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EXAMINATION OF THE PREDICTORS OF SUBCLINICAL CARDIOVASCULAR DISEASE IN A DIVERSE SAMPLE

A Thesis in

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ABSTRACT

Cardiovascular diseases are a complex set of diseases that affect the cardiovascular system and have fatal consequences if not identified and treated. There have been many studies that have examined risk factors for cardiovascular diseases over the years. In this thesis we examine a relatively new dataset –MESA dataset, which is the Multi Ethnic Study of Atherosclerosis for risk factors for sub clinical cardiovascular disease. We use maximal carotid artery stenosis as a marker of subclinical cardiovascular disease and treat this as our outcome variable and we look at both traditional and non traditional risk factors to estimate their effect on the risk for subclinical cardiovascular disease. We use traditional analytical methods including descriptive analyses, analyses of variance and regression analyses to estimate the risk. Our results indicate that while most of the traditionally studied risk factors do impact subclinical cardiovascular disease, there are also some non traditional factors that can be used to estimate risk. The added value of this theses is two fold: primarily it examines and identifies risk factors for subclinical disease thereby allowing us to target these risk factors even before clinical disease has begun and secondly it identifies risk factors with incremental value in predicting risk above and beyond those traditional risk factors previously reported in the literature

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Chapter 1: Introduction

Importance of the Problem:

Cardiovascular disease refers to the class of diseases that involve the heart or the blood vessels. There is no clear definition of cardiovascular disease; cardiovascular disease (CVD) includes acute myocardial infarction, other acute ischemic (coronary) heart disease, angina pectoris, atherosclerotic cardiovascular disease, and all other forms of chronic ischemic coronary heart disease. However, the risk factors for the different CVD, and the clinical manifestations, signs and symptoms are very similar, hence we consider these diseases under the broad umbrella term of cardiovascular disease. In 2005, the prevalence of CVD was 80.7 million while the mortality in 2004 was estimated to be 869,700 (American Heart Association, 2008). Because of the huge economic burden and suffering that CVD causes, it is of prime importance for prevention strategies. Sub clinical CVD is the presence of CVD before the appearance of clinical manifestations. It is very prevalent especially among older persons and associated with a high rate of progression to clinical CVD. Subclinical disease is probably an intermediary step in the progression from risk factors to clinical disease. Early identification of subclinical disease serves to limit the effects of the different risk factors on the cardiovascular system, and prevent the development or progression of subclinical disease and subsequent clinical disease. Thus, the measurement of subclinical disease therefore has implications for prevention and clinical medicine (Kuller et al., 1995). From an outcomes perspective, examining clinical outcomes and ignoring sub-clinical outcomes may result in delayed and less effective

preventive efforts. (Sibley et al, 2006).

CVD Prevention:

Over the past few decades, significant progress has been made in reducing death and disability from CVD by focusing on decreasing risk factors. Efforts to quantify the risks for CVD with the aim of decreasing such risks are significant to public health practice . There has been an aggressive effort to identify recurrent risk among CVD patients and treat them, which is a form of secondary prevention. Since the Framingham study, there has been considerable research and literature that has come under the heading of atherosclerotic cardiovascular disease (CVD) risk factor reduction (Brindle et al, 2003; Conroy et al, 2003). The major risk factors that are non-modifiable include age, sex, heredity/family history, and race (Berenson et al, 1989; Whitty et al. 1999). Cigarette and tobacco smoke, high blood cholesterol, high blood pressure (Kannel, 1993; Neaton, 1992; Vasan et al, 2001), physical inactivity, obesity and diabetes (Dokken 2008) are the six major independent risk factors for coronary heart disease that are modifiable (AHA). Each of these factors has been implicated in the etiology of heart disease. The risk scores in existence, which are used in clinical practice, are based on research identifying the risk factors for clinical CVD. A variety of risk calculators are available, as charts, tables, computer programs, and web based tools (Bild et al., 2002).

Most efforts at risk prediction and prevention use clinical outcomes to estimate risk. However, looking at clinical outcomes and ignoring sub-clinical outcomes may result in preventive efforts late in the disease process (Sibley et al., 2006). The focus now, is to be able

to accurately identify risk among non-CVD patients and prevent disease using risk prediction estimation which is a form of primary prevention. Estimating disease risk before the appearance of clinical CVD and preventing it through primary prevention strategies is paramount.

Scope of this Thesis:

The focus of this thesis is the identification of the risks for sub-clinical CVD before progression to clinically overt CVD. While most studies on risk estimation and prediction deal with clinical outcomes, we will consider risks as they relate to sub-clinical disease. In this study, we will examine risk factors for sub-clinical cardiovascular disease in a diverse sample of the population. We will examine the distribution of established (used for risk estimation in the established risk scores) and potential factors in this diverse sample and determine if they help predict the outcomes of subclinical CVD. Among the potential factors, we will examine behavioral, social and psychological factors which have been shown to have a conceptual link to subclinical CVD in the literature. We will look at the incremental value of these latter variables over and above the established variables to predict risk. The findings of this thesis will aid in the design of primary prevention strategies to prevent the development and progress of CVD.

Chapter 2: Literature Review

This section contains a review of the existing literature on the risk factors for CVD. We will examine the traditionally used risk predictors and make a case for the use of other variables in our domain categories of demographic, clinical, behavioral, social and psychological traits to be used as predictors of CVD risk.

Subclinical CVD versus Clinical CVD:

Subclinical disease is disease detected noninvasively before it produces clinical signs and symptoms (Bild et al., 2002). Carotid Stenosis is one of the sub clinical outcomes of CVD (Lutsey, 2008). Newer imaging techniques, such as Magnetic Resonance Angiography of the heart and Color Doppler Echocardiography are making it possible for these sub-clinical parameters to be measured (Wexler et al., 1996; Higgins et al., 1996).

