Examining the Base Rates of Atrial Fibrillation in Eastern North Carolina: Community Screening, Associated Risk Factors, and Psychological Correlates of Disease

by

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Background: Eastern North Carolina has historically high prevalence rates of cardiovascular disease. Novel solutions such as mobile screening technology may aid in reaching this region's vulnerable health population to prevent further disease progression. Additionally, symptoms of psychological distress are commonly comorbid with cardiovascular disease but often overlooked as formal predictors or modifiers of increased disease burden. Behavioral medicine providers recognize the importance of screening for psychological stress as it relates to cardiovascular disease as a way to reduce disease burden and advancement. Therefore, mobile-ECG screening for atrial fibrillation and exploration of adding psychological variables to a well-established cardiovascular stroke risk calculator (CHA_2DS_2-VASc) are discussed.

Methods: Participants (N = 250) were approached at pharmacies in Eastern North Carolina. Participants completed demographic and medical history questionnaires, the DASS-21, and were administered a single-lead mobile-ECG (mECG). All mECG readings were interpreted by the mECG device in addition to adjudication by three electrophysiologists. Medical referrals were

provided when indicated. Chi-squared statistics were utilized to investigate regional rates of atrial fibrillation and associated risk factors. Binary logistic regression modeling measured the capability of the CHA_2DS_2-VASc stroke risk calculator to predict abnormal mECG readings both with and without the addition of DASS-21 symptom scores.

Results: Rates of previously undiagnosed atrial fibrillation were much higher than rates found in studies of similar scope and design. Participants' average CHA_2DS_2-VASc scores (2.68 ± 1.35) signify an alarming rate of untreated ischemic stroke risk in a community sample. Additionally, the prevalence rates of six, known independent stroke risk factors were also significantly higher in the study sample than reported national US averages. Significant point-biserial correlations were not found between psychological endpoints and abnormal mECG readings or elevated CHA_2DS_2-VASc scores, but binary logistic regression modeling revealed that a longstanding stroke risk calculator could be potentially strengthened with the addition of one (anxiety) or three (depression, anxiety, and stress) psychological endpoints.

Discussion: The results of the current study further the knowledge of the utility of using mobile-health techniques to capture previously undiagnosed atrial fibrillation and associated risk factors. Prevalence of chronic disease and other health metrics in the Eastern North Carolina region are substantially worse than the general US population. Additionally, the results presented begin a compelling argument for the addition of psychological symptom scores to a long-standing stroke risk calculator.

EXAMINING THE BASE RATES OF ATRIAL FIBRILLATION IN EASTERN NORTH CAROLINA: COMMUNITY SCREENING, ASSOCIATED RISK FACTORS, AND PSYCHOLOGICAL CORRELATES OF DISEASE

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TABLE OF CONTENTS

List of Tables……. *vi*

CHAPTER 1: INTRODUCTION……1

Background……1

Study Purpose…… 2

CHAPTER 2: REVIEW OF LITERATURE……3

Cardiovascular Disease (CVD)…… 3

Atrial Fibrillation (AFib)……... 4

Risk factors…… 5

Stroke risk stratification……6

Screening with mECG……... 7

Community screening……... 8

Psychological Correlates of AFib…… 9

Summary, Aims, & Hypotheses……13

Aim 1…… 13

Aim 2…… 13

Aim 3…… 13

CHAPTER 3: METHOD……. 15

Participants……15

Measures…… 15

Medical and personal history variables……. 15

AFib eligibility screening……. 16

CHA_2DS_2-VASc…… 16

DASS-21…… 16

Study Design……. 17

Procedure……... 17

Data analysis……. 17

Significance of Study……22

Acknowledgements……23

CHAPTER 4: RESULTS.....20

Descriptive Analyses.....20

Aim 1.....21

Aim 2.....23

Aim 3.....25

CHAPTER 5: DISCUSSION.....28

Summary of Findings.....28

HRS Summary Report.....29

Considerations for Community Screening.....30

Clinical Implications.....32

Psychological Determinants of Health.....33

Limitations.....34

Conclusion & Future Directions.....35

Acknowledgements.....36

References…….……37

Appendix A: IRB Approval……...46

Appendix B: Measures……...47

List of Tables

Table 1. CHA_2DS_2-VASc Stroke Risk Calculator……...….....….....7

Table 2. Demographic Information…….....…….....…….....20

Table 3. Prevalence of AFib Risk Factors in ENC Compared to US National Samples.....22

Table 4. mECG Results from KardiaMobile and Electrophysiologist (EP) Review.....23

Table 5. Correlations Between Stroke Risk, Abnormal mECG, and Psychological Variables.....24

Table 6. CHA_2DS_2-VASc Original Model: Binary Logistic Regression.....25

Table 7. CHA_2DS_2-VASc Model + DAS Variables: Binary Logistic Regression.....26

Table 8. CHA_2DS_2-VASc Model + ANX: Binary Logistic Regression.....27

CHAPTER 1: INTRODUCTION

Atrial fibrillation (AFib) is a chronic cardiac condition of abnormal heart rhythm affecting more than 45 million patients worldwide, and more than 6 million adults in the United States (US) (Du, Dong, Ma, 2017). AFib is caused by irregular beats by the two upper chambers of the heart (the atria), during a period of problematic synchronicity with the two lower chambers of the heart (the ventricles). This type of arrhythmia can cause blood pooling susceptible to clot formation which can lead to cerebrovascular stroke. While AFib may have short-term symptoms, including shortness of breath and palpitations, its status as a primary risk factor for stroke is the greater public health concern (Morillo, Banerjee, Perel, Wood, Jouven, 2017). AFib is often under-diagnosed, as the symptoms may be inconsistent or misattributed to other comorbid disease states (January, Wann, Alpert, Calkins, Cigarroa, Conti et al., 2014). The feasibility and effectiveness of community-based screening for AFib is a new avenue with both population-wide and individual-level implications to further identify and address this burgeoning health problem.

Background: Eastern North Carolina (ENC) has been identified as a potential "hot spot" for increased rates of AFib due to high prevalence rates of associated risk factors (Tchwenko, 2012). It has been theorized that previously undiagnosed AFib rates may be significantly higher in this region, as compared to the national average, because of the elevated rates of comorbid disease states such as hypertension, obesity, and diabetes (Bennett, Coleman, Hayden, Holmes, Nelson, Puckett et al., 2012). The utilization of rapid, non-invasive mobile-electrocardiogram (mECG) technology may allow for more efficient AFib screenings for at-risk individuals who with no prior AFib diagnosis. Because of the dynamic disease continuum of AFib, it is imperative to investigate the psychological symptoms that AFib patients may experience. Understanding the role of psychological symptoms related to AFib and stroke risk may aid

patients and healthcare providers during shared decision-making processes and may increase patient engagement and decrease overall cardiovascular burden.

Study Purpose: Novel mECG technology has the ability to provide near-instant cardio-feedback to individuals at risk for AFib. AliveCor, Incorporated (AliveCor, 2018) has developed an FDA-cleared device that records a single-channel mECG rhythm with contact of an individual's fingertips. The mECG recordings are stored on the user's mobile device, as well as on AliveCor's encrypted servers, and can be printed or emailed to a health provider at any time. The mECG can currently report one of three heart rhythm statuses: (A) Normal, (B) Possible AFib, and (C) Indeterminable.

The purpose of the current study was to utilize mECG technology to detect previously undiagnosed AFib in individuals with two or more self-reported risk factors. Participants presenting to point-of-care pharmacies in rural, ENC were approached for study participation. A brief screening measure was used to determine participant eligibility, and collected data including demographics and self-reported AFib risk factors. mECG screenings were then administered to participants with two or more AFib risk factors. Negative AFib readings resulted in the patient receiving brief, verbal education on AFib and stroke, as well as a supplemental brochure. Positive AFib readings resulted in the patient receiving both educational support and a referral to a board-certified cardiologist and/or primary care provider of the participant's preference. In addition to the AFib screening measure, the Depression Anxiety and Stress Scales – Short Form (DASS-21; Henry & Crawford, 2005) was administered to gather self-reported psychological symptom scores. This research was reviewed and approved by the ECU Institutional Review Board.

