Jackson Heart Study Manuscript Proposal

Manuscript Proposal Outline (Upload)

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1. **Proposal Title: "The role of lipid biomarkers in predicting CVD in participants with Chronic Disease: Findings from the Jackson Heart Study"**

2. **Lead Author: Kia Monique Jones**

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3. **Overview**

The objective of this study is to determine the role of biomarkers in predicting cardiovascular disease among African Americans in the Jackson Heart Study with chronic kidney disease (CKD). The primary aim of this study is to evaluate the associations between key biomarkers, fasting triglyceride level, fasting high-density lipoprotein (HDL) cholesterol level, fasting low-density lipoprotein (LDL) cholesterol level and CVD such as Coronary Heart Disease (CHD), Ischemic Stroke, and Myocardial Infarction (MI) in participants with CKD. Exam one data will be used. We will use regression models adjusting for potential confounders, including demographics, anthropometrics, health behaviors, socioeconomic indicators and comorbidity, to assess the association between and certain types of CVD in participants with CKD. We hypothesize that key biomarkers, fasting triglyceride level, fasting HDL cholesterol level and fasting LDL cholesterol level identified at the baseline are positively associated with types of CVD even after adjustment for demographics and clinical characteristics. A secondary hypothesis is that JHS participants with CKD identified at the baseline have a higher unadjusted CVD risk in Hinds County than Madison and Rankin counties. We will use Geographic Information Systems (GIS) to outline how attribute values are distributed in the neighborhood and social environment of Hinds, Madison, and Rankin counties of Mississippi, whether there are spatial trends in the data, or whether the features form spatial patterns as it relates to this study.

4. **Background/Rationale**

The prevalence of CKD is paramount (Visconti et. al., 2016). Cardiovascular disease is one of the leading causes of morbidity and mortality in individuals with CKD. Literature distinguishes an association between abnormal levels of lipids such as triglycerides and cholesterol, particularly high levels of cholesterol (HDL-C) and low levels of cholesterol (LDL-C) increase CVD risk. Lipid abnormalities increases CVD risk in individuals with CKD. According to Sarnak et al., (2003), a prevalence of cardiovascular complications is becoming a prevailing cause of morbidity and mortality in individuals with CKD. CVD and kidney disease are significantly interrelated.Several epidemiological studies have found significant associations between CKD, increased lipid levels in the blood and CVD risk in individuals with CKD (Luca et. al., 2016). Trevisan et. al., (2006), also identified hyperlipidemia is stated to be a significant factor of prominent CVD risk and progression of renal disease. CVD risk factors can be categorized as modifiable and non-modifiable. A person's age, ethnicity and family history are classified as non-modifiable cardiovascular disease risk factors. Characteristics such as smoking, BMI, physical inactivity, neighborhood and social environment are classified as modifiable cardiovascular disease risk factors. Quang et al., (2012), stated from a population health standpoint, CVD

factors such as smoking, diabetes, history of hypertension, dietary patterns, physical activity, blood apolipoproteins and psychosocial factors account for more than 90% of the population-attributable risk. The purpose of this study is to address the emergence of chronic disease complications in the African American community that focuses on causative factors of CVD outcomes in the Jackson Heart Study.

Research Hypothesis

$H_0$1. Fasting Triglyceride Level is positively associated with CHD, Ischemic stroke, and Myocardial Infarction in participants with CKD.
$H_0$1. Fasting HDL Cholesterol Level is positively associated with CHD, Ischemic stroke, and Myocardial Infarction in participants with CKD.
$H_0$1. Fasting LDL Cholesterol Level is positively associated with CHD, Ischemic stroke, and Myocardial Infarction in participants with CKD.
$H_0$2. The positive association between key lipid biomarkers and CVD risk incidence persists despite adjustment for demographics, anthropometrics, health behaviors, socioeconomic indicators and comorbidity.
$H_0$3. JHS participants with CKD identified at the baseline have a higher unadjusted CVD risk in Hinds County than Madison and Rankin counties.

5. Inclusions/Exclusions

The proposed study will examine all participants from exam one in the Jackson, MS MSA (including Hinds, Rankin and Madison Counties) who reported that they have a history of CKD. Participants will be excluded if they did not have a cardiovascular disease diagnosis (CHD, Ischemic Stroke, and Myocardial Infarction).

6. Statistical Analysis Plan and Methods

Chronic Kidney Disease (CKD) is assessed by the JHS participants, who self-reported their CKD status/history. CKD will be measured using the Renal form and History of CKD form that was given as a questionnaire within the Jackson Heart Study during Examination 1 Period.

The proposed study involves specific variables: Coronary Heart Disease (CHD), Ischemic Stroke, Myocardial Infarction, Fasting Triglyceride Level (mg/dL), Fasting HDL Cholesterol Level (mg/dL), Fasting LDL Cholesterol Level (mg/dL).

