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Understanding Risk for Stroke Within the Context of COVID-19

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Understanding Risk for Stroke Within the Context of COVID-19

DNP Scholarly Project Paper

submitted in partial satisfaction of the requirements
for the degree of

DOCTOR OF NURSING PRACTICE

in Nursing Science

by

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2022

DEDICATION

This paper is dedicated to my parents, Beatriz and Jairo, who have been my constant source of inspiration. Their love and example have motivated me to continue this path of learning and serving. Without their support and unconditional love, this project would not have been possible.

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Above all, I want to thank God for this opportunity.

VITA

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FIELD OF STUDY

Doctor of Nursing Practice, Family Nurse Practitioner in Nursing Science

ABSTRACT OF THE DNP SCHOLARLY PROJECT PAPER

Understanding Risk for Stroke in the Context of COVID19

by

Maria del Pilar Giraldo Herrera

Doctor of Nursing Practice, Family Nurse Practitioner in Nursing Science

University of California, Irvine, 2022

Associate Professor Melissa D. Pinto, Chair

Early in Coronavirus disease-2019 (COVID-19) pandemic, frontline clinicians provided anecdotal observations there was an increase in the number of individuals presenting with a stroke who did not have traditional stroke factors. Current tools to evaluate stroke risks are based on decades of research-all conducted prior to COVID-19 pandemic and before the SARS-CoV-2 was in existence or circulating widely. Accurate stroke assessment is predicated on accurate identification of stroke risk factors. Little attention has been paid to re-examining stroke risk tools to consider the influence of COVID-19. This Quality Improvement (QI) project aimed to answer the question: Do established stroke tools capture factors that increase stroke risk during COVID and post-COVID illness? First, a review of literature was conducted to identify stroke risk assessment tools. Second, emerging risk factors for stroke related to COVID-19 were extracted from a literature search. Third, a survey, which included traditional and non-traditional risk factors found in the literature review, was developed and administered to 35 front-line clinical experts; this survey aimed to understand the reliability and content validity of stroke risk factors as they occur within the context of COVID-19. The clinical experts identified 23

traditional and 29 non-traditional risk factors as being highly associated with increased odds of stroke. The top traditional risk factors were atrial fibrillation, smoking (current or history), 2nd TIA in less than seven days, age >74, hypertension (>140/90 mmHg or SBP >140 or DBP >90). Non-traditional risk factors were metabolic syndrome, ipsilateral >50% carotid stenosis of the internal carotid artery and/or major cerebral artery, active COVID-19 infection that has lasted more than eight days, D-dimer >920 ng/m, and C-reactive protein >10.0 mg/L. This project provides a foundation for future QI projects and research with the goal of reducing risk for stroke within the context of COVID-19.

CHAPTER 1: INTRODUCTION

Stroke Prediction in the Context of COVID-19 Infections

There is emerging evidence that both the acute phase of COVID-19 infection and post-COVID phase are times of elevated risk for stroke in persons who would not traditionally be considered at risk (Oxley TJ, Mocco J, Majidi S, Kellner CP, Shoirah H, Singh IP, De Leacy RA, Shigematsu T, Ladner TR, Yaeger KA, et al., 2020). Multiple tools for assessing risk for strokes, mortality, or disability are currently being used, however, these tools were developed and tested prior to the existence of COVID-19. And thereby, it is not known if these tools fully capture stroke risk factors within the context of COVID-19. Given that SARS-CoV-2 will likely continue to circulate even after the pandemic, it is necessary to re-evaluate existing stroke tools to contracting the SARS-CoV-2 virus.

Our understanding of the pathophysiology for increased risk for stroke--during and following COVID-19 infection—is primary focus on how SARS-Co-V-2 infection induces hypercoagulation, exaggerated physiological responses to the cytokine storm, and multi-system inflammation (Agarwal, Pinho, Rai, Yu, Bathla, Achilleos, Oneill, Still & Maldijan, 2020). While some risk factors related to the pathophysiology are considered in existing tools, there is much to be learned from clinicians working on the frontlines about unique factors related to COVID-19 that are yet to be documented in the literature. In summary, tools that consider infection with SARS-CoV-2 virus, are needed to accurately assess stroke risk.

Background/Significance

In the United States, stroke is among the top five leading causes of death. (Ahmad, Anderson, 2021). It is also a major cause of chronic disability. The cost for chronic disability from stroke is substantial reaching $45.5 billion every year (Lo, Chan, & Flynn, S. 2021). When

compared to males, female stroke survivors are affected to a greater degree; females are less likely to be able to perform activities of daily living after surviving a stroke. Approximately 87% of all strokes are ischemic strokes and 13% are hemorrhagic (CDC, 2021).

It is estimated that approximately 800,000 individuals in the U.S. will have a new or recurrent stroke per year (Virani, S. S., Alonso, A., Aparicio, H. J., Benjamin, E. J., Bittencourt, M. S., Callaway, C. W., ... & American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee, 2021). Of these (800,000), three-quarters (610,000) are first-time strokes (U.S. Department of Health and Human Services. (n.d.). Among persons with a first stroke, 16% will die, and 40% will experience significant residual effects that impair their ability to do daily tasks (CDC, 2021). Of stroke survivors, approximately 185,000 will have a second stroke within five years. According to the CDC (2021) there is an opportunity to prevent approximately 80% of strokes in the U.S. with better assessment and education.

Prevention of first-time strokes is critical to reducing mortality and mitigating the negative impact on quality of life. The identification of traditional and nontraditional risk factors such as hypertension, smoking, and COVID19 infection is crucial to determine the risks of primary stroke, and once identified, these risks could be appropriately managed.

Problem Statement

COVID-19 and Stroke

Since the start of the pandemic (March 2020), there has been an increasing number of studies/case studies/anecdotal evidence on the impact of COVID-19 on the possibility of stroke among individuals who would not normally be considered at risk. It appears that during the acute phase of COVID-19 or Post COVID-19 are periods of high risk. With the context of COVID-19,

are just not beginning to appear in the literature and have not yet been translated into clinical practice in the form of a revision of stroke risk tools. In summary, stroke risk tools have not yet been revised to accounted for COVID-19 infection. Therefore, the goal of this project was to examine existing stroke tools within the context of COVID-19 through review of the literature and survey of expert clinical opinion.

PICOT

This PICOT question is considered to evaluate stroke risk factors in patients already suffering from COVID-19.

PICO Q1: Do established stroke tools capture factors that increase stroke risk during COVID and post-COVID illness?

CHAPTER 2: BODY OF EVIDENCE

Review of the Literature

Search Process

The purpose of the search was two-fold. First, we identified common tools for stroke prediction. Second, we identify emerging risk factors related to COVID for stroke. The search strategies involved using specified search terms on the search engines of databases to identify the existing literature on the possible association between COVID-19 and Stroke. The search results are indicated below:

PubMed Search

("COVID-19/pathology"[Mesh] OR covid-19 OR covid19 OR 2019-nCoV ORnCoV OR Coronavirus Disease-19 OR SARS-CoV-2 OR2 OR coronavirus OR "long hauler*") AND ("Stroke, Lacunar"[Mesh] OR "Ischemic Stroke"[Mesh] OR "Brain Infarction"[Mesh] OR "Stroke"[Mesh:NoExp] OR "Cerebrovascular Accident*" OR "Cerebrovascular Apoplexy" OR "Brain Vascular Accident*" OR "lacunar stroke*" OR "ischemic stroke" OR "Brain Infarction")

Filters applied: English, from 2020 - 3000/12/12. Results: 855

("COVID-19/pathology"[Mesh] OR covid-19 OR covid19 OR 2019-nCoV ORnCoV OR "Coronavirus Disease-19" OR SARS-CoV-2 OR2 OR "long hauler*") AND ("Stroke, Lacunar"[Mesh] OR "Ischemic Stroke"[Mesh] OR "Brain Infarction"[Mesh] OR "Stroke"[Mesh:NoExp] OR "Cerebrovascular Accident*" OR "Cerebrovascular Apoplexy" OR "Brain Vascular Accident*" OR "lacunar stroke*" OR "ischemic stroke" OR "Brain Infarction").

CINAHL Complete Search

(MH "COVID-19") OR (MH "SARS-CoV-2") OR covid-19 OR covid19 OR 2019-nCoV OR Coronavirus Disease-19 OR SARS-CoV-2 OR coronavirus OR "long hauler*" AND (MH "Ischemic Stroke+") OR (MH "Stroke") OR (MH "Stroke, Lacunar") OR (MH "Cerebral Infarction") OR (MH "Stroke Patients") OR "Cerebrovascular Accident*" OR "Cerebrovascular Apoplexy" OR "Brain Vascular Accident*" OR "lacunar stroke*" OR "ischemic stroke" OR "Brain Infarction" AND (MH "Survivors") OR survivor* Limiters - Published Date: 20200101, English Language. Expanders - Apply equivalent subjects Results: 8. Filters applied: Meta-Analysis, Systematic Review, English. Results: 41.

Appraisal of Evidence

PRISMA 2009 Flow Diagram

Please refer to appendix C – Flow Diagram

A search flow diagram is presented to show that overall, 216 records were identified through searching of the database. Additional records identified 47 of other sources. After removing duplicates, 142 search results were considered valid and relevant to our search. Of these 142, 36 records were screened or thoroughly examined and 7 of these articles were excluded. Overall, 34 full-text papers were examined for eligibility. Lastly, 26 papers were considered for qualitative synthesis and 11 papers were selected in the quantitative synthesis and analysis. The Johns Hopkins Nursing EBP was utilized to determine the levels of evidence of the articles. All of the articles were determined to be level I, II, III.

A literature review was conducted based on conditions associated with the prevention and development of primary stroke and the current assessments used in clinical practice. We screened papers from Pubmed, Cinahl, Google Scholar, and UptoDate, focusing on articles and/or EBP tools that could potentially assist us in improving or building a comprehensive risk stratification tool for primary stroke assessment.

We identified and reviewed several well-validated risk stratification tools such as the ATRIA (Singer, 2013), CHA□DS□-VASc Score for Atrial Fibrillation Stroke Risk (Lip, 2009) ABCD2 and ABCD3-I Score (Johnston, 2013), Metabolic Syndrome Severity Calculator (Gurka, and DeBoer, 2019), The Framingham Stroke Risk Score (FSRS) (D'Agostino et al., 1991), and Revised FSRS (Peter Flueckiger et al., 2017) for assessing stroke risk in specific populations like atrial fibrillation, transient ischemic attack, and metabolic syndrome.

Comprehensive Synthesis of Evidence

According to a study by Vogrig, Gigli, Bnà, & Morassi (2021) acute cerebrovascular disease, notably ischemic stroke, has emerged as a major consequence of infection with SARS-CoV-2, the causative agent of COVID-19. There is emerging evidence that COVID-19-related stroke revealed may differ in clinical presentation, neuroimaging results, and outcomes (Jain, R., Young, M., Dogra, S., Kennedy, H., Nguyen, V., Jones, S., Bilaloglu, S., Hochman, K., Raz, E., Galetta, S., & Horwtiz, L., 2020). Large vascular occlusion, multi-territory stroke, and involvement of otherwise seldom affected vessels are all examples of such unique characteristics (Vogrig, A., Gigli, G. L., Bnà, C., & Morassi, M., 2021). Cases of encephalopathy or encephalitis accompanied by seizures has been documented as a preceding factor prior to stroke. The reason for stroke and best practices for ischemic stroke within the context of COVID-19 are

unknown (Luo, W., Liu, X., Bao, K., & Huang, C., 2022). Emerging research suggests that cytokine storm-induced coagulopathy and endotheliopathy are potential contributing mechanism and therefore could be viable could be viable targets for treatment.

In a recent systematic review of 61 published research studies supports the notion that acute cerebrovascular diseases in COVID-19 are related to stroke (Nannoni, et al., 2021) With 108,571 patients with COVID-19, Nannoni, et al. (2021) found that acute cardiovascular event occurred in little over 1%, and ischemic stroke was the most common manifestation. Patients with Covid-19 who developed acute cerebrovascular disease, compared to those who did not were older and were more likely to have comorbidities. The authors concluded that acute cerebrovascular disorders are common in COVID-19 patients, particularly those who are highly infected and have vascular risk factors. The pattern of massive artery blockage and multi-territory infarctions suggests that cerebral thrombosis and/or thromboembolism may be plausible causes of cerebrovascular events in such patients. Trejo-Gabriel-Galán J. M. (2020) suggested stroke as a complication and prognostic variant of COVID-19 and concluded that a stroke history increases the incidence of mortality due to COVID-19 by 3 times and stroke is one of the principal complications of COVID-19.

In a review study conducted by Zakeri et al. (2021) the authors examine the mechanisms associated with the development of stroke in the settings of COVID-19 infections. The authors reviewed the histology of deceased COVID-19 patients and found that the organs of these patients demonstrated a large extent of thrombosis at a micro and macrovascular level. This is an important finding that reiterates the notion that besides infecting the respiratory system, COVID-19 also affects the vasculature, the authors added.

Li et al. (2020) conducted a retrospective observational study of 219 patients infected with SARS-CoV-2. The authors analyzed the incidence of stroke in these patients and estimated the risk to be significant. The author reported that from 219 individuals, those suffering from stroke account for 5.02 percent of the cases. The majority of strokes happened in older patients in the settings of other commodities.