CHAPTER 2: REVIEW OF LITERATURE

Cardiovascular Disease

Cardiovascular disease (CVD) comprises a wide range of heart and vessel disorders. The most common forms of CVD include hypertension, coronary artery disease, CVA, congestive heart failure (CHF), and AFib (American Heart Association, 2017). These conditions are often related and may be comorbid, resulting in significantly increased negative health outcomes (Benjamin, Blaha, Chiuve, Cushman, Das, Deo et al., 2017). Improved medical knowledge and rapidly advancing health technology has led to decreased mortality rates in developed nations; however, aging populations and high prevalence of risk factors continue to cause the global burden of CVD to be significant (Okwuosa, Lewsey, Adesiyun, Blumenthal, & Yancy, 2016; Roth, Forouzanfar, Moran, Barber, Nguyen, Feigin et al., 2015). CVD remains the leading cause of death worldwide, causing almost one third of total deaths (Okwuosa et al., 2016). In the US, CVD is the leading cause of death for both men and women, and accounts for more deaths than cancer and lower respiratory diseases combined (Benjamin et al., 2017). In 2015, more than 40% of the US population had at least one form of CVD (American Heart Association, 2017). This figure is projected to rise to approximately 45% of the U.S. population by 2035 (Benjamin et al., 2017).

CVD has been linked to a number of risk factors, preventable and non-preventable. These include age, gender, family history, obesity, poor diet, lack of exercise, diabetes, high cholesterol, and tobacco use (Benjamin et al., 2017). In the US, climbing rates of obesity and increasingly sedentary lifestyles have contributed to poor cardiovascular outcomes (Bennett, Coleman, Hayden, Holmes, Nelson, Puckett et al., 2012). Overall CVD rates in the US are decreasing, but its associated conditions remain a major burden on public health (Chen & Rizzo,

2012). Interestingly, there seems to be increasing geographical disparity regarding rates of CVD in American populations. While CVD mortality rates have steadily declined in the New England and Mid-Atlantic regions, the South has retained high mortality rates (Singh, Azuine, Siahpush, Williams, 2015). This is likely due to an increased concentration of those with one or more risk factors for CVD (Singh et al., 2015). Lastly, AFib and associated healthcare costs represent a significant financial burden in the US. When health expenditures and lost productivity are accounted for, cardiovascular disease and stroke cost the US more than $300 billion per annum (Benjamin et al., 2017).

Atrial Fibrillation

AFib is the most common cardiac arrhythmia worldwide affecting up to six million Americans, and this number is projected to double within the next 25 years (Du et al., 2017). AFib can occur in brief, paroxysmal episodes or more regular intervals, and is a disease state typically classified according to the duration of the episode (January et al., 2014). Symptoms of AFib can be overt or covert and include irregular heartbeat, palpitations, dizziness, fatigue, shortness of breath, and chest pain (January et al., 2014). The most troublesome statistic repeatedly conveyed in the literature is that AFib may increase a person's risk of ischemic stroke by five times (American Heart Association, 2017). Additionally, developing the condition may triple your risk of heart failure (Stewart, Hart, Hole, & McMurray, 2002) and double your risk of major neurocognitive disorder (Ott et al., 1997). For these reasons, the reduction of AFib prevalence and its associated risk factors continues to be an important public health objective.

Early identification of AFib is becoming a priority issue in medicine because the accompanying poor outcomes are thought to be highly preventable when appropriate medical treatment is provided (Lowres et al., 2013). At least one fifth of all strokes can be directly attributed

to AFib (Hannon et al., 2009), but AFib is asymptomatic in approximately 61% of patients (Barnett et al., 2016). A systematic review found that single timepoint screening is capable of identifying an overall AFib prevalence of 2.3%, and 4.4% in those individuals over the age of 65 (Lowres et al., 2013). Most importantly, they found a 1% incidence of previously undiagnosed AFib, a figure that increased to 1.4% in individuals 65 years of age and older (Lowres et al., 2013). Due to the heightened risk of stroke, myocardial infarction, and all-cause mortality that is known to be highest within months of initial diagnosis (Miyasaka et al., 2006), early diagnosis of AFib is paramount in medical settings (Atar et al., 2012). Therefore, medical technologies that permit and encourage more frequent screening for AFib may be extremely valuable.

Risk factors for AFib. As hypertension, diabetes, and cardiovascular disease rates have risen in the US, the portion of the population at risk of AFib has also risen (Du et al., 2017). However, the prevalence rates of these risk factors are not evenly dispersed. Certain regions of the US show higher rates of comorbid risk factors, and there is overlap with the US "stroke belt" which cover 11 states in the southern US, including North Carolina (Tchwenko, 2012). Of all annual NC deaths in persons aged 65 and older, more than one-fourth of those individuals die as a result of CVD and cerebrovascular disease, with stroke being the fourth leading cause of death in the state (Purcell et al., 2012; Tchwenko, 2012). The eastern most counties of NC have had some of the highest stroke mortality rates in the US for more than 35 years (North Carolina Institute of Medicine, 2014). There are currently nine potentially modifiable risk factors that account for more than 90% of the risk of heart attacks and stroke in ENC, including the following: hypertension, abnormal lipids, current smoking, obesity, unhealthy diet, physical inactivity, type II diabetes, alcohol intake, and various psychological factors (Kulshreshtha, Vaccarino, Judd, Howard, McClellan, Muntner et al., 2013). Early identification and expedient

treatment of risk factors has been identified as a potential cornerstone to reduce the state's cardiovascular disease burden.

Stroke risk stratification. Stroke represents the most injurious outcome that can be caused by AFib and one out of every twenty deaths in the US can be attributed to stroke (Ziegler, Glotzer, Daoud, Singer, Ezekowitz, Hoyt et al., 2012). Not only is AFib associated with a five times increased risk of stroke, but it is also associated with more severe and disabling stroke outcomes (American Heart Association, 2017). An individual's stroke risk is calculated from summative scores comprised of heterogeneous risk factors; each assigned a point value. In the past, there have been various stratification systems used to classify stroke risk (Lip, 2013). These systems have traditionally been based on a combination of expert opinion, clinical research trials, and the evolution of known risk factors. The current gold-standard of stroke risk stratification is the CHA_2DS_2-VASc score (Table 1), which was preceded by the CHA_2DS_2 calculator.

The CHA_2DS_2 score, originally termed the Birmingham schema algorithm, was developed from a multicenter research trial (SPAF-1, 1991). At that time, use of the calculation tool was widely encouraged to medical practitioners around the world. Subsequent validation studies and the development of new research on independent stroke risk factors paved the way for an enhanced version of this tool, the CHA_2DS_2-VASc calculator (Lip, Nieuwlaat, Pisters, Lane, Crijns, 2010). The new version of the stroke risk calculator has been found to be more robust than the original version and takes into account more recently discovered risk factors such as female sex, advanced age, and vascular disease (Olesen, Lip, Hansen, Hansen, Tolstrup, Lindhardsen, 2011). Scores range from 0 to 9 with a higher score denoting increased stroke risk. The criteria contain two major risk factors worth 2 points each – the history of previous stroke/TIA and age 75-years or greater. Not only is this new tool able to accurately predict high-

risk stroke patients, it is also able to more precisely discriminate low-risk patients disallowing incorrect or unnecessary medical treatment (Olesen & Torp-Pedersen, 2015). Accurate forecasting of an individual's stroke risk continues to be imperative to guide treatment. As detection methods for AFib become more sophisticated, stroke risk calculators will most likely continue to evolve as well. Current research is now focusing on the addition of possible biomarkers and other psychological risk factors that could strengthen the predictive capability of the CHA_2DS_2-VASc score (Jabati, Fareed, Liles, Otto, Hoppensteadt, Bontekoe et al., 2018).

Table 1. *CHA_2DS_2-VASc Stroke Risk Calculator*

CHA_2DS_2-VASc	**Score**
Congestive heart failure	1
Hypertension	1
Age ≥ 75	2
Diabetes	1
Previous stroke or TIA	2
Vascular disease	1
Age 65 – 74	1
Female sex	1
TOTAL	**0 – 9**

Screening with mECG. Traditional screening methods for AFib often require professional setup and operation such as a 12-lead electrocardiogram (ECG), or potentially burdensome wearable technologies and event recorders. The cost of these traditional methods of screening impose barriers to assessment and treatment for low SES individuals. Clinic-based screening before and after procedures is an important step in assessing the success of the procedure to guide management decisions for healthcare providers and patients (Calkins, Kuck, Cappato, Brugada, Camm, Chen et al., 2012). The early recurrence of AFib is common within the first three months of an ablation procedure and may predict high-risk patients who might require a second procedure or the addition of an antiarrhythmic drug therapy schedule (Calkins et

al., 2012). Recently, several medical technology companies have developed relatively low cost and convenient ECG technology options leveraging patient smartphone and internet access.