Dependent Variable:

The cardiovascular diseases that will be investigated in the proposed study will be CHD, Ischemic Stroke, and Myocardial Infarction.

Coronary Heart Disease (CHD) is assessed by the JHS participants, who self-reported their CHD status/history. CHD will be measured using the Cardiovascular History form that was given as a questionnaire within the Jackson Heart Study during Examination 1 Period.

Ischemic Stroke is assessed by the JHS participants, who self-reported whether they have had a physician diagnosis of stroke. Ischemic Stroke will be measured using the History of Stroke form that was given as a questionnaire within the Jackson Heart Study during Examination 1 Period.

Myocardial Infarction is assessed by the JHS participants, who self-reported whether they have had a physician diagnosis of Myocardial Infarction. Myocardial Infarction will be measured using the Cardiovascular History form that was given as a questionnaire within the Jackson Heart Study during Examination 1 Period.

Primary Independent Variables:

The key lipid biomarkers that will be discussed in the proposed study will be Fasting Triglyceride Level, Fasting HDL Cholesterol Level, and Fasting LDL Cholesterol Level.

Fasting Triglyceride Level (mg/dL) is defined by JHS based on triglycerides and fasting time. If fasting time

(in hours) < 8 hrs then fasting triglyceride level is set to missing.

Fasting HDL Cholesterol Level (mg/dL) is defined by JHS based on HDL cholesterol and fasting time. If fasting time (in hours) < 8 hrs then fasting HDL cholesterol is set to missing.

Fasting LDL Cholesterol Level (mg/dL) is defined by JHS based on LDL cholesterol and fasting time. If fasting time (in hours) < 8 hrs then fasting LDL cholesterol is set to missing.

Confounding Variables:

- Demographic Factors**:** Age, gender
- Anthropometry: Body Mass Index
- Health Behavior Factors**:** Smoking status, alcohol consumption, physical activity
- Comorbidity: Diabetes, Hypertension, Dyslipidemia
- Socioeconomic: Educational level, household income
- Neighborhood and Social Environment factor: Geographical location

Analysis Plan

The proposed study will be a cross-sectional study. Quantitative analysis will be utilized and numerical data will help to explain a particular phenomenon in the Jackson Heart Study data. Quantitative analysis of the data will be used to examine descriptive characteristics such as mean, median, mode, range, etc. Quantitative analysis will enable the creation of simple graphic analysis of the collected data. We will use SPSS Version 26 to summarize descriptive statistics to define the quantitative data. It will provide explanations about the sample of the vulnerable populations and their measures. Predictor variables will be entered in each step of the hierarchical regression analysis in an order based on the model. The variables will be entered as follows: Step 1, covariates (i.e., demographic characteristics); Step 2, CHD; Step 3, Ischemic Stroke; Step 4, Myocardial Infarction. Additional measures of data analysis will include independent t-tests, measures of regressions and correlation. A large range of statistical tests will be conducted to examine if there is correlation between the variables. The following confounding variables will be adjusted: for age, gender, BMI, smoking status, alcohol consumption, physical activity, BMI, diabetes, hypertension, dyslipidemia, educational level, household income, and geographical location (Mississippi Counties).

Inferential statistics will be used to test the hypotheses. We will gather numerical data and use inferential statistics and subsequently specify implications that can be generated regarding the relationships established in the sample. The determinations from the inferential statistics will help to confirm whether there is significance to support the hypotheses. We will do data screening to confirm the reliability of the data. We will examine the basic ethics of significance testing, such as normality, p-value, and significance level. The distribution of each biomarker will be tested for normality. The value of each biomarker will also be standardized into z-scores to obtain a graph of normality. SPSS Version 26 will be used to receive inferential statistics for correlation.

To determine whether there are spatial trends in the data, or whether the features form spatial patterns as it relates to this study, the use of Geographic Information Systems (GIS) will show the indication how attribute values are distributed in neighborhood and social environment of Hinds, Madison, and Rankin counties of Mississippi by data collected in the Jackson Heart Study (JHS).

7. References (maximum 15)

Quang Ngoc Nguyen, Son Thai Pham, Loi Doan Do, et al., "Cardiovascular Disease Risk Factor Patterns and Their Implications for Intervention Strategies in Vietnam," International Journal of Hypertension, vol. 2012, Article ID 560397, 11 pages, 2012. https://doi.org/10.1155/2012/560397

Sarnak M.J., Levey A.S., Schoolwerth A.C., Coresh J., Culleton B., Hamm L.L. (2003). Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Hypertension.42:1050–1065.

Trevisan R, Dodesini AR, Lepore G. (2016). Lipids and renal disease. J Am Soc Nephro.17(4 Suppl 2): S145–S147. doi: 10.1681/ASN.2005121320

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