The frequency and clinical features of stroke in COVID-19 patients were investigated in a systematic study by Yamakawa, Kuno, Mikami, Takagi, & Gronseth (2020). In hospitalized COVID-19 patients, the rate of identified stroke was 1%, and it was linked to older age and traditional stroke risk factors. COVID-19 patients with frequent cryptogenic stroke and elevated d-dimer levels had a higher risk of thromboembolism, which is linked to a higher death rate.

Belani et al. (2020) conducted a retrospective case-control study of 41 cases and 82 control subjects matched by age, sex, and risk factors. Cases were patients who had stroke and control subjects were those with no evidence of acute infarction. A univariate analysis performed showed that of individuals suffering acute ischemic stroke, 46% were affected by COVID-19 versus 18% of the control group. After adjusting the factors such as age, sex, and risk factors, patients with COVID-19 infection have increase odds for stroke when compared with the control cohort (Belani et al., 2020). Zhang et al. (2021) suggested that during the COVID-19 pandemic, patients with severe COVID-19 experienced consequences such as acute ischemic stroke (AIS), which was linked to a poor prognosis. These individuals frequently exhibited aberrant coagulation, such as increased D-dimer and fibrinogen values and a low platelet count. COVID-19 may cause AIS by inducing hypercoagulability, according to some research. Nonetheless, the exact methods through which COVID-19 causes infected patients to become hypercoagulable are

unknown. Understanding the underlying processes of hypercoagulability is critical for treating these patients effectively.

Review of Stroke Risk Tools

A review of several well-validated risk tools ATRIA, CHA2DS2-VASc score, ABCD2, and ABCD3-I Score, Metabolic Syndrome Severity Calculator, The Framingham Stroke Risk Score (FSRS) and Revised FSRS found tools captured risk for stroke in conditions like atrial fibrillation, transient ischemic attack, and metabolic syndrome. These tools are presented below (see table 1)

The ATRIA stroke risk score (Singer, 2013). ATRIA is designed to prognosticate risk of ischemic stroke among patients with atrial fibrillation not taking anticoagulants. The ATRIA tool was created and validated in two large California community Atrial fibrillation (AF) groups. (Aspberg, Chang, Atterman, Bottai, Go, & Singer, 2016). In people over the age of 65 years, atrial fibrillation (AF) is the most prevalent cardiac arrhythmia and 70% of those suffering from AF are between the ages of 65 and 85 years. AF is not directly life-threatening, but it is linked to an elevated risk of stroke and death (Karamichalakis, Letsas, Vlachos, Georgopoulos, Bakalakos, Efremidis, & Sideris, 2015). AF is also the principal risk factor for heart-related embolism to the brain resulting in acute ischemic stroke. Mortality rates are high among older patients with AF and these patients are also more likely to have frequent and often longer hospitalizations due to heart failure, strokes, pacemaker implantation, and antiarrhythmic treatment side effects.

CHA□DS□-VASc Score for Atrial Fibrillation Stroke Risk (Lip, 2009). CHA□DS□-VASc Score for AF Stroke Risk appraises ischemic stroke risk in people with AF. The tool was used in one retrospective cohort study by Tsadok, Senderey, Reges, Leibowitz, Leventer-Roberts, Hoshen, and Haim (2019) and found that CHADS2, CHA2DS2-VASc, and

R2CHADS2 risk scores has a moderate ability or less than 50% in predicting stroke in the context of AF. The C-statistic was 0.647 indicating that this system is particularly inaccurate in predicting stroke risk.

ABCD2 and ABCD3-I Score to Predict Stroke Risk After Transient Ischemic Attack (Johnston, 2013). The ABCD2 and ABCD3-I scores are validated tools to identify risk of stroke after a transient ischemic attack (TIA). A TIA, sometimes referred to as a mini stroke, is the abrupt and transient loss of neurological abilities due to localized brain ischemia. The biggest difference between stroke and TIA is the duration of the symptoms. TIA usually lasts from a few seconds to less than an hour. After the resolution of the symptoms, patients do not present with neurological deficits. Diagnosis of TIA is clinical (Chong, 2021). The ABCD2 and ABCD3-I tools are optimized to predict stroke risk within two days after a TIA but also predict risk up to 90 days. Scores range from 0 to 7. Scores greater than 3 are at significantly higher risk of stroke in the 2-day period after a TIA. These patients may need urgent assessment and treatment as inpatients. Validation analysis on these instruments stated that the ABCD3-I score had a better predictive value than the ABCD2 score for measuring the risk of an early stroke after a TIA (Song, Fang, Zhao, Gao, Tan, Lu, & Xu, 2013).

The Metabolic Syndrome Severity (MetS) Score Calculator (Gurka, and DeBoer, 2019). The metabolic syndrome (MetS) severity calculator is an online-based calculator that uses well-researched equations to compute an individual's metabolic syndrome severity score. The metabolic syndrome severity calculator (MetS Calc) evaluates the relationships between the different elements of MetS which are obesity, elevated blood pressure, increased triglycerides, low level of HDL cholesterol, and elevated level of fasting blood sugar. In comparison to the

average US adult, a score below zero or negative score indicates a reduced level of metabolic syndrome in people. Scores greater than 0 are linked to a higher risk of disease in the future, especially those above 1 (1 represent a risk of disease higher than 84.1 of the adults in the US) or 2 (which represent a risk of disease higher than 98% of the adult in the US) (Gurka, Lilly, Oliver, & DeBoer, 2014). People with metabolic syndrome are among the highest/or at high risk for stroke, CVD, and other chronic diseases like diabetes, and fatty liver disease. Additionally, stroke has been shown to be directly proportional to the severity of metabolic syndrome (DeBoer, Filipp, Sims, Musani, & Gurka, 2020).

The Framingham Stroke Risk Score (FSRS) (D'Agostino et al., 1991) and Revised FSRS (D'Agostino et al., 2017). The Framingham Stroke Risk Score (FSRS) is a tool that combines stroke risk element (age, gender, systolic blood pressure, antihypertensive medication use, presence, or absence of hypertrophy of the left ventricle on ECG, current cardiovascular illness, current smoking status, current or history of atrial fibrillation, and diabetes mellitus) to evaluate a 10-year stroke probability (Zhou, Wang, Duncan, & Zheng, 2017). The original FSRS (O-FSRS) used stroke data from the 1960s and 1970s and applied it to current cohorts to demonstrate that stroke risk is overestimated in certain patients (Flueckiger, Longstreth, Herrington, and Yeboah, 2018). The R-FSRS was created to reflect temporal trends in stroke rate incidence, and it can be used to investigate geographic/racial disparities in stroke risk and the use of nontraditional risk indicators in stroke prediction (Flueckiger, et al., 2018).

Review of traditional and Non-Traditional Stroke Risk factors

Estimation of stroke risk is especially important because it is the most common cause of death and the primary cause of neurological disability in the elderly. In an effort to better

understand risk factors in stroke, several studies have used an epidemiologic approach. The following are the risk factors associated with the increased incidence of stroke.

Blood pressure. Blood pressure (BP) has been identified as the single most important stroke risk factor in epidemiological studies. A meta-analysis of 844 by Forouzanfar, Liu, Roth, Biryukov, Marczak, ... and Murray, (2017) estimate the increased rate of systolic BP and its associated annual deaths. The authors report a direct lineal association between increased systolic blood pressure and significant morbidity and death. The study also categorized elevated SBP as a global health risk. Lastly, the authors reported that ischemic heart disease and stroke were associated with the majority of health loss.

Age. According to a Framingham study, the risk for stroke increases with age. After the age of 45 years, the risk of a stroke doubles with each decade. A longitudinal study by Kelly-Hayes (2010) reports that people aged 65 and older have the highest probability of stroke. The authors state that 70% of all strokes happen in these ranges of age. Women have a higher incidence of stroke compared with men for the most part because women live longer. In contrast, the incidence of stroke decreased in people aged 85 years and older despite a continued rise in stroke cases. This event is due to a more rapid decrease of remaining life expectancy than the risk of stroke increased. The authors also report that the overall lifetime risk (LTR) for stroke in men is 1 in 6 and 1 in 5 for women. Lastly, the author highlights that the incidence of stroke in men is higher in younger years, and for women, this incidence is higher in older ages.

Cigarette Smoking. A meta-analysis of 14 studies conducted by Pan, Jin, Jun, Qiu, Zheng, and Pan (2019) reported that smoking is a risk factor for stroke. In this study, the authors emphasized the role of smoking as a precursor to inflammation leading to the development of

stroke. The authors also reported a positive linear association between the incidence of stroke and the amount of smoking. This risk does not distinguish between women and men and exists throughout the life of a smoker. It is well known that smoking increases blood pressure, heart rate and the risk of atherosclerosis.

Physical Activity. It is well documented that physical activity exerts a beneficial protective effect on stroke risk and recurrence can be reduced throughout life, including in older persons. Physical activity and stroke risk were found to be lower in moderately and highly active people than in low-activity adults in a meta-analysis report. In moderately active adults, the incidence of stroke was reduced by 20%, while in very active adults, the risk was reduced by 27%. (Lee, Folsom, & Blair, 2003). Reduced plasma fibrinogen, decreased aggregability of platelets, reduced blood pressure, and weight loss are all possible pathways engaged by physical activity to reduce risk. (Alevizos, Lentzas, Kokkoris, Mariolis, & Korantzopoulos, 2005).

Diet. Diet has been linked to a higher or lower risk of stroke. Healthy eating habits and maintaining a normal weight are two components of food that should be considered for preventing strokes. Increased eating of fruits and vegetables was linked to a lower incidence of stroke in the Health Professionals Follow-Up Study, with a linear association between consumption of fruits and risk reduction. Another study by Haley, Krishnan, Burrows, de Hoog, Thakrar, Schiessl, I., ... and Lawrence (2019) examine the role of an acute high-fat diet and negative stroke outcome. The authors report that even a short period of high-fat ingestion has negative implications in glucose homeostasis, cerebral microvasculature, and neuron anatomy resulting in problems with learning and memory.

Psychological distress and Depression. A study by Gronewold, Engels, van de Velde, Cudjoe, Duman, Jokisch, and Hermann, (2021) shows that marital stress, job stress, and depression are linked to coronary heart disease, death, and stroke. Depression has also been linked to bad health habits such as inactivity, dietary changes, and increased smoking, and from middle age, its presence has been associated with increased risk of stroke in both men and women (Everson, Roberts, Goldberg, & Kaplan, 1998). Another study by Zhao, Yue, Jiang, & Yuan, Y. (2019) examines the shared genetic risk factors for depression and stroke. The authors report that people with variation in a specific DNA sequence of 4 genes, methylenetetrahydrofolate reductase, and apolipoprotein E are susceptible to major depressive disorder and stroke.

Obesity. The World Health Organization (2016) defines overweight and obesity as "abnormal or excessive fat accumulation that presents a risk to health. A body mass index (BMI) over 25 is considered overweight, and over 30 is obese". Obesity is associated with several comorbidities such as metabolic syndrome, type 2 diabetes mellitus and cardiovascular disease (Rhee, 2022). Obesity was also found to be a significant risk factor for ischemic stroke in both men and women. The connection between the greater indices of ischemic stroke and obesity was linear. Adjusting for other attributes that could mediate the link between stroke and obesity, such as diabetes and hypertension, the relationship between the two was dramatically reduced, implying that these other factors could account for much of the stroke risk related to obesity (Yatsuya, Folsom, Yamagishi, North, Brancati & Stevens, 2010).

Race. The Office of Minority Health (2021) reported that stroke is twice as common in blacks as it is in whites, and the black-white ratio is much higher in middle age. When compared

to white patients, the risk of stroke is higher in Black and Hispanic individuals. Ischemic stroke strikes black patients at a younger age, and the prevalence and age-standardized mortality from ischemic stroke are higher in black patients than in the other races and the general population. Hispanics seem to be at elevated risk for stroke than non-Hispanic whites living in the same communities.

Type 2 Diabetes Mellitus. Type 2 diabetes mellitus is a disease that impairs insulin secretion and causes insulin resistance resulting in elevated glucose in the blood (Brutsaert, 2020). Diabetes results in a variety of microvascular and macrovascular alterations, which can lead to serious clinical consequences, including stroke. Diabetic patients are particularly vulnerable to the effects of cerebral small vessel dysfunction. Hyperglycemia puts people at a higher risk of having a stroke. This elevated risk is common among diabetics and is linked to poorer clinical outcomes (including higher death), particularly after an ischemic stroke (Chen, Ovbiagele, Feng, 2016)

Hyperlipidemia. Hyperlipidemia is one of the leading causes of stroke in the United States. Lipid screening guidelines are defined by the US Preventive Service Task Force. Lower levels of low-density lipoprotein and higher levels of high-density lipoprotein are linked to a lower risk of stroke. Lifestyle changes and medical control are two treatment options for hyperlipidemia. Statins have been demonstrated to lower cholesterol levels while also having a pleiotropic effect on cerebral vasculature and inflammatory modulators, resulting in neuroprotection. Despite screening standards and proof of statin efficacy, there are a number of obstacles to maintaining sufficient or optimized cholesterol management (Lewis & Segal, 2010). (Lewis & Segal, 2010).

