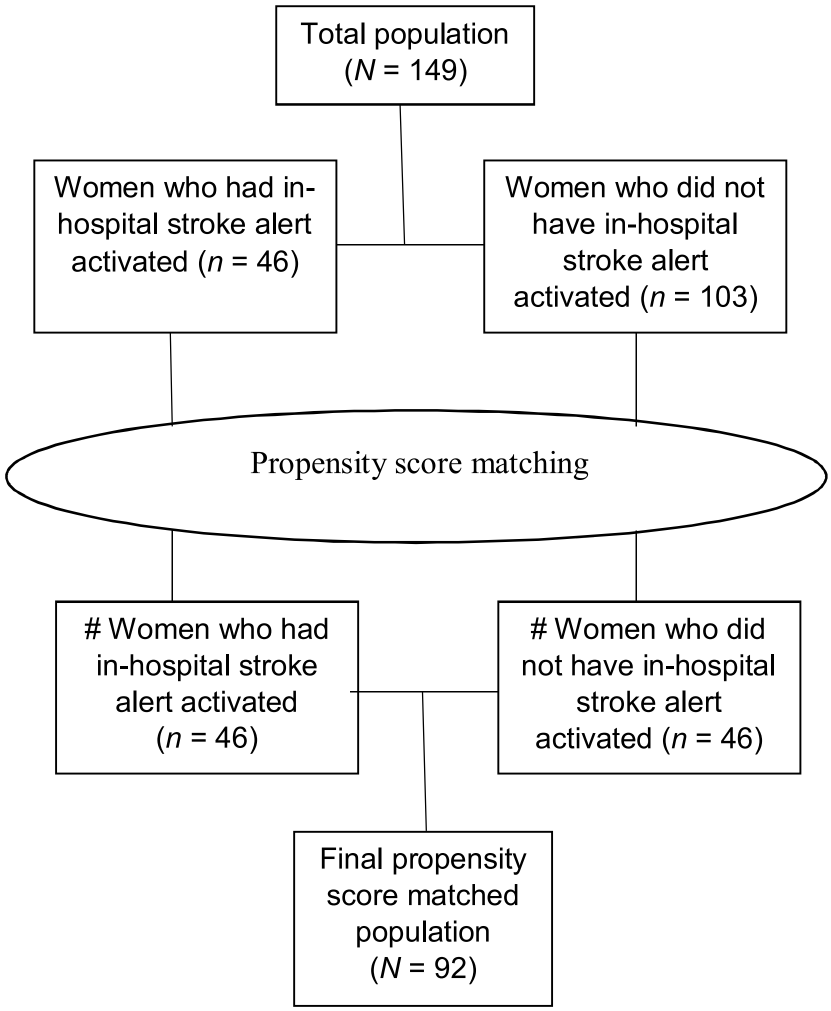
The third step in the propensity score analysis was to estimate propensity scores using logistic regression. In the propensity score model, the dichotomous treatment is treated as a dependent variable, where the observed covariates are considered to be predictors (Qin et al., 2008). Therefore, the independent treatment variable, in-hospital stroke alert was treated as the dichotomous dependent variable coded as 1 to represent that yes a stroke alert was activated, and 0 to represent that no in-hospital stroke alert was activated. Predictor variables included the 17 confounding variables (patient characteristics, clinical conditions and context of care) that are conceptually related to in-hospital stroke alert and thrombolytic therapy, as mentioned in procedures (Creswell, 2013; Polit & Beck, 2016; Tabachnick & Fidell, 2014). *A complete list of variable operational definitions and coding is presented in table 4.*

Lastly, a propensity score ranging from 0-1 was assigned to each case based on the probability that each subject received the treatment (in-hospital stroke alert). A propensity score is a conditional probability of receiving treatment and thus always has a value between 0 and 1 (Heinze & Jüni, 2011). The larger a propensity score, the more likely a patient was to receive the specified treatment (Heinze & Jüni, 2011). A key assumption of a propensity score is that participation is independent of outcomes conditional on Xi; this is false if there are unobserved outcomes affecting participation (Creswell, 2013; Heinze & Jüni, 2011; Polit & Beck, 2016; Tabachnick & Fidell, 2014). Therefore, for this study the probability that a patient received the treatment (in-hospital stroke alert) was identified as the propensity score closest to 1 and patients less likely to have the treatment (in-hospital stroke alert) were identified as a propensity score closest to 0. A population pyramid histogram was used to assess the distribution of propensity scores by treatment group, in-hospital stroke alert and no in-hospital stroke alert. When an overlap in the distribution of propensity scores exists it is possible to match groups. *See Chapter Four for figure and results.*

Aim 2. Match women who receive an in-hospital stroke alert activation to women with no in-hospital stroke alert. The analysis approach to achieve aim 2 included propensity score matching using the estimated propensity scores from aim 1 and 1:1 nearest neighbor matching Statistical Package for the Social Science software Propensity Score Matching to match participants and identify a successful distribution of variables over the treated (in-hospital stroke alert) to untreated (no in-hospital stroke alert) groups. *(Figure 3)* Matching entails that a single treated participant is matched to a single untreated participant who has the most similar estimated propensity score (Heinze & Jüni, 2011). The further away the closest 1:1 nearest neighbor is the higher the risk of bad matches in propensity score matching. Matching success and to ensure successful distribution, computing standardized differences of a caliper (maximum allowable difference between two participants) of less than .5 should be applied to matches (in a sense that the estimated propensity score from two matched units are very different from each other). Tolerance (caliper) matching means that the patients from the comparison group is chosen as a matching partner for a treated patient that lies within the caliper and closest in propensity score (Heinze & Jüni, 2011). For this study, the tolerance (caliper) was set to 0.5. However, following the first conditional (multinomial) logistic regression to evaluate the treatment (in-hospital stroke alert) effect on the primary outcome (thrombolytic therapy) with the reduction of confounding bias due to propensity score matching , no significance was reached. After adjusting the tolerance (caliper) to 0.10, significance was reached. However, the number of successful matches was also reduced. Therefore, the set tolerance (caliper) for this studies propensity score matching was 0.3 to avoid imposing a tolerance level on the maximum propensity score distance (caliper), to avoid bad matches and raise the quality of matching and significance.

Pseudo R^2 in logistic regression was completed to assess the balance of the 2 groups on baseline factors. Pseudo R^2 is a measure of predictive value of a logistic regression model, a reduction in pseudo R^2 from the propensity score match model in the raw data compared to the same model in the propensity score matched data means that the baseline factors are no longer predictive for determining treatment, in-hospital stroke alert group, as desired. A McFadden's pseudo R-squared ranging from 0.2 to 0.4 indicates a very good model fit (Staffa & Zurakowski, 2018). *See Chapter Four for the study results and respective tables and figures.*

Figure 3. Flowchart of Propensity Score Matching



Aim 3. Compare the effects and associated variables of an in-hospital stroke alert activation to no in-hospital stroke alert on outcomes in women admitted to the hospital for a separate condition. The analysis approach to achieve aim 3 included frequencies statistics and conditional logistic regression models.

The first step in aim 3 was to run descriptive statistics on the main continuous variables (e.g., age, delay time). Frequencies statistics were run on the nominal (e.g., gender, ethnicity) and ordinal variables (e.g. Emergency Severity Index) (Creswell, 2013; Polit & Beck, 2016). They are displayed per propensity score matched group with the means and standard deviation results.

The second step in aim 3 was to run a conditional logistic regression (NOMREG) on the new propensity score matched sample to evaluate a treatment effect with the reduction of confounding bias and determine whether any difference in any difference in effects (e.g., thrombolytic therapy, delay time) exist between the two related groups (women who have experienced a stroke who have in-hospital stroke alert activated to women who do not have in-hospital stroke alert activated). Conditional logistic regression model was needed to take into account the matched pairs created during propensity score matching. Conditional logistic regression allows the investigator to specify a group as being the matched pair from the propensity score matching (Heinze & Jüni, 2011; Polit & Beck, 2016). Conditional logistic regression provides estimates of regression coefficients associated with independent covariates variables that vary within and/or do not vary within at least one strata (Staffa & Zurakowski, 2018). Variables were statistically significant when $p < .05$. (Creswell, 2013; Polit & Beck, 2016). Therefore conditional logistic regression was the best fit for achieving this studies aim 3; compare the effects and associated variables of an in-hospital stroke alert activation to no in-hospital stroke alert on outcomes in women admitted to the hospital for a separate condition (Heinze & Jüni, 2011; Polit & Beck, 2016).

Assumptions for conditional logistic regression (NOMREG) were followed:

> ***Design.*** Assumption #1: There must be a 1:1 match where each case or observation with some condition is paired with one or several controls, observation, or risk factors (Staffa & Zurakowski, 2018). A propensity score matching was completed and a 1:1 successful match was achieved. *See Chapter Four for aim 2 results.*
>
> Assumption #2: The dependent variable must be constant, have only one level (Staffa & Zurakowski, 2018). The primary dependent variable for this study was thrombolytic therapy which was dichotomously measured as yes (1) or no (0) the patient did not receive thrombolytic therapy. The secondary dependent variable of discharge status was nominal (categorical) measured. To obtain constant dependent variables, discharge status was dummy coded and then each were transformed to the target variable and given one numeric expression.
>
> Assumption #3: Factors cannot enter the model. Variables have to be treated at the dichotomous level (Staffa & Zurakowski, 2018). Each continuous (age), and nominal, ordinal (marital status, ethnicity, admission floor, risk factors, comorbid conditions, primary medical diagnosis, Emergency Severity Index , number of units) were dummy coded to the appropriate level.
>
> Assumption #4: You should have an independence of observations, and the categories of the dichotomous dependent variable and all independent variables should be mutually exclusive and exhaustive(Staffa & Zurakowski, 2018). There was no relationship between the observations in each category of the dependent variable. Women were either "yes" or "no" placed into the dependent dichotomous variable of thrombolytic therapy, they did not have both. There was no relationship between the observations in each category of the nominal independent variables and no relationship between the categories. Each nominal variable category covered all potential groups. There was independence of residuals, as assessed by a Durbin-Watson statistic of 2.155.
>
> Assumption #5: The difference between each case and corresponding control must be constructed and this difference must be utilized as a covariate (Staffa & Zurakowski, 2018). More than one difference variable can be used. Each variable was transformed into difference variables by computing case (e.g. in-hospital stroke alert) – control (e.g. ethnicity).
>
> ***Data.*** Assumption #6: There must be no intercept within the model (Staffa & Zurakowski, 2018). During analysis the intercept was removed from the model. Success was obtained "The dependent variable has only one valid value. A conditional logistic regression model will be fitted."
>
> Assumption #7: Multicollinearity. (Correlation coefficients and Tolerance/VIF values). Multinomial conditional logistic regression procedures for categorical dependent variables do not have collinearity diagnostics. Therefore, the linear regression procedure was completed to check for multicollinearity. Utilizing the dummy variables that were

manually created for all categorical independent variables in Statistical Package for the Social Science software in order to correctly run the linear regression procedure. Collinearity statistics in regression analysis concerns the relationships among the predictors, ignoring the dependent variable. Therefore, the dependent variable was not dummy coded. Results of correlation coefficients indicated that all the Tolerance values for all variables, except 3, were much greater than 0.1 with only 2 variables slightly over 0.1 (the lowest range is 0.193 to 0.198). VIF values were much less than 10 for most variables except 3. However, conditional logistic regression refers to applying the logistic model to each of the stata individually (Staffa & Zurakowski, 2018). Therefore, after re-running correlation and Tolerance/VIF values for each variable individually, I was fairly confident that there was no problem with collinearity in this propensity score matching data set.

Assumption #8: There should be no significant outliers, high leverage points or highly influential points (Casewise diagnostics) (Creswell, 2013; Polit & Beck, 2016; Tabachnick & Fidell, 2014; Staffa & Zurakowski, 2018). There was two standardized residuals with values of 3.912, and 3.451 standard deviations. Each case was manually inspected and no case was determined to be unusual. Homoscedasticity was inspected to assess the variance of the errors (residuals). There was homoscedasticity, as assessed by visual inspection of a plot of standardized residuals versus standardized predicted values. Furthermore, residuals were normally distributed as assessed by visual inspection of a normal probability plot. *See Chapter Four for table and results*

Summary

The purpose of this descriptive quantitative study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition. The retrospective, descriptive propensity score with regression model design allowed for the examination of the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition.

CHAPTER IV

RESULTS

The purpose of this study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition. Specific Aims to address this purpose were to:

Aim 1 Determine the frequency of women receiving thrombolytic therapy after receiving in-hospital stroke alert during hospitalization for a separate condition.

Aim 2 Match women who receive an in-hospital stroke alert activation to women with no in-hospital stroke alert.

Aim 3 Compare the effects and associated variables of an in-hospital stroke alert activation to no in-hospital stroke alert on outcomes in women admitted to the hospital for a separate condition. This chapter provides an overview of the participants demographic characteristics and then identifies and describes the results related to the frequencies of in-hospital stroke alert, the likelihood of in-hospital stroke alert and finally the effect of in-hospital stroke alert.

Sample Demographics and Characteristics

A total of 149 adult women were selected based on inclusion and exclusion criteria. Detailed information regarding sampling is provided in chapter three.

Demographics of In-hospital Stroke Alert Participants

This section describes demographic characteristics of the women who had an in-hospital stroke alert activated during hospitalization. Table 5 displays the demographic characteristics of the women who had an in-hospital stroke alert activated (*n* = 46). The participants ranged from 46 and 89 years of age, mean 72.24 years. Almost half of this group of women were widowed (45.7%) and the vast majority (93.5%) were Caucasian, with the African American (2.2%), Alaskan Native (2.2%), and Middle Eastern American (2.2) ethnic groups being equal. Among the 46 participants within this group, half (50.0%) were admitted from the emergency floor for another condition, not ischemic stroke.

Table 5. Demographics of Women who had In-hospital Stroke Alert Activated (*n* = 46)

Variables	**Range/ Frequencies**	**Mean**	**SD**	**Percentage (%)**
Age				
Minimum	46	72.24	12.27	
Maximum	89			
Marital status				
Married	15	2.13	0.88	32.6
Separated/divorced or single	10			21.7
Widowed	21			45.7
Ethnicity				
Caucasian	43	1.20	0.86	93.5
African American	1			2.2
Native American	0			0
Alaskan Native	1			2.2
Pacific Islander	0			0
Middle Eastern American	1			2.2
Admission floor				
Critical care	11	2.87	1.28	23.9
Non-critical	7			15.2
Surgical	5			10.9
Emergency	23			50.0

Demographics of No In-hospital Stroke Alert Participants

This section describes demographic characteristics of the no in-hospital stroke alert was activated during hospitalization group. Table 6 displays the demographic characteristics of the women with no in-hospital stroke alert *(n* = 103). These women ranged from 18 to 88 years of age, with a mean age of 67.54 years. Almost half of the women were married (41.7%) and the vast majority (90.3%) were Caucasian, with the second highest ethnic group being African American (4.9%) and then Alaskan Native (3.9%) as the third highest ethnic group. Among the 103 women participants within this group, over half (56.3%) were admitted from the emergency floor for another condition, not ischemic stroke.

Table 6. Demographics of Women with no In-hospital Stroke Alert (*n* = 103)

Variables	Range/ Frequencies	Mean	SD	Percentage (%)
Age				
Minimum	18	67.54	14.55	
Maximum	88			
Marital status				
Married	43	1.90	0.86	41.7
Separated/divorced or single	27			26.2
Widowed	33			32.0
Ethnicity				
Caucasian	93	1.18	0.64	90.3
African American	5			4.9
Native American	1			1.0
Alaskan Native	4			3.9
Pacific Islander	0			0
Middle Eastern American	0			0
Admission floor				
Critical care	11	3.18	1.06	10.7
Non-critical	17			16.5
Surgical	17			16.5
Emergency	58			56.3

Sample Characteristics

Stroke patients often present with stroke risk factors and comorbid or coexisting conditions that influence stroke risk and outcomes. Stroke risk factors included modifiable risk factors for stroke per American Heart Association (ASA, 2019a). Comorbid conditions were selected and categorized based on the Charlson Comorbidity Index. Stroke risk factors and comorbid conditions were multiple response variables, in which each individual could have more than one stroke risk factor and/or more than one comorbid conditions. Therefore, risk factors and comorbid conditions were grouped for analysis. This first section of the sample characteristics describes sample characteristics of the in-hospital stroke alert was activated during hospitalization group. Table 7 displays the grouped risk factor characteristics of the women with in-hospital stroke alert activated (*n* = 46). Of this in-hospital stroke alert was activated group of women over three-quarters had the risk factor of high blood pressure (80%) and over half had atrial fibrillation or other heart disease (68.9). High cholesterol was present in 55.6%, diabetes and carotid or other artery disease was present in 48.9% of the sample. Slightly more than a quarter were obese (26.7%). Less than eight (17.8%) were smokers, only 6 (13.3) had sleep apnea, 5 (11.1%) had a prior transient ischemic attack, 3 (6.7%) had illegal drug use, and 2 (4.4%) had a prior stroke. None of the women in this group had the risk factors of physical inactivity, certain blood disorders, or excessive alcohol intake. Of this group of women (*n* = 46), 97.8% had at least one or more stroke risk factor. Only one (2.2%) had no stroke risk factors documented.