There are several advantages to examining risks for CVD using sub-clinical indices. Firstly, relying on clinical disease/events is misleading and an under-representation of the true prevalence of risk factors in the community. Using sub-clinical data along with clinical data gives us a better picture of risk prevalence. Sub-clinical disease usually progresses to clinical disease with time. In a study of 1938 Framingham participants with subclinical disease, 139 participants developed overt cardiovascular disease within 7 years. Furthermore these investigators found a two fold increase in the risk for overt cardiovascular disease associated with subclinical disease. Men with subclinical disease were 2.9 times more likely to experience clinical disease, and women were 1.7 times more likely to experience

clinical CVD (Kuller et al., 1995). The incidence of CVD is increased in patients with subclinical cardiovascular disease. Researchers followed patients from 1989 to 2001 and found incidence rates for CVD (coronary heart disease) to be 30.5 per 1000 patient years for white patients with subclinical CVD, and 16.3 per 1000 patient years for white patients without subclinical CVD. For black patients, the corresponding rates were 31.2 per 1000 patient years with subclinical CVD and 12.5 per 1000 patient years without subclinical CVD. Using indicators of sub-clinical disease to predict risk is advantageous as risk awareness for sub-clinical disease allows for primary preventive measures aimed at CVD risk in its incipient stages (Bild et al., 2002). Third, using clinical disease to predict risk can theoretically be inaccurate. Patients modify behaviors based on clinical signs and symptoms. (To restrict patients from doing so would be unethical). This may give us an inaccurate estimation of risk, and consequently an incorrect estimate of risk prediction. On the other hand, sub-clinical disease is asymptomatic and unknown to participants, and hence it is unlikely to impact health behaviors such as lifestyle modification or medication use that may alter risk of disease (Bild et al, 2002). Finally, sub-clinical measures represent processes as opposed to events, and are continuous in nature. This greatly increases the power to detect risk associations when compared with clinical measures which are more discrete and usually focused on the presence or absence of clinical disease (Bild et al, 2002; Kuller, 1998). Previous research has demonstrated that the risk of clinical events associated with sub-clinical measures is graded and continuous making it a reliable substitute (Bild et al., 2002; Levy et al.,1989; O'Leary et al., 1999; Chambless et al., 1997; Raggi et al., 2000), similar to the risk associated with conventional risk factors such as blood pressure and serum cholesterol. Therefore, interventions to reduce levels of sub-clinical disease could

potentially have a considerable impact on reducing CVD risk. This highlights the need for identification of factors contributing to the development and progression of sub-clinical as well as clinical disease.

Risk Factors for Cardiovascular Disease:

Cardiovascular disease is multi-factorial, as there are multiple factors working collectively to produce poor cardiovascular outcomes (Castelli, 1983). Clinical, psychological and social factors contribute individually and collectively to the development of CVD (AHA, 2008). The interactions of these risk factors with other variables have not been thoroughly examined (Marwick et al., 1999). Furthermore, the constellation of factors that cause poor cardiovascular outcomes may function differently for different subgroups of individuals.

Clinical risk factors for cardiovascular disease:

Clinical risk factors for CVD include high blood cholesterol, high blood pressure, obesity and diabetes (Kannel, 1993; Neaton, 1992; Vasan et al, 2001; Dokken 2008; McPhee et al., 2008; Wang et al., 2002; Hubert et al, 1983; Kannel et al., 1996; Lutsey 2008; AHA, 2008). Although risk-scoring systems that additionally evaluate traditional risk factors greatly improve risk prediction, multiple studies demonstrate that 20% to 25% of all future events occur in individuals with only one of these factors. Moreover, the prevalence of traditional risk factors is almost as high in those without disease as in affected individuals. Hence, there has been increased interest in other indices which may be utilized to predict risk at the sub-clinical stage. Some of these newer indices are measurable at the sub-clinical stage with improved technology.

For example, ankle brachial index which is the difference in the mean blood pressure between the upper and lower extremities has been shown to be linked to subclinical CVD

Behavioral Risk Factors for cardiovascular disease:

Several behavioral risk factors have been implicated in cardiovascular disease (Smith et al., 2002). These include alcohol intake (Ludwig et al 1999; Zarraga et al. 2006; Ignarro et al, 2007), compliance with medication, cigarette and tobacco smoking and physical inactivity (Dokken 2008; McPhee et al., 2008; Wang et al., 2002; Hubert et al, 1983; Kannel et al, 1996; Blair et al., 1989; Paffenbarger et al., 1986). Most of the behavioral risk factors are modifiable.

Social Factors: Included here are contextual and neighborhood risk factors:

Prior research has acknowledged the contribution of the neighborhood of residence to CVD risk (Diez-Roux et al., 2004). Nordstrom et al. (2004) found that, even after controlling for behavioral and biomarker differences, lower neighborhood socioeconomic level was associated with cardiovascular disease. Even after controlling for personal socioeconomic indicators, persons living in the most disadvantaged neighborhood were more likely to develop coronary heart disease than those living in advantaged neighborhoods (Diez-Roux et al, 2004). This association between disadvantaged neighborhoods and cardiovascular disease mortality was found to be greater among the elderly (Diez-Roux et al, 2004). Neighborhood characteristics could contribute to both, the development and propagation of established risk factors, and risk

factors in neighborhoods mediate the effects of neighborhoods on the health of the individuals living in them. Characteristics of neighborhoods include number of parks, number of shops for groceries, amount of tobacco advertising, the amount of spending on health promotion campaigns, the level of awareness regarding cardiovascular health, availability and quality of public spaces, parks, walkways, bicycle paths and recreational facilities, as well as the perceived safety of the neighborhood. Several neighborhood properties such as noise, violence, traffic congestion and poverty itself, as well as social support, social cohesion and neighborliness may contribute to, or alleviate stress and impact CVD risk.

There is an abundance of literature linking SES with established cardiovascular risk factors . There has been a consistent inverse relation between cardiovascular disease, primarily coronary heart disease and many of the indicators of SES. In the few studies of multiple risk factors, there has generally been an inverse relation between SES indicators and hypertension, smoking, total cholesterol level, body mass index, excess alcohol use, and sometimes diabetes. There is also evidence for an inverse relation between SES and individual risk factors. While the literature is most abundant and striking for the relationship between SES, hypertension and cigarette smoking, the data are more limited for hemostatic factors, cholesterol levels, diabetes, obesity, and physical activity. Keeping in mind the complexities of measurement and confounding, it does appear that the association between SES and cardiovascular events is substantial when accepted cardiovascular risk factors are simultaneously considered.