Atrial Fibrillation. Cardiovascular risk factors such as congestive heart failure, elevated blood pressure, diabetes mellitus, previous stroke or TIA as well as the patients' age have a significant influence on stroke development. A meta-analysis by Tereshchenko, Henrikson, Cigarroa, and Steinberg (2016) compares the effectiveness of pharmacological and surgical interventions for stroke prevention in AF. The authors report that the use of anticoagulants and other surgical interventions as the watchman procedure significantly reduces the risk of stroke when compared to no treatment or placebo, although it significantly raises the risk of serious bleeding.

Chronic Kidney Disease and End-Stage Renal Disease. Chronic kidney disease (CKD) and its advanced stage known as an end-stage renal disease (ESRD) are conditions characterized by the inability of the kidneys to function. These diseases have been recognized as a global health concern due to the incidence of high morbidity and mortality. CKD and ESRD have been linked with a broad variety of neurological implications. The incidence of stroke in these patients is frequently due to increased chronic inflammation, elevated acidity stage, elevated homocysteine in the blood which result in endothelium dysfunction, platelet aggregation, and vascular injury (Cherng, Lin, Shih, Hsu, Yeh, Hu, & Liao, 2018).

Atherosclerotic Cardiovascular Disease (ASCVD). Atherosclerotic cardiovascular disease (ASCVD) is an illness resulting from elevated levels of low-density lipoproteins (LDL) in the blood. The hallmark feature of this condition is the accumulation of cholesterol plaque on the wall of the vessels. These plaques' collection affects the integrity of the cells in the endothelium. This plaque can also fall off and spread to the brain, causing a stroke. Individuals with prior coronary heart disease (CHD) are classified as extremely high risk for having another

incident, according to clinical practice recommendations. These incidents include but are not limited to conditions such as stroke MI, angina, and sudden death. Factors that influence the development of ASCD are smoking, obesity, high fat intake, inactivity, and family history. (Rosenblit, 2019).

COVID -19 Risk Factors. COVID-19 and post COVID-19 patients not only have a high burden of pulmonary complications but also an increased risk for stroke. While overall stroke risk in COVID-19 and post COVID-19 patients is up to 1.4 times greater than the general population. Studies in the general population indicate that elevated IL6 independently increases stroke risk by fivefold (Jenny, 2019). Studies examining the independent association of COVID-19 with stroke in COVID-19 and post COVID-19 patients have shown conflicting and more modest associations.

COVID-19 infection is linked with pathological inflammation, hypercoagulability, higher D-dimer levels, and the induced production of antiphospholipid antibodies. These events result in multi-vascular thrombosis in these patients (Panigada, 2020). Medical problems such as AF and other cardiac arrhythmias, MI, CHF, myocarditis, and venous thrombosis are more common in COVID-19 infected patients, all of which increase the risk of ischemic stroke (Goyal, 2020).

Evidence-Based Recommendation for the Project

Multiple tools for predicting secondary strokes, mortality, or disability are currently being used. Despite multiple studies reporting an increased incidence of stroke in patients suffering from COVID-19 infections, risk factors from COVID-19 have not been included in these tools. Strokes, especially ischemic strokes, continues to be a clinical manifestation in

patients who are acutely ill with COVID-19 and post-COVID infection. This is due to systemic dysregulation in the respiratory, cardiovascular, gastrointestinal, and neurological systems. These dysregulations are associated with a hypercoagulable state and system inflammation (Agarwal, Pinho, Rai, Yu, Bathla, Achilleos, Oneill, Still &Maldijan, 2020). Moving forward, risk tools specific to the COVID-19 and post-COVID-19 population are needed to accurately assess and balance stroke risks in patients with COVID-19 and post-COVID-19 infection.

CHAPTER 3: PROJECT FRAMEWORK

Conceptual Framework Logic Model

The logic model framework was developed to articulate the underlying components needed for the stroke prediction project. The elements consider knowledge process, specialized assistance and dissemination, leadership and cooperation, and assessment activities. The different components are connected and influence one another through an iterative process. This model has also been developed as a general guide about how resources and activities can be connected. This framework helps with project management, resource allocation, and strategic planning. The process of developing the logic model also facilitated critical thinking through the process of planning and communicating network objectives and outcomes. Please see appendix E – Logic Model.

CHAPTER 4: METHODS

Project Goals

The purpose of this project was to assess if the established stroke tools capture factors that increase stroke risk during COVID and post-COVID illness. This QI project also attempted to identify risk factors from previously published tools, expert opinion of front-line clinicians, and the scientific literature on stroke and stroke within the context of COVID-19 as It appears as COVID-19 and Post COVID-19 infections have not been accounted for by traditional approaches.

Project Description

Project Type/Design

Project Type/Design Quality improvement (QI) is a systematic approach to enhancing care through the evaluation of the process and implementation of activities to improve it. For this DNP paper, a QI project was chosen to help identify risk factors for stroke within the context of COVID-19 that have not been accounted for by traditional approaches. This QI project assisted in the examination of factors where clinical stroke assessments are sub-optimal. A review of the literature helped identify traditional stroke risk factors. The literature review also aided in the identification of possible non-traditional risk factors associated with stroke in the context of COVID-19. An online survey was created by the investigator adapted from Aber, A. et al. (2020), Lip et al., (2010) that contained traditional risk factors and new factors to assess risk. The survey was distributed to frontline clinical experts in stroke and COVID-19 for stroke factors validation. We hope this project offers use information that would reduce risk for stroke and increase the quality of care and improve patient outcomes. The results of this QI study were analyzed in Excel, SPSS, phyton, and Redcap. These programs assisted in the creation of run

charts and statistical analysis tables to highlight probability-based tests necessary to understand the effect of a comprehensive stroke tool assessment.

Project Setting/Population

An electronic survey was sent to health care providers with expertise in stroke and COVID-19 infections. This survey was created and distributed using an electronic platform known as Redcap, an online program that assists individuals in the creation and management of electronic files and surveys. We used Excell, SPSS, Python, and Redcap for the analysis and displacement of data to illustrate findings.

Health care providers with expertise in stroke and COVID-19 infections represented the population needed for content validity. These professionals work at acute care and comprehensive stroke center institution that has agreed to facilitate the dissemination of these surveys.

Please refer to appendix A - Site approval/authorization letter.

Participants and Recruitment

Participants were physicians, advanced practice nurses, physician assistants, and critical care nurses specializing in stroke, emergency medicine, and vascular-related conditions working in the emergency department (ER) at Mission Hospital. The inclusion criteria were based on expertise related to stroke and COVID-19 given by a minimum of 1 year of experience working with this population.

`According to Haynes, Richard, Kubany (1993) and Boateng, Neilands, Frongillo, Melgar-Quiñonez, & Young (2018), the minimum number of experts needed for content validity to be significant statistical ranges from 5 to 7. However, due to the novelty of the disease, the survey was sent to all eligible providers to increase the chance of getting the most

comprehensive information. The survey was distributed to 65 qualified experts. Thirty-five clinical experts completed the survey.

i. Inclusion Criteria

1. Physicians, advanced practice nurses, physician assistants, and critical care nurses working for the designated acute care facility.

2. Expertise in stroke and COVID-19 infections were given by at least one year of experience working with these population.

3. Aged 18 or older

3. Ability to speak and understand English

ii. Exclusion Criteria

1. Healthcare professionals employed but have not worked in the capacity at the designated facility throughout the pandemic.

Description of Intervention

This project has no intervention. This project aimed to collect additional information from clinicians that will provide new information to inform the beginning stage of developing a risk assessment tool that can be assessed and refined in the future through research. Consequently, the results of these surveys were analyzed using SPSS, REDCap, and python to help support the findings.

Measures/Instruments

The instrument used to collect data was a survey. The survey was adapted from Aber, A. et al. (2020), Lip et al., (2010) and distributed among health care providers working at Mission Hospital, Emergency Department. The questionnaire was developed with a Likert scare rating.

The survey was divided into three questions about demographics and 56 questions related to potential risk factors for stroke in COVID-19 patients. In addition, participants were asked to rate each risk factor's degree of validity and relevance on a 4-point Likert scale of "very true" (=1) to "not true" (=4), "very relevant" (=6) to "not relevant" (=9). There was also an option to enter free text. The survey was developed using REDCap. This program provides computerized tools for data downloads to statistical packages. This program also has several reporting tools and other advanced features utilized to manage and analyze the data results.

Please refer to appendix G - Survey.

Data Collection Procedures

Data for this project were collected between December 4, 2021, and March 31, 2022, using a secure online survey (REDCap). The results of the surveys were organized in electronic folders for better management and control. Data for this project were kept in a secure MySQL database secured using encryption provided by the Research Electronic Data Capture (REDCap) web-based application.

Data Analysis

Python, SPSS, Excel, and REDCap were used to perform statistical analysis. Survey results based on expert clinical opinion were evaluated to determine whether they represent each specific risk factor. These results were analyzed using the content validity ratio for quantifying consensus and Cronbach’s Alpha to measure reliability and internal consistency on the Likert scale questions. Exploratory data analysis was utilized to generate summary statistics and create graphical representations of the traditional and non-traditional stroke risk factors. Please refer to table 2.

Ethical Considerations

This project is considered quality improvement and not research. Though, the University of California, Irvine Institutional Review Board (IRB) approval was sought, and the project was deemed by IRB as self-exempt. The record for this approval can be found in the UCI Kaui computer-based platform where we received self-exemption. Please refer to Appendix L.

Stakeholders/Barriers

The resources utilized for this project encompass using a computer and knowledge and management of the REDCap application. The primary stakeholders were the physician practice manager and the ER clinical director. They facilitate the dissemination of the survey among ER clinical experts. The setting of the QI project was in the Providence Health System (Mission Viejo and Laguna Beach). The results should not be generalized to other facilities. Larger groups can be surveyed in future research.

Formative Process Evaluation

Formative evaluations were conducted before, during, and after starting data collection. The purpose was to identify any pitfalls and problematic, unanticipated issues with the execution of the project. The feedback enabled us to modify the activities midstream based on their effectiveness, impact, and value. The formative evaluation was focused on the process of survey delivery, data management, and interpretation of results.

The following pitfalls/problems were identified, (1) initial format of questions and (2) single email with the invitation to participate in the survey. To address the pitfalls and problematic issues, the following steps were implemented: (1) the questions were formatted using the REDCap platform that assisted with clarity; (2) Programmer reminders in REDCap

were predetermined to motivate participants to complete the survey. These strategies were successful in incrementing participation and completion of the survey.

CHAPTER 5: RESULTS AND CONCLUSION

Results

Overall, this chapter presents a summary of the findings of this QI project and captures risk factors for stroke in the context of COVID-19 infections. The findings from a comparison of stroke tools, the literature review, and survey results from front-line clinicians are described. Additionally, recommendations for future QI projects and implications of research in clinical practice are noted.

Description of the Sample

There were 35 participants, and information about recruitment can be found in participants section (page 28). Participants were identified in four groups: (1) physicians (Doctor of Medicine (M.D) and Doctor of Osteopathic Medicine (D.O.)), (2) advance practice (nurse practitioner (NP), physician assistant (PA), clinical nurse specialist (CNS)), (3) nurse (registered nurse), (4) other (therapist). Physicians account for 66%, advance practice 9%, nurse 17% and other 9% (Figure 5).

On average, the number of years of practice was M=15.69 (SD=11.29). The range was 1 - 44 years (see figure 6).

Figure 5 - Demographic – Professional Role

What is your professional role?