Table 7. Demographic Stroke Risk Factors of Women with In-hospital Stroke Alert Activated (n = 46)

Variables	Total (n)	Percentage (%)	Percent (%) per Cases
High blood pressure	36	20.9	80.0
Smoking	8	4.7	17.8
Diabetes	22	12.8	48.9
High cholesterol	25	14.5	55.6
Physical inactivity	0	0	0
Obesity	12	7.0	26.7
Carotid or other artery disease	22	12.8	48.9
Transient ischemic attacks	5	2.9	11.1
Atrial fibrillation or other heart disease	31	18.0	68.9
Certain blood disorders	0	0	0
Excessive alcohol intake	0	0	0
Illegal drug use	3	1.7	6.7
Sleep apnea	6	3.5	13.3
Prior stroke	2	1.2	4.4

Table 8 displays the grouped comorbid conditions characteristics of the women with in-hospital stroke alert activated during hospitalization (n = 46). Of this in-hospital stroke alert was activated group of women almost half had the comorbid conditions of congestive heart failure (42.9%), diabetes with chronic complications (42.9%) and renal disease (42.9%). Almost a quarter had myocardial infarction (20.0%). Only 5 (14.3%) had peripheral vascular disease, chronic pulmonary disease, diabetes without complications, 4 (11.4%) had dementia, 3 (8.6%) had cerebrovascular disease, and 1 (2.9%) had connective tissue or rheumatic disease, paraplegia/hemiplegia, cancer, moderate or severe liver disease, and metastatic cancer. None of this group of women had the comorbid conditions of peptic ulcer disease, mild liver disease, human immunodeficiency virus or acquired immunodeficiency syndrome. Of this group of women (n = 46), 76.1% had at least one or more comorbid conditions. Eleven (23.9%) had no comorbid conditions documented.

Table 8. Demographic Comorbid Conditions of Women with In-hospital Stroke Alert Activated (*n* = 46)

Variables	**Total (n)**	**Percentage (%)**	**Percent (%) per Cases**
Myocardial Infarction	7	8.9	20.0
Congestive Heart Failure	15	19.0	42.9
Peripheral Vascular Disease	5	6.3	14.3
Cerebrovascular Disease	3	3.8	8.6
Dementia	4	5.1	11.4
Chronic Pulmonary Disease	5	6.3	14.3
Connective Tissue Disease-	1	1.3	2.9
Rheumatic Disease	0	0	0
Peptic Ulcer Disease	0	0	0
Mild Liver Disease	0	0	0
Diabetes without Chronic Complications	5	6.3	14.3
Diabetes with Chronic Complications	15	19.0	42.9
Paraplegia and Hemiplegia	1	1.3	2.9
Renal Disease	15	19.0	42.9
Cancer	1	1.3	2.9
Moderate or Severe Liver Disease	1	1.3	2.9
Metastatic Carcinoma	1	1.3	2.9
HIV/AIDS	0	0	0

Abbreviations: HIV/AIDS, human immunodeficiency virus, acquired immunodeficiency syndrome

Table 9 displays the risk factor characteristics of the women with no in-hospital stroke alert activated during hospitalization (*n* = 103). Nearly, three-quarters of the sample had the stroke risk factor of high blood pressure (78%) and over half of the sample had atrial fibrillation or other heart disease (62.6%) as risk factors. Diabetes was present in 37.4%, high cholesterol was present in 35.2%, and carotid or other artery disease was present in 33.0%. Slightly less than a quarter of these women were smokers (18.7%), had a prior transient ischemic attack (16.5%) and were obese (14.3%). Less than 5 (5.5%) had sleep apnea, 2 (2.2) had a prior stroke, and 1 (1.1%) had illegal drug use. None of this group of women had the risk factors of physical inactivity, certain blood disorders, or excessive alcohol intake. Of this group of women (*n* = 103), 88.3% had at least one or more stroke risk factor. Only twelve (11.7%) women had no stroke risk factors documented.

Table 9. Demographic Risk Factors of Women with No In-hospital Stroke Alert (n = 103)

Variables	Total (n)	Percentage (%)	Percent (%) per Cases
High blood pressure	71	25.6	78.0
Smoking	17	6.1	18.7
Diabetes	34	12.3	37.4
High cholesterol	32	11.6	35.2
Physical inactivity	0	0	0
Obesity	13	4.7	14.3
Carotid or other artery disease	30	10.8	33.0
Transient ischemic attacks	15	5.4	16.5
Atrial fibrillation or other heart disease	57	20.6	62.6
Certain blood disorders	0	0	0
Excessive alcohol intake	0	0	0
Illegal drug use	1	0.4	1.1
Sleep apnea	5	1.8	5.5
Prior stroke	2	0.7	2.2

Abbreviations: HIV/AIDS, human immunodeficiency virus, acquired immunodeficiency syndrome

Table 10 displays the grouped comorbid conditions characteristics of the women with no in-hospital stroke alert activated during hospitalization (n = 103). Of this no in-hospital stroke alert group of women almost half had the comorbid conditions of cerebrovascular disease (42.7%). Slightly over a quarter had renal disease (29.3%) and almost a quarter had congestive heart failure (22.0%). Fifteen (18.3%) had diabetes with chronic complications, 11 (13.4%) had myocardial infarction, 10 (12.2%) had peripheral vascular disease, 7 (8.5%) had diabetes without complications, 5 (6.1%) had chronic pulmonary disease, 5 (6.1%) had cancer, 4 (11.4%) had dementia, 2 (2.4%) had moderate or severe liver disease, and 1 (1.2%) had connective tissue or rheumatic disease, mild liver disease, and metastatic cancer. None of this group of women had the comorbid conditions of peptic ulcer disease, human immunodeficiency virus or acquired immunodeficiency syndrome. Of this group of women (n = 103), 79.6% had at least one or more comorbid conditions. Twenty-one (20.4%) women had no comorbid conditions documented.

Table 10. Demographic Comorbid Conditions of Women with No In-hospital Stroke Alert (n = 103)

Variables	Total (n)	Percentage (%)	Percent (%) per Cases
Myocardial Infarction	11	7.7	13.4
Congestive Heart Failure	18	12.6	22.0
Peripheral Vascular Disease	10	7.0	12.2
Cerebrovascular Disease	35	24.5	42.7
Dementia	4	2.8	4.9
Chronic Pulmonary Disease	5	3.5	6.1
Connective Tissue Disease-Rheumatic Disease	1	0.7	1.2
Peptic Ulcer Disease	0	0	0
Mild Liver Disease	1	0.7	1.2
Diabetes without Chronic Complications	7	4.9	8.5
Diabetes with Chronic Complications	15	10.5	18.3
Paraplegia and Hemiplegia	4	2.8	4.9
Renal Disease	24	16.8	29.3
Cancer	5	3.5	6.1
Moderate or Severe Liver Disease	2	1.4	2.4
Metastatic Carcinoma	1	0.7	1.2
HIV/AIDS	0	0	0

Abbreviations: HIV/AIDS, human immunodeficiency virus, acquired immunodeficiency syndrome

The second section of this chapter describes findings related specifically to aim 1: **Determine the frequency of women receiving thrombolytic therapy after receiving in-hospital stroke alert during hospitalization for a separate condition.** Frequencies, independent samples t-test and logistic regression models with distributions were used in the analysis for aim 1. Frequencies statistics assessed the entire group of participants with in-hospital stroke, the participants with in-hospital stroke alert activated and participants with no in-hospital stroke alert baseline relationship between variables and outcomes.

A preliminary analysis before propensity score matching showed that 46 of 149 women had an in-hospital stroke alert activated (mean .309) and 15 women (mean .100) received thrombolytic therapy. The participants ages ranged from 18 to 89 years of age (mean 69.2). Of the 149 women, 38.9% were married, 36.2 widowed, and 24.8% were either separated, divorced, or single. Majority of the group of women were Caucasian (91.3%) and only 8.7% were from other ethnicity groups. Of the 149 women, 55.4% (n = 81) were admitted from the emergency room, 91.3% had stroke risk factors, 78.5% had comorbid conditions and over half (55.7%) had a cardiovascular disease or disorder as their primary medical diagnosis. Only 24.2% had common stroke symptoms and 28.9% had unique stroke symptoms. In addition, only 32.2% had a Time Last Known Well documented, 51% had an Emergency Severity Index documented with 42 of these women classified as emergent, 26 as urgent, and 8 as most urgent. Of the 149 women, 41.6% or 62 women were on a total of 2 hospital units, 35.6% or 53 women were on 3 hospital units, 13.4% or 20 were on 1 unit, and 9.4% or 14 women were on 4 units. Of the 149 women, 141 (94.6%) women did not have a computed tomographic scan or magnetic resonance imaging completed at all or within the 45 minutes of Time Last Known Well. Outcomes included only 15 (10.1%) of the 149 women received thrombolytic therapy, 37 (24.8%) were discharged to a skilled nursing facility, 23 (15.4%) to home, 22 (14.8%) to home care, 21 (14.1%) to an inpatient rehabilitation, 18 (12.1%) to long term care, 14 (9.4%) expired, 10 (6.7%) to hospice, 3 (2.0%) transferred to another hospital and 1 (0.7%) woman went to intermediate care. *Please see table 11 for the baseline sample frequencies. Please see figure 4 for the baseline sample age frequencies.*

Table 11. Frequencies of Women Before Propensity Score Matching (N = 149)

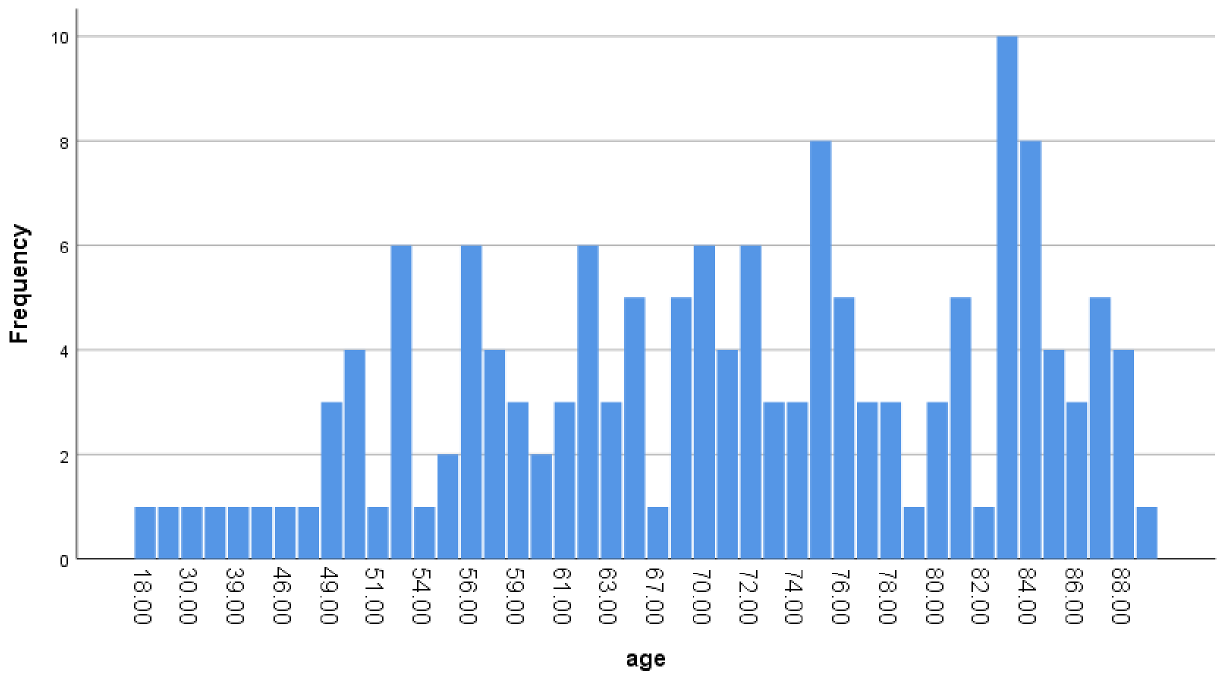
Analysis	**Frequency**		**Percent**		**Mean**	**SD**
In-hospital stroke alert = Yes	46	103	30.9	69.1	.309	.046
Patient Characteristics						
Age					69.2	.870
18-39	5		3.5			
40-49	6		4.1			
50-59	27		18.1			
60-69	25		16.8			
70-79	42		28.2			
80-89	44		29.3			
Marital status					1.97	.870
Married	58		38.9			
Separated/divorced/single	37		24.8			
Widowed	54		36.2			
Ethnicity					1.19	.711
Caucasian	136		91.3			
Other	13		8.7			
Admission floor					3.09	1.14
Critical care	22		14.8			
Non-critical	24		16.1			
Surgical	22		14.8			
Emergency	81		54.4			
Clinical Conditions						
Risk factors = Yes	136	13	91.3	8.7	.912	.283
Comorbid conditions = Yes	117	32	78.5	21.5	.790	.412
Primary medical diagnosis = Other; cardiovascular	66	83	44.3	55.7	4.58	3.22
Common stroke symptoms = Yes	36	113	24.2	75.8	.242	.430
Unique stroke symptoms = Yes	43	106	28.9	71.1	.290	.454
Context of Care						
Last Known Well = Yes	48	101	32.2	67.8	.322	.469
ESI = Yes	76	73	51.0	49.0	2.24	.630
Most urgent	8		5.4			
Emergent	42		28.2			
Urgent	26		17.4			
Number of units						
1	20		13.4		2.41	.838
2	62		41.6			
3	53		35.6			
4	14		9.4			
>5	0		0			
Diagnostic imaging = Yes	8	141	5.4	94.6	.053	.226
Outcome						
Thrombolytic therapy = Yes	15	134	10.1	89.9	.100	.30

Table 11. cont.

Analysis	**Frequency**	**Percent**	**Mean**	**SD**
Discharge status			4.56	3.04
Home/self-care	23	15.4		
SNF	37	24.8		
Long term care	18	12.1		
Intermediate care	1	.7		
Another hospital	3	2.0		
IP rehab	21	14.1		
Home care	22	14.8		
Hospice	10	6.7		
Expired	14	9.4		

Abbreviations: ESI, Emergency Severity Index; SNF, skilled nursing facility; IP, inpatient

Figure 4. Demographic Age Frequencies of Women Before Propensity Score Matching (*N* = 149)



In this second frequencies section, the preliminary, before propensity score matching, analysis for the in-hospital stroke alert was activated group of women (*n* = 46) showed that age ranged from 40 to 89 years of age with the majority of the group between 70 to 79 years of age (34.9%) and between 80 to 89 years of age (32.6%). Of the 46 women, 45.7% were widowed, 32.6% were married, and 21.7% were either separated, divorced, or single. Forty-three of the 46 women (93.5%) were Caucasian and 3 (6.5%) were from other ethnicity groups. Fifty percent (*n*

= 23) of the women were admitted from the emergency room. Of the 46 women, 97.8% had stroke risk factors, 76.1% had comorbid conditions and half of the group (50.0%) had a cardiovascular disease or disorder as their primary medical diagnosis. Only 7 of the 46 women (15.2%) had common stroke symptoms and 16 women (34.8%) had unique stroke symptoms in women. In addition, 43.5% had a Time Last Known Well documented and 45.7% had an Emergency Severity Index documented with 16 of these women classified as emergent, 4 as urgent, and 1 as most urgent. Of the 46 women, 39.1% or 18 women were on a total of 3 hospital units, 30.4% or 14 women were on 3 hospital units, 17.4% or 8 were on 4 units, and only 13% or 6 women were on just 1 unit. In-hospital stroke alert occurred on the critical care unit the majority of the time (n = 32; 69.6%), with the non-critical unit being second (n = 11; 23.9%), surgical (n = 2; 4.3%), and emergency room (n = 1; 2.2%). The average nurse patient ratio was 2:1 (n = 32; 69.6%), with the second average being 4:1 (n = 11; 23.9%). Only 5 (10.9%) of these women had a computed tomographic scan or magnetic resonance imaging and 41 (89.1%) of these women did not have a computed tomographic scan or magnetic resonance imaging completed at all or within the 45 minutes of Time Last Known Well. Then considering outcomes two (4.3%) women received thrombolytic therapy, 18 (39.1%) were discharged to a skilled nursing facility, 9 (19.6%) to an inpatient rehabilitation unit, 7 (15.2%) to home, 5 (10.9%) to home care, 4 (8.7%) to hospice and three (6.5%) women expired. Of the 46 women, 17.6% had an average of 1 to 2 hour delay time in diagnostics and 17.4% had an average of 1 hour delay time in in-hospital stroke alert. *Please see table 12 for the demographic frequencies of women who had an in-hospital stroke alert activated before propensity score matching. See figure 5 for the demographic age frequencies of women with in-hospital stroke alert activated before propensity score matching, See figure 6 for the demographic diagnostics delay time* *frequencies for in-hospital stroke alert before propensity score matching. See figure 7 for the demographic in-hospital stroke alert delay time frequencies when in-hospital stroke alert is activated before propensity score matching.*

Table 12. Frequencies of Women with In-hospital Stroke Alert Activated (Before Propensity Score Matching) ($N = 46$)

Analysis	Frequency		Percent	
Patient Characteristics				
Age				
18-39	0		0	
40-49	3		6.5	
50-59	6		13	
60-69	6		13	
70-79	16		34.9	
80-89	15		32.6	
Marital status				
Married	15		32.6	
Separated/divorced/single	10		21.7	
Widowed	21		45.7	
Ethnicity				
Caucasian	43		93.5	
Other	3		6.5	
Admission floor				
Critical care	11		23.9	
Non-critical	7		15.2	
Surgical	5		10.9	
Emergency	23		50.0	
Clinical Conditions				
Risk factors = Yes	45	1	97.8	2.2
Comorbid conditions = Yes	35	11	76.1	23.9
Primary medical diagnosis = Other; cardiovascular	23	23	50.0	50.0
Common stroke symptoms = Yes	7	39	15.2	84.8
Unique stroke symptoms = Yes	16	30	34.8	65.2
Context of Care				
Last Known Well = Yes	20	26	43.5	56.5
ESI = Yes ($n = 21$)	21	25	45.7	54.3
Most urgent	1		2.2	
Emergent	16		34.8	
Urgent	4		8.7	
Number of units				
1	6		13.0	
2	14		30.4	
3	18		39.1	
4	8		17.4	
>5	0		0	
Unit stroke alert occurred				
Critical care	32		69.6	
Non-critical	11		23.9	
Surgical	2		4.3	
Emergency	1		2.2	

Table 12. cont.