One of the major barriers to regular ECG screening is the time and inconvenience that is associated with getting a 12-lead reading (Orchard, Freedman, Lowres, Peiris, Neubeck, 2014). AliveCor, Incorporated has recently developed an innovative way to procure a 1-lead ECG using only a mobile device and a user's fingertips (AliveCor, 2018). This device is a single lead, wireless ECG technology that connects to a free application on a user's smartphone or tablet. Using the app and Bluetooth connectivity, users can take a 30-second reading of their heart rate, with immediate feedback on whether they may be experiencing an AFib episode. Users then have the option to forward their reading to cardiac care specialists. Participants in a pilot study in the ENC region reported high levels of technology satisfaction with the AliveCor device and reliably used the device as prescribed (Kropp, Ellis, Nekkanti, Sears, 2018). The associated AliveCor app can be found on all major mobile phone platforms.

Community screening. A notable benefit of these new mECG technologies is their ease of application in non-traditional health settings. These devices allow for quick, accessible AFib screenings in locations that are highly utilized by at-risk individuals. Comparisons between mECG recordings and traditional trans-telephonic monitor recordings have revealed excellent agreement between the two methods (Tarakji, Wazni, Callahan, Kanj, Hakim, Wolski, 2015). mECG devices have demonstrated up to 100% sensitivity and 97% specificity rates for the detection of AFib and atrial flutter (Tarakji et al., 2015).

Point-of-care locations such as pharmacies, primary care offices, and nursing homes have been identified as locations with high volumes of potentially at-risk patients that could benefit from screening. Screening research at pharmacies in the SEARCH-AF project by Lowres and

colleagues (2016) identified undiagnosed AFib rates of 1.5% in a population of 1,000 individuals. Nurses utilizing mECG technology at a flu walk-in clinic uncovered an overall prevalence rate of 3.8% in a population of 973 individuals, and the screenings were rated as efficacious and timely by staff (Orchard, Lowres, Freedman, Ladak, Lee, Zwar et al., 2016). Other community-focused studies have compared mECG readings to traditional 12-lead ECGs and found high sensitivity (98%), specificity (97%), and overall accuracy (97%) of mECG devices (Galloway, Albert, Freedman, 2013). Non-governmental organizations, triage centers, and various outpatient locations have benefitted from the easy usability of mECG devices to complete screenings for individuals who otherwise would not have access. The further sophistication of these screening technologies will continue to make mECG tools ideal for community screening and the regular monitoring of ECG patients.

Psychological Correlates of AFib

AFib is psychologically burdensome primarily because the symptoms can be 'silent' and/or unpredictable, while posing long-term, and possibly deadly, health risks including thromboembolic stroke. AFib can be particularly problematic in the post-operative period because of its association with increased mortality (Jung, Meyerfeldt, Birkmeyer, 2006), higher rate of stroke (Mariscalco, Lorusso, Klersy, Ferrarese, Tozzi, Vanoli et al., 2007), and longer hospital stays (Aranki, Shaw, Adams, Rizzo, Couper et al., 1996). The relationship between anxiety/depression and AFib is complex and decreasing AFib symptom severity does not always reduce psychological distress (Thompson, Barksdale, Sears, Mounsey, Pursell, Gehi, 2014). Rather, anxiety and depression are primarily conceptualized as exacerbating factors to common AFib symptoms (Thompson et al, 2014). These findings further increase the interest of identifying areas of interventions related to the psychological AFib correlates.

Psychological distress is frequently present in AFib patients (Wändell, Carlsson, Gasevic, Wahlström, Sundquist, 2016), and symptoms of depression and anxiety are associated with heightened symptom severity in AFib (Gehi, Sears, Goli, Walker, Chung, Schwartz, Mounsey, 2012; Thompson et al., 2014; von Eisenhart-Rothe, Hutt, Baumert, Breithardt, Goette, Kirchhof et al., 2015). Multiple AFib risk factors (female sex, younger age, new-onset AFib) have been found to be independent predictors of overall lower QoL (Steinberg, Holmes, Ezekowitz, Fonarow, Kowey, Mahaffey et al., 2013). Symptoms of anxiety and depression have routinely been found to be associated with increased AFib symptom severity, and resistant to improvement, even when overall disease burden is lessened with antiarrhythmic drug therapy and catheter ablation (Thompson et al., 2014). Symptoms of depression and reported physical inactivity are closely correlated with worsened AFib outcomes (Garimella, Sears, Gehi, 2016).

Depression can be a significant mediator for poor health-related QoL outcomes in patients with coronary artery disease (Akintade, Chapa, Friedmann, Thomas, 2015), myocardial infarctions (Frasure-Smith, Lespérance, Habra, Talajic, Khairy, Dorian et al., 2009), and AFib (Ong, Irvine, Nolan, Cribbie, Harris, Newman et al., 2006). Symptoms of depression in CVD patients are known to worsen AFib-related symptoms, and men with AFib have been observed to be at 30% greater mortality risk when concomitant symptoms of depression are present (Akintade et al., 2015; Wändell et al., 2016). Patients with AFib are significantly more likely to be depressed (Dąbrowski, Smolis-Bąk, Kowalik, Kazimierska, Wójcicka, Szwed, 2010), and depression heightens recurrent risk in some AFib patients (Lange & Herrmann-Lingen, 2007). Many patients with AFib disengage in their daily activities and can develop maladaptive cognitions about their AFib symptoms – further contributing to a low mood state (Ong et al., 2006). Depressive symptoms manifested by AFib can be maintained by the persistent and

excessive anxiety that often afflicts AFib patients. This persistent worry can lead to autonomic arousal, general restlessness, and even insomnia putting patients at further risk for developing depressive symptoms (Lane, Langman, Lip, Nouwen, 2009).

Anxiety symptoms occur in approximately 38% of all patients with AFib (Thrall, Lip, Carroll, Lane, 2007), and have been established as an independent risk factor of adverse cardiac events (Frasure-Smith & Lespérance, 2008). Symptoms of anxiety are often the principal affective response to an AFib diagnosis, and Lane and colleagues discovered prevalence rates of 39%, 31%, and 36% occurring at baseline, 3-month, and 6-month time points in this population (Lane et al., 2009). These findings mirror prevalence rates of anxiety commonly found in ICD patients, a patient group with known psychological difficulties (Sears & Conti, 2002). Symptoms of anxiety are endorsed by more than half of patients with paroxysmal AFib at the time of the arrhythmia "attack" (Hansson, Madsen-Härdig, Olsson, 2004). One explanation of the relationship between AFib and anxiety is dysregulation of the autonomic nervous system, subsequently having effects on both the reduction of parasympathetic activity and increase in sympathetic activity (Carney, Freedland, Veith, 2005). Given the overlap of symptoms between AFib and anxiety (e.g. shortness of breath, palpitations), it is understandable that autonomic arousal symptoms have been shown to be associated with AFib (Thomas, Chapa, Friedmann, Durden, Ross, Lee et al., 2008).

Stress, in general, is associated with cortisol imbalances and hypertension both of which can be damaging to heart function (Graff, Prior, Fenger-Grøn, Christenson, Glümer, Larson et al., 2017). Some research has shown acute, episodic stress to be associated with CVD, particularly in myocardial infarction and sudden cardiac death (Li, Hansen, Mortensen, Olsen, 2002; Carey, Shah, DeWilde, Harris, Victor, Cook, 2014; Steptoe & Kivimäki, 2012). The

relationship between general stress and AFib is lesser known, but several theories posit plausible explanations as to why stress could lead to AFib episodes. These theories include parasympathetic modulation, excessive sympathetic activity, and pro-inflammatory cytokines as possible physiologic mechanisms of stress related AFib symptoms (Graff et al., 2017). Cognitive appraisals of physical symptomology also have some effect on AFib-related symptoms, and psychological stress is the most commonly endorsed "trigger" for idiopathic arrhythmias (Li et al., 2002).

Negative emotions, such as anxiety and sadness, have been shown to precipitate ventricular arrhythmias and myocardial infarctions in limited sample studies (Lampert, Joska, Burg, Batsford, McPherson, Jain, 2002), and there is growing interest on negative emotions having the ability to trigger an AFib episode. Research findings include a significant unadjusted increase in the likelihood of an AFib episode when accompanied with the endorsement of sadness, anxiety, anger, or stress (Lampert et al., 2014). Furthermore, the endorsement of stress on an end-of-day summary report almost doubled the likelihood of an AFib episode the following day and an overall dose-response was observed for reported stress and AFib episodes (Lampert et al., 2014). In summary, a growing body of research is beginning to capture the possible role of psychological distress as an antecedent to AFib episodes.