Total Count (N)	Missing*	Unique
35	1 (2.8%)	4

Counts/Frequency: Physician (23, 65.7%), Nurse (6, 17.1%), Advance Practice Provider (3, 8.6%), Other (3, 8.6%)

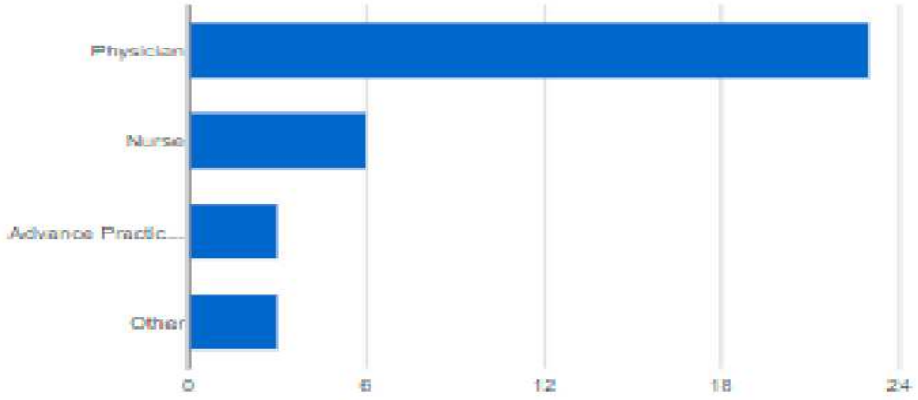


Figure 6 - Demography – Years of Experience

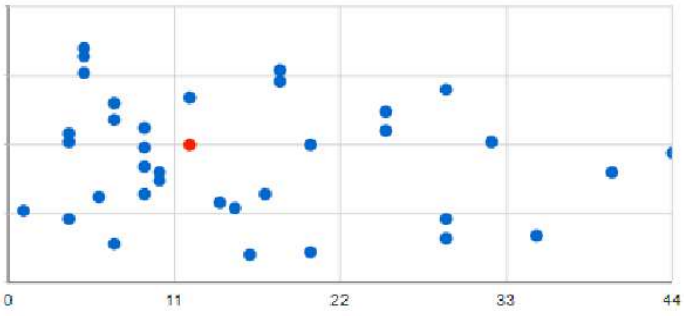
How many years have you worked in your professional role? (if less than a year, enter 0)

(yrs_role)

Total Count (N)	Missing*	Unique	Min	Max	Mean	StDev	Sum	Percentile						
								0.05	0.10	0.25	0.50 Median	0.75	0.90	0.95
35	1 (2.8%)	20	1	44	15.69	11.29	549	4	4.40	7	12	22.50	30.80	36.50

Lowest values: 1, 4, 4, 4, 5

Highest values: 29, 32, 35, 40, 44



Review of Existing Stroke Risk Tools

There were 22 stroke risk factors identified from the existing tools. A comparison of risk factors by specific tools can be found in Table 1. The stroke factors in existing tools included: (1) age (males >65 and females >74), (2) gender, (3) race (African American), (4) BMI, (5) smoking (current or past history), (6) atrial fibrillation, (7) congestive heart failure (CHF), (8) history of heart attack before the age of 60 years, (9) vascular disease (prior myocardial infarction (MI), peripheral artery disease (PAD), or aortic plaque), (10) enlarged heart or presence of left ventricular hypertrophy on ECG, (11) parent with MI before age 60 years, (12) hypertension (>140/90 mmHg or SBP >140 or DBP >90), (13) diabetes mellitus (current or past history), (14) history of stroke, (15) transient ischemic attack (TIA) that lasted < 10 min, 10-59 min, or >60 min, (16) 2nd TIA in less than 7 days, (17) dyslipidemia, (18) metabolic syndrome, (19) estimated glomerular filtration rate (eGFR) <45 or end stage renal disease, (20) Proteinuria, (21) c-reactive protein (CRP), and (22) ipsilateral >50% stenosis of internal carotid artery and/or cerebral major artery.

As shown in Table 1, the most common risk factors across tools were hypertension, diabetes mellitus, and age. Some tools had a single item with three risk factors (conditions). The criteria for a positive score on such item involved meeting 2 or more of the conditions. For example, the ABCD2 tool noted having either TIA and age >59 years or TIA and HTN (SBP>139 and/or DBP>89) or TIA and DM were sufficient to denote risk on that item. Stroke factors also included vascular disease and atrial fibrillation. While age for stroke is a risk factor there is a difference by gender, specifically, women 45 years or older were more likely to have a stroke if they had an underlying condition.

Table 1 - Summary of the comparative analysis among stratification tools

Tool name	Age <65, 65-74, >75	Age >60	Sex Female, Male	CHF	HTN	BP >140/90 mmHg. Either SBP>140 or DBP>90	Clinical features of TIA Unilateral weakness, speech disturbance without weakness, other symptoms	Duration of TIA's symptoms <10 min, 10-59 mins, >60 mins	Stroke/TIA/ Thromboembolism hx	Vascular disease hx (prior MI, PAD or aortic plaque)	DM	Smoker	Dyslipidemia	Race	Tx HTN	Proteinuria	eGFR < 45 or end-stage renal disease	CRP	BMI	Parent with MI before age 60 years	2nd TIA in <7 days	**Imaging** Acute diffusion-weighted hyperintensity on imaging. Ipsilateral >50% stenosis of internal carotid artery and/or cerebral major artery
CHA_2DS_2-VASc	X		X	X	X				X	x	x										
$ABCD^2$ Score for TIA		X				X	X	X			X										
ABCD3I		X				X	X	X			X									X	X
ASCVD	X		X		x						x	x	x	X	x						
ATRIA	X		x	x	x				x		x					x	x				
Reynolds Risk Score for Cardiovascular Risk in Women	x		x		x						x	x	x					x		x	
NINDS	x		x		x					X	x	x		x							
MetS Calc, the metabolic syndrome (MetS)	x		x		x						x		x	x					x		
Framingham Risk Score	x		x	x	x					X	x	x									
Modified Framingham Risk Score	x		x	x	x					X	x	x									

Age, HTN, and DM were the most common factors included in 7/7 tools
Sex was considered in all the tools except $ABCD^2$ tool
CHF and Stroke/TIA/Thromboembolism hx were considered by CHA_2DS_2-VASc and ATRIA
Vascular disease hx (prior MI, PAD or aortic plaque) were consider by CHA_2DS_2-VASc, Reynolds Risk Score and NIDS
5/7 tools were computed by medical personnel
4 of the tools were found to be reliable to predict stroke pre COVID-19
1 tool had descriptive items for each measure and was augmented with questions related to imaging.
2 tools assess stroke within the context of atrial fibrillation
2 tools assess stroke within the context of TIA
1 tool assess stroke in women 45 years of age and older
1 tool assess stroke within the context of metabolic syndrome
7 tools can be complete by clinicians using discrete questions as noted above under factors included.

The Framingham Stroke Risk Score (FSRS) is the most widely used assessment tool for determining the risk of stroke.
The revised Framingham Stroke Risk Score (R-FSRS) is more accurate, and thus more useful in reducing stroke risk while improving stroke discriminatory ability.
All CHA2DS2-VASc risk factors are included in the ATRIA. The ATRIA, CHADS2, and CHA2DS2-VASc scores tend to overlap in terms of factors.
When the ATRIA, CHADS2, and CHA2DS2-VASc stroke risk results were assessed in terms of stroke prediction, the ATRIA score was most accurate.
The ATRIA score's accuracy, especially when compared to the entire range of scores, is partly due to the inclusion of a wider range of age groups and formal statistical modeling.

Literature Review: Stroke Risks Factors Associated with COVID-19

Because SARS-Cov-2 is an emerging and novel virus, literature is limited; pathogenesis has not been well explicated. The results of the literature can be found in chapter 2-page 11. Also, see PRISMA page 12, Appendix D. Because of the limited scientific literature, the literature review was used to justify the need for this QI project and was examined to identify specific stroke risk factors associated with COVID-19. Specific risk factors are expanded upon in this section.

Overall, the literature did not ultimately show a direct causal link between COVID-19 and stroke. However, all studies from the literature search showed an increased risk of stroke during and following COVID-19 infection. These observations underscore the critical need to understand stroke risk factors within the context of COVID-19.

The risk for stroke is thought to be related to SARS-CoV-2–induce hypercoagulability and blood clot formation. SARS-CoV-2, a neurotropic virus, stimulates glial cells and causes a pro-inflammatory response in patients. Proinflammatory cytokines activate endothelial and mononuclear cells, enhancing tissue factor expression. This causes thrombosis by coagulation, thrombin production, and platelet activation. Elevated d-dimer, ferritin, and interleukin six values reflect the patient's proinflammatory and prothrombotic condition. The lungs, as well as infected neurons, produce interleukin 6. Interleukin concentrations are inversely proportional to the number of T cells in the body and predict symptom severity, outcome, and stroke risk. These factors show why the incidence of COVID-19 and stroke risk may be highly correlated.

Survey Findings

As noted in the methods section, the survey was adapted from Aber, A. et al. (2020) and Lip et al., (2010) (Appendix H). The adaptation was informed by examination of existing stroke tools and literature review discussed in this prior section.

Thirty-five clinical experts with medical training who worked frontline in the emergency department during COVID-19 completed the survey. The survey assessed reliability and content validity, and specificity of 23 traditional and 29 non-tradition risk factors for stroke in the context of COVID-19 infections. Content validity was operationalized as the degree to which the clinician believes the factor should be included as a risk factor. Reliability was operationalized as the degree/probability to which they have seen the risk factor in COVID-19 patients since the start of the pandemic.

With regards to reliability and content validity of traditional risk factors, 100% of participants rated atrial fibrillation, roughly 98% rated smoking, TIA and vascular disease as factors associated with stroke in COVID-19. Regarding non-traditional risk factors, participants identified metabolic syndrome, active COVID-19 that has lasted >8 days, ipsilateral >50% carotid stenosis, and limited physical activity as factors influence stroke risk (for full results see Tables 3, 4 and 5).

The participants rated 10 traditional and 10 non-traditional risk factors as being highly associated with increased odds of stroke. The traditional risk factors were (1) Atrial fibrillation, (2) smoking (current or history), (3) 2nd TIA in less than seven days, (4) TIA's symptoms >60 min, (5) vascular disease history (prior MI, PAD, or aortic plaque), (6) TIA's symptoms lasted 10-59 mins, (7) diabetes mellitus (current or history), (8) age >74 (9) hypertension (>140/90 mmHg or SBP >140 or DBP >90), and (10) history of stroke. Non-traditional risk factors were:

(1) metabolic syndrome, (2) ipsilateral >50% carotid stenosis of the internal carotid artery and/or major cerebral artery, (3) carotid stenosis, (4) BMI, (5) active COVID-19 infection that has lasted more than eight days, (6) limited physical activity, (7) use of hormone replacement, (8) Cancer, (9) D-dimer >920 ng/m, and (10) C-reactive protein >10.0 mg/L (see Table 3, 4, 5 and Figures 1, 2).

Table 3 - Validity and Reliability of Common and Traditional Stroke Risk Factors in the Context of COVID19

Total Responders 35 - Traditional Factors

Total Risks Factors	52
Traditional	23

Color represents top 10 factors per category

Traditional Factors Complete Sample	Validity %	Reliability %	Total %
Age >65	85.7	88.6	87.15
Age >74	94.3	97.1	95.7
Female	65.7	74.2	69.95
Male	80	82.9	81.45
African American	82.9	85.8	84.35
Currently Smoking	100	97.2	98.6
History of Smoking	94.3	94.3	94.3
History of stroke or heart attack before the age of 60 years	88.6	88.5	88.55
Hypertension >140/90 mmHg. Either SBP >140 or DBP >90	97.1	94.3	95.7
Use anti-hypertension medication	77.1	77.1	77.1
Diabetes mellitus (DM) or history of DM	97.2	94.3	95.75
Congestive heart failure (CHF) chronic heart failure	82.9	88.6	85.75
Vascular disease history (prior MI, PAD, or aortic plaque)	100	97.1	98.55
Enlarge heart or presence of left ventricular hypertrophy on ECG	88.6	91.4	90
Atrial fibrillation	100	100	100
Dementia	65.7	71.4	68.55
Traumatic brain injury history	65.7	71.4	68.55

History of stroke	97.2	94.2	95.7
TIA's symptoms < 10 min	85.7	82.9	84.3
TIA's symptoms lasted 10-59 min	97.2	94.3	95.75
TIA's symptoms >60 min	100	97.1	98.55
2nd TIA in less than 7 days	100	97.1	98.55
Dyslipidemia	91.5	88.6	90.05

Table 4

Validity and Reliability of Novel and Non-Traditional Stroke Risk Factors in the Context of COVID-19

Total Responders 35 – Non-Traditional Factors

Total Risks Factors	52
Non-Traditional	29

Non-Traditional Factors Complete Sample	Total Validity %	Total Reliability %	Total %
Active COVID-19 infection. Day 0 to 8	80	82.8	81.4
Active COVID-19 infection that has lasted more than 8 days	88.6	88.6	88.6
History of prior COVID-19 infection	77.1	77.1	77.1
Decrease SpO2 less than 90%	77.2	80	78.6
Ipsilateral >50% stenosis of the internal carotid artery and/or cerebral major artery	97.1	94.3	95.7
	97.1	94.2	95.65
White blood cells>10.4 K/uL	68.5	74.3	71.4
Lymphocytes < 1.00 K/uL	65.7	71.4	68.55
Hemoglobin < 11.5 g/dL	60	68.5	64.25
aPTT >36.3 seconds	71.4	74.3	72.85
INR >1.20	74.2	80	77.1
D-dimer >920 ng/ml	85.7	88.6	87.15
C-reactive protein >10.0 mg/L	82.9	85.8	84.35
Ferritin >1200 ng/mL	77.1	82.9	80
LDH >484 U/L	80	85.7	82.85
ALT >90.0 U/L	74.3	80	77.15
Creatinine >1.30 mg/dL	65.7	68.6	67.15
Proteinuria	62.9	68.6	65.75
eGFR < 45 or end-stage renal disease	71.4	77.1	74.25
Troponin >0.04 ng/mL	71.4	74.3	72.85
Hispanic	80	85.8	82.9
BMI >30kg/m2	88.5	91.5	90

Abuse Alcohol	82.8	85.7	84.25
History of Alcohol Abuse	80	80	80
Limited Physical Activity	88.6	88.5	88.55
Hormone Replacement Therapy	88.6	85.8	87.2
Significant emotional stress or depression in the last year	68.6	74.3	71.45
Metabolic syndrome	97.2	94.3	95.75
Cancer	85.8	88.6	87.2