Demographic risk factors:

The major risk factors that are non-modifiable include age, sex, heredity/family history, and race (Berenson et al, 1989; Whitty et al. 1999). Demographic factors include age, race and gender. Aging is an independent mechanism via which CVD occurs. Aging causes the arteries to lose their elasticity leading to high blood

pressure. The work load on the heart increases as the heart has to pump blood against greater resistance. This facilitates the development of CVD (Kuller et al. 1994). Racial differences in CVD have been documented, clearly indicating that race plays some role in predicting CVD risk. CVD deaths disproportionately affect racial minorities (Kurian et al., 2007) and racial disparities in cardiovascular risk factors and outcomes have been well-recognized (Yusuf et al., 2004). Recent research has shown that African Americans have the highest age-adjusted death rate from CVD, followed by Whites, Hispanics, and Asians . Racial differences exist in the prevalence of risk factors for CVD. For instance, hypertension is more prevalent in blacks, manifests at an earlier age, is more difficult to control, is more often associated with target organ injury such as left ventricular hypertrophy and other cardiovascular complications (Kurian et al. 2007; Yusuf et al., 2004; Flack et al., 2003). In addition, certain clinical factors like diabetes, blood pressure and cholesterol levels differ by race and are more significant for blacks (Kurian et al., 2007). Gender-specific behaviors and physiological states influence the development of CVD. These include the use of oral contraceptive pills and states such as menarche, menopause and matriarchy, which affect estrogen exposure and CVD risk. This thesis will not focus on differences

between race and gender groups, however, the importance of these variables to subclinical CVD will be tested.

Psychological risk factors:

A psychological factor may be defined as a measurement that potentially relates psychological phenomena to the social environment and to pathophysiological changes. Recent studies provide clear and convincing evidence that psychosocial factors contribute significantly to the pathogenesis and expression of coronary artery disease. This evidence is composed largely of data relating cardiovascular risk to 5 specific psychosocial domains: (1) depression, (2) anxiety, (3) personality factors and character traits (4) social isolation and (5) chronic life stress (Strike et al., 2004; Siegler et al., 1992; Williams et al., 2001; Frasure-Smith et al, 1995; Barefoot et al, 1996; Ahern et al., 1990). Prior research suggests three independent pathways to consider for the effects of psychosocial factors Firstly, health related behaviors like smoking, diet, alcohol consumption or physical activity, which may influence the risk of heart disease, may be affected by psychosocial factors. Secondly, psychosocial factors may directly impact acute or chronic pathophysiological changes (neuro-endocrine and platelet activation) and have a relationship with CVD risk. Finally, psychosocial factors may impact other factors which have a bearing on CVD risk such as access to care, propensity for healthy behaviors and propensity for preventative care (Rozanski et al., 1999; Hemingway et al., 1999).

Interactive nature of Risk factors:

Even though we can categorize the various risk and protective factors into characteristic

groupings such as demographic, behavioral, clinical, and social, these risk factors are interactive. Each risk factor may interact with other risk factors and thus influence the development of CVD (Yusuf et al. 2004). Differences in one or more risk factors may have an impact on other risk factors even across risk factor categories. Behavioral Risk factors interact with other risk factors such as clinical indices and are also affected by demographic characteristics (Shea et al, 1991). For example, increasing daily physical activity and controlling dietary intake have an impact on cholesterol levels as well as blood pressure. Gender, weight status and blood pressure interact with each other to affect CVD risk (American Heart Association, 2008). These interactions are significant, because most therapeutic and behavioral prevention strategies target individual risk factors or risk categories, without considering how this changes other risk factors for any given patient. It is this interactive nature of the risk factors that makes the use of standard techniques to analyze risk redundant and mandates a different approach.

Chapter 3: Framework for this study

This section presents a conceptual model which guides our choice of variables and determines which variables are candidate risk or protective factors. It also helps us understand the two different methodological approaches we will employ to understand Subclinical CVD risk.

Different domains of risk and protective factors:

Subclinical CVD is multi factorial (Kuller et al, 1995). The theories underlying this model enable us to understand the necessity to examine risk factors in multiple domains such as clinical, behavioral and psychosocial factors. The theory highlights the need to look beyond traditional risk factors when considering cardiovascular risk and to consider factors in other domains that may have a risk or protective effect on cardiovascular health.

Methodological Approach:

The theoretical framework also suggests the need for a methodological approach when examining risk and protective factors for subclinical CVD. We will use a variable specific approach, examining the predictive capability of individual risk factors/variables on subclinical CVD.

Conceptual Model:

The conceptual model highlights the different aspects of the study. Firstly, by choosing to look at risks for subclinical CVD, we are trying to prevent disease early in the process.

Secondly, it gives us a theoretical basis for examining different risk and protective factors. Engel's Biopsychosocial model gives us a framework for our choice of variables.

Subclinical CVD

Subclinical CVD may progress to clinical CVD over time. Empirical data on the progression from subclinical CVD to clinical CVD are scarce and lacking, because the focus on subclinical disease is recent with the implementation of non invasive technology that allows measurement of different subclinical pathologies. Furthermore, it will be difficult to document the true rate of progression from subclinical to clinical CVD because of the effect of behavior changes and treatments. There is a new focus on measuring subclinical disease. Measurement of subclinical disease requires measurement of discreet pathological processes in the body, including the heart and vasculature compared with distinct cardiovascular events in clinical CVD. New technology has made these measurements possible (Wexler et al., 1996; Higgins et al, 1996). The Multi Ethnic Study of Atherosclerosis, is a longitudinal cohort study aimed at identifying risks and outcomes in subclinical CVD. This study, together with the "Progression of Subclinical Atherosclerosis Study" sponsored by the NHLBI, will throw light on subclinical CVD in the near future.