AFib is a condition amenable to psychological intervention due to its number of modifiable risk factors. Symptoms of depression, anxiety, and stress may be contributory to the AFib disease state and/or exacerbating factors. Further research is needed in this area to determine which psychological symptoms, if any, are most inflammatory to the AFib disease process to discover what lifestyle changes can be made to lessen overall illness burden.

Summary, Aims, & Hypotheses

The primary aim of the current study was to examine the base rates of known risk factors associated with AFib, to determine the average CHA_2DS_2-VASc stroke risk scores, and to uncover the rates of previously undiagnosed AFib in an ENC community sample (N = 250). The secondary aim of the project was to evaluate the relationships between self-reported psychological symptoms and correlates of AFib and its risk factors (N = 157). The third and final aim was to evaluate predictors of abnormal mECG readings (N = 157).

Aim 1: To report on the prevalence of risk factors associated with AFib, calculated CHA_2DS_2-VASc stroke risk scores, and previously undiagnosed AFib incidence in a community sample of 250 participants. ***Hypothesis 1a***: The prevalence rates reported in the community sample of at least three, grant specified AFib risk factors will be greater than reported national averages. ***Hypothesis 1b:*** The rates of previously undiagnosed AFib discovered using the mECG device will be greater than 2%. ***Hypothesis 1c:*** The average CHA_2DS_2-VASc score in the study sample will be greater than 2.

Aim 2: To examine which psychological endpoints, if any, are significantly correlated with abnormal mECG readings and/or elevated CHA_2DS_2-VASc scores ($\geq$ 2). ***Hypothesis 2a***: At least one psychological endpoint will be significantly correlated with abnormal mECG readings. ***Hypothesis 2b***: At least one psychological endpoint will be significantly correlated with elevated CHA_2DS_2-VASc scores ($\geq$ 2).

Aim 3: To evaluate the predictive capabilities of the CHA_2DS_2-VASc component parts and their relationship(s) with abnormal mECG readings. mECG readings will be dichotomized into 'Normal' or 'Abnormal' categories. Abnormal mECG readings will include both 'Possible AFib' or 'Indeterminable' readings. ***Hypothesis 3a***: Each of the components of the CHA_2DS_2-

VASc model will predict abnormal mECG readings independently and significantly. ***Hypothesis 3b***: The strongest psychological endpoint, when added to the pre-existing CHA_2DS_2-VASc component parts, will strengthen its predictive capability of abnormal mECG readings.

CHAPTER 3: METHOD

Participants

Residents of ENC presenting to one of two point-of-care pharmacy locations were approached for study participation. Individuals who denied any previous diagnosis of AFib or atrial flutter and also endorsed two or more AFib risk factors were offered a free mECG screening. Consenting participants were also given educational materials on AFib, medical referrals when indicated, and were asked to complete brief psychological questionnaires. Other eligibility requirements included being 18-years of age or older, self-reported reading ability at fifth grade or greater, and being able to fluently speak and understand English.

Measures

An IRB-approved waiver of consent was approved to administer a screening questionnaire comprised of demographics and self-reported AFib risk factors prior to full study participation. mECG screenings were administered to participants with two or more AFib risk factors. Negative AFib readings resulted in the patient receiving education on AFib and stroke, and all participants were given a supplemental AFib brochure. Positive AFib readings resulted in the patient receiving the aforementioned educational support, in addition to an appropriate referral to a board-certified cardiologist. Additionally, positive readings were sent confidentially to a primary care physician or cardiologist of the participant's choosing.

Medical and personal history variables. Demographic and medical variables collected include age, sex, race, marital status, and formal education. Participants were asked to consent to medical record review and were also asked to provide their date of birth, telephone number, and email address.

AFib eligibility screening. A screening questionnaire quickly determined whether or not participants were eligible for study participation. First, participants reported whether or not they had a pre-existing diagnosis of AFib or atrial flutter. If they answered 'No' to the first question, they were asked to self-report on the presence of pre-specified AFib risk factors including the following: congestive heart failure, hypertension, age, diabetes, previous stroke, peripheral vascular disease, sex, obstructive sleep apnea, and obesity. If the participant endorsed two or more risk factors, they were eligible for the mECG screening and further study participation.

CHA_2DS_2-VASc. A CHA_2DS_2-VASc score is a commonly-used stroke risk calculator that uses a 0 – 9 scoring method, with higher scores denoting higher stroke risk. Points are assigned to certain characteristics as shown in Table 1. Based on participants self-reported symptoms and diagnoses, each participant was assigned an overall stroke risk score.

DASS-21. The Depression Anxiety and Stress Scales – Short Form (DASS-21) is an empirically validated measure of the emotional states of depression, anxiety and stress with excellent reliability and validity (Lovibond & Lovibond, 1995). The depression subscale assesses for symptoms of dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest, and anhedonia. The anxiety subscale assesses for symptoms of autonomic arousal, skeletal-muscle effects, situational anxiety, and the subjective experience of being anxious. Lastly, the stress subscale assesses symptoms of difficulty relaxing, nervous arousal, agitation/irritability, and over-reactivity/impatience. Cronbach's alphas for the subscales in clinical samples has been found to be .94 (depression), .87 (anxiety), and .91 (stress) (Antony et al., 1998). Both the full version of the DASS and the DASS-21 have been found to have good convergent and discriminant validity when compared to other widely used and validated measures of depression and anxiety (Henry et al., 2005). Each consenting participant was

offered the opportunity to complete the DASS-21 in addition to their mECG reading. A total of 157/250 participants completed both the mECG recording and the DASS-2.

Study Design

Procedure. Following eligibility screening and informed consent, participants were administered a 1-lead mECG reading with an AliveCor KardiaMobile device. Then, participants were asked to complete questionnaires on demographic and medical history data, symptoms of psychological distress, and were given educational materials on AFib. Medical referrals were provided at the conclusion of their participation when indicated. All mECG readings were assigned an initial report of 'Normal,' 'Possible AFib,' or 'Indeterminable' by the KardiaMobile device to acquire an initial AFib prevalence rate. After study conclusion, three board-certified cardiologists independently reviewed each mECG reading for official adjudication and accuracy of an AFib study prevalence rate.

Data analysis. Descriptive statistics are reported for age, sex, race, marital status, level of education, and average household income. *Aim 1*. The chief aim of the proposed study was to report on the prevalence of risk factors associated with AFib, calculated stroke risk scores, and rates of previously diagnosed AFib in an ENC sample. It was hypothesized that the prevalence of at least three AFib risk factors in a community sample would be greater than reported national averages. National averages reported in the American Heart Association's 2018 Heart Disease and Stroke Statistics Update (Benjamin, Virani, Callaway, Chamberlain, Chang, Cheng et al., 2018) were used for comparison. Chi-squared cross-tabulation methods were used to measure differences of weighted proportions to compare percentages of prevalence in both groups. Power analyses for a chi-square test with a total sample size of 250 and a medium effect size ($w = 0.3$) yielded 99% power. It was hypothesized that rates of previously undiagnosed AFib in the study

sample would be greater than 2%; and the average CHA_2DS_2-VASc score would be greater than 2 as measured by a one-sample t-test. Means, standard deviations, relative risk ratios, and 95% confidence intervals are reported.

Aim 2. The second aim of the proposed study was to examine which psychological endpoints, if any, were correlated with abnormal mECG readings and elevated CHA_2DS_2-VASc scores (≥ 2). mECG readings were dichotomized into 'Normal' or 'Abnormal' categories with the latter group containing both 'Possible AFib' and 'Indeterminable' readings. It was hypothesized that at least one psychological endpoint (depression, anxiety, or stress) would be correlated with abnormal mECG readings. It was also hypothesized that at least one of the aforementioned psychological endpoints would be correlated with elevated CHA_2DS_2-VASc scores (≥ 2). A Pearson *r* correlation matrix was utilized to reveal relationships between CHA_2DS_2-VASc component parts, abnormal mECG readings, and psychological variables. Power analysis for a two-tailed point-biserial correlation given $a = 0.05$, medium effect size ($d = 0.3$), and sample of 157 participants yielded 97% power.

Aim 3. The third and final aim of the study was to evaluate the predictive capabilities of the CHA_2DS_2-VASc component parts and their relationship(s) with abnormal mECG readings. It was hypothesized that each of the components of the CHA_2DS_2-VASc model would be a significant and independent predictor of abnormal mECG readings. It was also hypothesized that the strongest psychological end-point score, when added to the pre-existing CHA_2DS_2-VASc component parts, would strengthen its overall predictive capability of abnormal mECG readings. Binary logistic regression modeling was utilized to investigate the original CHA_2DS_2-VASc components as predictors of abnormal mECG readings, as well as to discern the most salient psychological endpoint when added to the model. The strongest psychological endpoint,

evidenced by beta weight and significance, was then added to the original CHA_2DS_2-VASc component equation to measure for statistically significant changes in the chi-squared statistic and -2 Log likelihood.