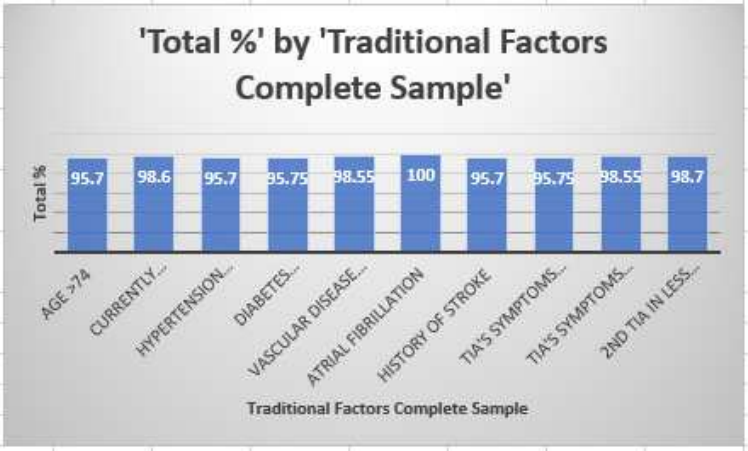
Table 5, Figure 1

Top 10 Traditional Risk Factors and Non-Traditional Risk Factors - Complete Sample

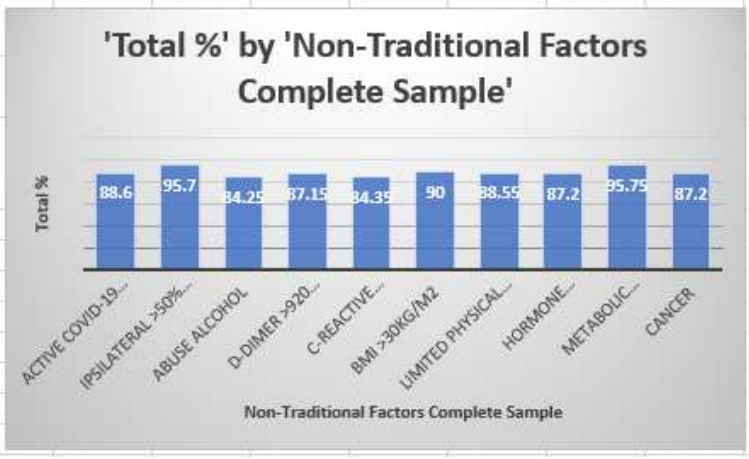
Total Responders 35

Total Risks Factors	**52**
Non-Traditional	29

Traditional Factors Complete Sample	Total %
Age >74	95.7
Currently Smoking	98.6
Hypertension >140/90 mmHg. Either SBP >140 or DBP >90	95.7
Diabetes mellitus (DM) or history of DM	95.75
Vascular disease history (prior MI, PAD, or aortic plaque)	98.55
Atrial fibrillation	100
History of stroke	95.7
TIA's symptoms lasted 10-59 min	95.75
TIA's symptoms >60 min	98.55
2nd TIA in less than 7 days	98.7



Non-Traditional Factors Complete Sample	Total %
Active COVID-19 infection that has lasted more than 8 days	88.6
Ipsilateral >50% stenosis of the internal carotid artery and/or cerebral major artery	95.7
Abuse alcohol	84.25
D-dimer >920 ng/ml	87.15
C-reactive protein >10.0 mg/L	84.35
BMI >30kg/m2	90
Limited Physical Activity	88.55
Hormone Replacement Therapy	87.2
Metabolic syndrome	95.75
Cancer	87.2



Because of the difference in disciplinary perspective and level of practice, it was important to understand any differences in discipline view. From the sample of 35 participants, physicians account for 66%, advance practice 9%, nurses 17%, and other 9%. Participant responses were organized by discipline – (see Tables 6, 7, and 8, Figures 3 and 4). Subsequently, the top ten factors per discipline were identified and compared against each other. The perspectives of each discipline were similar. All the disciplines agreed on seven traditional risk factors and five non-traditional risk factors. Traditional risk factors were: (1) age >74, (2) smoking (currently), (3) hypertension, (4) vascular disease (history), (5) atrial fibrillation, (6) TIA's symptoms >60 min, and (7) 2nd TIA in <7 days. Non-traditional risk factors were: (1) active COVID-19 infections lasted >8 days, (2) ipsilateral >50% carotid stenosis and or cerebral major artery, (3) D-dimer >920 ng/ml, (4) BMI >30kg/m2, and (5) cancer. For complete results, refer to Tables 9 and 10.

Table 6 - Figure 2

Top 10 Traditional & Non-Traditional Risk Factors – Physician Perspective

 # Physicians 24/35

Traditional Risk Factors - Physician	Total %
Age >74	95.65
Currently Smoking	97.85
History of stroke or heart attack before the age of 60 years	95.65
Hypertension >140/90 mmHg. Either SBP >140 or DBP >90	97.85
Vascular disease history (prior MI, PAD, or aortic plaque)	97.85
Atrial fibrillation	100
History of stroke	97.85
TIA's symptoms lasted 10-59 min	97.8
TIA's symptoms >60 min	97.8
2nd TIA in less than 7 days	97.8

Non-Traditional Factors - Physician	Total %
Active COVID-19 infection that has lasted more than 8 days	86.95
Decrease SpO2 less than 90%	84.8
Ipsilateral >50% stenosis of the internal carotid artery and/or cerebral major artery	97.8
D-dimer >920 ng/ml	84.8
BMI >30kg/m2	89.1
History of Alcohol Abuse	86.9
Limited Physical Activity	91.3
Hormone Replacement Therapy	97.8
Metabolic syndrome	93.5
Cancer	84.8

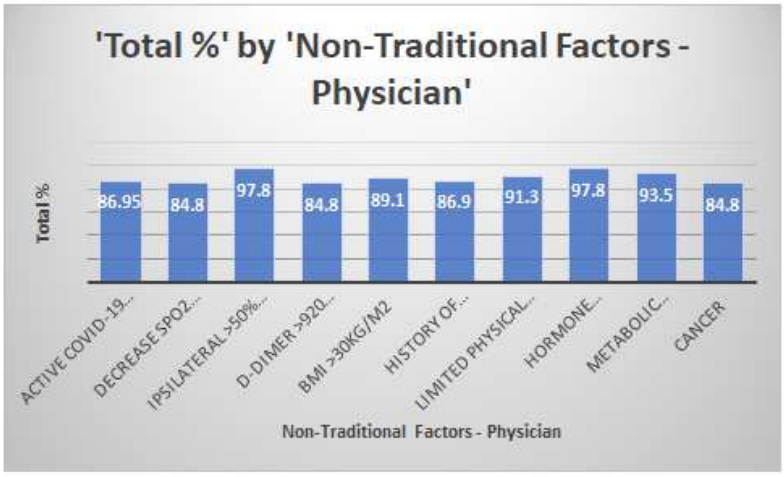


Table 7 - Figure 3

Top 10 Traditional & Non-Traditional Risk Factors – Nurse Perspective

 # Nurses 6/35

Traditional Factors - Nurse	Total %
Age >74	91.7
Currently Smoking	100
Hypertension >140/90 mmHg. Either SBP >140 or DBP >90	83.4
Diabetes mellitus (DM) or history of DM	100
Vascular disease history (prior MI, PAD, or aortic plaque)	100
Atrial fibrillation	100
TIA's symptoms < 10 min	91.7
TIA's symptoms lasted 10-59 min	100
TIA's symptoms >60 min	100
2nd TIA in less than 7 days	100

Non-Traditional Factors - Nurse	Total %
Active COVID-19 infection. Day 0 to 8	83.3
Active COVID-19 infection that has lasted more than 8 days	83.35
Ipsilateral >50% stenosis of the internal carotid artery and/or cerebral major artery	83.35
Carotid stenosis	83.35
D-dimer >920 ng/ml	83.3
LDH >484 U/L	83.4
Hispanic	100
BMI >30kg/m2	83.3
Abuse Alcohol	83.3
Metabolic syndrome	100
Cancer	83.3

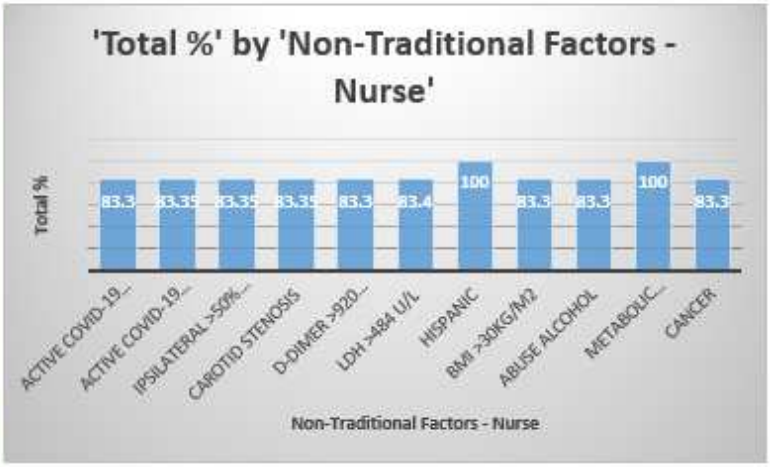
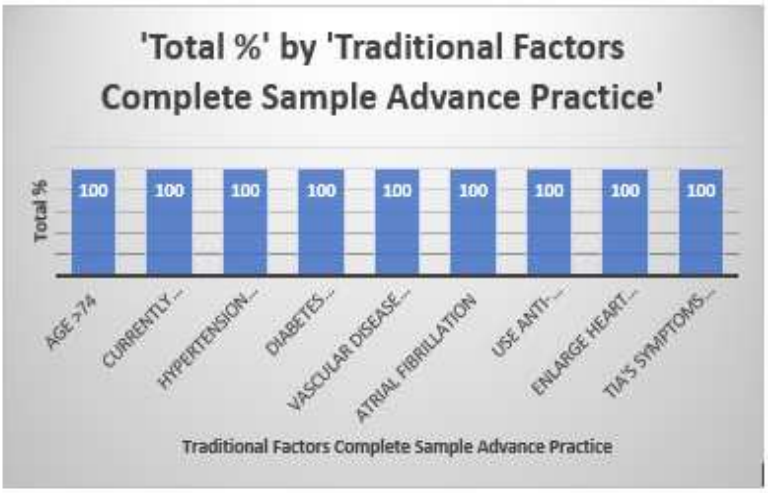


Table 8 - Figure 4

Top 10 Traditional & Non-Traditional Risk Factors – Advance Practice & Other

 # Advance Practice & Other 6/35

Traditional Factors Complete Sample Advance Practice	Total %
Age >74	100
Currently Smoking	100
Hypertension >140/90 mmHg. Either SBP >140 or DBP >90	100
Diabetes mellitus (DM) or history of DM	100
Vascular disease history (prior MI, PAD, or aortic plaque)	100
Atrial fibrillation	100
Use anti-hypertension medication	100
Enlarge heart or presence of left ventricular hypertrophy on ECG	100
TIA's symptoms >60 min	100



Non-Traditional Factors - Advance Practice	Total %
Active COVID-19 infection that has lasted more than 8 days	100
History of prior COVID-19 infection	100
Ipsilateral >50% stenosis of the internal carotid artery and/or cerebral major artery	100
Lymphocytes < 1.00 K/ul	100
aPTT >36.3 seconds	100
D-dimer >920 ng/ml	100
Hispanic	100
BMI >30kg/m2	100
Hormone Replacement Therapy	100
Cancer	100

Table 9

Top 10 Traditional Risk Factors comparison table among Disciplines

Repeat 1	Repeat 2	Repeat 3	Repeat 4

Traditional Factors Complete Sample	Total %
Age >74	95.7
Currently Smoking	98.6
Hypertension >140/90 mmHg. Either SBP >140 or DBP >90	95.7
Diabetes mellitus (DM) or history of DM	95.75
Vascular disease history (prior MI, PAD, or aortic plaque)	98.55
Atrial fibrillation	100
History of stroke	95.7
TIA's symptoms lasted 10-59 min	95.75
TIA's symptoms >60 min	98.55
2nd TIA in less than 7 days	98.7

Traditional Risk Factors Physician	Total %
Age >74	95.65
Currently Smoking	97.85
History of stroke or heart attack before the age of 60 years	95.65
Hypertension >140/90 mmHg. Either SBP >140 or DBP >90	97.85
Vascular disease history (prior MI, PAD, or aortic plaque)	97.85
Atrial fibrillation	100
History of stroke	97.85
TIA's symptoms lasted 10-59 min	97.8
TIA's symptoms >60 min	97.8
2nd TIA in less than 7 days	97.8

Traditional Factors - Nurse	Total %
Age >74	91.7
Currently Smoking	100
Hypertension >140/90 mmHg. Either SBP >140 or DBP >90	83.4
Diabetes mellitus (DM) or history of DM	100
Vascular disease history (prior MI, PAD, or aortic plaque)	100
Atrial fibrillation	100
TIA's symptoms < 10 min	91.7
TIA's symptoms lasted 10-59 min	100
TIA's symptoms >60 min	100
2nd TIA in less than 7 days	100

Traditional Factors Complete Sample Advance Practice	Total %
Age >74	100
Currently Smoking	100
Hypertension >140/90 mmHg. Either SBP >140 or DBP >90	100
Diabetes mellitus (DM) or history of DM	100
Vascular disease history (prior MI, PAD, or aortic plaque)	100
Atrial fibrillation	100
Use anti-hypertension medication	100
Enlarge heart or presence of left ventricular hypertrophy on ECG	100
TIA's symptoms >60 min	100
2nd TIA in less than 7 days	100