Analysis	**Frequency**		**Percent**	
Average nurse patient ratio	2		4.3	
1	32		69.6	
2	1		2.2	
3	11		23.9	
4				
Diagnostic imaging = Yes	5	41	10.9	89.1
Diagnostics delay time (hours) (*n* = 15)				
.10 – .99	5		11.0	
1 – 1.99	8		17.6	
17 – 22	2		4.4	
In-hospital stroke alert delay time (hours) (*n* = 15)				
.10 - .99	8		17.4	
1 – 1.99	3		6.6	
16 – 21	2		4.4	
264 - 265	2		4.4	
Outcome				
Thrombolytic therapy = Yes	2	44	4.3	95.7
Discharge status				
Home/self-care	7		15.2	
SNF	18		39.1	
IP rehab	9		19.6	
Home care	5		10.9	
Hospice	4		8.7	
Expired	3		6.5	

Abbreviations: ESI, Emergency Severity Index; PSM, propensity score matching; SNF, skilled nursing facility; IP, inpatient

Figure 5. Age Frequencies of Women with In-hospital Stroke Alert Activated (Before Propensity Score Matching) ($N = 46$)

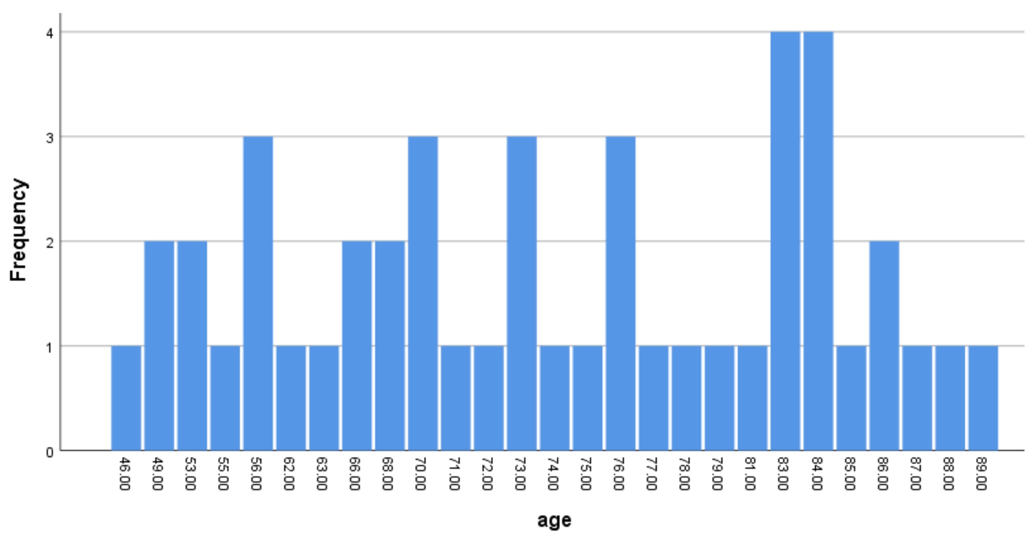
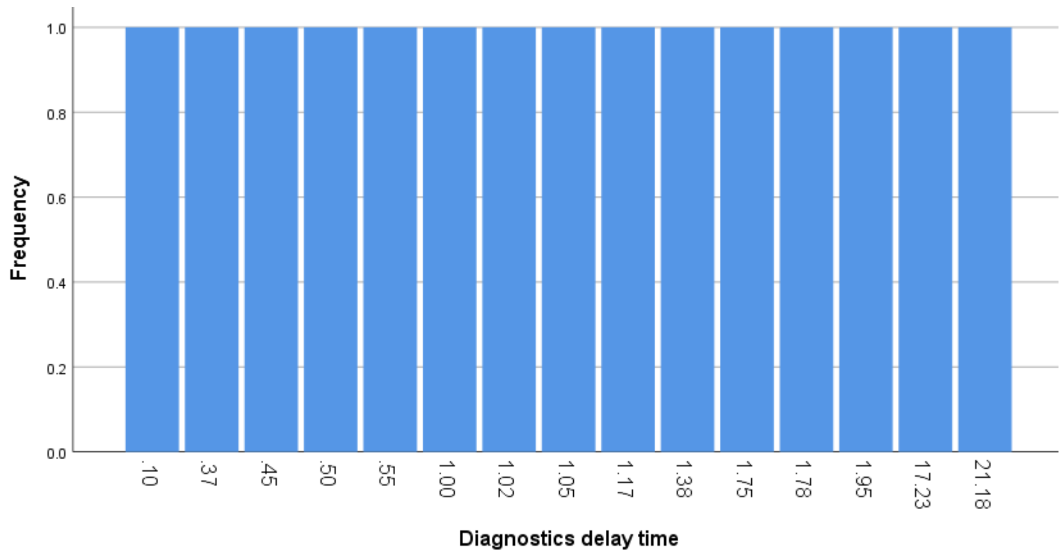
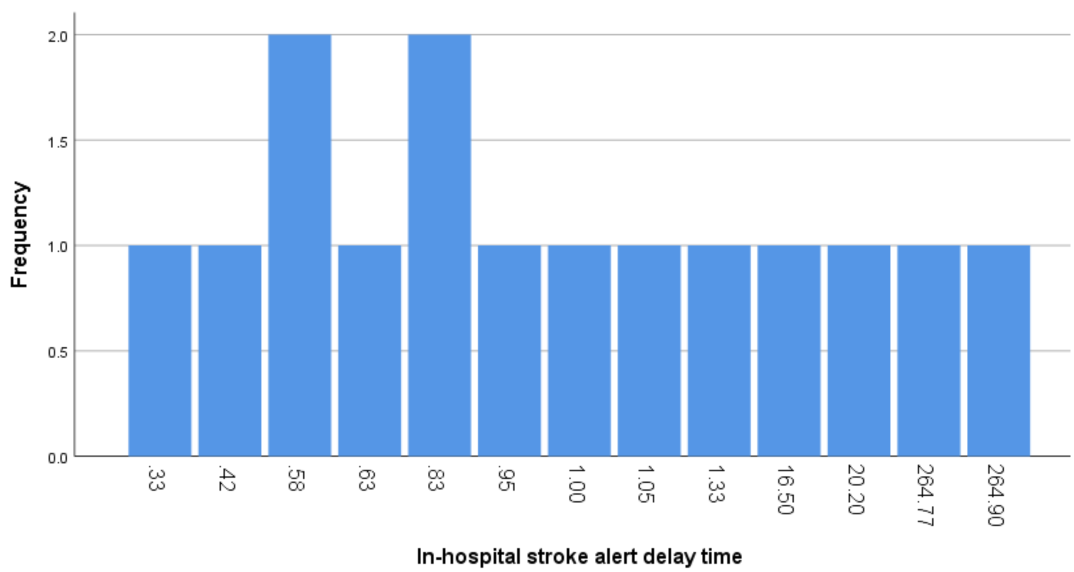


Figure 6. Diagnostics Delay Time Frequencies of Women with In-hospital Stroke Alert Activated (Before Propensity Score Matching) ($N = 46$)



Note: Time in hours

Figure 7. Demographic In-hospital Stroke Alert Delay Time Frequencies of Women with In-hospital Stroke Alert Activated (Before Propensity Score Matching) ($N = 46$)



Note: Time in hours

A t-test was completed to assess for an imbalance of the baseline demographics and other covariates between the in-hospital stroke alert activated and no in-hospital stroke alert groups. Table 13 shows the baseline comparison characteristics of women who had a stroke during hospitalization for a separate condition (N = 149). Of the 149 women who had a stroke during hospitalization, 103 of these women did not have a stroke alert activated compared to the 46 women who had an in-hospital stroke alert activated. A standardized difference greater than 10% was recognized in 6 variables when comparing baseline covariates between women with in-hospital stroke alert activated and women with no in-hospital stroke alert. Age had a 24.7 standardized difference (p = .088). Marital status had a 15.4 standardized difference (p = .141). Ethnicity had a 12.6 standardized difference (p = .930). Admission floor had a 21.4 standardized difference (p = .148). Primary medical diagnosis had a 58.8 standardized difference (p = .105) and the number of units had a 14.7 standardized difference (p = .052). These large standardized differences exhibited indicate an imbalance within covariates which is large enough to be adjusted for by a propensity score. *See table 13 for the observed covariates for women with in-hospital stroke alert activated compared to women with no in-hospital stroke alert.*

Table 13. Comparison of Observed Covariates for Women with In-hospital Stroke Alert Activated vs. Women with no In-hospital Stroke Alert (N = 149)

	Yes (n = 46)		**No (n = 103)**		**Standardized Difference %**	**Significance Test**
Variables	**Mean**	**SD**	**Mean**	**SD**		
Patient Characteristics						
Age	72.1	12.0	67.9	14.7	**24.7**	.088
Marital status	2.13	.885	1.90	.858	**15.4**	.141
Ethnicity	1.20	.860	1.19	.638	**12.6**	.930
Admission floor	2.87	1.27	3.19	1.06	**21.5**	.148
Clinical Conditions						
Risk factors	.978	.147	.884	.322	3.85	.015
Comorbid conditions	.760	.431	.796	.405	7.33	.631
Primary medical diagnosis	5.21	3.04	4.29	3.27	**56.8**	.105
Common stroke symptoms	.152	.363	.282	.452	6.96	.066
Unique stroke symptoms	.348	.482	.262	.442	8.33	.307
Context of Care						
Last Known Well	.435	.501	.272	.447	8.60	.062
ESI	.478	.505	.534	.501	8.91	.533
Number of units	2.60	.930	2.32	.782	**14.7**	.052
Diagnostic imaging	.109	.315	.030	.169	4.93	.112
Outcome						
Thrombolytic therapy	.044	.206	.126	.334	4.48	.067
Discharge status	.740	.444	.680	.469	1.56	.468

Note: **Bold** = standardized difference greater than 10%
Abbreviations: ESI, Emergency Severity Index

A logistic regression was performed to describe the baseline, before propensity score matching, effects of in-hospital stroke alert (in-hospital stroke alert yes/no) and the associated variables: age, marital status, ethnicity, admission floor, stroke risk factors, comorbid conditions, primary medical diagnosis, common and unique stroke symptoms, Time Last Known Well, Emergency Severity Index, number of hospital units, diagnostic imaging, and thrombolytic therapy.

The logistic regression model was statistically significant, $\chi2(4) = 6.259$, $p > .0005$ (Hosmer & Lemeshow). The model explained 22.7% (Nagelkerke R^2) of the variance in in-hospital stroke alert and correctly classified 75.8% of cases ($N = 149$). Sensitivity 41.3% and specificity 91.3%. Of the 13 predictor variables only the number of hospital units was statistically significant ($p = .034$). This low significance observed by logistic regression could be due to the potential bias and influence each covariate has to each other. Age was positively associated with in-hospital stroke alert, the odds for older women to have in-hospital stroke alert were higher than younger women ($p = .334$; OR 1.02). Marital status was positively associated with in-hospital stroke alert, the odds of in-hospital stroke alert increased when a women was separated/divorced/single or widowed ($p = .405$; OR 1.23). Ethnicity was positively associated with in-hospital stroke alert, the odds of in-hospital stroke alert were higher for Caucasians than for non-Caucasian ethnic groups ($p = .933$; OR 1.07). Stroke risk factors and unique stroke symptoms were positively associated with in-hospital stroke alert, the odds of in-hospital stroke alert increased when a women had stroke risk factors ($p = .143$; OR 5.12), unique stroke symptoms ($p = .562$; OR 1.32). Emergency Severity Index ($p = .764$; OR 1.26) and diagnostic imaging completed ($p = .292$; OR 2.62). As the number of hospital units increased the odds for in-hospital stroke alert increased ($p = .034$; OR 1.84). However, the admission floor ($p = .126$;

OR .595), comorbid conditions (p = .477; OR .702), primary medical diagnosis (p = .366; OR .676) and common stroke symptoms (p = .798; OR .873) were associated with a reduction in the likelihood of in-hospital stroke alert activation. In addition, the primary outcome of receiving thrombolytic therapy (p = .103; OR .241) was negatively associated with in-hospital stroke alert. Therefore, when no in-hospital stroke alert was activated the odds for receiving thrombolytic therapy decreased. In addition, the secondary outcome of discharge status (p = .466; OR 1.34) was positively associated with in-hospital stroke alert. The odds for discharge to a skilled nursing facility, home care, hospice, or expiring increased with in-hospital stroke alert activation. *See table 14 for the baseline effects of in-hospital stroke alert and associated variables.*

Table 14. Baseline Effects of In-hospital Stroke Alert and Associated Variables in Women (Before Propensity Score Matching) (N = 149)

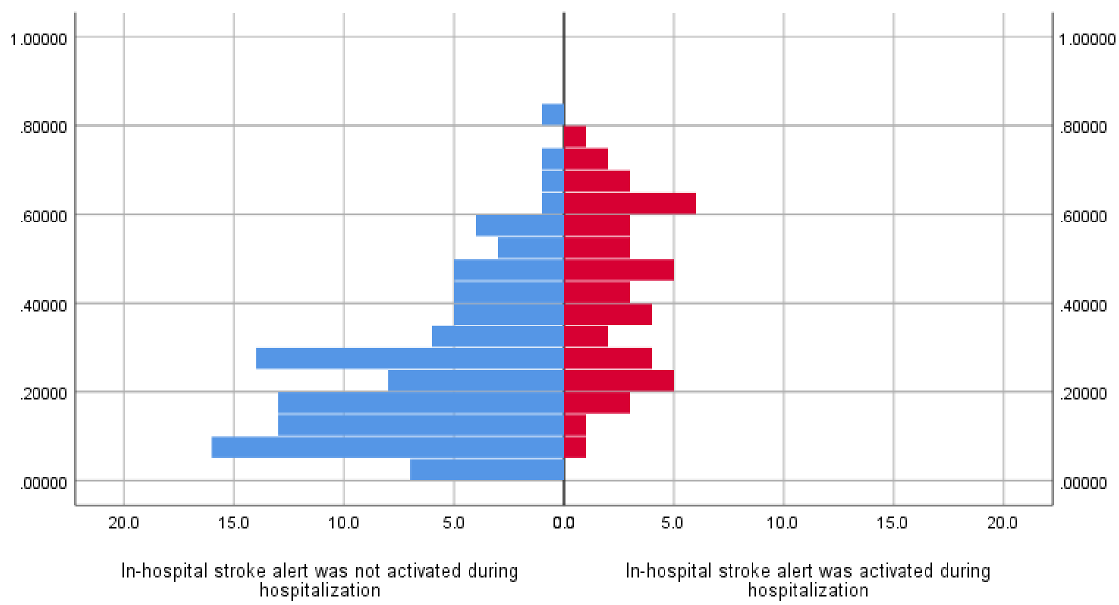
Variables	*B*	SE	Wald	*df*	*p*	Odds Ratio	95% CI for Odds Ratio	
							Lower	Upper
Patient Characteristics								
Age	.017	.018	.932	1	.334	1.02	.982	1.05
Marital status = Married; separated/divorced/single; widowed	.210	.253	.693	1	.405	1.23	.752	2.03
Ethnicity = Caucasian	.067	.799	.007	1	.933	1.07	.223	5.13
Admission floor	-.520	.339	2.34	1	.126	.595	.306	1.16
Clinical Conditions								
Risk factors = Yes	1.63	1.12	2.14	1	.143	5.12	.575	45.59
Comorbid conditions = Yes	-.354	.500	.505	1	.477	.702	.264	1.87
Primary medical diagnosis = Other; cardiovascular	-.391	.432	.819	1	.366	.676	.290	1.58
Common stroke symptoms = Yes	-.136	.532	.066	1	.798	.873	.308	2.47
Unique stroke symptoms = Yes	.279	.481	.336	1	.562	1.32	.515	3.40
Context of Care								
Last Known Well = Yes	.340	.443	.591	1	.442	1.41	.590	3.35
ESI = Yes	.232	.772	.090	1	.764	1.26	.278	5.72
Number of units, 1;2;3;4;>5	.611	.288	4.50	1	**.034**	1.84	1.05	3.24
Diagnostic imaging = Yes	.964	.914	1.11	1	.292	2.62	.437	15.7
Outcome								
Thrombolytic Therapy = Yes	-1.42	.873	2.70	1	.103	.241	.044	1.34
Discharge status = Home; SNF, hospice, expired	.289	.397	.533	1	.466	1.34	.614	2.91

Note: **Bold** = within p<0.05 trim threshold, in-hospital stroke alert yes = n = 46
Abbreviations: ESI, Emergency Severity Index; SNF, skilled nursing facility

Lastly for **aim 1, propensity scores** were generated using the 1:1 nearest neighbor matching Statistical Package for the Social Science software Propensity Score Matching for the entire group of participants ($N = 149$). Each case was assigned a propensity score ranging from 0 to 1 based on whether they had or did not have the primary treatment of an in-hospital stroke alert. Propensity scores ranged from 0.01 to 0.86. Forty nine cases had propensity scores < 0.2, 30 cases between 0.2 – 0.3, 15 cases between 0.3 – 0.4, 21 cases between 0.4 – 0.5, 11 cases between 0.5 – 0.6 and 23 cases > 0.6.

A population pyramid histogram was used to assess the distribution of propensity scores by treatment group, in-hospital stroke alert activated and no in-hospital stroke alert. The overlap in the distributions of propensity scores shows that matching can be performed between the groups. *See figure 8 for the distribution of propensity scores by in-hospital stroke alert.*

Figure 8. Distribution of Propensity Scores by In-hospital Stroke Alert was Activated or No In-hospital Stroke Alert



The third section of this chapter describes findings related specifically to **aim 2: Match women who receive an in-hospital stroke alert activation to women with no in-hospital stroke alert.** The analysis for aim 2 used 1:1 nearest neighbor propensity score matching frequencies and logistic regression models with distributions and links appropriate to the part of research aim under analysis.