CHAPTER 4: RESULTS

Descriptive Analyses

The current study sample included a total of 250 participants. The mean participant age was 61.69 $\pm$ 15.31 with a range of 22 – 91. The majority of participants were female (60%), Caucasian (83%), and married (64%). Most participants reported completing 12 years of formal education and earning an annual household income averaging $50,000 - $59,999. Demographic data is shown in Table 2.

Table 2. *Demographic Information*

Characteristic	Percentage
Gender	---
Female	60%
Male	40%
Race/Ethnicity	---
African American	12%
Caucasian	83%
Hispanic	3%
Native American	1%
Other	1%
Marital Status	---
Married	64%
Single	14%
Divorced	12%
Widowed	10%
Household Income	
$0 – 9,999	4%
$10k – 19,999	7%
$20k – 29,999	7%
$30k – 39,999	10%
$40k – 49,999	9%
$50k – 59,999	13%
$75k – 99,999	9%
$100k – 149,999	10%
$150k and above	4%
Prefer not to disclose	27%

Aim 1 - Prevalence of Risk Factors, Stroke Risk, and Rates of AFib

The primary aim of this research was to report on the prevalence of risk factors associated with AFib, calculated stroke risk scores, and rates of previously diagnosed AFib in an ENC sample. It was hypothesized that the prevalence rates of at least three risk factors with AFib in a community sample would be greater than reported national averages found in the American Heart Association's 2018 Heart Disease and Stroke Statistics Update (Benjamin et al., 2018). It was also hypothesized that prevalence rates of previously undiagnosed AFib would be greater than 2% and the average CHA_2DS_2-VASc score would be greater than 2.

Chi-squared analyses of AFib risk factor prevalence rates. Prevalence rates were analyzed with chi-squared cross-tabulation methods that controlled for differences in proportions with weighted sample sizes. Hypothesis 1a predicted that prevalence rates of at least three major risk factors of stroke risk would be significantly greater in the current sample as compared to US national averages. This hypothesis was confirmed as 6 of 7 risk factor scores in the community sample were significantly greater than national prevalence rates. Prevalence rates, relative risk ratios, and chi-squared values can be found in Table 3.

Participants in the current study had significantly higher rates of hypertension (75% of 250) than the average US adult (35% of 252M), $\chi^2(1, N = 252{,}059{,}074) = 187.11$, $p < .001$. Participants in the current study had significantly higher rates of obstructive sleep apnea (24.8% of 250) than the average US adult (2.5% of 252M), $\chi^2(1, N = 226{,}559{,}242) = 510.04$, $p < .001$. Participants in the current study had significantly higher rates of obesity (65.2% of 250) than the average US adult (36.3% of 226M), $\chi^2(1, N = 257{,}142{,}857) = 90.3$, $p < .001$. Participants in the current study had significantly higher rates of type 2 diabetes (29.6% of 250) than the average US adult (9.1% of 257M), $\chi^2(1, N = 257{,}142{,}857) = 127.01$, $p < .001$. Participants in the current

study had significantly higher rates of peripheral vascular disease (14.8% of 250) than the average US adult (2.74% of 247M), $\chi^2(1, N = 247{,}813{,}910) = 136.44$, $p < .001$. Participants in the current study had significantly higher rates of previous stroke (7.6% of 250) than the average US adult (2.7% of 266M), $\chi^2(1, N = 266{,}666{,}667) = 22.85$, $p < .001$. Lastly, there were no significant differences in the rates of congestive heart failure (3.2% of 250) in the study sample compared to the average US adult (2.5% of 260M), $\chi^2(1, N = 260{,}000{,}258) = 142.9$, p (two-sided) = 0.42.

Table 3. *Prevalence of AFib Risk Factors in ENC Compared to US National Samples*

AFib Risk Factor	Sample Prevalence	National Prevalence	Relative Risk Ratio [95% CI]	χ^2 value
Congestive Heart Failure	3.2%	2.5%	1.51 [0.26; 8.79]	142.9
Hypertension	75.2%	35%	2.14 [1.61; 2.92]	187.11**
Age ≥ 75	21.6%	---	---	---
Diabetes Mellitus	29.6%	9.1%	3.35 [1.67; 6.66]	127.01**
Previous Stroke / TIA	7.6%	2.7%	2.67 [0.73; 9.76]	22.85**
Peripheral Vascular Disease	4.8%	2.7%	1.67 [0.41; 6.79]	136.44**
Age 65 – 74	25.6%	---	---	---
Female Sex	60.8%	---	---	---
Obstructive Sleep Apnea	24.8%	2.5%	8.33 [2.60; 26.72]	510.04**
Obesity	65.2%	36%	1.81 [1.34; 2.43]	90.3**

*significant at the $p < .05$ level
**significant at the $p < .01$ level

Previously undiagnosed rates of AFib and CHA_2DS_2-VASc means. Hypothesis 1b predicted that rates of previously undiagnosed AFib in the current study would be greater than 2%, which is the average percentage found in research studies of similar scope and design examined in the literature. Hypothesis 1b was supported as the KardiaMobile device discovered a total of 10/250 (4%) mECG readings were positive for AFib, 202/250 (81%) resulted in normal sinus rhythm readings, and 38/250 (15%) were indeterminable readings. However, when the mECG readings were separately reviewed by three electrophysiologists, the rates of AFib were not definitive. Due to adjudication variance and the inability to confirm each mECG with a 12-

lead reading, a true prevalence rate of AFib in the study sample remained elusive. An overall range of possible AFib rates is reported between 1-8%. mECG percentages and differences in electrophysiologist adjudications are listed in Table 4.

Lastly, hypothesis 1c predicted that the average CHA_2DS_2-VASc score would be greater than 2, which is the standard cut-off score for the recommendation of oral anti-coagulant treatment. This hypothesis was also confirmed as the average CHA_2DS_2-VASc score in the study sample was 2.68 ± 1.35. A one-sample t-test revealed the average CHA_2DS_2-VASc score in the current sample ($M = 2.68$, $SD = 1.35$) to be much higher than expected averages, $t(249) = 7.96$, $p < .001$.

Table 4. *mECG Results from KardiaMobile and Electrophysiologist (EP) Review*

EP Adjudications	EP 1	EP 2	EP 3
Possible AFib	19/250 (8%)	4/250 (2%)	2/250 (1%)
-----	-----	-----	-----
KardiaMobile Reading			
Sinus Rhythm	202/250 (81%)		
Unclassified	38/250 (15%)		
Possible AFib	10/250 (4%)		

Aim 2 - Correlations of Stroke Risk, Abnormal mECGs, and Psychological Variables

The second aim of the current study was to investigate point-biserial correlations between CHA_2DS_2-VASc stroke risk scores, abnormal mECG readings, and three psychological variables (depression, anxiety, stress symptom scores). These correlations were completed under the assumption that increased CHA_2DS_2-VASc scores would be significantly correlated with abnormal mECG readings, which was confirmed ($r = .46$, $p < .05$) prior to additional analyses.

There were two hypotheses within this aim. Hypothesis 2a predicted that at least one psychological endpoint (depression, anxiety, or stress symptom score) would be correlated with abnormal mECG readings. Hypothesis 2b predicted that at least one psychological endpoint

would be significantly correlated with CHA_2DS_2-VASc scores greater than or equal to 2. Both of these hypotheses were rejected as no significance was found between psychological endpoints, abnormal mECGs, or CHA_2DS_2-VASc scores. Point-biserial correlations and significance levels can be found in Table 5.