Table 10

Top 10 Non-Traditional Risk Factors comparison table among Disciplines

Repeat 1	Repeat 2	Repeat 3	Repeat 4

Non-Traditional Factors Complete Sample	Total %
Active COVID-19 infection that has lasted more than 8 days	88.6
Ipsilateral >50% stenosis of the internal carotid artery and/or cerebral major artery	95.7
Abuse alcohol	84.25
D-dimer >920 ng/ml	87.15
C-reactive protein >10.0 mg/L	84.35
BMI >30kg/m2	90
Limited Physical Activity	88.55
Hormone Replacement Therapy	87.2
Metabolic syndrome	95.75
Cancer	87.2

Non-Traditional factors Physician	Total %
Active COVID-19 infection that has lasted more than 8 days	86.95
Decrease SpO2 less than 90%	84.8
Ipsilateral >50% stenosis of the internal carotid artery and/or cerebral major artery	97.8
D-dimer >920 ng/ml	84.8
BMI >30kg/m2	89.1
History of Alcohol Abuse	86.9
Limited Physical Activity	91.3
Hormone Replacement Therapy	97.8
Metabolic syndrome	93.5
Cancer	84.8

Non-Traditional Factors - Nurse	Total %
Active COVID-19 infection. Day 0 to 8	83.3
Active COVID-19 infection that has lasted more than 8 days	83.35
Ipsilateral >50% stenosis of the internal carotid artery and/or cerebral major artery	83.35
D-dimer >920 ng/ml	83.3
LDH >484 U/L	83.4
Hispanic	100
BMI >30kg/m2	83.3
Abuse Alcohol	83.3
Metabolic syndrome	100
Cancer	83.3

Non-Traditional Factors - Advance Practice	Total %
Active COVID-19 infection that has lasted more than 8 days	100
History of prior COVID-19 infection	100
Ipsilateral >50% stenosis of the internal carotid artery and/or cerebral major artery	100
C-reactive protein >10.0 mg/L	100
aPTT >36.3 seconds	100
D-dimer >920 ng/ml	100
Hispanic	100
BMI >30kg/m2	100
Hormone Replacement Therapy	100
Cancer	100

Narrative Data

Participants noted the omission of the following factors from the survey: (1) history of pulmonary embolism/ deep vein thrombosis (PE/DVT), (2) history of hypercoagulation state, (3) obstructive sleep apnea (OSA), (4) recent surgery, (5) clotting factors, (6) family history of stroke, (7) blood thinner use, and (8) hyperhomocysteinemia (Table 11).

Table 11

Missing Factors Associated with Stroke Risk in COVID-19 According to Clinical Expert Opinions

Is there anything that should be included in the assessment form?
Patients with history of PE/DVT
Patients with history of hypercoag stage (you included cancer, but this broadens it out
Patients with history of OSA
Recent or hx of surgeries
Family history of stroke
Blood thinner use
Hyperhomocysteinemia

Discussion

This QI project presented existing gaps in stroke prediction based on a literature review of existing validated stroke tools. Based on clinicians' perspectives, the surveys' results indicate that 27 stroke risk factors are not covered in the current stroke tools and should be explored in more extensive samples using appropriate research methods. The findings of the narrative comments are aligned with recent research. For example, concerning PE/DVT, the CDC (n.d.) reports that even though DVT is not directly associated with stroke, a history of PE/DVT can be associated with inflammation-driven coagulation that is also seen in conditions like stroke.

About OSA, a recent study conducted by Jehan et al. (2018), the mechanisms associated with the development of stroke in OSA and found that blood vessel damage contributes to a pronounced inflammatory process caused by hypoxic episodes in OSA. OSA stimulates the sympathetic system leading to elevation of blood pressure. In addition, it depresses the parasympathetic system resulting in more inflammation, platelet accumulation, and endothelium dysfunction. In a review study by Baufreton (2010), there is an increased possibility of stroke after surgery associated with thromboembolism. In another study by Boehme et al. (2017), the authors investigated a genetic predisposition for stroke and concluded that gene disorders might be plausible causes of stroke events in such patients. According to a study by Spence et al. (2006), hyperhomocysteinemia is related to improper coagulation, diminished endothelial compliance, elevated oxidative stress, and low-density lipoprotein. The authors suggest that these processes are linked to higher stroke risk.

The findings of this QI project are not to be generalized. The findings of this QI project provide initial evidence that suggests that stroke tools may be updated for a more comprehensive assessment of risk for stroke when considering the influence of COVID-19.

Increasing our understanding of stroke risk within the context of COVID-19 could serve as a basis for early intervention and prevention. This QI is a starting point of questions that can be used to advance the detection of stroke in COVID-19 that are to be tested in research studies and larger samples in the future.

The limitation of the project refers to a small sample size within one health system.

Conclusion

Stroke is the fifth leading cause of death in the US. However, the CDC reports that 80% of strokes can be prevented. The impact of COVID-19 on stroke incidence has been discussed since the beginning of the pandemic. There are various pathways on how the SARS-CoV-2 virus can cause stroke, including the direct affection of the neurological system by the virus, the secondary inflammation resulting from pro-inflammatory substances and mechanisms triggered by the virus, the effects on the heart and circulatory system that result in systemic clotting formation and finally, the impact on the respiratory system resulting in hypercapnia and brain hypoxia leading to acidity and cell death. Zakeri et al. (2021) examines these pathways and state that COVID-19 is associated with hypercoagulability and inappropriate immune responses. These manifestations influenced the release of cytokines and other pro-inflammatory markers, causing an exaggerated inflammation and destruction of endothelial cells. Similarly, the virus also causes a dysregulation of the renin-angiotensin-aldosterone system (RASS) associated with increased inflammation leading to vessel damage and the formation of blood clots.

Fifty-two stroke risk factors in the context of COVID-19 infection were identified. Risk factors for stroke should be considered when assessing patients with active or history of COVID-19 infections with or without commodities, especially those hospitalized. We hope this QI project will serve as a basis for future QI and research projects that will aid in the development of a more precise assessment of stroke within the context of COVID-19. Ultimately, we hope this project will contribute to future work that increases the quality of care and improve patient outcomes.

DNP Essentials

Nursing education at the doctoral level reflects the Scientific Underpinnings for Practice.

The application of the DNP Essentials facilitated the activities associated with the planning, delivery, analysis, and completion of this QI project. The DNP essentials and competencies related to the activities documented in this project were: (1) Scientific Underpinnings for Practice and (2) Clinical Prevention and Population Health for Improving the Nation's Health.

The essentials of Scientific Underpinnings for Practice and the Clinical Prevention and Population Health for Improving the Nation's Health were used in the application of knowledge to find gaps in the system, select and review appropriate information and suggest approaches that could help inform and improve future processes. This project also used science-based theories and concepts that required the integration of nursing science with knowledge from the biophysical and analytical sciences. The project encompasses individual, aggregate, and population health based on concepts related to clinical prevention in addressing gaps in stroke assessment of individuals suffering from COVID-19 infections.

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Appendix A

Site approval/authorization letter

Letter of Cooperation with Outside Organization for UCI DNP Project

Date: December 2021

Dear: (name of DNP Student): Maria del Pilar Giraldo Herrera

This letter confirms that I, as an authorized representative of
allow the above-named Doctor of Nursing Practice student access to conduct a leadership, policy, quality improvement, or evidence-based practice project activities at the listed site(s) as discussed with the DNP student and outlined below. These activities may commence after the DNP student has consulted with UCI IRB about the proposed project.

- **Project site(s):** (list specific site name and address for all sites within which the organization is providing student access to conduct the project)

  Mission Hospital Emergency Group.
  27700 Medical Center Rd, Mission Viejo, CA 92691

- **Project purpose:** (briefly summarize the project purpose, plan and expected outcomes)

  The purpose of this project is to identify potential risk factors that may predict risk for stroke for patients with a history of SARS-Co-V-2 infection. This is a quality improvement project, deemed self-exempt through UCI IRB.

- **Project activities:** (briefly summarize the activities that will commence at the site, including any baseline data collected, educational interventions, PDSA cycle proposed...)

  Online survey. The survey will take approximately 10 minutes. Participants will be asked a few questions about demographics. Then participants will see a list of potential risk factors for stroke for COVID-19 patients, and they will be asked to rate the degree of relevance and validity of each risk factor as it is worded on the survey.

- **Target population:** (identify the population upon whom the project will focus)

  Emergency department doctors, physician assistants, nurse practicioners.

- **Site(s) support:** (briefly describe the support the project site(s) agree to provide to support the project, such as space to conduct project activities, data retrieval from electronic records, facilitation of educational activities....)

  The site agreed to facilitate disemination of survey via email

- **Data management plan:** (briefly describe the plan for management of data such as what data will be collected, whether it will be identified/de-identified, what protections will be in place for data protection...)

  Data will be mana and secute in privite folders and only will be share with UCI School of Nursing departmenut for educational purposes
  Providers personal/professional identifiers will NOT be collected. participants will be identify by a number.

- **Other agreements:** (briefly describe any additional agreements that have been made to support the project, if applicable)

  No applicable

- **Anticipated end date:** (indicate the anticipated date that the project will be concluded at the site)

  March 15, 2022

It is understood that all DNP Scholarly Project related activities must cease if directed by UCI IRB. It is also understood that any activities that involve Personal Private Information or Protected Health Information must comply with HIPAA Laws and institutional policy.

Our organization agrees to the terms and conditions stated above. If there are any concerns related to this project, we will contact the DNP student named above and their DNP Scholarly Project Chair. For concerns regarding IRB policy or human subject welfare, we may also contact our own institutional IRB.

UCI IRB: https://www.research.uci.edu/compliance/human-research-protections/researchers/irb-faqs.html

With regards,

(Signature of project site-authorized representative)

James Keany, MD

(Job title of authorized representative)

Dec, 2021

(Date signed)

Appendix B

Conflict of Interest Disclosure Form

DNP Scholarly Project Conflict of Interest Disclosure Form

Directions: Students must complete this form and acquire all signatures prior to beginning work on their scholarly project at their place of employment. Once form has been approved, students must upload the signed and approved form to Typhon, along with your Clinical Practice Site Mentor's CV/resume.

Student:

I, Maria del Pilar Giraldo Herrera, understand the guidelines for clinical practicum hours required in association with the DNP Scholarly Project. These practice hours may be carried out in my place of employment but are not to be done during work hours. The Faculty of Record for the DNP Practicum or DNP APRN Practicum course and the Clinical Practice Site Mentor at my clinical site will supervise my DNP practice hours. I agree and abide by these guidelines.

Student Signature: _____ Date: December, 2021

Clinical Practice Site Mentor:

I, Hubbard, MaryAnn, have read and understand the guidelines for the UC Irvine DNP clinical practicum hours. These hours will not be accrued during the student's work hours. I will be mentoring (student) Maria del Pilar Giraldo Herrera at (name of institution) Mission Hospital.

Clinical Practice Site Mentor Signature: _____ Date: December, 2021

DNP Scholarly Project Chair:

I, MaryAnn Hubbard, understand the guidelines for the DNP clinical practicum hours. The Scholarly Project may be carried out at the student's place of employment but required clinical practice hours may not be accrued during the student's work time or interfere with student's work obligations.

Chair Signature: _____ Date: December, 2021

DNP Faculty of Record for DNP Practicum or DNP APRN Practicum course:

I, Melissa Dawn, understand the guidelines for the DNP clinical practicum hours. The Scholarly Project may be carried out at the student's place of employment but required clinical practice hours may not be accrued during the student's work time or interfere with student's work obligations.

Appendix C

Kuali Approval Email

Kuali Notifications <no-reply@kuali.co> Thu, Jan 6, 8:48 AM

to me

Dear Maria Del Pilar Giraldo Herrera,

The University of California, Irvine (UCI) Human Research Protections (HRP) Program complies with all review requirements defined in 45 CFR Part 46 and 21 CFR 50.3.