The analysis approach to achieve aim two included propensity score matching using the estimated propensity scores from aim 1 and 1:1 nearest neighbor matching Statistical Package for the Social Science software Propensity Score Matching to match participants and identify a successful distribution of variables over the treated (in-hospital stroke alert activated) to untreated (no in-hospital stroke alert) groups.

Propensity Score Matching tolerance (caliper) was set to 0.3 to avoid imposing a tolerance level on the maximum propensity score distance (caliper), to avoid bad matches, and raise the quality of matching. A McFadden's Pseudo R^2 in logistic regression was completed to compare the balance of the 2 groups on baseline factors. The pseudo R^2 in binary logistic regression for in-hospital stroke alert unmatched raw data indicated 0.146 and in the propensity score matched group, conditional regression the pseudo R^2 is 0.279. There was a reduction in the pseudo R^2, so the propensity score matching successfully reduced the predictive value of age, marital status, ethnicity, admission floor, risk factors, comorbid conditions, common stroke symptoms, unique stroke symptoms, Time Last Known Well , Emergency Severity Index, number of units, and diagnostic imaging. Box plots were also plotted to assess the quality of propensity score matching. Absolute standardized mean differences before and after matching for all variables in the propensity score were generated. Propensity score matching was successful in all variables except primary diagnosis because match tolerance level was > 0.30

before matching, and after matching, they are < 0.30 match tolerance level. After grouping and reassessing primary diagnosis the absolute standardized mean difference was < 0.10 after matching (Creswell, 2013; Heinze & Jüni, 2011; Polit & Beck, 2016; Tabachnick & Fidell, 2014). *See figure 9* for the *distribution of observed covariates before and after propensity score matching.*

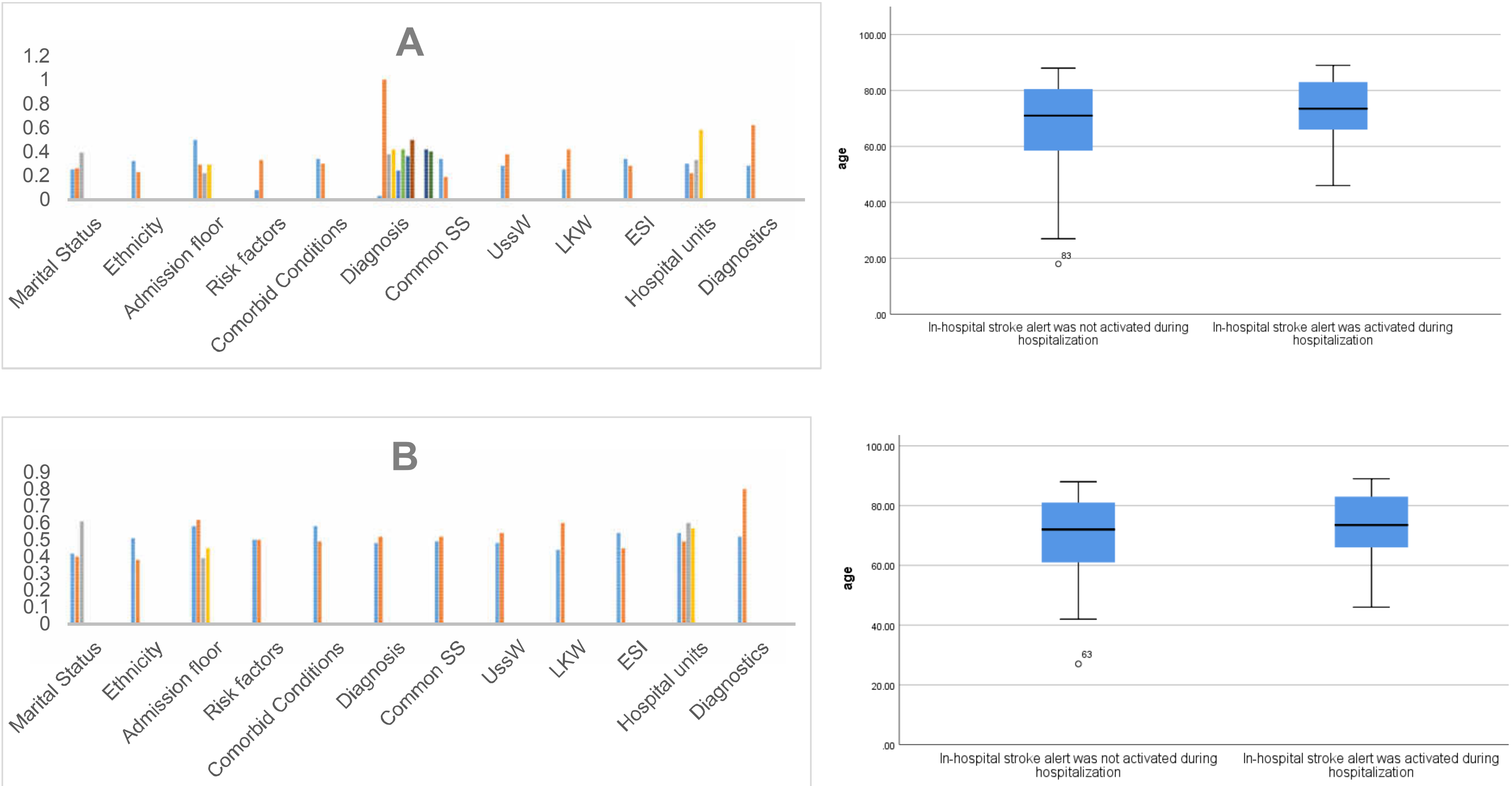
Following propensity score matching, a conditional logistic regression was performed, taking into account the propensity-matched pair, to evaluate the treatment (in-hospital stroke alert activated) effect on the primary outcome (thrombolytic therapy) with the reduction of confounding bias due to propensity score matching. With propensity score matching in-hospital stroke alert is a statistically significant predictor of thrombolytic therapy ($p < .001$; OR 8.80) compared to before and with no propensity score matching ($p = .139$; OR 3.18). *See table 15 for the comparison of in-hospital stroke alert effect on thrombolytic therapy before propensity score matching and after propensity score matching.*

Table 15. Comparison of In-hospital Stroke Alert Effect on Thrombolytic Therapy in Women Before and After Propensity Score Matching

	Thrombolytic Therapy			
Analysis	**Odds Ratio**	**95% CI**		***P* Value**
		Lower	**Upper**	
Before propensity score matching	3.18	.687	14.7	.139
After propensity score matching	8.80	3.49	22.2	<.001

Abbreviations: CI, confidence interval

Figure 9. Distribution of Observed Covariates Before and After Propensity Score Matching



Note: Before (A) and after (B) propensity score matching

The last section of this chapter describes findings related specifically to **aim 3: Compare the effects and associated variables of an in-hospital stroke alert activation to no in-hospital stroke alert on outcomes in women admitted to the hospital for a separate condition.** The analysis for aim 3 used frequencies statistics and conditional regression models with distributions and links appropriate to the part of research aim under analysis. The first step in aim 3 included frequencies statistics to assess the propensity score matched group relationship between variables, in-hospital stroke alert and outcomes.

The frequencies analysis for the propensity score matched group of women showed that age ranged from 18 to 89 years of age with the majority of the group between 70 to 79 years of age (33.8%) and between 80 to 89 years of age (30.5%). Of the 92 women, 37.0% of women were widowed, 35.9% were married, and 27.2% were either separated, divorced, or single. Of the 92 women, 91.3% were Caucasian and 8.7% were from other ethnic groups. Fifty three percent (n = 49) of the women were admitted from the emergency room, 97.8% had stroke risk factors, 79.3% had comorbid conditions and over half of the group (52.2%) had a cardiovascular disease or disorder as their primary medical diagnosis. Only 14.1% had common stroke symptoms. However, 31.5% had unique stroke symptoms in women. In addition, 35.9% had a Time Last Known Well documented, 50.0% had an Emergency Severity Index documented with 29 of these women classified as emergent, 14 as urgent, and 3 as most urgent. Of the 92 women, 40.2% or 37 women were on a total of 2 hospital units, 32.6% or 30 women were on 3 hospital units, 15.2% or 14 were on 4 units, and only 12.0% or 11 women were on just 1 unit. In-hospital stroke alert activation occurred on the critical care unit the majority of the time (n = 32; 34.8%), with the non-critical unit being second (n = 11; 12.0%), surgical (n = 2; 2.2%), and emergency room (n = 1; 1.1%). The average nurse-patient ratio was 2:1 (n = 32; 34.8%), with the second average being 4:1 (*n* = 11; 12.0%). Only 6 (6.5%) of the women had a computed tomographic scan or magnetic resonance imaging and 86 (93.5%) of the women did not have a computed tomographic scan or magnetic resonance imaging completed at all or within the 45 minutes of Time Last Known Well. Thirteen percent or 12 women had an average of 1 to 2 hour delay time in diagnostics and 8.8% had an average of 1 hour delay time in in-hospital stroke alert. Outcomes included only 7 (7.6%) of these women receiving thrombolytic therapy, 27 (39.3%) were discharged to a skilled nursing facility, 16 (17.4%) to home care, 14 (15.2%) to home, 14 (15.2%) to an inpatient rehabilitation, 7 (7.6%) to hospice, 7 (7.6%) expired, 5 (5.4%) to a long term care facility, 1 (1.1%) to intermediate care facility and 1 (1.1%) to another hospital. *Please see table 16 for the demographic frequencies of in-hospital stroke alert after propensity matching. See figure 10 for the demographic age frequencies of women with in-hospital stroke after propensity score matching. See figure 11 for the demographic diagnostics delay time frequencies for in-hospital stroke alert after propensity score matching. See figure 12 for the demographic in-hospital stroke alert delay time frequencies when in-hospital stroke alert is activated after propensity score matching.*

Table 16. Frequencies of In-hospital Stroke Alert in Women (After Propensity Score Matching) (*N* =92)

Analysis	**Frequency**		**Percentage**		**Mean**	**SD**
Patient Characteristics						
Age					70.9	12.5
18-39	1		1.1			
40-49	5		5.5			
50-59	14		15.4			
60-69	13		14.2			
70-79	31		33.8			
80-89	28		30.5			
Marital status					2.01	.860
Married	33		35.9			
Separated/divorced/single	25		27.2			
Widowed	34		37.0			
Ethnicity					.090	.283
Caucasian	84		91.3			
Other	8		8.7			
Admission floor					3.00	1.22
Critical care	19		20.7			
Non-critical	11		12.0			
Surgical	13		14.1			
Emergency	49		53.3			
Clinical Conditions						
Risk factors = Yes	90	2	97.8	2.2	.980	.147
Hypertension	12	42.8				
Smoking	71	9.6				
Diabetes	16	23.5				
High cholesterol	39	24.1				
Comorbid conditions = Yes	73	19	79.3	20.7	.794	.407
Myocardial Infarction	12	7.9				
Congestive Heart Failure	24	15.9				
Peripheral Vascular Disease	12	7.9				
Cerebrovascular Disease	14	9.3				
Dementia	7	4.6				
Chronic Pulmonary Disease	9	6.0				
Connective Tissue Disease	2	1.3				
Diabetes without Chronic Complications	7	4.6				
Diabetes with Chronic Complications	24	15.9				
Paraplegia and Hemiplegia	3	2.0				
Renal Disease	31	20.5				
Cancer	3	1.3				
Moderate or Severe Liver Disease	3	2.0				
Metastatic Carcinoma	1	0.7				
Primary medical diagnosis = Other; cardiovascular	44	48	47.8	52.2	5.16	3.09
Common stroke symptoms = Yes	13	79	14.1	85.9	.141	.350
Unique stroke symptoms = Yes	29	63	31.5	68.5	.315	.467
Context of Care						
Last Known Well = Yes	33	59	35.9	64.1	.360	.482
ESI = Yes	46	46	50.0	50.0	.500	.503

Table 16. cont.

Analysis	**Frequency**	**Percentage**	**Mean**	**SD**
Most urgent	3	3.3		
Emergent	29	31.5		
Urgent	14	15.2		
Number of units			2.51	.896
1	11	12.0		
2	37	40.2		
3	30	32.6		
4	14	15.2		
>5	0	0		
Unit stroke alert occurred			1.39	.682
Critical care	32	34.8		
Non-critical	11	12.0		
Surgical	2	2.2		
Emergency	1	1.1		
Average nurse patient ratio			2.46	.912
1	2	2.2		
2	32	34.8		
3	1	1.1		
4	11	12.0		
Diagnostic imaging = Yes	6 86	6.5 93.5	.065	.248
Diagnostics delay time (hours) (*n* = 15)			6.10	16.9
.10 – .99	7	7.7		
1 – 1.99	12	13.2		
4 – 4.99	1	1.1		
17 – 22	3	3.3		
In-hospital stroke alert delay time (hours) (*n* = 15)			38.3	92.2
.10 - .99	8	8.8		
1 – 1.99	3	3.3		
16 – 21	2	2.2		
264 - 265	2	2.2		
Outcome				
Thrombolytic therapy = Yes	7 85	7.6 92.4	.076	.267
Discharge status			4.58	.316
Home/self-care	14	15.2		
SNF	27	29.3		
LTC	5	5.4		
Intermediate care	1	1.1		
Another hospital	1	1.1		
IP rehab	14	15.2		
Home care	16	17.4		
Hospice	7	7.6		
Expired	7	7.6		

Abbreviations: ESI, Emergency Severity Index; SNF, skilled nursing facility; IP, inpatient

Figure 10. Age Frequencies of Women with In-hospital Stroke (After Propensity Score Matching) (N = 92)

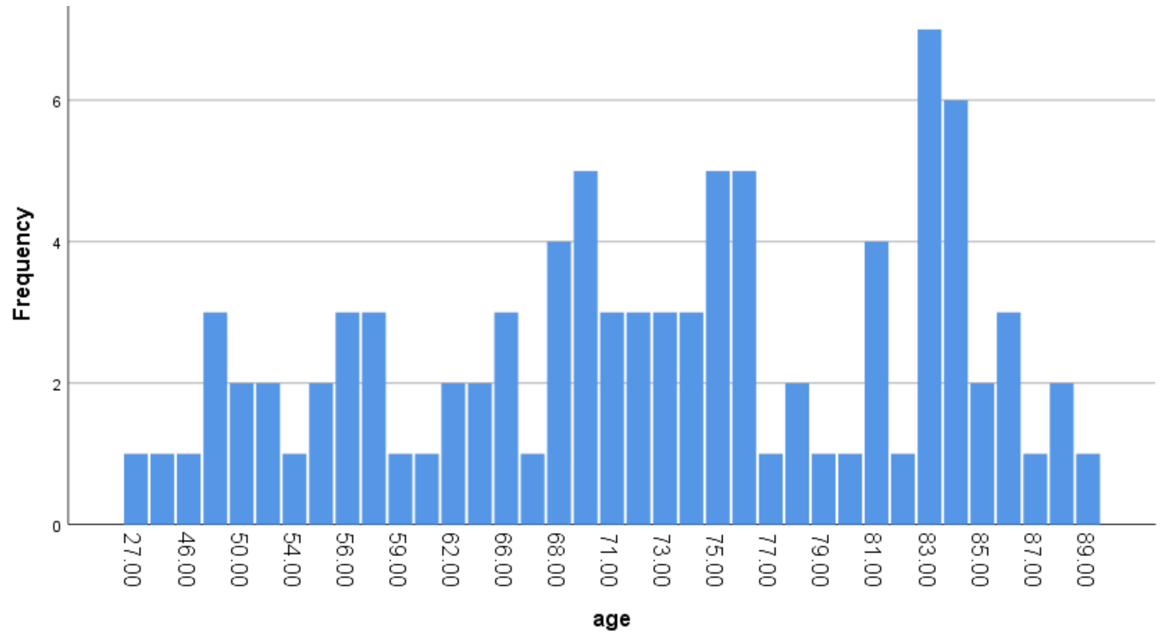
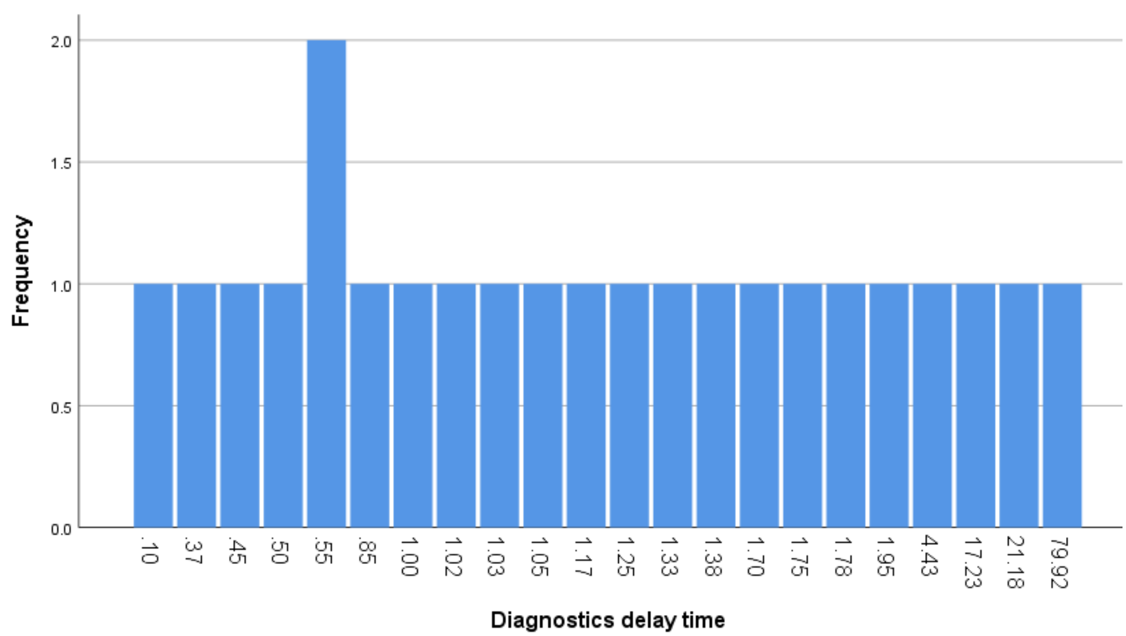
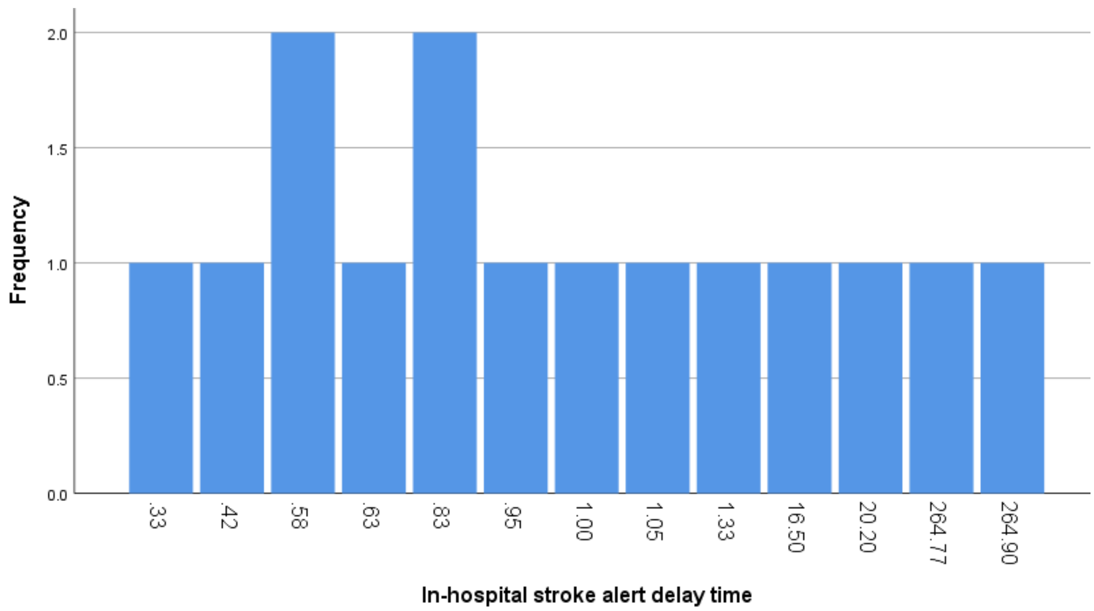