Table 5. *Correlations Between Stroke Risk, Abnormal mECG, and Psychological Variables*

	Depression	**Anxiety**	**Stress**
CHA_2DS_2-VASc (>= 2)	Pearson *r* = .042 Sig. two-tailed = .601	Pearson *r* = .046 Sig. two-tailed = .565	Pearson *r* = -.090 Sig. two-tailed = .260
Abnormal mECG	Pearson *r* = -.110 Sig. two-tailed = .169	Pearson *r* = .094 Sig. two-tailed = .242	Pearson *r* = -.121 Sig. two-tailed = .130

*****Denotes Pearson *r* significance at the $p < .05$ level

Aim 3 - Predictive Capabilities of CHA_2DS_2-VASc on Abnormal mECG Readings

The third and final aim of the current study was to evaluate the predictive capabilities of the CHA_2DS_2-VASc component parts and their relationship(s) with abnormal mECG readings. mECG readings were dichotomized into 'Normal' or 'Abnormal' categories. Abnormal mECG readings were comprised of 'Possible AFib' and 'Indeterminable' readings. Hypothesis 3a predicted that each of the components of the CHA_2DS_2-VASc model would be significant and independent predictors of abnormal mECG readings. After mECG dichotomization there were 118 'Normal' mECG readings and 39 'Abnormal' mECG readings. Hypothesis 3b predicted that the strongest psychological end-point score, when added to the pre-existing CHA_2DS_2-VASc component parts, would strengthen its overall predictive capability of abnormal mECG readings. Binary logistic regression modeling was utilized to test the original CHA_2DS_2-VASc components as predictors of abnormal mECG readings, as well as to discern the most salient psychological endpoint in a model with all three psychological scores added. The strongest psychological

endpoint, evidenced by beta weight and significance, was then added to the original CHA_2DS_2-VASc component equation to measure for statistically significant changes in -2 Log likelihood.

A binary logistic regression model with only the original components of the CHA_2DS_2-VASc stroke risk calculator was completed first. As expected, the model was highly predictive of abnormal mECG readings, $\chi 2$ (7, N = 157) = 18.73, $p < .01$. However, hypothesis 3a predicted that each of the components of the CHA_2DS_2-VASc model would be significant and independent predictors of abnormal mECG readings and this hypothesis was rejected. Only the risk factors of hypertension ($p < .05$, OR = 2.809), age ($p < .05$, OR = 1.032), and sex ($p < .01$, OR = 3.298) were significant, independent risk factors associated with abnormal mECG readings. Full statistics on this model can be found in Table 6.

Table 6. *CHA_2DS_2-VASc Original Model: Binary Logistic Regression*

		Chi-square	**df**	**Sig.**	**-2 Log likelihood**
Step 1: Variables	**Step**	18.73	7	0.009**	157.29
	Block	18.73	7	0.009**	
	Model	18.73	7	0.009**	
	B	**df**	**Sig.**	**Exp(B)**	**CI (95%)**
CHF	.017	1	.987	1.017	[.129, 8.013]
HTN	1.033	1	.032*	2.809	[1.093, 7.216]
Age	.032	1	.040*	1.032	[1.001, 1.064]
DM2	.461	1	.317	1.585	[.643, 3.907]
Sex	1.193	1	.008**	3.298	[1.360, 8.000]
Vasc. Disease	-.248	1	.631	.283	[.283, 2.150]
Previous Stroke	-.283	1	.698	.180	[.180, 3.151]

*****Denotes significance at the $p < .05$ level
**Denotes significance at the $p < .01$ level
***Denotes significance at the $p < .001$ level

Then, a binary logistic regression model with both the original components of the CHA_2DS_2-VASc stroke risk calculator and symptoms scores for depression, anxiety, and stress was completed. The addition of these psychological endpoints was implemented to isolate the

most salient psychological endpoint, as well as to determine if the addition of these psychological factors improved the predictive capability of the model. The model was strengthened significantly as evidenced by an increase in the chi-squared statistic, $\chi 2$ (10, N = 157) = 37.705, $p < .001$ and reduction in -2 Log likelihood (157.29 to 138.317). In this model inclusive of all three psychological endpoints, the variables of hypertension ($p < .05$, OR = 3.428), sex ($p < .01$, OR = 4.149), and anxiety ($p < .001$, OR = 1.235) were the most significant predictors of abnormal mECG readings. Full statistics for this model can be found in Table 7.

Table 7. *CHA_2DS_2-VASc Model + DAS Variables: Binary Logistic Regression*

		Chi-square	**df**	**Sig.**	**-2 Log likelihood**
Step 1: Variables	**Step**	18.972	3	< .001***	138.317
	Block	18.972	3	< .001***	
	Model	37.705	10	< .001***	
	B	**df**	**Sig.**	**Exp(B)**	**CI (95%)**
CHF	-.289	1	.797	.749	[.083, 6.754]
HTN	1.232	1	.020*	3.428	[1.212, 9.698]
Age	.026	1	.124	1.026	[.993, 1.060]
DM2	.649	1	.197	1.915	[.714, 5.132]
Sex	1.423	1	.005**	4.149	[1.543, 11.160]
Vasc. Disease	-.090	1	.875	.914	[.296, 2.823]
Previous Stroke	-.501	1	.557	.606	[.114, 3.226]
DEPRESSION	-.098	1	.108	.906	[.804, 1.022]
ANXIETY	.211	1	.000***	1.235	[1.104, 1.382]
STRESS	-.101	1	.058	.904	[.814, 1.003]

*****Denotes significance at the $p < .05$ level
**Denotes significance at the $p < .01$ level
***Denotes significance at the $p < .001$ level

Lastly, a binary logistic regression model with both the original components of the CHA_2DS_2-VASc stroke risk calculator and an anxiety symptom score were completed. Hypothesis 3b predicted that the strongest psychological end-point score, when added to the pre-existing CHA_2DS_2-VASc component parts, would strengthen its overall predictive capability of abnormal mECG readings. This hypothesis was confirmed, however, the regression model

including the anxiety score was not as strong as the model that included all three psychological endpoints. The addition of an anxiety endpoint alone significantly improved the predictive capability of the model as evidence by an increase in the chi-squared statistic, $\chi 2$ (8, N = 157) = 22.967, $p < .01$ and reduction in -2 Log likelihood (157.29 to 153.055). In this model including an anxiety symptom score endpoint, the variables of hypertension ($p < .05$, OR = 2.809), age ($p < .05$, OR = 1.032), sex ($p < .01$, OR = 3.298), and anxiety ($p < .05$, OR = 1.060) were the most significant predictors of abnormal mECG readings. Full statistics for this model can be found in Table 8.

Table 8. *CHA_2DS_2-VASc Model + ANX: Binary Logistic Regression*

		Chi-square	**df**	**Sig.**	**-2 Log likelihood**
Step 1: Variables	**Step**	4.234	1	.040*	153.055
	Block	4.234	1	.040*	
	Model	22.967	8	.003**	
	B	**df**	**Sig.**	**Exp(B)**	**CI (95%)**
CHF	.071	1	.948	1.017	[.126, 9.116]
HTN	1.196	1	.018*	2.809	[1.231, 8.887]
Age	.037	1	.021*	1.032	[1.006, 1.071]
DM2	.459	1	.318	1.585	[.643, 3.894]
Sex	1.338	1	.004**	3.298	[1.528, 9.514]
Vasc. Disease	-.083	1	.877	.283	[.322, 2.635]
Previous Stroke	-.324	1	.664	.180	[.167, 3.124]
ANXIETY	.058	1	.034*	1.060	[1.004, 1.118]

*****Denotes significance at the $p < .05$ level
**Denotes significance at the $p < .01$ level
***Denotes significance at the $p < .001$ level

CHAPTER 5: DISCUSSION

Summary of Findings

The purposes of the current study included broad, community-wide aims and also exploratory methods of integrating psychological factors into traditional ischemic stroke risk prediction. The primary aim of the study was to examine the base rates of known risk factors associated with AFib, to determine the average CHA_2DS_2-VASc stroke risk scores, and to uncover the rates of previously undiagnosed AFib in an ENC community sample (N = 250). The secondary aims were to evaluate the relationships between self-reported psychological symptoms and correlates of AFib and its risk factors (N = 157). The third aim was to evaluate predictors of abnormal mECG readings (N = 157).

The current study produced several meaningful findings from offering single-lead mECG readings to an opportunistic sample of individuals presenting to their local pharmacies. The rates of previously undiagnosed AFib were much higher than rates found in studies of similar scope and design. Preliminary AFib rates of approximately 4% based on KardiaMobile mECG readings were blindly and independently reviewed by board-certified electrophysiologists, revealing an AFib prevalence rate ranging from 1-8% dependent upon the reviewer. This number represents a rate of previously undiagnosed AFib that is unmatched in similar literature. Not only were AFib rates higher than expected, the participants' average CHA_2DS_2-VASc scores were greater than 2 (2.68 ± 1.35) signifying an alarming rate of often untreated ischemic stroke risk in a community sample. Additionally, the prevalence rates of six, known independent stroke risk factors were also significantly higher in the study sample than reported national US averages.