Based on the responses provided in Non Human Subjects Research (NHSR): #684 - "Stroke Prediction in the Context of COVID-19 Infections", and per the definitions cited below, the activities do not constitute human subject research or a clinical investigation, as applicable. Therefore, *UCI IRB review is not required and will not be provided.*

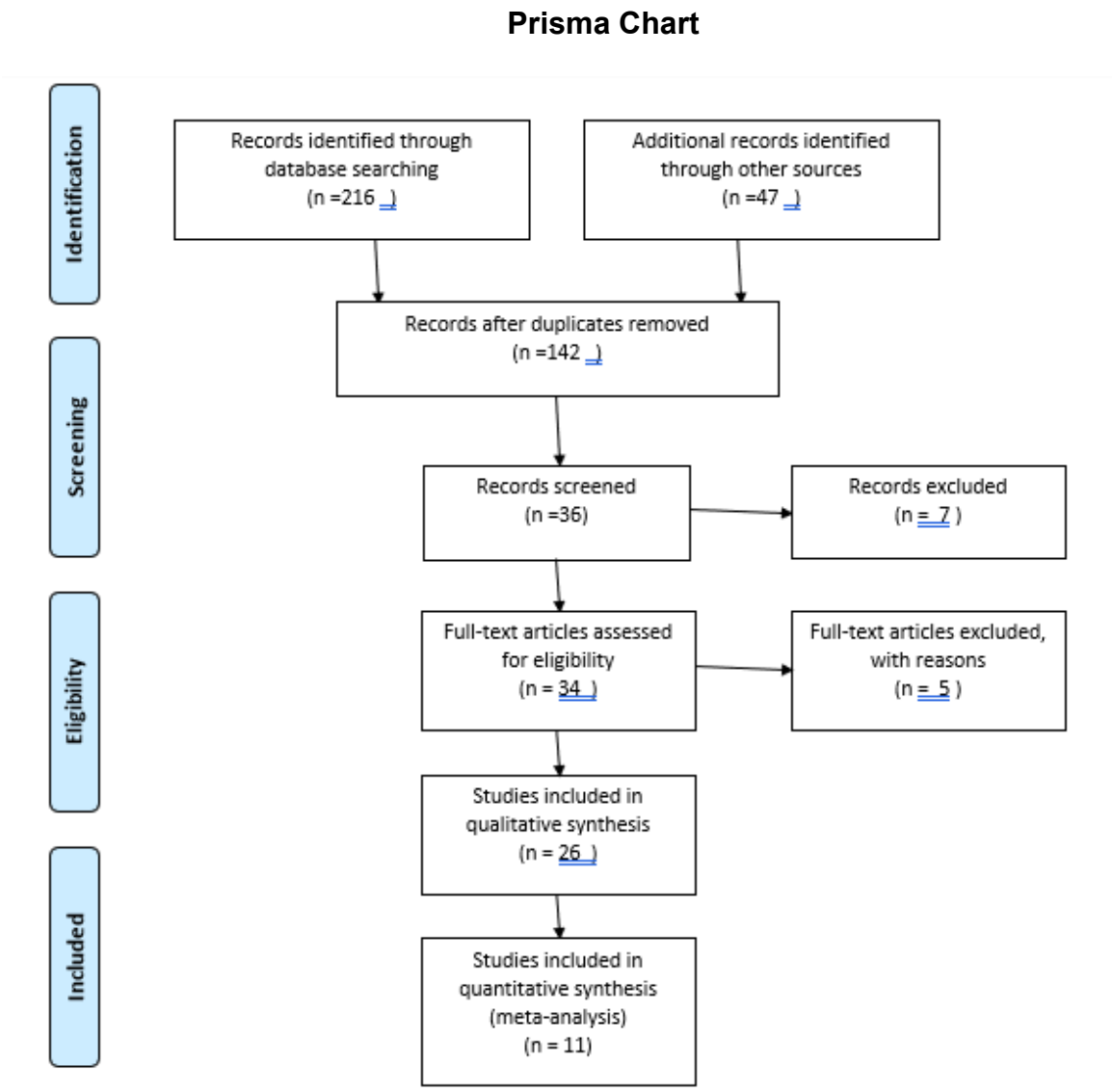
45 CFR 46.102(l) defines research as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge; and 45 CFR 46.102(e)(1) defines a human subject as "a living individual about whom an investigator conducting research obtains (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens."

21 CFR 50.3(c) defines a clinical investigation as "any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit."

To view the determination for your submission, click here: uci.kuali.co/protocols/protocols/61bcf073650fe9002c68f71f

Please DO NOT REPLY to this email as this mailbox is unmonitored. If your project changes in ways that may affect this determination, please contact the HRP staff for additional guidance: irb@uci.edu.

Appendix D



Appendix E

Table of Evidence

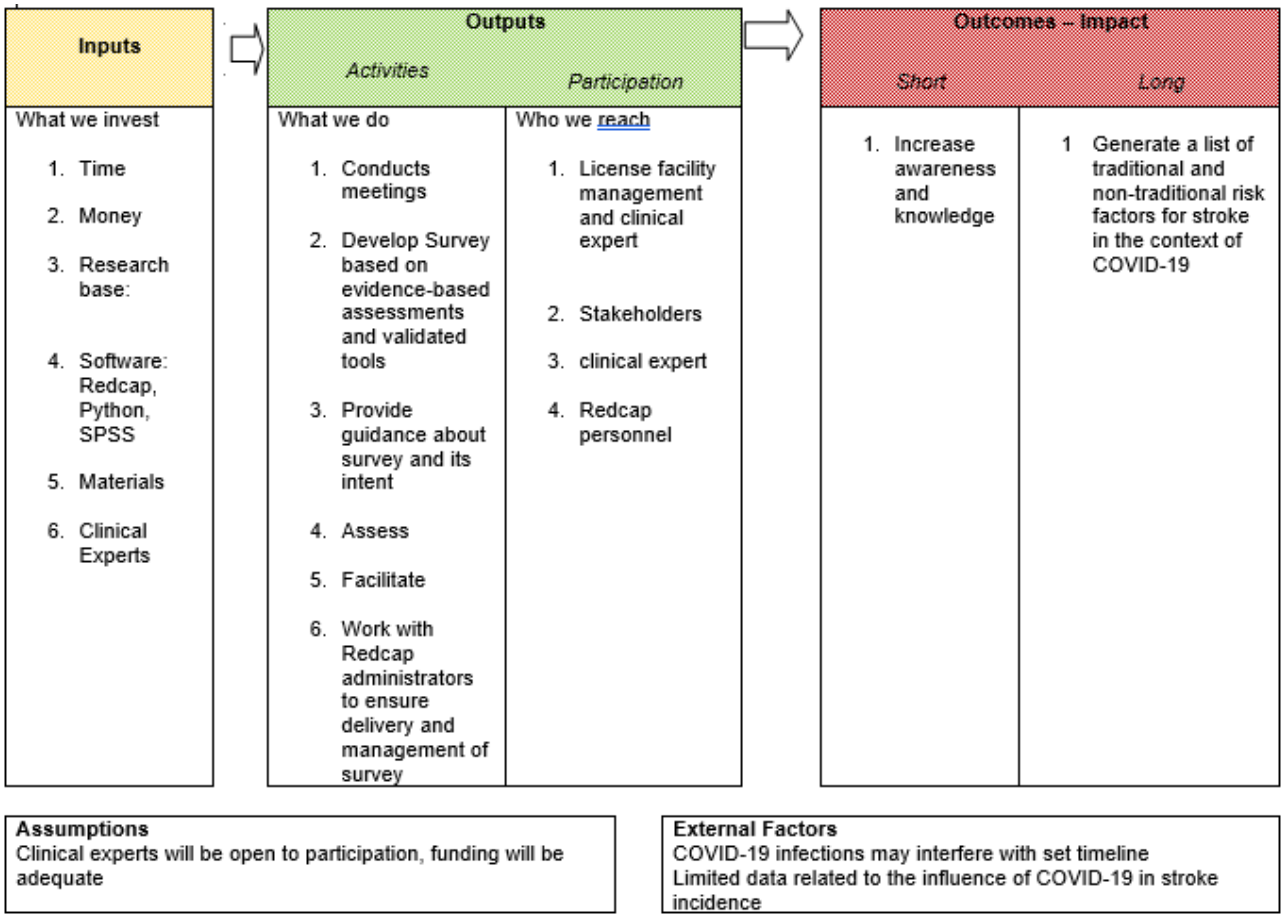
	THEME	SOURCE 1	SOURCE 2	SOURCE 3	SOURCE 4
SOURCE (AUTHOR, DATE)		Agarwal, A., Pinho, M., Raj, K., Frank, F. Y., Bathla, G., Achilleos, M., ... & Maldjian, J. (2020)	Belani, P., Schefflein, J., Kihira, S., Rigney, B., Delman, B. N., Mahmoudi, K., Mocco, J., Majidi, S., Yeckley, J., Aggarwal, A., Lefton, D., & Doshi, A. H. (2020)	Beyrouti, R., Adams, M. E., Benjamin, L., Cohen, H., Farmer, S. F., Goh, Y. Y., ... & Werring, D. J. (2020).	Goyal, P., Choi, J. J., Pinheiro, L. C., Schenck, E. J., Chen, R., Jabri, A., ... & Safford, M. M. (2020)
THEME 1	COVID-19 infections are associated with increase stroke risk.	The study suggest that although a wide range of neurological manifestations has been found in COVID-19 cases, ischemic stroke is the most common neurological feature of the disease, mainly because COVID-19 is associated with a condition of hypercoagulation, exaggerated physiological responses to the cytokine storm, and multi-system inflammation	In this retrospective case-control study of 41 cases and 82 control subjects matched by age, sex, and risk factors an analysis performed showed that of individuals suffering acute ischemic stroke, 46.3% were affected by COVID-19 versus 18.3% of control group. After adjusting the factors such as age, sex, and risk factors, patients with COVID-19 infection have increase odds for stroke when compared with the control cohort.	The study report that data cannot confirm a causal relationship between COVID-19 and ischaemic stroke, since most patients had other risk factors for stroke. Nevertheless, the findings suggest that IS associated with COVID-19 infection can haapen in the context of a systemic hypercoagulopathy	Medical problems such as AF and other cardiac arrhythmias, MI, CHF, myocarditis, and venous thrombosis are more common in COVID-19 infected patients, all of which increase the risk of ischemic stroke

	THEME	SOURCE 5	SOURCE 6	SOURCE 7
SOURCE (AUTHOR, DATE)		Nannoni, S., de Groot, R., Bell, S., & Markus, H. S. (2021).	Panigada, M., Bottino, N., Tagliabue, P., Grasselli, G., Novembrino, C., Chantarangkul, V., ... & Tripodi, A. (2020)	Trejo-Gabriel-Galán, J. M. (2020).
THEME 1	COVID-19 infections are associated with increase stroke risk.	research papers on acute cerebrovascular diseases in COVID-19 and the data showed that of the 108,571 patients with COVID-19, acute cardiovascular event occurred in 1.4%, the ischemic stroke being the most common manifestation. Patients with Covid-19 who developed acute cerebrovascular disease, compared to those who did not were older and were more likely to have comorbidities. The authors concluded that acute cerebrovascular disorders are common in COVID-19 patients, particularly those who are highly infected and have vascular risk factors.	this study suggest that COVID-19 infection is linked with pathological inflammation, hypercoagulability, higher D-dimer levels, and the induced production of antiphospholipid antibodies. These events result in multi-vascular thrombosis in these patients	The study suggested stroke as a complication and prognostic variant of COVID-19, and concluded that a stroke history increases the incidence of mortality due to COVID-19 by 3 times and stroke is one of the principal complication of COVID-19.

	THEME	SOURCE 8	SOURCE 9	SOURCE 10
SOURCE (AUTHOR, DATE)		Vogrig, A., Gigli, G. L., Bnà, C., & Morassi, M. (2021).	Yamakawa, M., Kuno, T., Mikami, T., Takagi, H., & Gronseth, G. (2020).	Zhang, S., Zhang, J., Wang, C., Chen, X., Zhao, X., Jing, H., Liu, H., Li, Z., Wang, L., & Shi, J. (2021).
THEME 1	COVID-19 infections are associated with increase stroke risk.	The study states acute cerebrovascular disease, notably ischemic stroke, has emerged as a major consequence of infection with SARS-CoV-2, the causative agent of Coronavirus disease-2019 (COVID-19). Data on people who have had a COVID-19-related stroke revealed some differences in clinical presentation, neuroimaging results, and outcomes in these cases.	The study report that in hospitalized COVID-19 patients, the rate of identified stroke was 1.1 percent, and it was linked to older age and stroke risk factors. COVID-19 patients with frequent cryptogenic stroke and elevated d-dimer levels had a higher risk of thromboembolism, which is linked to a higher death rate.	The study suggested that during the COVID-19 pandemic, patients with severe COVID-19 experienced consequences such as acute ischemic stroke (AIS), which was linked to a poor prognosis. These individuals frequently exhibited aberrant coagulation, such as increased D-dimer and fibrinogen values and a low platelet count. The authors conclude that COVID-19 may cause AIS by inducing hypercoagulability.

Appendix F

Logic Model



Appendix G

Recruitment Material

Stroke prediction in COVID-19 patients

Dear Sir or Madam,

I am a family nurse practitioner student, enrolled in a Doctor of Nursing Practice program at the University of California, Irvine (UCI). I am required to complete a final project to fulfill the degree requirements at UCI. The purpose of this project is to identify potential risk factors that may predict risk for stroke for patients with a history of SARS-Co-V-2 infection. This is a quality improvement project, deemed self-exempt through UCI IRB. The project is being overseen by my project chair Melissa Pinto, Ph.D., RN, FSAHM, FAAN, Associate Professor at UCI, and Jung-Ah Lee, Ph.D., RN, FAAN, Associate Professor at UCI.

The survey will take approximately 5-10 minutes. You will be asked a few questions about your demographics. Then you will see a list of potential risk factors for stroke for COVID-19 patients, and you will be asked to please rate the degree of relevance and validity of each risk factor as it is worded on the survey. There is also an option to enter free text. This is designed to provide me with any information that was not captured in the survey or information you think I should know about stroke in COVID-19 patients. Please answer each question based on your experience and starting at the beginning of the **COVID-19 pandemic (March 2020) until now.**

Thank you very much for considering. Upon completion, I intend to share the survey findings with the unit in the form of a written summary report.

You may open the survey in your web browser by clicking the link below:
Stroke prediction in COVID-19 patients

If the link above does not work, try copying the link below into your web browser:
https://redcap.providence.org/redcap/surveys/?s=HPXLP4K4L8YENF8D

Participation in this survey is voluntary.