Figure 11. Diagnostics Delay Time Frequencies for In-hospital Stroke Alert Activation (After Propensity Score Matching) (N = 92)



Note: Time in hours

Figure 12. Frequencies of In-hospital Stroke Alert Delay Time for In-hospital Stroke Activation (After Propensity Score Matching) ($N = 92$)



Note: Time in hours

The second step in aim 3 included conditional logistic regression on the propensity score matched group to evaluate a treatment effect with the reduction of confounding bias.

The conditional logistic regression model was statistically significant when analyzing the in-hospital stroke alert as a dependent treatment variable $\chi2(4) = 35.633$, $p < .001$ (Chi-Square). The McFadden's pseudo R-squared test indicated that the model was a good fit to the observed data, pseudo R^2 is 0.279. Eight of the thirteen predictor variables were statistically significant when analyzing for in-hospital stroke alert: age ($p < .001$), ethnicity ($p <.001$), stroke risk factors ($p <.001$), comorbid conditions ($p < .001$), common stroke symptoms ($p < .001$), unique stroke symptoms ($p = 012$), Time Last Known Well ($p = .041$) and diagnostic imaging ($p < .001$). Both outcome variables were statistically significant: thrombolytic therapy ($p < .001$) and discharge status ($p = .014$).

An increase in age was associated with an increase in the odds for an in-hospital stroke alert being activated (p < .001 OR 3.89). Marital status was positively associated with in-hospital stroke alert, the odds of in-hospital stroke alert activation increased when a women was separated/divorced/single or widowed (p = .067; OR 1.72). The odds of in-hospital stroke alert activation were higher for women of Caucasian ethnicity than for non-Caucasian ethnic groups (p < .001; OR 8.60). A primary diagnosis of a cardiovascular disease was associated with an increase in the odds for in-hospital stroke alert being activated (p =.763; OR 1.10). The odds for an in-hospital stroke alert activation increased when the woman had common (p = <.001; OR 6.50) or unique (p = .012; OR 2.31) stroke symptoms. When the Time Last Known Well (p = .041; OR 2.00) was documented the odds for an in-hospital stroke alert activation increased. The documentation of the Emergency Severity Index made no difference between groups (p = 1.00; OR 1.00). The increase in the number of hospital floors was associated with an increase in the odds for in-hospital stroke alert being activated (p = .746; OR 1.11). When diagnostic imaging was completed within the 45 minutes from the Time Last Known Well the odds for in-hospital stroke alert activation increased (p <.001; OR 41.0). However, being admitted from the emergency floor (p = .668; OR .885) was associated with a reduction in the odds for an in-hospital stroke alert activation. In addition, having stroke risk factors (p <.001; OR .022) and comorbid conditions (p <.001; OR .289) were negatively associated with the odds for an in-hospital stroke alert activation. The primary outcome of thrombolytic therapy (p < .001; OR 8.80) was significantly associated with in-hospital stroke alert being activated. In addition, the secondary outcome of discharge status (p = .014; OR .429) was negatively associated with in-hospital stroke alert. The odds for discharge to a skilled nursing facility, home care, hospice, or expiring decreased with in-hospital stroke alert activation. *See table 17 for the relevant clinical* *effects for in-hospital stroke alert after adjusting for confounders with propensity score matching.*

Table 17. Relevant Clinical Effects for In-hospital Stroke Alert in Women (After Propensity Score Matching) (*N* = 92)

Variables	***B***	**SE**	**Wald**	***df***	***p***	**Odds Ratio**	**95% CI for Odds Ratio**	
							Lower	**Upper**
Patient Characteristics								
Age = 18 – 59; 60 – 89	1.36	.374	13.2	1	**< .001**	3.89	1.87	8.1
Marital status = Married; separated/divorced/single; widowed	.544	.296	3.37	1	.067	1.72	.963	3.08
Ethnicity = Other; Caucasian	2.15	.472	20.8	1	**< .001**	8.60	3.45	21.7
Admission floor = Other; Emergency	-.123	.286	.183	1	.668	.885	.505	1.55
Clinical Conditions								
Risk factors = Yes	-3.81	1.01	14.2	1	**< .001**	.022	.003	.161
Comorbid conditions = Yes	-1.24	.342	13.1	1	**< .001**	.289	.148	.566
Primary medical diagnosis = Other; Cardiovascular	.091	.302	.091	1	.763	1.10	.606	1.98
Common stroke symptoms = Yes	1.87	.439	18.2	1	**< .001**	6.50	2.75	15.4
Unique stroke symptoms = Yes	.836	.332	6.34	1	**.012**	2.31	1.20	4.42
Context of Care								
Last Known Well = Yes	.693	.340	4.16	1	**.041**	2.00	1.03	3.89
ESI = Yes	.000	.283	.000	1	1.00	1.00	.574	1.74
Number of units = 1-2; 3-4	.105	.325	.105	1	.746	1.11	.588	2.10
Diagnostic imaging = Yes	3.71	1.01	13.4	1	**< .001**	41.0	5.64	298
Outcome								
Thrombolytic Therapy = Yes	2.18	.472	21.3	1	**< .001**	8.800	3.49	22.2
Discharge status = Home; SNF, hospice, expired	-.847	.345	6.03	1	**.014**	.429	.218	.843

Abbreviations: ESI, Emergency Severity Index; SNF, skilled nursing facility

Summary of Results

The purpose of this study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition. In-hospital stroke alert activation for women who had a stroke while being hospitalized for a separate condition in this study had an overall incidence of 31%. Thrombolytic therapy was administered to 15 (N = 149) women. The mean age for the entire group of women (N = 149) was 69 years, 91.3% women were Caucasian and 8.7% were from other ethnic groups. In-hospital stroke alert was significantly associated with the primary and secondary outcomes of thrombolytic therapy and discharge status. In addition, there was a total of eight confounding variables significantly associated with in-hospital stroke alert; age, ethnicity, stroke risk factors, comorbid conditions, common stroke symptoms, unique stroke symptoms, Time Last Known Well, and diagnostic imaging. Three variables were positively associated with in-hospital stroke alert, indicating an increase in an in-hospital stroke alert activation, and included: marital status, primary diagnosis and the number of hospital floors. Therefore, the odds of in-hospital stroke alert activation increased when: a women was separated/divorced/single or widowed; the primary diagnosis was a cardiovascular disease; and when there was an increase in the number of hospital floors. One variable was negatively associated with in-hospital stroke alert, indicating a decrease in an in-hospital stroke alert being activated, and included: admission floor. Therefore, the odds of in-hospital stroke alert activation increased when a women was admitted to the hospital from different floor, such as surgery or direct clinic admission, not an emergency room admission. The Emergency Severity Index had the same outcome for both groups (p = 1.00; OR 1.00). Therefore, there was no difference for in-hospital stroke alert activation whether the Emergency Severity Index was documented or not documented.

CHAPTER V

DISCUSSION

The purpose of this study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition. The primary outcome for this study was whether the stroke patient received thrombolytic therapy or not. The secondary outcome included discharge status. The following Specific Aims were accomplished during this study: aim 1) determine the frequency of women receiving thrombolytic therapy after receiving in-hospital stroke alert during hospitalization for a separate condition; aim 2) match women who receive an in-hospital stroke alert activation to women with no in-hospital stroke alert; aim 3) compare the effects and associated variables of an in-hospital stroke alert activation to no in-hospital stroke alert on outcomes in women admitted to the hospital for a separate condition. This final chapter contains a discussion of this study, the findings from chapter four, and important conclusions from those findings. Implications of the results for nursing science, practice and education are discussed.

This descriptive observational study was guided by the Model for Nursing Effectiveness Research developed by Shever et al., (2008). This model was influenced by Titler, Dochterman, and Reed's (2004) Effectiveness Research Model and is similar to the Outcomes Conceptual Model by Kane (1997; 2006). The overall goal of this study was to isolate the treatment (in-hospital stroke alert) and outcome (thrombolytic therapy), while controlling the effects of other influential variables (Shever et al., 2008).

The relationship between an in-hospital stroke alert activation for women and the effects on outcomes are not clear. Furthermore, the implementation of in-hospital stroke alert processes varies widely. Therefore the purpose of this study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition.

In this study, there are a number of variables that are associated with and may influence the results related to in-hospital stroke alert. Variable selection for this study was guided by the Model for Nursing Effectiveness Research, in addition to clinical knowledge and empirical evidence. The identified potential confounding variables are: patient characteristics (age, marital status, ethnicity, and admission hospital floor); clinical conditions (stroke risk factors, comorbid conditions, primary medical diagnosis, common and unique stroke symptoms); and the context of care (Time Last Known Well, Emergency Severity Index, diagnostic imaging, number of hospital units/floors, unit the stroke alert occurred, delay time, and average nurse-patient ratio). Therefore, the first section of this chapter will discuss the sample demographics and next aims 1 and 2 will be discussed first with intentness that aims 1 and 2 were conducive to assess for confounding variables and to reach aim 3 with a precise estimation of in-hospital stroke alert response.

Sample

This section of chapter 5 will discuss the demographic characteristics of the entire cohort (N = 149), the participants who received in-hospital stroke alert (n = 46), the participants with no in-hospital stroke alert (n = 103), and lastly the propensity score matched group of participants (N = 92). This study took place at a Midwestern hospital which annually serves roughly 12,000 stroke patients. About 21.2% of the hospital's patient population lived below the poverty line.

Sample Demographics

Patient characteristics. Patient characteristics of age, marital status, ethnicity, and admission hospital floor all have a potential relationship to stroke risk, diagnosis, treatment, and outcomes (ASA, 2019a; Mozaffarian et al., 2016).

Age. The *entire cohort* consisted of 149 women who had an in-hospital stroke, age ranged from 18 to 89 years of age with a mean age of 69 years. Before propensity score matching, 46 women with an *in-hospital stroke alert was activated* ranged from 40 to 89 years of age with a mean age of 72 years. Before propensity score matching, 103 women had *no in - hospital stroke alert* during hospitalization ranged from 18 to 88 years of age with a mean age of 67 years. After propensity score matching, 92 women were successfully matched, 46 women from the in-hospital stroke alert was activated group and 46 women from the no an in-hospital stroke alert during hospitalization. The age range for the *propensity score matched* women ranged from 18 to 89 years of age with a mean age of 70 years. Age for the sample in this study are consistent with other studies and stroke statistics. Other studies and stroke statistics indicate that nearly three-quarters of strokes occur in individuals 65 years of age or older (Benjamin et al., 2017; Mozaffarian et al., 2016) Also, the risk of stroke doubles each decade after the age of 55 (Benjamin et al., 2017; Mozaffarian et al., 2016).

Marital status. Of the 149 women from the *entire cohort,* almost 40% of these women were either married or widowed, and about 25% were either separated, divorced or single. Of the 46 women with an *in-hospital stroke alert was activated,* almost 50% of these women were widowed. Of the 103 women who had *no in-hospital stroke alert,* almost 50% of these women were married. Of the 92 *propensity score matched* women, almost 40% of these women were married, about 35% were widowed and about 27% were either separated, divorced or single.

Marital status for the sample in this study are consistent with other studies and stroke statistics. Similarly, in a study of 60,507 stroke patients stroke rate per marital status was about: 52% were married, 10% were unmarried, 14% were divorced, and 26% were widowers (Anderson & Olsen, 2018).

Ethnicity. Of the 149 women from the *entire cohort,* nearly 92% of women were Caucasian and about 9% were from other ethnicity groups. Of the 46 women with an *in-hospital stroke alert was activated,* nearly 94% of women were Caucasian and about 7% were from other ethnicity groups. Of the 103 women who had *no an in-hospital stroke alert,* about 90% of women were Caucasian and about 9% were from other ethnicity groups. Of the 92 *propensity score matched* women, about 91% of women were Caucasian and nearly 9% were from other ethnicity groups. The composition of the sample in this study was more homogenous than anticipated given the proportions of similar studies from this upper Midwestern urban hospital (60% Caucasians, 15% Asian, and 10% African American) (Brown, Luby, Shah, Giannakidis, & Latour, 2015). Ethnicity, as a risk factor for stroke, for the sample in this study are consistent with other studies and stroke statistics. Similar to other studies and stroke statistics, the risk of stroke is nearly two times higher for African American ethnic populations when compared to Caucasian ethnicity (Benjamin et al., 2017; Mozaffarian et al., 2016). In addition, stroke death rate is the highest for African American ethnic populations and has increased in Hispanic ethnic populations (Benjamin et al., 2017; Mozaffarian et al., 2016).

Admission floor. Of the 149 women from the *entire cohort,* over half of the women (n = 81; N = 149) were admitted from the emergency room (54.4%). Of the 46 women with an *in-hospital stroke alert was activated,* half of these women (n = 23; N = 46) were admitted from the emergency room (50%). Of the 103 women who had *no an in-hospital stroke alert,* almost half of these women (*n* = 58; *N* = 103) were admitted from the emergency room (56.3). Of the 92 *propensity score matched* women, slightly over half of these women (*n* = 49; *N* = 92) were admitted from the emergency room (53.3%). Admission floor for the sample in this study are not consistent with other studies and stroke statistics. In this study, women who were admitted to the hospital from the emergency room were less likely to have an in-hospital stroke alert activated. Whereas, in a study of 983 stroke patients, about 50% of stroke cases that occurred in the emergency department compared to other hospital floors had a higher rate of stroke alert activation and thrombolytic therapy (Stecker, Michel, Antaky, Wolin, & Koyfman, 2015).

Clinical conditions. Clinical conditions of common and unique stroke symptoms, stroke risk factors, comorbid conditions and primary medical diagnosis all can contribute to the risk, recognition, and severity of stroke (ASA, 2019a; Mozaffarian et al., 2016).

Stroke risk factors. Of the 149 women from the *entire cohort,* 136 of the 149 women had stroke risk factors. Of the 46 women with an *in-hospital stroke alert was activated,* 36 of the 46 women who had an in-hospital stroke alert activated had at least 1 or more stroke risk factors. Almost 80.0% of them had high blood pressure, almost 70% had atrial fibrillation or another heart disease and almost 60% had high cholesterol. Of the 103 women who had *no an in-hospital stroke alert,* 100 of the 103 women who had no in-hospital stroke alert had at least 1 or more stroke risk factors. Almost 80.0% of them had high blood pressure, almost 63% had atrial fibrillation or another heart disease and almost 40% had diabetes. Of the 92 *propensity score matched* women, 90 of the 92 matched women had at least 1 or more stroke risk factors. Almost 43% of them had high blood pressure, almost 25% had high cholesterol, almost 24% had diabetes, and almost 10% women were smokers. Stroke risk factors for the sample in this study are consistent with other studies and stroke statistics. Similar to other studies and stroke statistics, heart disease and stroke are linked, several types of heart disease are risk factors for stroke (Benjamin et al., 2017; Mozaffarian et al., 2016). In this study, high blood pressure, high cholesterol, heart disease, diabetes and smoking increased the chance of stroke. Current stroke statistics indicate that smokers are at a double risk for stroke compared to non-smokers, atrial fibrillation increases stroke risk about five-fold and high blood pressure is the number one risk factor for a stroke (Benjamin et al., 2017; Mozaffarian et al., 2016). In other study findings, as many as 1 in 3 adults had at least one of the following stroke risk factors: high blood pressure, high cholesterol, smoking, and obesity (Benjamin et al., 2017; Mozaffarian et al., 2016). In a study of 4,780 predominantly Caucasian adults with stroke all had at least one of the following cardiovascular disease risk factors: older age, smoking, high blood pressure, high cholesterol, and obesity (Wilson et al., 2008 as cited in Dad & Weiner, 2015).