Significant correlations were not found between psychological endpoints and abnormal mECG readings or elevated CHA_2DS_2-VASc scores, but binary logistic regression modeling

revealed that a longstanding stroke risk calculator could be potentially strengthened with the addition of one (anxiety) or three (depression, anxiety, and stress) psychological endpoints. These results represent novel findings with broad implications for community AFib screening. These results suggest that the addition of psychological endpoints may have a value-added effect on an established stroke risk calculator to predict ischemic stroke risk.

The CHA_2DS_2-VASc stroke risk calculator will continue to require updating based on dynamic health trends found in the US population. Further independent risk factors for stroke that will likely be added to the CHA_2DS_2-VASc calculator include obesity and obstructive sleep apnea. This research makes an inaugural argument for the addition of a psychological endpoint to be included in the CHA_2DS_2-VASc calculator. The biopsychosocial relationships between psychological symptoms and cardiovascular outcomes continue to be established, but there is ample preliminary evidence to support the further investigation of possible direct and indirect links between poor psychological health and increased ischemic stroke risk.

HRS Summary Report

The current study was part of a larger AFib screening and education initiative conducted by the Heart Rhythm Society (HRS). The initiative had two primary goals: to encourage innovative screening for AFib and to provide education to local communities about the risks associated with AFib. East Carolina University's Department of Psychology was one of eight locations chosen to conduct mECG community screenings and one of six sites to fulfill all project requirements. HRS provided an internal summary report based on the 1,383 individuals screened across all sites. Positive AFib readings taken by a KardiaMobile device were found in 2.8% of individuals meeting project criteria. Hypertension was the most common risk factor

(70.5%), followed by obesity (39.3%) and type 2 diabetes (27.7%). More information on this initiative can be found in Tables 9 and 10.

Table 9. *Site Characteristics from the HRS AFib Screening Summary Report*

Site	**Region**	**Participants**	**Indeterminable**	**Possible AFib**
University of Buffalo	Buffalo, NY	141	Not reported	9
East Carolina University	Greenville, NC	250	37	10
Edwards-Elmhurst Healthcare	Chicago, IL	262	35	10
Mayo Clinic	Rochester, MN	229	19	1
University of Massachusetts	Worcester, MA	250	23	7
Wellness Center of Eastern ID	Idaho Falls, ID	251	12	2
	Total	1383	126	39
	mECG %		9.10%	2.80%

Table 10. *Site Reported Risk Factors from the HRS AFib Screening Summary Report*

Site	**Age > 75 years**	**DM2**	**Female**	**HTN**	**Obesity**	**PVD**	**OSA**
University of Buffalo	139	39	116	117	9	66	2
East Carolina University	54	74	152	188	163	37	62
Edwards-Elmhurst Healthcare	226	37	205	166	61	42	23
Mayo Clinic	140	63	204	169	104	10	67
University of MA	80	79	98	191	108	42	5
Wellness Center of Eastern ID	17	91	178	144	98	12	86
Total	656	383	953	975	543	209	245
% of Total Screened	47.40%	27.70%	68.90%	70.50%	39.30%	15.10%	17.70%

Considerations for Community Screening

The utilization of novel screening techniques for AFib continues to be proven as a safe, convenient, cost-saving, and potentially life-saving way to prevent patients from experiencing a stroke. Practical and philosophical questions remain about how and why to use technology such as AliveCor's KardiaMobile device to detect the presence of AFib. The obvious benefits include the potential to treat stroke risk before a debilitating medical event occurs. AFib is a major

contributor to overall stroke risk and its early detection is an effective preventive strategy for mitigating overall stroke risk. The interventions of anticoagulation, ablation, and use of antiarrhythmic medications prevent stroke incidence and are usually initiated by an AFib diagnosis. The psychological impact of novel, mobile-based screening for AFib appears to be minimal. Patients and families have reported that the technology is easy to use, increases their healthcare confidence, and can give them peace of mind (Kropp et al., 2018).

There are also downsides to increased screening for AFib. In some instances, AFib screening may seem unnecessary or even burdensome to patients. These screenings can also potentially increase health-related anxiety in a small subset of patients due the desire for increased health-related hypervigilance and amplified checking behaviors. From a healthcare point of view, these additional screenings may increase the workload of medical practitioners by creating a more constant stream of medical information requiring review. A perfect balance between utilization of this technology and integration into complex medical systems is still being pursued and represents a significant challenge. However, some universal truths are beginning to emerge and are also evidenced by the results of the current study.

Devices such as KardiaMobile are most useful when used in screening initiatives targeting individuals with 1-2 known risk factors for AFib, and this technology allows for more routine screening that can better capture AFib episodes from outside a medical facility (Rosenfeld, Alpesh, Hsu, Oxner, Hills, Frankel, 2019). These benefits of using these 1-lead recordings are undoubtedly enhanced by immediate confirmation via 12-lead ECG when possible. At-home or community screening methods may also increase patient engagement in their own healthcare and give patients and their families an increased sense of control (Rosenfeld et al., 2019).

Clinical Implications

AFib is a growing health crisis that affects different regions and groups disproportionately. Known as one the leading risk factors for increased frequency and severity of ischemic stroke, AFib risk is comprised of several co-morbid risk factors that commonly exist in areas with low access to healthcare, increased levels of poverty, and decreased level of health literacy. Because of these barriers and others, this condition is often under-diagnosed, and symptoms may be inconsistent or misattributed to other disease states. Traditional means of AFib identification including 12-lead ECG often elude individuals in rural settings, making the design of the current study novel and participant-centered.

Unprecedented levels of previously undiagnosed AFib in the study sample further highlight the ENC region's unmet medical needs and increased levels of co-morbid disease states. The estimated base rates of AFib found in the current study further justify the use of novel, mECG technology to screen for AFib in at-risk populations. There is increasing evidence to suggest that more US adults have AFib than is reported. A multi-center randomized controlled trial of almost exactly the same sample size recently reported that individuals with AFib-related symptoms using mECG technology across a 90-day period were five times more likely to capture at least one episode of AFib (Reed et al., 2019). Because AFib is so strongly linked to ischemic stroke, it is imperative that this type of arrhythmia is detected and treated as early as possible. mECG technology represents a low-cost, non-invasive solution to this problem.

The results of the current study provide evidence to support the practice of opportunistic community screening for previously undiagnosed AFib in at-risk populations. Medical technology development and the burgeoning field of at-home digital health screening may continue to outpace the academic community's ability to critically evaluate these technologies

prior to their existence on the consumer market. However, a growing body of research points to mECG technology as a low-cost, non-invasive, safe strategy to reduce overall cardiovascular disease burden in the US.

There are still several questions that remain about the diagnostic implementation of these devices. At-home screening is convenient but may not be indicated for all consumers, and not all individuals will want to pay the fees commonly associated with on-demand cardiologist interpretation. This technology may be best utilized in peripheral medical settings such as pharmacies and nursing homes where screenings can be initiated by either patient or health staff. Regulations and standards of use for these devices are still in their infancy, but the potential upside of catching AFib symptoms sooner in the general population far outweigh the disadvantages and difficulties associated with questions of implementation, feasibility, and cost-effectiveness.

Psychological Determinants of Health

Many studies have now investigated the accuracy and practicality of using mECG devices. To the authors' knowledge, the current study is the first of its kind to investigate psychological improvements to the CHA_2DS_2-VASc stroke risk calculator. Our results are only preliminary but warrant further investigation of adding psychological components to the measurement of stroke risk. The symptoms associated with depression, anxiety, and stress have been demonstrated in the literature to be linked to, at the very least, the exacerbation of common cardiovascular symptoms. These psychological factors are pervasive to mental, physical, and behavioral components of individuals' health and should continue to be investigated as potential independent risk factors for poor cardiovascular outcomes.

Limitations

The current study was impacted by several limitations common to novel study designs. The first limitation is a caveat that should be taken into consideration when interpreting the positive AFib readings described in the results section. Our study recorded an 8% positive AFib rate among our participants, but these readings were taken by a 1-lead mECG device and were not confirmed via 12-lead ECG. However, they were blindly adjudicated by three, independent cardiologists improving the perceived accuracy of our findings. Inter-rater reliability was a barrier to the identification of a true prevalence rate of AFib, as was the research team's inability to immediately confirm each mECG reading with a 12-lead ECG.

Participant recruitment took place at rural pharmacy locations. It could be assumed that a research sample presenting to pharmacy locations may be 'sicker' than a study sample from the general public. However, recruitment included individuals presenting to the pharmacy for medication purchase, as well as those shopping for household items commonly found in community pharmacies. Lastly, participant selection and prevalence rates of AFib risk factors were determined by participant self-report and were not confirmed via medical record review. So, it is possible that our research included participants who were not aware of a prior AFib diagnosis or over- or under-reported known risk factors.