In a study of 1938 Framingham participants with subclinical disease, 139 participants developed overt cardiovascular disease within 7 years. Furthermore these investigators found a two fold increase in the risk for overt cardiovascular disease associated with subclinical disease. Researchers followed patients from the Cardiovascular Health Study for 2.3 years and found that the incidence for coronary disease was increased among patients who had subclinical CVD after

adjusting for age and other risk factors (Kuller et al, 1995). The presence of subclinical CVD increases the likelihood of progression to clinical CVD . If we focus on subclinical CVD, we may be able to identify the risk and protective factors that predispose to subclinical CVD and stem the disease very early.

Risk Factors for Subclinical CVD:

The same risk factors which bring about clinical CVD are also responsible for subclinical CVD. Consequently researchers have used subclinical risks as indicators of clinical CVD (Newman et al, 2003; Psaty et al., 1999; Kuller et al. 1995). Researchers have shown that risk factors for subclinical CVD can be used as a substitute for risk for clinical CVD ((Bild et al., 2002; Levy et al., 1989; O'Leary et al., 1999; Chambless et al., 1997; Raggi et al., 2000).

Risk Factor Domains:

We will examine different factors for their risk and protective effects on Subclinical CVD. These risk factors belong to several domains including clinical, social, psychological and behavioral risk factors. However, most models of cardiovascular disease risks have focused on the biological risk factors which predispose to CVD (Bild et al, 2002; Brindle et al, 2003). We need to look beyond these traditional risk factors to develop a better understanding of CVD and tackle it more effectively.

Biopsychosocial model of Disease:

The biopsychosocial model (Engel G, 1977) posits that biological, psychological and social factors play a role in the disease process. This model goes beyond "reductionist biomedical model" which explains disease as an aberration caused by a pathogen, injury or a genetic or developmental problem (Engel G, 1977). While the biological model is considered in this framework, it also suggests the importance of psychological and social factors which impact the disease process. Essentially this model posits that there are factors which affect the body and the mind that impact the disease process.

Applying the Biopsychosocial Model to Sublcinical CVD:

With regards to subclinical cardiovascular disease, we want to examine how different biological, social and psychological factors impact the disease process. Traditionally researchers have focused their attention on clinical risk factors such as blood pressure, cholesterol, age and behavioral risks such as cigarette smoking (Bild et al, 2002). However, we need to consider factors beyond these clinical and behavioral risks. We will consider risk and protective factors across different domains including biological, clinical, behavioral, social & psychological factors.

Biological Factors impacting subclinical CVD:

Biological factors such as varying blood pressure levels, cholesterol levels & blood glucose levels impact the cardiovascular disease process. Even in this realm, there are newer factors which merit consideration such as HDL, LDL, total cholesterol and triglycerides

considered separately, ankle-brachial index and body mass index. The literature review section of this thesis documents evidence why these factors should be considered. Many of these factors impact or are the result of disease processes involving the cardiovascular system.

Psychological Factors impacting subclinical CVD:

There are different psychological factors which impact CVD including stress, anxiety, depression, emotional stability. These factors have a direct bearing on the working of the cardiovascular system through the neurohumoral axis. They also impact other factors such as behavioral and clinical variables as documented in the literature review section.

Social Factors impacting subclinical CVD:

Social factors such as neighborhood of residence, neighborhood problems, neighborhood cohesion have a bearing on the individual's cardiovascular health. These factors affect the level of physical activity a person can achieve, the type of diet that is person is afforded as well as the psychological variables such as anxiety and stress due to the society one is part of. Extending the biopsychosocial model, in this proposal, we also consider the behavioral factors which impact CVD.

Behavioral Factors impacting subclinical CVD:

These factors include cigarette smoking, physical activity and dietary behavior. While cigarette smoking and physical activity have been considered as risk factors before, dietary

behavior has not been stressed as much. All the behavioral variables impact CVD health directly as well as have a bearing on other variables. For example the levels of physical activity and dietary behavior affect clinical indices such s blood pressure, cholesterol and blood sugar.