Comorbid conditions. The Charlson Comorbidity Index was the method used for categorizing comorbidities based on all the ICD–9–CM has been validated as a measure of mortality risk and burden of disease; it has been extensively used in research to address the confounding influence of comorbidities (Frenkel, Jongerius, Mandjes-van Uitert, Munster, & Rooij, 2014; Quan et al., 2011). The Charlson Comorbidity Index scoring was considered and determined to not be a good fit for this study because examining scores and mortality related to comorbid conditions were not this study's purpose and aims. Of the 149 women from the *entire cohort,* nearly 80% of these women had comorbid conditions. Over half of these women had a cardiovascular disease. Of the 46 women with an *in-hospital stroke alert was activated,* nearly 80% of these women had comorbid conditions. Comorbid conditions were nearly equally spread across the following 3 conditions: congestive heart failure (42.9%), diabetes with chronic complications (42.9%), and renal disease (42.9). Of the 103 women who had *no an in-hospital* *stroke alert,* nearly 80% of these women had comorbid conditions. The top three comorbid conditions were spread across the following 3 conditions: cerebrovascular disease (29.3), renal disease (29.3%), and congestive heart failure (22.0%). Of the 92 *propensity score matched* women, nearly 80% of these women had comorbid conditions. The top three comorbid conditions were spread across the following 3 conditions: renal disease (20.5%), congestive heart failure (15.9%), and diabetes with chronic complications (15.9%). Comorbid conditions for the sample in this study are consistent with other studies and stroke statistics. Similar to other studies and stroke statistics, as many as 1 in 3 adults has at least one of the following comorbid conditions: cardiovascular disease and diabetes (Benjamin et al., 2017; Mozaffarian et al., 2016). A meta-analysis of 21 studies found that renal disease with an eGFR less than 60 mL/min per 1.73 m2 was associated with a 43% higher risk of incidence of stroke (Dad & Weiner, 2015).

Primary medical diagnosis. Of the 149 women from the *entire cohort,* over half of these women had a primary medical diagnosis of a cardiovascular disease. Of the 46 women with an *in-hospital stroke alert was activated,* half of these women had a primary medical diagnosis of cardiovascular disease. Of the 103 women who had *no an in-hospital stroke alert,* slightly over half of these women had a primary medical diagnosis of a cardiovascular disease. Of the 92 *propensity score matched* women, nearly half of these women had a primary medical diagnosis of a cardiovascular disease. The primary medical diagnosis for the sample in this study are consistent with other studies and stroke statistics. Patients who are hospitalized for cardiac disease or surgery are vulnerable to in-hospital stroke (Berglund et al., 2015; Boden-Albala et al., 2015; Hanselman, 2014; Park, Shin, Ro, Song, & Oh, 2013; Sobolewski et al., 2015). Similarly, in a study by Kes (2016) of 396 stroke patients, the older patients presented more often with greater heart conditions and the women had higher odds of hypertension, chronic heart failure and atrial fibrillation than men (Kes, 2016).

Stroke symptoms. Of the 149 women from the *entire cohort,* about 25% of these women had common stroke symptoms and nearly 30% had unique stroke symptoms. Of the 46 women with an *in-hospital stroke alert was activated,* about 25% of these women had common stroke symptoms and nearly 30% had unique stroke symptoms. Of the 103 women who had *no an in-hospital stroke alert,* about 76% of these women had common stroke symptoms and nearly 72% had unique stroke symptoms. Of the 92 *propensity score matched* women, about 15% of these women had common stroke symptoms and nearly 32% had unique stroke symptoms. Stroke symptoms for the sample in this study are consistent with other studies and national stroke statistics. Early identification (the process of identifying stroke symptoms less than 3 to 4.5 hours of symptom onset) is crucial to timely thrombolytic treatment and better patient outcomes (Boden-Albala et al., 2015; Boehme et al., 2014; Hanselman, 2014; Powers et al., 2015; Sobolewski et al., 2015). In a study by Cumbler et al. (2015), evidence has demonstrated that response time to stroke symptoms, adherence to quality processes of care, treatment rates, and overall outcomes were lower for in-hospital strokes when compared to patients who had a stroke in the community and were treated by emergency services. In addition, studies have highlighted the difference in stroke symptoms among gender, acknowledge there is a low recognition of unique stroke symptoms in women and that more women are initially misdiagnosed on presentation (Berglund et al., 2015; Colsch & Lindseth, 2018; Dupre et al., 2014; Fothergill et al., 2013; Hodell et al., 2016; Kes, 2016; Lever et al., 2013; Madsen et al., 2016; Park et al., 2013).

In-hospital Stroke Alert and Thrombolytic Therapy

This section of chapter five will discuss the findings related to each Specific Aim:

Aim 1) Determine the frequency of women receiving thrombolytic therapy after receiving in-hospital stroke alert during hospitalization for a separate condition

Aim 2) Match women who receive an in-hospital stroke alert activation to women with no in-hospital stroke alert

Aim 3) Compare the effects and associated variables of an in-hospital stroke alert activation to no in-hospital stroke alert on outcomes in women admitted to the hospital for a separate condition.

Aims 1 and 2 will be discussed with intentness that these aims were conducive to assess for confounding variables and to reach aim 3 with a precise estimation of in-hospital stroke alert response.

Frequencies

This section of this chapter discusses the results related specifically to aim 1:

Aim 1. Determine the frequency of women receiving thrombolytic therapy after receiving in-hospital stroke alert during hospitalization for a separate condition.

Aim 1 consisted of obtaining a baseline frequencies of the entire cohort of women who had an in-hospital stroke. In addition, aim 1 also obtained a primary dataset for analysis of the observed covariates along with the baseline effects of in-hospital stroke alert with identification of potential confounding variables. Lastly, aim 1 obtained a distribution of propensity scores to assess for balance across both groups.

Baseline frequencies. The baseline frequencies were analyzed for the *entire cohort*, before propensity score matching. In this study, 46 of 149 or 30.9% (n = 46 of an N of 149) women had an in-hospital stroke alert activated. Only 48 of the 149 women had the Time Last

Known Well documented (32.2%). Of the 149 women in this study, 76 (51.0%) had an Emergency Severity Index score documented and 42 women were classified as emergent, 26 as urgent, and 8 as most urgent. Of the 149 women in this study, 41.6% or 62 women were on a total of 2 hospital units, 35.6% or 53 women were on 3 hospital units, 13.4% or 20 were on 1 unit, and 9.4% or 14 women were on 4 units. Of the 149 women in this study, only 8 (5.4%) women had a computed tomographic scan or magnetic resonance imaging completed within the 45 minutes of the Time Last Known Well . The use of activating emergency and in-hospital stroke alert have shown to improve time to diagnosis and reduce thrombolytic treatment times (Meretoja et al., 2012). Studies that specifically focus on in-hospital stroke alert are minimal and to the author's knowledge no study currently exists that investigated in-hospital stroke alert and stroke as manifested in women. However, similar to emergency stroke alert studies found the median in-hospital stroke alert to computed tomography scan time decreased to 29.5 minutes from 69.0 minutes pre-intervention time ($p = 0.0001$) (Cumbler et al., 2012).

The primary outcome of thrombolytic therapy consisted of 15 of 149 or 10.1% of women who received thrombolytic therapy. In addition, only 2 of 46 or 4.3% ($n = 46$ of an N of 149) women who had in-hospital stroke alert activated received thrombolytic therapy. This low incidence of thrombolytic therapy is similar to another study of 1193 stroke patients in which only 51 (4.3%) of the participants were treated with thrombolytic therapy (Boden-Albala et al., 2015). The study by Boden-Albala et al., (2015) suggested that the low incidence of thrombolytic therapy was due to the delay time in arriving to the emergency room. Similarly, the low incidence of thrombolytic therapy for this study could have been impacted by the delay time in recognition of stroke symptoms, the delay in stroke alert activation or because no in-hospital stroke alert was activated.

Comparison of observed covariates. Prior to the application of a propensity score model, a baseline comparison of observed covariates was completed on the *entire cohort* (*N* = 149). This comparison of covariates was completed to assess for imbalances and identify potential confounding variables between women with in-hospital stroke alert activation compared to women with no stroke alert. A t-test analysis identified a standardized difference greater than 10% in the following 6 variables: age, marital status, ethnicity, admission floor, primary medical diagnosis, and the number of hospital units. In this study, before propensity score matching, the standardized difference was greater than 10% suggesting an imbalance and potential bias from confounding variables. Similar to other studies and propensity score methods, when the absolute standardized difference is greater than 10% and the match tolerance level (caliper) exceeds set level the covariates are not balanced increasing potential bias from confounding variables (Creswell, 2013; Heinze & Jüni, 2011; Polit & Beck, 2016; Tabachnick & Fidell, 2014). This imbalance indicates the need to do matching in order to reduce the bias and influence of the confounding variables (Creswell, 2013; Heinze & Jüni, 2011; Polit & Beck, 2016; Tabachnick & Fidell, 2014). Therefore, similar to these other studies, after propensity score matching. the standardized difference in this study was less than 10% and the set tolerance (caliper) of 0.3 was met which positively reduced the bias and influence of confounding variables.

Baseline effects of in-hospital stroke alert and associated variables. A baseline, before propensity score matching, of the effects of in-hospital stroke alert and the associated variables was completed on the *entire cohort* (*N* = 149). A logistic regression model was applied to describe the baseline effects and to further identify potential confounding variables between women with in-hospital stroke alert activation compared to women with no stroke alert. Due to potential bias and the influence each covariate has on each other a low significance was observed. The number of hospital units (p = .034) was the only significant variable. Similar to other observational studies, significant findings may not always be a valid result because obtaining the treatment effect is not always independent of the confounding variables (Heinze & Jüni, 2011; Littnerova et al., 2013; Qin et al., 2008; Shever et al., 2008). Therefore, obtaining sufficiently unbiased results in observational studies requires statistical methods that can adjust for the impact of confounding factors (Littnerova et al., 2013). The propensity score matching is a statistical method that can reduce bias and study causal effects in observational studies (Heinze & Jüni, 2011; Littnerova et al., 2013; Qin et al., 2008; Shever et al., 2008).

Distribution of propensity scores. Propensity scores were generated for the *entire cohort* (N = 149). Propensity scores were assessed by score range and visually by a histogram. Distributions of propensity scores overlapped and were balanced between groups indicating matching could be successfully performed. Similar to other studies, in observational studies before matching the covariates are typically not balanced between groups (Heinze & Jüni, 2011; Littnerova et al., 2013; Qin et al., 2008; Shever et al., 2008). When observed covariates are balanced at each propensity score an equal distribution will be obtained (Heinze & Jüni, 2011; Littnerova et al., 2013; Qin et al., 2008; Shever et al., 2008).

Participant Group Matching

This section of this chapter discusses the results related specifically to aim 2:

Aim 2. Match women who receive an in-hospital stroke alert activation to women with no in-hospital stroke alert.

Aim 2 consisted of matching participants based on in-hospital stroke alert and assess for a successful distribution and matching across groups.

Matching. Women were successfully grouped and matched using propensity score matching. The final balanced propensity score matched group of women consisted of 92 women

(61.7% of original dataset): 46 women who had an in-hospital stroke alert activated and 46 women who had no in-hospital stroke alert. The effectiveness of propensity score matching was confirmed by a McFadden's Pseudo R2 in logistic regression (0.279), a match tolerance level (< .30) and an absolute standardized mean difference (< 0.10). Similar to other studies and propensity score methods, when the covariates after matching absolute standardized differences are below 10% this is considered to be a successful balance. (Creswell, 2013; Heinze & Jüni, 2011; Polit & Beck, 2016; Tabachnick & Fidell, 2014).

The purpose of this study was to investigate the effects and associated variables of having an in-hospital stroke alert activation on outcomes in women admitted to the hospital for a separate condition. In the original dataset, in-hospital stroke alert and thrombolytic therapy was not statistically significant ($p = .139$). After propensity score matching, in-hospital stroke alert and thrombolytic therapy was statistically significant ($p < .001$). The in-hospital stroke alert and thrombolytic therapy significance in this study are consistent with other studies. In a different study, a high urgency stroke alert protocol decreased the median door to thrombolytic therapy (103 min to 37 min with the stroke alert, $p < 0.001$; and decreased the median onset-to-treatment time, 177 min to 114 min with the new stroke alert, $p < 0.001$) (Candelaresi et al., 2017). Similarly, another study that initiated a stroke alert found that the rate of thrombolytic therapy among ischemic stroke patients increased from 33.3% to 59.2% ($p = 0.0001$) (Kim et al., 2015).

Effects of In-hospital Stroke Alert and Associated Variables

This section of this chapter discusses the results related specifically to aim 3:

Aim 3. Compare the effects and associated variables of an in-hospital stroke alert activation to no in-hospital stroke alert on outcomes in women admitted to the hospital for a separate condition.

Aims 1 and 2 allowed for the analysis of confounding variables and lead to obtaining a successfully balanced propensity score matched group. The success of aims 1 and 2 created unbiased results for aim 3 to generate a precise estimation of an in-hospital stroke alert response in women hospitalized for a separate condition. Aim 3 consisted of obtaining frequencies of the propensity score matched group and an analysis of the final dataset with the reduced potential bias of confounding variables.

A discussion on the frequencies and effects of the associated variables are as follows:

Age. Of the 92 *propensity score matched* women age ranged from 18 to 89 years of age with a mean age of 70 years. Of the 46 women who had an in-hospital stroke alert activated age ranged from 46 and 89 years of age. Only one out of the 11 women between 18 to 49 years of age had an in-hospital stroke alert activated and 6 out of the 27 women between 50 to 59 years of age had an in-hospital stroke alert activated. Similar to other study findings, an increase in age was significant. The findings in this study indicate that older women were more likely to have an in-hospital stroke alert activated ($p < .001$; OR 3.89). Patient characteristics of age, marital status, ethnicity, and admission floor have all been found in the literature to be related to stroke risk, diagnosis, treatment, and outcomes. In a literature review by Girijala, Sohrabji, and Bush (2017) data was found to be consistent among the studies in that women faced greater rates of stroke at older ages and worse outcomes.

Marital status. Of the 92 *propensity score matched* women, almost 40% of these women were married, about 35% were widowed and about 27% were either separated, divorced or single. Almost half of the 46 women who had an in-hospital stroke alert activated were widowed (45.7%). Similar to other study findings, marital status was a factor in stroke. In this study, women who were separated/divorced/single or widowed were more likely to have an in-hospital stroke alert activated when compared to women who were married (p = .067; OR 1.72). In a study of 60,507 patients with stroke the case fatality was lower among unmarried, divorced and widowed compared to married stroke patients (51.19% were married, 9.47% were unmarried, 13.29% were divorced, and 26.05% were widowers) (Anderson & Olsen, 2018).

Ethnicity. Of the 92 *propensity score matched* women, about 91% of women were Caucasian and nearly 9% were from other ethnicity groups. The vast majority (93.5%) of the 46 women who had an in-hospital stroke alert activated were Caucasian, with the African American (2.2%), Alaskan Native (2.2%), and Middle Eastern American (2.2) ethnic groups being equal. Similar to other study findings and national statistics, ethnicity was significant. In this study, women of Caucasian ethnicity were more likely to have an in-hospital stroke alert activated when compared to women of other ethnic groups (p < .001; OR 8.60). In one study, African-American women suffer from a significantly higher number of strokes than Caucasian women who have experienced a stroke being the leading cause of death for Hispanic women (Benjamin et al., 2017; Mozaffarian et al., 2016). In addition, nationally African Americans are twice as likely to die from stroke and survivors are more likely to have disabilities compared to Caucasians (Benjamin et al., 2017; Mozaffarian et al., 2016; National Stroke Association, 2018).

Admission hospital floor. Of the 92 *propensity score matched* women, slightly over half of these women (n = 49; N = 92) were admitted from the emergency room. Half (50.0%) of the 46 women who had an in-hospital stroke alert activated were admitted from the emergency floor for another condition, not ischemic stroke. Contradictory to other study findings, this study findings indicate that women who were admitted from the emergency floor (p = .668; OR .885) were less likely to have an in-hospital stroke alert activated compared to women admitted directly to critical care, non-critical and surgical floors. Stroke alert evidence and clinical guidelines are robust for activation within the emergency department (El Husseini & Goldstein, 2013; Meretoja et al., 2012; Meretoja et al., 2013; Middleton Grimley and Alexandrov, 2015). The use of activating emergency room stroke alert have shown to improve time to diagnosis and reduce thrombolytic treatment times (Meretoja et al., 2012). In a prospective interventional study by Kassardjian et al., (2017), in-hospital strokes were more commonly found on cardiovascular wards (45%) and during the perioperative period (60%).