The current study included a majority of female participants, which may have elevated the average stroke risk score due to the automatic 1-point value of being a female on the stroke risk calculator. Females in the US also live longer which may have also contributed to additional disease representation in this study sample.

Conclusion & Future Directions

The current study contains important implications for the ENC region and beyond. The burden of stroke on individuals and their healthcare systems is well-documented, and stroke survivors are affected by a wider of disabilities than most other disease populations (Adamson, Beswick, Ebrahim, 2004). Reports approximate that up to 80% of all strokes could be avoided with the mitigation of associated risk factors (National Stroke Association, 2016). The risk factors of stroke including AFib are relatively well-known and studied by medical professionals, and the list of modifiable risk factors is much longer than the list of non-modifiable risk factors. AFib is thought to be generally manageable or even prevented with targeted identification and treatment. Low access, cultural norms, and maladaptive health behaviors are all regional barriers to treatment. Preventive medical solutions and novel modes of intervention will continue to be required to reach our region's vulnerable population.

The future health of individuals in the ENC region depends on the coordinated efforts of healthcare systems and area-specific inventions that are broadly accessible by even the most unreachable patients. mECG technology and other remote monitoring devices have the potential of more quickly identifying the precipitants of disease so that interventions can occur before a disabling medical event occurs. The current study represents a small step forward to a future of enhanced diagnostic capability and treatment of potentially deadly cardiovascular diseases.

One possible way to enhance the identification of AFib in the ENC region and beyond is to continue to investigate the relationships between psychological distress and maladaptive cardiovascular outcomes. The current study provides compelling preliminary data to suggest that psychological symptoms, ones associated with anxiety in particular, may be a stronger predictor

of abnormal ECGs and thus cardiovascular abnormalities than other known independent risk factors.

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Appendix A: IRB Approval

EAST CAROLINA UNIVERSITY
University & Medical Center Institutional Review Board Office
4N-70 Brody Medical Sciences Building· Mail Stop 682
600 Moye Boulevard · Greenville, NC 27834
Office **252-744-2914** · Fax **252-744-2284** · **www.ecu.edu/ORIC/irb**

Notification of Initial Approval: Expedited

From:	Biomedical IRB
To:	Caley Kropp
CC:	Samuel Sears Caley Kropp
Date:	8/18/2017
Re:	UMCIRB 17-001397 Smartphone-ECG Screening for Atrial Fibrillation

I am pleased to inform you that your Expedited Application was approved. Approval of the study and any consent form(s) is for the period of 8/17/2017 to 8/16/2018. The research study is eligible for review under expedited category #4,7. The Chairperson (or designee) deemed this study no more than minimal risk.

Changes to this approved research may not be initiated without UMCIRB review except when necessary to eliminate an apparent immediate hazard to the participant. All unanticipated problems involving risks to participants and others must be promptly reported to the UMCIRB. The investigator must submit a continuing review/closure application to the UMCIRB prior to the date of study expiration. The Investigator must adhere to all reporting requirements for this study.

Approved consent documents with the IRB approval date stamped on the document should be used to consent participants (consent documents with the IRB approval date stamp are found under the Documents tab in the study workspace).

The approval includes the following items:

Name	Description
AFib initiative_final.pdf	Study Protocol or Grant Application
Afib screening script.docx	Additional Items
AFib_consent_2.2.doc	Consent Forms
AFib_demographics_final.pdf	Surveys and Questionnaires
AFib_eligibility screener + CHADS.docx	Information Sheet
AFib_eligibility screener.docx	Surveys and Questionnaires
DASS - 21	Surveys and Questionnaires
Fax cover letter + info sheet.docx	Additional Items
HRS_AF-Patient-Broch_FINAL.pdf	Additional Items
KMASQ-SF.docx	Surveys and Questionnaires
Recruitment Flyer	Recruitment Documents/Scripts
referral information.docx	Additional Items
SF-12.docx	Surveys and Questionnaires

The Chairperson (or designee) does not have a potential for conflict of interest on this study.

Appendix B: Measures

To the best of your knowledge, have you ever been given a diagnosis of Atrial Fibrillation or Atrial Flutter? [circle one]

YES [if yes, please discontinue questionnaire]

NO

Please indicate which of the following, if any, risk factors you have currently:

^(1) _____Do you identify as female

^(2) _____Are you 75-years old, or older?

_____Sleep Apnea

^(1) _____Vascular Disease

^(1) _____Diabetes

_____Obesity

^(1) _____High blood pressure (hypertension)

---

^(1) _____Congestive Heart Failure

^(2) _____Previous Stroke, TIA, or TE

^(1) _____Are you aged 65-74?

Administrative Use Only:
CHA_2DS_2-VASc score = _____ / 9 (maximum)

AFib Screening Initiative

ID #: Date of Birth:

Town of Residence: Telephone Number:

Email Address: Screening Site:

Screened by:

What is your age?

What is your gender? [circle one]

Male Female Other [specify] _____

What is your race? [circle one]

Black/AA White/Caucasian Hispanic/Latino

Asian/Pacific Islander Other [specify] _____

What is your marital status? [circle one]

Single Married Divorced Widowed

What is your level of education? [circle one]

Grade School Some High School High School Graduate

Technical School Some College College Graduate

Graduate School

How often do you exercise? [circle one]

Never Some (1-2x per week)

Moderate (3-4x per week) Advanced (5x or more per week)

What is your annual household income? [circle one]

$0 – 9,999 $10,000 – 19,999 $20,000 – 29,999 $30,000 – 39,999

$40,000 – 49,999 $50,000 – 74,999 $75,000 – 99,999 $100,000 – 149,999

$150,000 and above Prefer not to answer

AFib Screening Initiative

Do you use a CPAP (Continuous Positive Airway Pressure) device when you sleep?

YES NO

If yes, describe how often you use it:

None Some of the time Most of the time All of the time

Do you use alcohol ever? [circle one]

YES NO

If yes, how many drinks per week (including the weekend) do you have on average? One drink is defined as one beer, one shot or mixed drink, or one glass of wine.

1 drink or less per week 2-3 drinks per week 4-7 drinks per week

8-10 drinks per week 11-14 drinks per week 15 or more drinks per week

Do you use tobacco products of any kind? [circle one]

YES NO

If yes, describe:

I smoke cigarettes/cigars

< pack a day
pack a day
> pack a day

I use dip/snuff/chew

> 5 times a day
2-5 times a day
< 2 times a day

I use an E-Cigarette (E-Cig)

> 10 times a day
6-10 times a day
2-5
< 2 times a day

DASS 21 NAME _____ DATE _____

Please read each statement and circle a number 0, 1, 2 or 3 which indicates how much the statement applied to you over the past week. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 Did not apply to me at all - NEVER

1 Applied to me to some degree, or some of the time - SOMETIMES

2 Applied to me to a considerable degree, or a good part of time - OFTEN

3 Applied to me very much, or most of the time - ALMOST ALWAYS

		N	S	O	AA	FOR OFFICE USE D	A	S
1	I found it hard to wind down	0	1	2	3			
2	I was aware of dryness of my mouth	0	1	2	3			
3	I couldn't seem to experience any positive feeling at all	0	1	2	3			
4	I experienced breathing difficulty (eg, excessively rapid breathing, breathlessness in the absence of physical exertion)	0	1	2	3			
5	I found it difficult to work up the initiative to do things	0	1	2	3			
6	I tended to over-react to situations	0	1	2	3			
7	I experienced trembling (eg, in the hands)	0	1	2	3			
8	I felt that I was using a lot of nervous energy	0	1	2	3			
9	I was worried about situations in which I might panic and make a fool of myself	0	1	2	3			
10	I felt that I had nothing to look forward to	0	1	2	3			
11	I found myself getting agitated	0	1	2	3			
12	I found it difficult to relax	0	1	2	3			
13	I felt down-hearted and blue	0	1	2	3			
14	I was intolerant of anything that kept me from getting on with what I was doing	0	1	2	3			
15	I felt I was close to panic	0	1	2	3			
16	I was unable to become enthusiastic about anything	0	1	2	3			
17	I felt I wasn't worth much as a person	0	1	2	3			
18	I felt that I was rather touchy	0	1	2	3			
19	I was aware of the action of my heart in the absence of physicalexertion (eg, sense of heart rate increase, heart missing a beat)	0	1	2	3			
20	I felt scared without any good reason	0	1	2	3			
21	I felt that life was meaningless	0	1	2	3			
					TOTALS			