Interdependent nature of biological, psychological and social risks

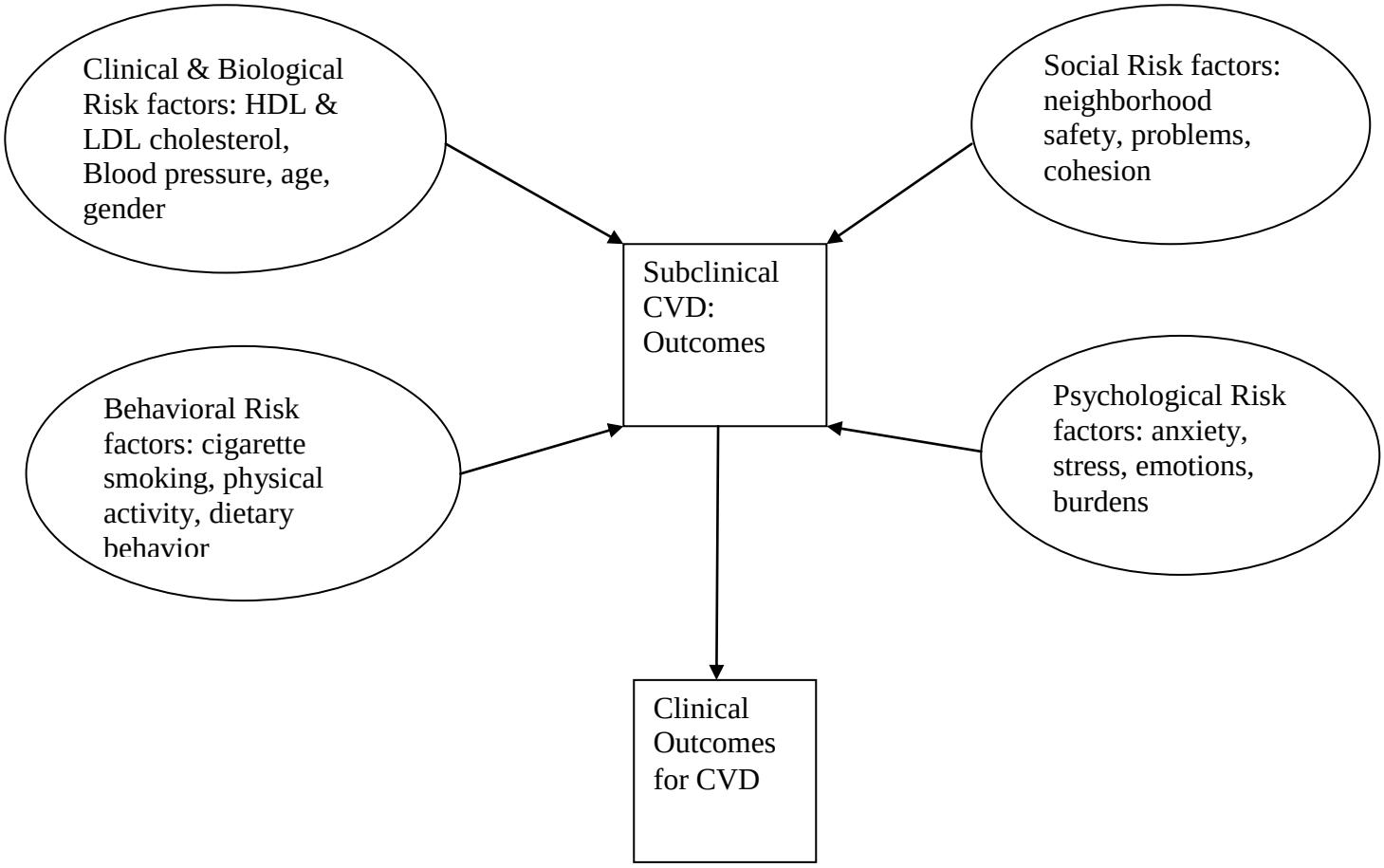
The risk factors mentioned in the different domains above interact at the level of the individual to produce a cardiovascular risk profile. . For example, biological factors such as blood pressure regulation and endocrine mechanisms such as insulin-glucagon axis which are disrupted in diabetics impact CVD outcomes. However, based on this theory, one could argue that social factors such as socio economic status impact the ability of an individual to have regular blood pressure and blood glucose examinations which impacts the cardiovascular health. Neighborhood characteristics such as the availability of recreational facilities and neighborhood safety and cleanliness impact physical activity levels which have an effect on stress, blood pressure and body mass index. Psychological factors such as anxiety levels and stress have an effect on the blood pressure levels of an individual and also on the hormonal axis of the body (cortisol levels and levels of insulinogenic versus non-insulinogenic hormones). This model suggests looking at factors in these different domains and how they relate to subclinical CVD risk. Since so many different factors have a bearing on cardiovascular health, it is necessary that we look beyond the traditional Framingham factors to assess risk.

Schematic representation of the conceptual Model:

The schematic representation of the conceptual model is detailed in Figure 1. We utilize regression models to examine which variables are best predictors of subclinical CVD. Each box represents a set of risk factors that falls within a particular domain. Each risk factor will be examined for its ability to predict a poor outcome. Each risk factor in a particular domain affects the outcome namely subclinical cardiovascular disease which in turn progresses to clinical cardiovascular disease.

Figure 1. Conceptual Model

Variable Specific Approach: Using regression determining which variables best affect/predict the outcome. Variables are considered across different domains to determine their effect on the subclinical CVD outcomes.



Schematic Representation of the Conceptual Model representing variable specific approach. Different sets of variables are grouped together.

Purpose of this research:

Given the multi-factorial nature of CVD, individual differences in the correlates of CVD and the interactive nature of the risks, it can be difficult to identify the most relevant risk factors to target for prevention of CVD in diverse groups of adults. Prevention efforts require comprehensive knowledge of the risk factors for CVD and an understanding of the most significant risk factors. In this study, we will use a variable specific approach to identify risk and protective factors.

Variable Specific Approach:

In this approach, we will use regression models to determine which risk and protective factors best predict subclinical CVD in our sample. These models identify which variables best serve to predict the outcomes.

Nature of the study:

In this study, we will examine risks for sub-clinical cardiovascular disease using the Multi Ethnic Study of Atherosclerosis (MESA). We will employ a variable specific approach to determine the most significant risk factors within the study population. Cardiovascular risk will be modeled as a function of predictor variables in logistic regression models.

Research goals:

To identify behavioral, psychological, social and clinical predictors of sub-clinical cardiovascular disease in the MESA dataset which explain variance in subclinical disease beyond that explained by the traditional risk measures used by previous researchers.

Hypothesis:

Behavioral, psychological, social, demographic and newer clinical variables explain some of the variance in the subclinical outcomes over and above that explained by established risk factors

Significance of the study:

The global risk profile represents the totality of risk factors exhibited by an individual. Accurate and comprehensive risk prediction is a vital tool in clinical practice, as it allows primary care physicians to target patients with specific risk factors for behavioral change and therapeutic intervention. In addition, it allows physicians to focus on controlling risk factors depending on the relative importance of each individual factor. It allows public health professionals to allocate resources aimed at controlling risks in the population. Risk prediction is also significant for epidemiological reasons as it determines the risks for cardiovascular disease in populations based on the prevalence of clinically measurable indices. In addition, it provides information to target intervention strategies (primary prevention). Risk scores and charts are beneficial in getting treatment decisions made alongside realistic estimates of patient

susceptibility to cardiovascular disease . Therefore risk estimation and quantification to predict disease has a significant role in clinical and public health practice. Furthermore predicting risk at the subclinical level, even before clinical disease begins is beneficial in targeting the disease early in its course and modifying the path of the disease and its outcomes.

Chapter 4: Methodology

Data Set:

For our analyses, we will be using the Multi Ethnic Study of Atherosclerosis (MESA) dataset.

Brief description of the MESA study:

This study is a prospective longitudinal cohort study, initiated in July 2000 to investigate the prevalence, correlates, and progression of sub-clinical cardiovascular disease (CVD) in a population-based sample of 6,814 men and women aged 45-84 years. All subjects were free of clinical CVD at baseline (Bild et al., 2002; Lutsey, 2008). The MESA cohort is drawn from six regions in the U.S.: Forsyth County, NC, Northern Manhattan and the Bronx, NY, Baltimore City and Baltimore County, MD, St. Paul, MN, Chicago, IL, Los Angeles County, CA .The source population for each field center varies in size and ethnic composition. Each site will recruit 1,100 eligible participants, equally divided between men and women, and according to specified race/ethnicity proportions.