Feel free to contact me if you have any questions.

Maria Giraldo H.

Email: mdgirald@uci.edu

Cell: (949) 637-2213

Appendix H

Data Collection Instrument

1) **COVID-19** patients have a higher probability of stroke when they are **Age >65**
* must provide value
- Very true
- True
- Somewhat true
- Not true

2) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they are **Age >65**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

3) COVID-19 patients have a higher probability of stroke when they are **Age >74**
* must provide value
- Very true
- True
- Somewhat true
- Not true

4) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they are **Age >74**
* must provide value
- Very relevant
- Relevant
- Somewhat Relevant
- Not relevant

5) COVID-19 patients have a higher probability of stroke when they are **Female**
* must provide value
- Very true
- True
- Somewhat true
- Not true

6) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they are **Female**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

7) COVID-19 patients have a higher probability of stroke when they are **Male**
* must provide value
- Very true
- True
- Somewhat true
- Not true

8) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they are **Male**
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

9) COVID-19 patients have a higher probability of stroke when they are **African American**
* must provide value
- Very true
- True
- Somewhat true
- Not true

10) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they are **African American**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

11) COVID-19 patients have a higher probability of stroke when they are **Hispanic**
* must provide value
- Very true
- True
- Somewhat true
- Not true

12) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they are **Hispanic**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

13) COVID-19 patients have a higher probability of stroke when **BMI >30 kg/m2**
* must provide value
- Very true
- True
- Somewhat true
- Not true

14) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when **BMI >30 kg/m2**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

15) COVID-19 patients have a higher probability of stroke when they Currently **Smoke**
* must provide value
- Very true
- True
- Somewhat true
- Not true

16) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they Currently **Smoke**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

17) COVID-19 patients have a higher probability of stroke when they have **a history of Smoking**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

18) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **a history of Smoking**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

19) COVID-19 patients have a higher probability of stroke when they **abuse alcohol**

* must provide value

- ○ CHOOSE 1 OPTION
- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

20) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they **abuse alcohol**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

21) COVID-19 patients have a higher probability of stroke when they have **history of alcohol abuse**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

22) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **history of alcohol abuse**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

23) COVID-19 patients have a higher probability of stroke when they have **limited physical activity**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

24) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **limited physical activity**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

25) COVID-19 patients have a higher probability of stroke when they use **hormone replacement therapy**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

26) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they use **hormone replacement therapy**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

27) COVID-19 patients have a higher probability of stroke when they have had/have been having **significant emotional stress or depression in the past year**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

28) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have had/have been having **significant emotional stress or depression in the past year**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

29) COVID-19 patients have a higher probability of stroke when their **parents had a history of stroke or heart attack before the age of 60 years**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

30) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when their **parents had a history of stroke or heart attack before the age of 60 years**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

31) COVID-19 patients have a higher probability of stroke when they have **hypertension >140/90 mmHg. Either SBP >140 or DBP >90**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

32) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **hypertension >140/90 mmHg. Either SBP >140 or DBP >90**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

33) COVID-19 patients have a higher probability of stroke when they use **hypertension medication**
* must provide value
- Very true
- True
- Somewhat true
- Not true

34) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they use **hypertension medication**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

35) COVID-19 patients have a higher probability of stroke when they have **diabetes mellitus (DM) or history of DM**
* must provide value
- Very true
- True
- Somewhat true
- Not true

36) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they have **diabetes mellitus (DM) or history of DM**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

37) COVID-19 patients have a higher probability of stroke when they have **congestive heart failure (CHF) chronic heart failure**
* must provide value
- Very true
- True
- Somewhat true
- Not true

38) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they have **congestive heart failure (CHF) chronic heart failure**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

39) COVID-19 patients have a higher probability of stroke when they have **vascular disease history (prior MI, PAD, or aortic plaque)**
* must provide value
- Very true
- True
- Somewhat true
- Not true

40) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they have **vascular disease history (prior MI, PAD, or aortic plaque)**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

41) COVID-19 patients have a higher probability of stroke when they have **enlarge heart or presence of left ventricular hypertrophy on ECG**
* must provide value
- Very true
- True
- Somewhat true
- Not true

42) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they have **enlarge heart or presence of left ventricular hypertrophy on ECG**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

43) COVID-19 patients have a higher probability of stroke when they have **atrial fibrillation**
* must provide value
- Very true
- True
- Somewhat true
- Not true

44) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they have **atrial fibrillation**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

45) COVID-19 patients have a higher probability of stroke when they have **dementia**
* must provide value
- Very true
- True
- Somewhat true
- Not true

46) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they have **dementia**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

47) COVID-19 patients have a higher probability of stroke when they have a **traumatic brain injury history**
* must provide value
- Very true
- True
- Somewhat true
- Not true

48) Test for relevant - same question as above
COVID-19 patients have a higher probability of stroke when they have a **traumatic brain injury history**
* must provide value
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

49) COVID-19 patients have a higher probability of stroke when they have a **history of stroke**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

50) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have a **history of stroke**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

51) COVID-19 patients have a higher probability of stroke when they have **TIA's symptoms < 10 min**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

52) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **TIA's symptoms < 10 min**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

53) COVID-19 patients have a higher probability of stroke when their **TIA's symptoms lasted 10-59 min**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

54) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when their **TIA's symptoms lasted 10-59 min**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

55) COVID-19 patients have a higher probability of stroke when their **TIA's symptoms >60 min**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

56) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when their **TIA's symptoms >60 min**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

57) COVID-19 patients have a higher probability of stroke when they have a **2nd TIA in less than 7 days**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

58) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have a **2nd TIA in less than 7 days**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

59) COVID-19 patients have a higher probability of stroke when they have **dyslipidemia**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

60) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **dyslipidemia**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

61) COVID-19 patients have a higher probability of stroke when they have **metabolic syndrome**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

62) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **metabolic syndrome**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

63) COVID-19 patients have a higher probability of stroke when they have **cancer**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

64) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **cancer**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

65) COVID-19 patients have a higher probability of stroke when they have an **active COVID-19 infection. Day 0 to 8**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

66) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have an **active COVID-19 infection. Day 0 to 8**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

67) COVID-19 patients have a higher probability of stroke when they have an **active COVID-19 infection that has lasted more than 8 days**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

68) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have an **active COVID-19 infection that has lasted more than 8 days**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

69) COVID-19 patients have a higher probability of stroke when they have a **history of prior COVID-19 infection.**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

70) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have a **history of prior COVID-19 infection.**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

71) COVID-19 patients have a higher probability of stroke when they have **decrease SpO2 less than 90%**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

72) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **decrease SpO2 less than 90%**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

73) COVID-19 patients have a higher probability of stroke when they have **ipsilateral >50% stenosis of the internal carotid artery and/or cerebral major artery**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

74) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **ipsilateral >50% stenosis of the internal carotid artery and/or cerebral major artery**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

75) COVID-19 patients have a higher probability of stroke when they have **carotid stenosis**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

76) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **carotid stenosis**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

77) COVID-19 patients have a higher probability of stroke when they have **white blood cells>10.4 K/uL**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

78) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **white blood cells>10.4 K/uL**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

79) COVID-19 patients have a higher probability of stroke when they have **lymphocytes < 1.00 K/uL**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

80) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **lymphocytes < 1.00 K/uL**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

81) COVID-19 patients have a higher probability of stroke when they have **hemoglobin < 11.5 g/dL**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

82) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **hemoglobin < 11.5 g/dL**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

83) COVID-19 patients have a higher probability of stroke when they have **aPTT >36.3 seconds**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

84) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **aPTT >36.3 seconds**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

85) COVID-19 patients have a higher probability of stroke when they have **INR >1.20**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

86) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **INR >1.20**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

87) COVID-19 patients have a higher probability of stroke when they have **D-dimer >920 ng/ml**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

88) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **D-dimer >920 ng/ml**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

89) COVID-19 patients have a higher probability of stroke when their **C-reactive protein >10.0 mg/L**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

90) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when their **C-reactive protein >10.0 mg/L**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

91) COVID-19 patients have a higher probability of stroke when their **ferritin >1200 ng/mL**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

92) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when their **ferritin >1200 ng/mL**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

93) COVID-19 patients have a higher probability of stroke when their **LDH >484 U/L**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

94) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when their **LDH >484 U/L**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

95) COVID-19 patients have a higher probability of stroke when their **ALT >90.0 U/L**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

96) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when their **ALT >90.0 U/L**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

97) COVID-19 patients have a higher probability of stroke when their **Creatinine >1.30 mg/dL**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

98) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when their **Creatinine >1.30 mg/dL**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

99) COVID-19 patients have a higher probability of stroke when they have **proteinuria**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

100) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when they have **proteinuria**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

101) COVID-19 patients have a higher probability of stroke when **their eGFR < 45 or end-stage renal disease**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

102) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when **their eGFR < 45 or end-stage renal disease**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

103) COVID-19 patients have a higher probability of stroke when their **troponin >0.04 ng/mL**

* must provide value

- ○ Very true
- ○ True
- ○ Somewhat true
- ○ Not true

104) Test for relevant - same question as above

COVID-19 patients have a higher probability of stroke when their **troponin >0.04 ng/mL**

* must provide value

- ○ Very relevant
- ○ Relevant
- ○ Somewhat relevant
- ○ Not relevant

105) **Does the assessment form include all the factors essential to evaluate stroke in the context of COVID-19?**

- ○ Yes
- ○ No

reset

106) **Is there anything else that should be included in the assessment form?**

(optional)

107) **Any additional comments or suggestions?**

(optional)

Submit

Save & Return Later

Table 2

Cronbach's Alpha

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Age >65	82.46	1370.961	.611	.983
Age >74	82.71	1371.622	.716	.983
Female	82.06	1319.703	.933	.983
Male	82.34	1341.644	.813	.983
African American	82.43	1346.958	.847	.983
Hispanic	82.37	1347.476	.775	.983
BMI >30 kg/m2	82.60	1359.071	.773	.983
Smoking (currently)	82.86	1390.832	.573	.983
Smoking (history)	82.66	1370.938	.828	.983
Alcohol abuse (currently)	81.77	1382.005	.102	.988
Alcohol (history)	82.37	1349.182	.917	.983
limited physical activity	82.54	1371.138	.707	.983
hormone replacement therapy	82.57	1371.193	.705	.983
significant emotional stress or depression in the past year	82.14	1329.244	.930	.983
parents had a history of stroke or heart attack before the age of 60 years	82.51	1365.375	.735	.983
hypertension >140/90 mmHg. Either SBP >140 or DBP >90	82.74	1378.373	.755	.983
Use of hypertension medication	82.37	1357.829	.749	.983

diabetes mellitus (DM)	82.86	1383.714	.694	.983
congestive heart failure (CHF) or chronic heart failure	82.46	1347.020	.902	.983
vascular disease history (prior MI, PAD, or aortic plaque)	82.89	1386.339	.768	.983
enlarge heart or presence of left ventricular hypertrophy on ECG	82.57	1353.723	.859	.983
atrial fibrillation	82.94	1394.408	.574	.983
dementia	82.00	1327.941	.828	.983
traumatic brain injury history	82.03	1328.087	.849	.983
history of stroke	82.86	1382.420	.731	.983
TIA's symptoms < 10 min	82.51	1377.198	.556	.983
TIA's symptoms lasted 10-59 min	82.77	1382.476	.664	.983
TIA's symptoms >60 min	82.83	1387.205	.661	.983
2nd TIA in less than 7 days	82.86	1389.008	.634	.983
dyslipidemia	82.63	1367.593	.736	.983
metabolic syndrome	82.71	1378.151	.747	.983
Cancer	82.46	1351.020	.812	.983
active COVID-19 infection. Day 0 to 8	82.34	1346.467	.841	.983
active COVID-19 infection that has lasted more than 8 days	82.60	1364.071	.758	.983
history of prior COVID-19 infection	82.31	1350.104	.771	.983
decrease SpO2 less than 90%	82.31	1337.692	.847	.983
ipsilateral >50% stenosis of the internal carotid artery and/or	82.74	1375.961	.817	.983

cerebral major artery				
carotid stenosis	82.80	1382.106	.692	.983
white blood cells>10.4 K/uL	81.97	1319.558	.912	.983
lymphocytes < 1.00 K/uL	82.00	1321.824	.894	.983
hemoglobin < 11.5 g/dL	82.00	1321.765	.895	.983
aPTT >36.3 seconds	82.14	1321.185	.927	.983
INR >1.20	82.17	1329.264	.882	.983
D-dimer >920 ng/ml	82.57	1356.664	.847	.983
D-dimer >920 ng/ml	82.49	1354.375	.851	.983
C-reactive protein >10.0 mg/L	82.37	1345.652	.874	.983
ferritin >1200 ng/mL	82.43	1344.193	.859	.983
LDH >484 U/L	82.20	1327.165	.900	.983
ALT >90.0 U/L	82.14	1329.361	.908	.983
Creatinine >1.30 mg/dL	82.03	1322.676	.926	.983
Proteinuria	82.23	1332.593	.930	.983
eGFR < 45 or end-stage renal disease	82.17	1325.087	.951	.982

Scale Statistics

Mean	Variance	Std. Deviation	N of Items
84.06	1408.350	37.528	52