Stroke risk factors. Of the 92 *propensity score matched* women, 90 of the 92 matched women had at least 1 or more stroke risk factors. Almost 43% of them had high blood pressure, almost 25% had high cholesterol, almost 24% had diabetes, and almost 10% women were smokers. Interestingly, in this study, women who had stroke risk factors ($p < .001$; OR .022) were less likely to have an in-hospital stroke alert activated. In this study, the top stroke risk factors included: high blood pressure, atrial fibrillation, and high cholesterol. These risk factors were similar to other study findings. Modifiable and non-modifiable risk factors for ischemic stroke have been identified and include: high blood pressure; smoking; diabetes; high cholesterol; physical inactivity and obesity; carotid or other artery disease; transient ischemic attacks; atrial fibrillation or other heart disease; certain blood disorders; excessive alcohol intake; illegal drug use; sleep apnea; increasing age; gender; heredity and race; and prior stroke (ASA, 2019a; Capriotti, & Frizzell, 2016). In a study by Kes (2016) of 396 stroke patients, women had higher odds of hypertension, chronic heart failure and atrial fibrillation than men. About 15% of all embolic strokes occur in individuals with the stroke risk factor of atrial fibrillation (ASA, 2019a). High cholesterol is a common stroke risk factor for large vessel strokes and lacunar strokes are closely linked to high blood pressure (ASA, 2019a).

Comorbid conditions. Of the 92 *propensity score matched* women, nearly 80% of these women had comorbid conditions. The top three comorbid conditions were spread across the following 3 conditions: renal disease (20.5%), congestive heart failure (15.9%), and diabetes with chronic complications (15.9%). Interestingly, in this study, women who had comorbid conditions ($p < .001$; OR .289) were less likely to have an in-hospital stroke alert activated. This studying's findings of congestive heart failure, diabetes, and renal disease were similar to other study findings. In a study by Kes (2016) of 396 stroke patients, the older patients had greater comorbid heart conditions and went to rehabilitation treatment more often than the younger patients.

Primary medical diagnosis. Of the 92 *propensity score matched* women, nearly half of these women had a primary medical diagnosis of a cardiovascular disease. Similar to other study findings, primary medical diagnosis was significant. Women with a primary diagnosis of a cardiovascular disease were more likely to have an in-hospital stroke alert activated compared to women with other diseases or disorders ($p = .763$; OR 1.10). In other study findings, patients who are hospitalized for a primary admission diagnosis of cardiac disease or surgery were vulnerable to in-hospital stroke, a stroke occurring during a hospital stay in a patient originally admitted for another diagnosis, (Berglund et al., 2015; Boden-Albala et al., 2015; Hanselman, 2014; Park et al., 2013; Sobolewski et al., 2015).

Stroke symptoms. Of the 92 *propensity score matched* women, about 15% of these women had common stroke symptoms and nearly 32% had unique stroke symptoms. Similar to other study findings, early recognition of stroke symptoms were significant. This study found that women who had common ($p < .001$; OR 6.50) or unique ($p = .012$; OR 2.31) stroke symptoms were more likely to have an in-hospital stroke alert activated. Up to 135,150 (17%)

of all stroke cases have stroke symptom onset during an in-patient hospital stay for a separate condition (Cumbler, 2015; Messé et al., 2016). Younger women have greater unique symptoms than older women, when compared to women aged 46 years and older (CDC, 2019). Early identification (the process of identifying stroke symptoms less than 3 to 4.5 hours of symptom onset) is crucial to timely thrombolytic treatment and better patient outcomes (Boden-Albala et al., 2015; Boehme et al., 2014; Hanselman, 2014; Powers et al., 2015; Sobolewski et al., 2015). Evidence indicates that a percentage of stroke patients' are initially misdiagnosed due to either unique symptoms or stroke mimics; nonvascular conditions that present with stroke-like symptoms (Madsen et al., 2016).

Time last known well. The Time Last Known Well is documented when a stroke alert is activated. The Time Last Known Well is used in determining if the patient meets thrombolytic therapy inclusion or not (The Joint Commission, 2018). The Time Last Known Well is part of the stroke alert guidelines and informs the benchmark times to diagnostics and treatment (Benjamin et al., 2017; Mozaffarian et al., 2016). Of the 92 *propensity score matched* women, 33 (35.9%) had the Time Last Known Well documented. Similar to The Joint Commission stroke guidelines (2019), The Time Last Known Well was significant. Women who had the Time Last Known Well documented were more likely to have an in-hospital stroke alert activated compared to women who did not have a Time Last Known Well documented (p = .041; OR 2.00).

Emergency Severity Index. Of the 92 *propensity score matched* women, 46 (50.0%) women had an Emergency Severity Index documented with 29 women classified as emergent, 14 as urgent, and 3 as most urgent. Contradictory to other study findings, Emergency Severity Index was not significant. In this study, there was no difference in women who had an

Emergency Severity Index score documented or not documented (p = 1.00; OR 1.00). Other studies have found that stroke misdiagnosis has led to longer hospital stays, and woman have been found to have higher odds for less severe Emergency Severity Index and increased Modified Rankin Scale than men (Kes et al., 2016; Madsen et al., 2016; Park et al., 2013). This unexpected insignificant finding could be due to the small sample size of this study; the fact that only 46 women had an Emergency Severity Index documented with the majority of the Index classified as emergent.

Number of hospital units/floors. Of the 92 *propensity score matched* women, 40.2% or 37 women were on a total of 2 hospital units, 32.6% or 30 women were on 3 hospital units, 15.2% or 14 were on 4 units, and only 12.0% or 11 women were on just 1 unit. Contradictory to other study findings, the number of hospital floors/units was not significant. Interestedly, women who were on more hospital units were more likely to have an in-hospital stroke alert activated compared to women on less hospital floors (p = .746; OR 1.11). Previous studies have indicated that multiple unit transfers affect the quality of care and stroke outcomes (Solano et al., 2017). The difference in multiple unit transfers and outcomes noted in this study could be attributed to the patient having an initial assessment indicating a stroke by the nurse each time the patient transferred to a different unit/floor. Further investigation is warranted to understand the process of multiple patient hospital unit floor transfers to the nursing process and the effect on outcomes.

Average nurse patient-ratio. Of the 92 *propensity score matched* women, the average nurse patient-ratio was 2:1 (n = 32; 34.8%), with the second average being 4:1 (n = 11; 12.0%). There are no reports on the relationship of the average nurse patient-ratio and in-hospital stroke alert in women in the literature. Although, a study of 2,388 acute stroke patients, found that when the nurse-patient ratio was increased to one trained nurse per 10 beds the stroke patient had a reduction in 30-day mortality of 11–28% ($p < 0.0001$) and a reduction in 1-year mortality of 8–12% ($p < 0.001$) (Myint et.al., 2016). However in a different study, involving 175,755 patients admitted to the intensive care unit and/or cardiac/cardiothoracic units showed that a higher nurse staffing level decreased the risk of in-hospital mortality by 14% (0.86, 95% confidence interval 0.79–0.94) (Driscoll, et.al., 2017). Further investigation is needed to identify the associations of nurse-to-patient ratios with nurse-sensitive patient outcomes for optimal nurse-to-patient ratios and early stroke detection and better stroke outcomes.

Diagnostic imaging. Of the 92 *propensity score matched* women, only 6 (6.5%) of the women had a computed tomographic scan or magnetic resonance imaging and 86 (93.5%) of women did not have a computed tomographic scan or magnetic resonance imaging completed at all or within the 45 minutes of the Time Last Known Well. Similar to other study findings, a computed tomographic scan or magnetic resonance imaging within 45 minutes of the Time Last Known Well was significant. Women who had a diagnostic imaging completed within the 45 minutes time from the Last Known Well time were more likely to have an in-hospital stroke alert activated ($p < .001$; OR 41.0). Therefore, those women who had an in-hospital stroke alert activated early were more likely also to have a computed tomographic scan or magnetic resonance imaging completed within the 45 minutes of the Last Known Well time increasing time to diagnosis and treatment.

Delay time. Of the 92 *propensity score matched* women in this study the *diagnostic delay time*, the time from when the patient was last known well (without stroke symptoms) to the time of computed tomographic scan or magnetic resonance imaging, ranged from 0.1 to 80 hours with 12 (13.2%) of women who had an average of 1 to 2 hour delay time in diagnostics delay time. There are no reports on the relationship of the diagnostic delay time and in-hospital stroke alert in women in the literature. Although, according to the American Heart and Stroke Association 2018 guidelines, “centers should attempt to obtain a non-contrast head computed tomography scan within 20 minutes of arrival in ≥ 50% of stroke patients who may be candidates for IV tissue plasminogen activator or mechanical thrombectomy” (Powers et al., 2018, para 4).

Of the 92 *propensity score matched* women in this study the *in-hospital stroke alert delay time*, the time from when the patient was last known well (without stroke symptoms) to the time the stroke alert response team was activated, ranged from 0.3 to 264 hours with 8 (8.8%) of women who had an average of 1 hour delay time for in-hospital stroke alert activation. There are no reports on the relationship of the in-hospital stroke alert delay time and in-hospital stroke alert in women in the literature. Although, evidence suggests that low symptom recognition and misdiagnosis of stroke all contribute to delayed thrombolytic therapy and has led to longer hospital stays (Boden-Albala et al., 2015; CDC, 2019; Kes, 2016; Madsen et al., 2016; Mellon et al., 2015; Park et al., 2013).

Thrombolytic therapy. The outcome of receiving thrombolytic therapy is associated with and potentially influenced by stroke risk, recognition, and severity of stroke (ASA, 2019a; Mozaffarian et al., 2016). Thrombolytic therapy was measured as either the stroke patient received thrombolytic therapy or not. Of the 92 *propensity score matched* women in this study, only 15 of the 149 women who had an in-hospital stroke received thrombolytic therapy. Thrombolytic therapy was significantly associated with in-hospital stroke alert (p < .001; OR 8.80). Therefore, the activation of in-hospital stroke alert is significant to receiving thrombolytic therapy (p < .001). Similarly, the use of activating in-hospital stroke alert have shown to improve thrombolytic treatment times (Meretoja et al., 2012). Other studies have found that the activation of stroke alert increased the rate of thrombolytic therapy from 33.3% to 59.2% among ischemic stroke patients ($p = 0.0001$) (Kim et al., 2015); and stroke alert improved the use of thrombolytic therapy ($p = 0.001$) (Chen et al., 2014).

Discharge status. The outcome of discharge status is associated with and potentially influenced by stroke risk, recognition, and severity of stroke (ASA, 2019a; Mozaffarian et al., 2016). Discharge status is an outcome indicator which suggests good versus poor outcome status. Of the 92 *propensity score matched* women in this study, the odds for discharge to a skilled nursing facility, home care, hospice, or expiring decreased with in-hospital stroke alert activation ($p = .014$; OR .429). Women who had an in-hospital stroke alert activated were more likely to discharge to home ($p = .014$). Therefore, women who had no in-hospital stroke alert fared worse in stroke outcomes and women who had an in-hospital stroke alert activated had better stroke outcomes. Similarly, another study found that stroke alert improved patient outcomes at discharge ($p = 0.001$) (Chen et al., 2014). In addition, studies indicate that early recognition of stroke is crucial to timely thrombolytic treatment and better patient outcomes (Boden-Albala et al., 2015; Boehme et al., 2014; Hanselman, 2014; Powers et al., 2015; Sobolewski et al., 2015).

Summaries and Conclusions

Effects of In-hospital Stroke Alert and Associated Variables

This study was unique in that it only evaluated women and the relationship between in-hospital stroke alert and thrombolytic therapy. This study also used a propensity score matching model to isolate the treatment (in-hospital stroke alert) and outcome (thrombolytic therapy), while controlling the effects of other influential variables (Shever et al., 2008). Before propensity score matching, there was no significance between in-hospital stroke alert and thrombolytic therapy ($p = .103$). However, after propensity score matching, and controlling for the effects of other influential variables, activation of an in-hospital stroke alert and thrombolytic therapy was significant ($p < .001$). This difference in significance demonstrates the confounding influence the other covariates had on an examination of in-hospital stroke alert and thrombolytic therapy.

Patient characteristics. This propensity score matching and regression models demonstrate the strength of association between the covariates to in-hospital stroke alert. Age was a factor whether in-hospital stroke alert was activated or not. Younger women were less likely to have an in-hospital stroke alert activated compared to older women. Only seven woman out of thirty-eight women between 18 to 59 years of age had an in-hospital stroke alert activated.

Ethnicity was also a factor whether in-hospital stroke alert was activated or not. Only three of the thirteen women from non-Caucasian ethnic groups had an in-hospital stroke alert activated. None of these women had a computed tomographic scan or magnetic resonance imaging scan within 45 minutes of the Time Last Known Well. In addition, none of these women received thrombolytic therapy. The age ranges for women of non-Caucasian ethnic groups were: a) one woman between the ages of 30-40 years; b) two women between the ages of 40-50 years; c) seven women between the ages of 50 – 60 years; and d) three women between the ages of 70 – 89 years.

Contraindications to thrombolytic therapy were reviewed. Two women may not have had thrombolytic therapy due to the contraindication of surgery within the last 14 days, and 23 may have been excluded due to advanced age. This study was retrospective and therefore, it is possible that thrombolytic therapy exclusion was not documented and thus not entered into this study. Future research should include collection of detailed data on why thrombolytic therapy was not given.

Clinical conditions. The major contributing risk factors for the propensity score matched women ($N = 92$) were smoking ($n = 71$) and high cholesterol ($n = 39$). The major contributing comorbid conditions were renal disease ($n = 31$), congestive heart failure ($n = 24$) and diabetes with chronic complication ($n = 24$). Interestingly, two women from the non-Caucasian ethnic group ($n = 13$) were smokers and neither of them had an in-hospital stroke alert activated and four of these women had high cholesterol with only two of these women had an in-hospital stroke alert activated. In addition, three women from the non-Caucasian ethnic group ($n = 13$) had congestive heart failure and neither of these women had an in-hospital stroke alert activated, five women had diabetes with chronic conditions and one of them had an in-hospital stroke alert activated. Also, four women from the non-Caucasian ethnic group ($n = 13$) had renal disease and none of these women had an in-hospital stroke alert activated. Therefore, this study findings indicate that stroke risk factors and comorbid conditions were major contributors to whether an in-hospital stroke alert was activated or not. The more risk factors and comorbid conditions a women had the less likely an in-hospital stroke alert was activated. This risk factors and comorbid incidence of no in-hospital stroke alert increased when a women was also from other ethnic groups.

Common and unique stroke symptoms in women were also contributors to whether an in-hospital stroke alert was activated or not. When stroke symptoms were present women were more likely to have an in-hospital stroke alert activated. Within the propensity score matched women ($N = 92$), 13 women had common stroke symptoms present which included: weakness, speech, headache and dizziness. Twenty-nine women had unique stroke symptoms in women present which included: vomiting, trouble breathing, general weakness, nausea and altered mental status. This study was retrospective and therefore, it is possible that not every stroke symptom was documented and thus entered into this study. Future research is necessary to further investigate common and unique stroke symptoms in women, the relationship to early stroke detection and in-hospital stroke alert in women.

Context of care. The Time Last Known Well is documented when a stroke alert is activated and a stroke alert is activated when a stroke is suspected based on signs and symptoms of a stroke (The Joint Commission, 2018). Not surprisingly, in this study, the documentation of the Time Last Known Well was directly linked to whether an in-hospital stroke alert was activated or not. Thirty-three women (n = 46; N = 92) who had in-hospital stroke alert activated also had a Last Known Well time documented. This directly linked to whether a computed tomographic scan or magnetic resonance imaging was completed within 45 minutes of the Last Known Well time or not. Six women (n = 46; N = 92) who had the Last Known Well time documented and an in-hospital stroke alert activated had a computed tomographic scan or magnetic resonance imaging completed within the recommended stroke guideline timeframe. Delay time varied between Time Last Known Well to when an in-hospital stroke alert was activated ranging from 0.10 – 265 hours. Further investigation in delay time is needed to better understand this disconnect. The delay time from Last Known Well time to having a computed tomographic scan or magnetic resonance imaging completed ranged from 0.10 – 22 hours. The delay time for diagnostics suggests that the health care team may have had to stabilize the patient and make priority decisions.

Outcomes. This study found that in-hospital stroke alert was a major determinant to whether the patient received thrombolytic therapy or not. After the two groups were matched and compared there is an excellent chance that the difference in thrombolytic therapy would not have been observed if in-hospital stroke alert had no benefit whatsoever ($p < .001$). Therefore in-hospital stroke alert is indeed effective to women receiving thrombolytic therapy or not. Interestingly in this study, most women who had an in-hospital stroke alert activated were admitted through the emergency room. The critical care unit with an average 2:1 nurse-patient ratio activated the majority of the in-hospital stroke alerts. However, only 2 of the 15 women that received thrombolytic therapy had an in-hospital stroke alert activated on the critical care unit with a 2:1 nurse patient ratio. The other 13 women who received thrombolytic therapy were on either non-critical or surgical hospital units. The reason for this small percentage of women receiving thrombolytic therapy on the critical care floor where in-hospital stroke alert was activated could be due to patient conditions being acute increasingly the possibility of contraindications to thrombolytic therapy. Further investigation is warranted on the relationship between admitting emergency diagnosis and in-hospital stroke alert.

Discharge to home status was directly linked to having an in-hospital stroke alert activated or not. After the two groups were matched and compared there was a good chance that the difference in discharge status would not have been observed if in-hospital stroke alert had no benefit whatsoever ($p = .014$). Therefore in-hospital stroke alert is indeed effective to women discharging to home or not. Women were more likely to discharge to home when they had an in-hospital stroke alert activated. Seven women from the in-hospital stroke alert was activated group ($n = 46$) discharged to home. However, the only 2 women who had both, in-hospital stroke alert and thrombolytic therapy went to hospice and/or expired. Only 1 of the 15 women who received thrombolytic therapy discharged to home and the majority discharged to skilled nursing facilities.