Features of the MESA study and data:

The MESA study follows participants through 2008 to identify and characterize CVD events, including acute myocardial infarction and other coronary heart disease, stroke, peripheral

vascular disease, and congestive heart failure; therapeutic interventions for CVD; and mortality. MESA was initiated by the National Heart, Lung, and Blood Institute.

- The purpose of the study is to improve our knowledge of the pathogenesis of atherosclerosis and other CVDs by making available accurate, quantifiable measures of early CVD, and allowing for the characterization of CVD before it becomes clinically manifest.
- This also allows us to study the disease before any interventions, therapeutic or behavioral.
- The MESA data provide for an optimal study of the sub-clinical factors and progression of sub-clinical disease.
- An important feature of the MESA study is its inclusion of ethnic populations which allows us to gather information on ethnic minorities and make group level comparisons for CVD risk (Bild et al., 2002).
- The MESA study employs computed tomography, cardiac magnetic resonance imaging, doppler flow studies and ultrasonography techniques, which allow for measurement of coronary artery and aortic calcification, different flow parameters and ventricular parameters used as estimators of risk.

The study also contains data on standard risk factors, socio demographic factors and psycho social factors (Bild et al, 2002). During data collection researchers targeted households and individuals so as to get required numbers of participants from the desired ethnic

communities. Self- report of conditions was generally considered satisfactory. None of the patients had CVD at the time of entrance into the study.

Goals of MESA study:

The goal of the MESA study is to examine sub-clinical cardiovascular disease and risk, and identify new indices which have incremental predictive value over established risk factors. In addition the purpose of the study is to develop methods to identify risk at the asymptomatic stage of disease and prevent it (Bild et al, 2002).

Objectives of the MESA study (adapted from MESA NHLBI)

Primary Objectives (from MESA website of the NHLBI):

- "To determine characteristics related to progression of subclinical to clinical cardiovascular disease.
- To determine characteristics related to progression of subclinical cardiovascular disease."

Secondary Objectives (from MESA website of the NHLBI):

- "To assess ethnic, age, and gender differences in subclinical disease prevalence and risk of progression and clinical cardiovascular disease.
- To describe the interrelationships of newly identified factors, established risk factors, and subclinical disease, and to determine the incremental predictive value for clinical

cardiovascular disease of newly identified factors and subclinical disease measures above that of established risk factors.

- To develop population-based methods, suitable for application in future screening and intervention studies, for characterizing the risk of asymptomatic persons."

Details of the recruitment procedures as well as eligibility and exclusion criteria can be found on the MESA website. For this thesis study, we will use cross-sectional data from the first exam. This study looks beyond the traditional risk factors for CVD as well as uses a variable specific and group specific approach to predicting CVD risk.

Measures:

Dependent Variables- Subclinical CVD Outcomes:

Maximum carotid artery stenosis R:

This variable is recoded from maximum carotid artery stenosis. The recoded variable has two categories 0-no stenosis and 1- any degree of stenosis. The original variable had 6 categories and was measured with a carotid ultrasound. The original categories were 0-no lesion, 1-24%, 2-25-49%, 3- 50-74%, 4-75-99%, 5-100%. The original stenosis was calculated using the maximum function and was equal to MAXSTN1c=max (rsten1,lsten1), which was the maximum stenosis of the right and left carotid arteries. When one side had a bad image or could not tell, then the other side with the valid value or measure was taken as the maximum stenosis. We recoded this variable into two categories as mentioned above, the first category included persons

with no stenosis and the second category included persons with any degree of stenosis. Hence groups 1-5 were collapsed into a single category where 1=yes (some degree of stenosis). The N for the original variable was 6716. The original variable MAXSTN1c had 3927 (57.6%) in category 0 (no lesion) and 1914 (28.1%) in category 1, 824 (12.1%) in category 2, 30 (.4%) in category 3, 16 (.2%) in category 4 and 5 (.1%) in category 5. 98 persons or 1.4% of the sample were missing data on this variable). The recoded variable has 3927 (57.6%) in category 0/no stenosis and 2789 (40.9%) in category 1/any degree of stenosis.

Independent Variables:

The independent variables are listed in categories below

Demographic variables:

These variables include age, race, gender, socioeconomic status, marital status, education and insurance status. The demographic information was obtained from the personal history forms.

Age:

Age is reported as a continuous variable and was calculated from the enrollment date and birth date using the following formula trunc[(enrolldt1 – birthdt1)/365.25]. It was truncated to the next whole number. We collapsed the Age variable into 4 categories, 45-54 (N

Race categories:

Race was coded into 4 categories as follows: 1= Caucasian, 2= Asian (predominantly Chinese), 3= African American and 4=Hispanic.

Gender categories:

Gender was coded as 0=female and 1=male.

Socioeconomic Status:

This variable was recorded from the Personal History questionnaire. The original variable has 13 categories 1=<$5,000, 2=$5,000-7,999, 3=$8,000-11,999, 4=$12,000-15,999, 5=$16,000-19,999, 6=$20,000-24,999, 7=$25,000-29,999, 8=$30,000-34,999, 9=$35,000-39,999, 10=$40,000-49,999, 11=$50,000-74,999, 12=$75,000-99,999, 13=$100,000 +. Table 1 in the results section details the distribution of the income categories in the sample. Since there are 13 categories we will treat this variable as a continuous variable with values ranging from 1-13.

Education:

This variable is recoded from the original variable developed from the personal history questionnaire. The original variable had 8 categories detailed as 0=no schooling, 1=grades 1-8, 2=grades 9-11, 3=completed high school/GED, 4=some college but no degree, 5=technical school certificate, 6=associates degree, 7=bachelor's degree, 8=graduate/professional school. The recoded variable has two categories 0=less than high school and 1=high school or greater . Therefore records in the original variable which

were coded as 0 or 1 (no schooling or grades 1-8) were recoded as 0 and records coded from 2-8 (2=grades 9-11, 3=completed high school/GED, 4=some college but no degree, 5=technical school certificate, 6=associates degree, 7=bachelor's degree, 8=graduate/professional school) were recoded as 1.

Insurance Status:

For the purposes of this analyses we are interested in whether a person had any/some health insurance versus no health insurance. We used the variable hinone`1 which is a categorical variable with two values 0=No and 1=Yes.

Clinical variables:

This domain includes Ankle Brachial index, Body mass index, Triglycerides, Total cholesterol, HDL cholesterol, LDL cholesterol calculated, Hypertension by JNC-7 criteria, hypertension meds, Diabetes by ADA 2003 criteria.

Ankle Brachial Index (ABI:

The ankle brachial index is calculated as the minimum ratio of the ankle blood pressure in the posterior tibial artery to the arm blood pressure in the brachial artery. The minimum ratio between that of the right and left side is taken. Ratios are calculated separately for the left and right side, and the minimum is then selected. ABI1C = min (rtabi , ltabi). The right ABI is calculated as the ratio of the pressure on the right dorsalis pedis or the right posterior tibial (maximum or greater of the two) to the average of the right brachial or left brachial pressure.

[where rtabi = (max (rdpedis1, rptib1)) / (avg (rbrach1,lbrach1), ltabi = (max (ldpedis1, lptib1)) / (avg (rbrach1,lbrach1)]. If the right and left brachial pressures differed by 10 mm Hg then the higher arm pressure is sued as the denominator.

Body mass (BMI):

BMI is measured in kg/m^2 (continuous variable) was calculated from measurements of height and weight recorded on the anthropometric form. The height was measured using a Stadiometer (Accu-Hite Measure Device with level bubble) and the weight was measured with a Detecto Platform Balance Scale in lbs/kg.

Triglycerides:

This is a continuous variable measured in mg/dl. Triglycerides are measured in EDTA plasma using Triglyceride GB reagent (Roche Diagnostics, Indianapolis, IN 46250) on the Roche COBAS FARA centrifugal analyzer. This assay performs an automated glycerol blank by taking a spectrophotometric reading after endogenous glycerol has reacted and before lipase is added to release the glycerol from the triglyceride. This method is calibrated with a frozen serum standard prepared in our laboratory and frozen at -70°C. We have assigned this calibrator by comparison to CDC reference materials. The accuracy and precision The NCEP program recommends reference range of <150 mg/dL. Measurements are made at the Collaborative Studies Clinical Laboratory at Fairview-University Medical Center (Minneapolis, MN). The laboratory CV is 4.0%

Total Cholesterol:

Total cholesterol is a continuous variable. Total cholesterol is measured in EDTA plasma using a cholesterol oxidase method (Roche Diagnostics, Indianapolis, IN 46250) on a Roche COBAS FARA centrifugal analyzer at the Collaborative Studies Clinical Laboratory at Fairview-University Medical Center (Minneapolis, MN). This method incorporates cholesterol esterase and peroxidase in the reagent and monitors cholesterol oxidation at 500 nm upon conversion of 4-aminoantipyrine to quinoneimine. This enzymatic method is standardized with a serum standard prepared in our laboratory and frozen at -70°C. The assigned value of this standard is set by replicate Abell-Kendall cholesterol analysis performed by a CDC/NHLBI Cholesterol Reference Method Laboratory Network laboratory. The calibration of this assay is regularly monitored by the CDC/NHLBI Lipid Standardization Program. The NCEP program recommends reference range of <200 mg/dL. The laboratory CV is 1.6%.

HDL-Cholesterol:

HDL-Cholesterol is a continuous variable measured in EDTA plasma using the cholesterol oxidase cholesterol method (Roche Diagnostics) after precipitation of non-HDL-cholesterol with magnesium/dextran. This method is standardized as described for the cholesterol assay; and calibration of the assay is regularly monitored by the CDC/NHLBI Lipid Standardization Program. The NCEP program recommends reference range of >40 mg/dL. Measurements are made at the Collaborative Studies Clinical Laboratory at Fairview-University Medical Center (Minneapolis, MN). The laboratory CV is 2.9%.

LDL-Cholesterol Calculated:

This is a continuous variable. LDL-cholesterol is calculated in plasma specimens having a triglyceride value <400 mg/dL using the formula of Friedewald et al. 1972 . The NCEP program recommends reference range of <100 mg/dL. Measurements are made at the Collaborative Studies Clinical Laboratory at Fairview-University Medical Center (Minneapolis, MN).

Hypertension by JNC criteria:

This is a computed categorical variable with two categories (0-No, 1-Yes) defined as systolic blood pressure >=140 and diastolic blood pressure >=90 or self reported history of hypertension and hypertensive medications. Self reported hypertension and hypertensive medications were obtained from the medical history form. This variable was chosen since it incorporates hypertension by measurement of systolic blood pressure, by self report and patients on hypertensive medications.

Hypertension meds:

This is a categorical variable with two categories (0=No, 1=Yes), indicting if the patient is taking any anti hypertensive medications or not. The information for this variable is obtained from the medications form.

Diabetes Mellitus by 2003 ADA fasting criteria:

This is a categorical variable with four categories as follows:-0=normal, if fasting glucose <100mg/dl and the patient does not fall into the category of treated diabetes, 1=impaired fasting glucose, if fasting glucose=100-125mg/dl and the patient does not belong to category 3/treated diabetics, 2=untreated diabetes if fasting glucose>=126mg/dl and patient does not belong to category 3, and 3=treated diabetes if patient is on insulin or oral hypoglycemic agents on medication form or by self report.

Family history of a heart attack:

This is a categorical variable with two categories (0=No, 1=Yes). This is a computed variable from the medical history questionnaire and includes patients with either parent/ sibs or children with a history of heart attack.

Psychological Variables:

This domain of variables includes Center for Epidemiologic Studies Depression scale, Chronic burden scale> 6 months, perceived discrimination over a lifetime, emotional social support index, everyday hassles, Spielberger trait anger scale and Spielberger trait anxiety scale.