Implications for Action

In-hospital stroke alert activation is a system, a protocol that can be further developed to be sensitive and specific to women. Previous studies and this study have identified that activation of in-hospital stroke alert is an effective tool for stroke patients receiving thrombolytic therapy and better stroke outcomes. However, nursing or other health professionals may not recognize stroke symptoms, or the symptoms may be attributed to another condition which then can hinder the activation of an in-hospital stroke alert and thus delay the administration of thrombolytic therapy. Therefore, strategies to improve the identification of all common and unique stroke symptoms in women is needed. Current in-hospital stroke protocols should include the nationally accepted and published stroke symptoms recognized as “f” for face drooping, “a” for arm weakness, “s” for speech difficulty, and “t” for time to call 911 (ASA, 2019b). In-hospital stroke alert protocols should also include the common symptoms of stroke, which includes sudden “(1) Numbness or weakness of face, arm or leg, especially on one side of the body, (2) Confusion, trouble speaking, or understanding, (3) Trouble seeing in one or both eyes, (4) Trouble walking, dizziness, loss of balance or coordination, and (5) Severe headache with no known cause” (ASA, 2019b). In addition, in-hospital stroke alert protocols should recognize the following 11 unique stroke symptoms in women which includes: (1) loss of consciousness or fainting, (2) general weakness, (3) difficulty breathing or shortness of breath, (4) confusion, unresponsiveness or disorientation, (5) sudden behavioral change, (6) agitation, (7) hallucination, (8) nausea or vomiting, (9) pain, (10) seizures, and (11) hiccups (National Stroke Association, 2018). Special attention should be made to younger women under 59 years of age and women of non-Caucasian ethnic groups. Given the influence risk factors and comorbid conditions have on in-hospital stroke alert, nurses and other health professionals should be alert to careful stroke assessment of women that have more than 1 risk factor and any comorbid conditions, especially if they are smokers, have high cholesterol, have renal disease, congestive heart failure, and/or diabetes with chronic complication. In addition, special attention needs to made to ensuring that the Time Last Known Well and timely diagnostic imaging is part of the in-hospital stroke alert protocol. Timely and adequate documentation of the Time Last Known Well should be a priority.

Significance for Nursing Science, Practice and Education

This study contributes to the growing evidence regarding stroke in women, in-hospital stroke alert and stroke outcomes by contributing to the knowledge related to women and stroke. This study provides the preliminary evidence for the development of a stroke assessment tool specific and sensitive to women. There is a current gap in our current data and knowledge on criteria specific to in-hospital stroke alert for women and means to increase the frequency of thrombolytic therapy and thus decrease disability and cost. Prior studies have focused on patients who are hospitalized for cardiac disease or surgery as being vulnerable to having an in-hospital stroke (Berglund et al., 2015; Boden-Albala et al., 2015; Hanselman, 2014; Park et al., 2013; Sobolewski et al., 2015) and how the use of activating in-hospital stroke alert has been shown to improve time to diagnosis as well as reduce thrombolytic treatment times (Cumbler, Zaemisch, Graves, Brega, & Jones, 2012; Meretoja et al., 2012; Meretoja et al., 2013). Prior to this study, the effects of in-hospital stroke alert specifically in women have not been examined. Additional research is needed to learn what additional variables affect in-hospital stroke alert in women, with special consideration to stroke mimics and other nonvascular conditions that present with stroke-like symptoms. With the increase in stroke in women and stroke in the younger population, there is a need to further investigate unique stroke symptoms in women and the development of stroke tools that are sensitive and specific to women. Additional research is also needed to better understand nursing knowledge, education, and decisions to activate an in-hospital stroke alert in women. Furthermore, investigation is warranted to understand the process of transferring hospital unit floors to the nursing process and the effect on outcomes. There is also a need for nurse scientists to increase comparative effectiveness research as a means to facilitate linking nursing practice and health outcomes, development and disseminate best practices.

Educating nurses and other health professionals about the effects of in-hospital stroke alert in women will be necessary to improve both early stroke detection in women and early activation of in-hospital stroke alert. Awareness to the factors that facilitate and hinder stroke detection and in-hospital stroke alert activation may increase early stroke treatment in women who have a stroke while hospitalized for a separate condition. Because stroke symptoms may go undetected, nurses are encouraged to educate themselves on stroke in women, recognize the importance of early stroke detection and to report early when a woman presents with symptoms that are unusual for them. Furthermore, nurses are encouraged to assist in the development or revision of an in-hospital stroke alert protocol. Strategies for in-hospital stroke alert protocol may include recognizing factors that are barriers to an in-hospital stroke alert being activated in women and discuss how these barriers could be addressed and removed.

APPENDICES

Appendix A

Signed Consent Form: Model for Nursing Effectiveness Research

CONSENT FORM

I, ___Leah L. Shever_______________ hereby grant permission, including non-exclusive world rights, to _____Renee Colsch___to use the portion of the work here cited for the purpose described below:

Work:

- Model for nursing effectiveness research using propensity scores.
- Shever LL, Titler MG, Kerr P, Qin R, Kim T, Picone DM. The effect of high nursing surveillance on hospital cost. Journal of Nursing Scholarship. 2008 Jun 1;40(2):161-9.

Portion:

- Figure for the Model for Nursing Effectiveness Research Using Propensity Scores.

Purpose:

- To utilize the model as a framework for proposed study: Determine the effect of In-hospital code stroke on delivering thrombolytic therapy. Specific aims will be applied to subjects' 18 years of age and older with a diagnosis of ischemic stroke obtained during hospitalization:
- Aim 1. Describe the imbalance of patient characteristics (age, marital status, ethnicity, and site admitted from) and covariates (clinical conditions, context of care, and treatments) between those who had In-hospital code stroke to those who did not.
- Aim 2. Determine the relationship between each covariate variable to the treatment (In-hospital code stroke) and to the outcome (STK-4 Thrombolytic Therapy).
- Aim 3. Determine which patient characteristics; clinical conditions; context of care; and treatments are associated with the probability of In-hospital code stroke and administration of STK-4 Thrombolytic Therapy.

Signed: Leah L. Shever on 11/20/2017
[Signature of copyright holder] [Date]

Name: Leah L. Shever
[Please Print]

Director of Nursing Research, Quality and Innovation
[Title]

11/20/17
[Date]

Other persons to contact for consent:

Name(s): ______________________________

Address(es): ______________________________

Telephone No(s): ______________________________

Email address(es): ______________________________

1

Appendix B

Example of Participating Medical Center's In-Hospital Stroke Alert Protocol

Table. Example of Participating Medical Center's In-Hospital Stroke Alert Protocol

The in-hospital Stroke Alert Team consists of a Hospitalist, Critical Care flyer, Special Care Unit RN, CT Technician, Respiratory Therapist, Lab technician, Pharmacist, Tele-Stroke (TS) Neurologist, Administrative Nursing Supervisor, and Emergency Department Technician (EDT).

After recognition of acute neurologic impairment, any team member may activate the Rapid Response Team by calling X. The team will then determine the need to activate a stroke alert based on predetermined criteria:
Sudden onset of any one of the following;
1. Numbness or weakness in the face, arms or legs, particularly on one side of the body.
2. Confusion
3. Aphasia (difficulty speaking or understanding what others are saying
4. Difficulty walking, loss of balance or coordination.
5. Severe headache that does not have obvious or known cause.
6. Nonspecific visual complaints with Partial, Complete or Bilateral visual field loss or double vision.
7. Sudden onset of continuous vertigo and ANY of the following:
   - 65 years of age or older
   - Younger than 65 with risk factors (i.e. Smoking, diabetes, HTN, etc.)
   - Posterior neck pain in setting of recent manipulation or injury

The stroke alert can be activated by a nurse caring for the patient or during a Rapid Response Team Activation by calling X and stating "Stroke Alert in room_________".
The HMC assigned to the unit in which the stroke alert is being activated will immediately contact Patient Placement to connect with the TS Neurologist. Be prepared to give primary RN's phone number.

Role	Responsibility/Action
Bedside RN	1. Identify neurologic signs/symptoms and confirm time last known well (patient, family, hospital staff) 2. Activate RRT by calling X 3. Obtain stat finger stick blood sugar and blood pressure 4. Remain available at the bedside during the stroke alert to provide information re: time last known well (in military time), symptoms, baseline neuro status, reason for hospitalization, medications received during hospitalization, (anticoagulants, narcotics, sleep meds), kidney function, sleep status, and pre-existing dementia 5. Locate most recent accurate weight of patient and confirm that it is entered into Excellian immediately for Pharmacy reference if IV Alteplase administration is indicated. If necessary, obtain an estimated weight.

Table cont.

Role	**Responsibility/Action**
	6. Contact radiology staff to ensure they are prepared for the patient's arrival 7. May need to accompany patient and CC RN to CT to provide additional history to TS Neurologist (hand off assignment to partner)
Hospitalist	~~1.~~ Respond to stroke alert and assess the patient's symptoms, time of onset and perform a brief exam. 2. Initiate the STROKE ALERT if not already done 3. If not already done, instruct the Health Monitor Coordinator to contact TS Neurologist through Patient Placement 4. Connect with the TS neurologist and develop a treatment plan 5. Order entry– CT head without contrast and computed tomography angiography (CTA) head and CTA neck (STAT) 6. Consider ordering the following laboratory tests: BMP, CBC, PTT, INR / Protime, urine pregnancy (if appropriate) and EKG to be done prior to IV alteplase administration 7. If possible accompany patient to CT to be available to connect with TS Neurologist 8. Discuss treating hypertension with TS Neurologist if indicated 9. Once connected with TS Neurologist, review additional history and perform National Institute of Health Stroke Scale (NIHSS) with TS Neurologist before CT is done 10. Review non-contrast CT with TS Neurologist 11. If indicated, enter In House Ischemic Stroke with Alteplase orderset and call pharmacy to mix and send (while CTA is being done) 12. Upon arriving back to department, review labs, EKG and perform any additional exam with TS Neurologist 13. Assist TS Neurologist in completing informed verbal consent 14. Collaboratively make decision regarding continued treatment at hospital or need for transfer to center providing higher level of neurological care 15. Enter orders as appropriate for care decisions

Table. cont.

Role	Responsibility/Action
Telestroke Neurologist	1. Call back to primary nurse and confirm code stroke candidate 2. Connect via telestroke cart in CT within 10 minutes of moving forward with code stroke 3. Give orders for code stroke diagnostics / workup 4. Make decision re: if additional labs needed – direct nurse to call phlebotomy if needed 5. Review imaging as completed – collaborate with radiologist when appropriate 6. Make treatment decision and direct Nurse or Hospitalist to call pharmacy to order IV Alteplase 7. Obtain verbal consent if IV Alteplase is indicated 8. Discuss options with Hospitalist for continued care at hospital vs. transfer to another center providing a higher level of neurological care
Flyer and or CC RN	1. Confirm stroke-like symptoms and time last known well 2. Notify Hospitalist immediately and initiate a Code Stroke, if not already done 3. Begin every 15 minute vital signs and neuro checks 4. Initiate 2 IV sites (prefer #18 gauge antecubital for at least one site) – this can be completed in CT – do NOT delay transport to CT for IV placement 5. Place on cardiac monitor 6. Assist patient to CT. Patient must be on a cardiac monitor with a critical care nurse in attendance throughout transport. 7. Assist TS neurologist with exam 8. Continue every 15 minute VS and neuro checks/ throughout transport 9. Be prepared to treat hypertension as requested 10. Transport patient back to the appropriate unit for further monitoring. (If IV alteplase is indicated the patient will need to be transferred to the SCU
Additional CC RN Responsibilities (CC RN only in the SCU)	<u>Administration of IV Alteplase</u> 1. Participate in “Time Out” prior to any administration of IV Alteplase

Table. cont.

Role	Responsibility/Action
	2. Double check IV Alteplase dose and pump rate with SCU RN prior to administration 3. Support SCU staff and team as needed until patient is stabilized or transferred to another facility 4. If IV Alteplase will not be given, confirm that call has been made to Pharmacy to not mix and order to be discontinued 5. If IV Alteplase is delivered and not given, return the medication to the pharmacy
Lab Technician	1. Draws blood per MD order 2. Call lab to notify them of urgency and prioritization of tests.
Respiratory therapist	1. Respond immediately 2. Obtain an EKG but do not delay the patient going to CT (EKG may be completed after CT) 3. Hand results to Hospitalist for interpretation. Must be done prior to decision to administer Alteplase
Pharmacist	1. When stroke alert is paged overhead, watch for orders related to possible Alteplase administration. Immediately check that patient weight is available in the EMR 2. Pharmacist to verify IV Alteplase order, print label and wait for MD phone call indicating that medication should be mixed 3. Alteplase to be prepared immediately, pharmacist to hand deliver drug promptly to nurse caring for patient at patient location 4. Pharmacist to discontinue order if decision is made not to mix and administer IV Alteplase.
Administrative Supervisor	1. Participate in management of patient flow and work flow as needed to assure efficient care during the code stroke process 2. Bring the ED Telestroke Machine to CT if ED Tech is unavailable 3. Keep the family informed if present at bedside
Charge RN	1. Transport a portable cardiac monitor/ electrodes to patient room for immediate monitoring during a code stroke

Table. cont.

Role	Responsibility/Action
	2. Locate and bring a cart with portable oxygen to the room for immediate transport of patient to the CT Scan area
CT Technologist	3. Respond appropriately to code stroke page by preparing the area 4. Perform non-contrast head CT 5. Load CT images into Ultravisual (PACS) system 6. Send non-contrast head CT scan results while waiting for CTA
ED Technician	1. Bring telestroke equipment to CT Scan and assist with initial set-up

Permission to adapt and reprint granted by participating medical center 09.12.18

Appendix C

Allina Health IRB Approval

Allina Health
Human Research Protection Program
Institutional Review Board

P.O. Box 43 Mail Route 10105
Minneapolis, MN 55440-0043
Tel: 612-262-4920
Fax: 612-262-4953
www.allinahealth.org

DATE:	October 5, 2018
TO:	Dimitrios Giannakidis, MD
FROM:	Allina Health IRB Office
PROJECT TITLE:	Effect of In-Hospital Stroke Alert on Thrombolytic Therapy in Women
REFERENCE #:	1313192-1
SUBMISSION TYPE:	New Project
SUBMISSION DATE:	September 13, 2018
ACTION:	DETERMINATION OF EXEMPT STATUS
ACTION DATE:	October 4, 2018
REVIEW CATEGORY:	Exemption category # 4

Thank you for your submission of New Project materials for this project for exempt determination.

The following items were included in this submission:

- Allina Health - Application Part 1 - Allina Health - Application Part 1 (UPDATED: 09/28/2018)
- Application Form - ALLINA - Application 2 - Chart Review doc (UPDATED: 09/28/2018)
- Conflict of Interest - Other - Glenda Lindseth FY18 UND COI.pdf (UPDATED: 09/13/2018)
- Conflict of Interest - Other - Colsch Project Specific COI Disclosure Form v 11-10-17-1 signed.pdf (UPDATED: 09/12/2018)
- Conflict of Interest - Other - Giannakidis Project Specific COI Disclosure Form v 11-10-17-2.pdf (UPDATED: 09/12/2018)
- CV/Resume - Giannkidiscv feb18.docx (UPDATED: 09/17/2018)
- CV/Resume - G Lindseth Vita Signed 07.2018.pdf (UPDATED: 08/29/2018)
- CV/Resume - Renee Colsch Curriculum Vitae Signed.pdf (UPDATED: 08/26/2018)
- Other - UND IRB Board Approval Letter.pdf (UPDATED: 09/28/2018)
- Other - Memo of acknowledgement.signed.pdf (UPDATED: 09/12/2018)
- Protocol - Allina Protocol Expedited.docx (UPDATED: 09/28/2018)
- Training/Certification - G Lindseth citiCompletionReport5407262-1.pdf (UPDATED: 08/29/2018)

The Allina Health IRB has determined this project is EXEMPT FROM IRB REVIEW according to federal regulations 45 CFR 46.101(b).

Modifications which may impact this exempt determination (e.g., addition of or changes to research procedures) should be submitted in advance of implementation via the submission of an Amendment for determination of whether the project continues to qualify for exemption.

When the research is complete Study Closure report must be completed and submitted to the IRB.

Exempt studies are subject to institutional oversight including reviews and audits by the Human Research Protection Program.

If you have any questions, please contact the Allina Health IRB Office at (612) 262-4920 or irb@allina.com. Please include your project title and IRBNet ID# in all correspondence.

This letter has been electronically signed in accordance with all applicable regulations, and a copy is retained within Allina Health IRB Office's records.

Appendix D

University of North Dakota IRB Approval

UNIVERSITY OF NORTH DAKOTA

DIVISION OF RESEARCH & ECONOMIC DEVELOPMENT

UND.edu

Institutional Review Board
Twamley Hall, Room 106
264 Centennial Dr Stop 7134
Grand Forks, ND 58202-7134
Phone: 701.777.4279
Fax: 701.777.6708
Email: UND.irb@research.UND.edu

September 19, 2018

Principal Investigator(s):	Renee Colsch
Project Title:	Effect of In-Hospital Stroke Alert on Thrombolytic Therapy in Women
IRB Project Number:	IRB-201809-050
Project Review Level:	Exempt 4
Date of IRB Approval:	09/19/2018
Expiration Date of This Approval:	09/18/2021

The application form and all included documentation for the above-referenced project have been reviewed and approved via the procedures of the University of North Dakota Institutional Review Board.

If you need to make changes to your research, you must submit a Protocol Change Request Form to the IRB for approval. No changes to approved research may take place without prior IRB approval.

This project has been approved for 3 years, as permitted by UND IRB policies for exempt research. You have approval for this project through the above-listed expiration date. When this research is completed, please submit a Termination Form to the IRB.

The forms to assist you in filing your project termination, adverse event/unanticipated problem, protocol change, etc. may be accessed on the IRB website: http://und.edu/research/resources/human-subjects/

Sincerely,

Michelle L. Bowles

Michelle L. Bowles, M.P.A., CIP
IRB Manager

MLB/sb

Cc: Glenda Lindseth, Ph.D.

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