Center for Epidemiologic Studies Depression Scale (CES-D):

This score is a continuous created variable which is a sum of scores for the 20 items in the CES-D scale. Details of the CES-D scale can be found in the appendix A. The CES-D is a self-report scale developed in the general population to measure symptoms of depression.

Depression is gauged using mood, feelings of guilt, worthlessness, psychomotor retardation, appetite loss and sleep disturbance (Radloff, 1977). The CES-D was developed in the 1970s by Lenore Radloff. (Murphy, 2002; Naughton & Wiklund,1993; Snaith, 1993; Nezu et al., 2002). Sample questions used in the CES-D score included "I was bothered by things that usually don't bother me, I did not feel like eating; my appetite was poor, I felt that I could not shake off the blues even with help from my family or friends, I felt I was just as good as other people, I had trouble keeping my mind on what I was doing, I felt depressed, I felt that everything I did was an effort, I felt hopeful about the future, I thought my life had been a failure, I felt fearful, My sleep was restless, I was happy, I talked less than usual, I felt lonely, People were unfriendly, I enjoyed life, I had crying spells, I felt sad, I felt that people dislike me, I could not get "going". Respondents answered "Rarely or none of the time (less than 1 day), Some or a little of the time (1-2 days), Occasionally or a moderate amount of time (3-4 days) or Most or all of the time (5-7 days)". In the MESA sample the range of the CES-D score is 0-53. The CES-D is a well established scale with internal consistency (alpha coefficient) of 0.85 (Radloff, 1997, Hann et al. 1999).

Chronic burden scale > 6 months:

This scale is a computed sum of scores to five items- details of the individual items used to compute the scores as well as assignment of values can be found in Appendix A), Sample questions included "Serious ongoing health problem (self), Serious ongoing health problem (someone close to you), Ongoing job difficulties, Ongoing financial strain & Ongoing relationship problems". Minimum possible score was 0 and maximum score was 5.

Perceived discrimination over a lifetime:

This is a computed sum of scores to six items. Sample questions include "Unfairly fired or denied a promotion, Unfairly not hired for a job, Treated unfairly by the police, Unfairly discouraged by a teacher from continuing education, Unfairly prevented from moving into a neighborhood, Neighbors made life difficult during last twelve months. Scores were assigned from 1 for none of the time to 5 for all of the time. The minimum score was 0 and the maximum score was 6

Emotional Social Support Index:

This variable is a computed sum of scores for six items. Sample questions include "Someone available to listen to you, advice, Someone available to give you advice, Someone available to show you love and affection, Someone available to help with daily chores, Someone available to provide emotional support, Sufficient contact with someone you can confide in". Scores were assigned from 1 for none of the time to 5 for all of the time.

Everyday hassles:

This is a computed sum of scores for nine items. Sample questions include "Treated with less courtesy than others, Treated with less respect than others, Receive poorer service than others, People act as if you are not smart, People act as if they are afraid of you, People act as if you are dishonest, People act as if they are better than you, You are called names or insulted, You are threatened or harassed". Scores were assigned from 6-almost every day to 1 for never. The minimum possible score was 9 and the maximum possible score was 54.

Spielberger Trait Anger Scale:

This is a computed sum of scores for ten items. Sample questions include "I am quick tempered, I have a fiery temper, I am a hotheaded person, I get angry when slowed by others' mistakes, I am annoyed when not recognized for good work, I fly off the handle, I say nasty things when mad, I get furious when criticized in front of others, I feel like hitting someone when frustrated, I feel infuriated when I do a good job and get a poor evaluation". Scores were assigned from 1 for 'almost never' to 4 for 'almost always'. Minimum score was 10 and maximum score was 40. The internal consistency (alpha coefficient) for this scale is .86.

Spielberger Trait Anxiety Scale:

This variable is a computed sum of scores for responses to ten questions on the Health and Life questionnaire. Sample questions include "I am a steady person, I feel satisfied with myself, I feel nervous and restless, I wish to be as happy as others seem to be, I feel like a failure, I feel tension when I think of recent concerns/interests, I feel secure, I lack self-confidence, I feel inadequate, I worry too much over something that does not matter. Scored were assigned from 1-almost never to 4 for almost always for -I feel nervous and restless, I wish to be as happy as others seem to be, I feel like a failure, I feel tension when I think of recent concerns/interests, I lack self-confidence, I feel inadequate, I worry too much over something that does not matter". The range of this score in the MESA sample is 10-37. The Spielberger trait anxiety scale is a well established scale with tested internal consistency and reliability.

Behavioral Risk Factors:

This domain of risk factors includes current aspirin use, pack years of cigarette smoking, current cigarette smoker, current alcohol use, number of years of alcohol consumption, number of drinks per week and reported total physical activity hours per day.

Current Aspirin Use:

This is a created categorical variable with two categories 0=no and 1=yes. It was calculated from two variables: 1)ASPDAYS1 (which is a continuous variable indicating aspirin: days per week. If the value of this variable was > 3, indicating that the patient took aspirin for more than 3 days per week, then the patient was considered a current user of aspirin) and 2)ASA1C (which is a categorical variable, from the medications form indicating aspirin use. If this variable was coded as 1=yes then the patient was considered a current aspirin user).

Cigarette smoking Status:

This is a computed categorical variable with 3 categories. It was computed from two variables- 1) smoked at least 100 cigarettes in a lifetime and 2) current smoking status from the personal history questionnaire. It was coded as 0=never smoked if the person replied no to smoked at least 100 cigarettes in a lifetime. It was coded as 1=former smoker, if the person smoked at least 100 cigarettes in a lifetime but the current smoking status was 0/ no. It was coded as 2 =current smoker if the person had answered yes to the current smoking status question.

Pack years of cigarette smoking:

This is a computed continuous variable. It was calculated using the following variables from the personal history questionnaire: the cigarette smoking status variable, age started smoking cigarettes, age quit smoking and the average number of cigarettes smoked per day. It was coded as 0 if the cigarette smoking status indicated that the patient had never smoked (cig1c=0, then PKYRS1C=0, where cig1c is cigarette smoking status and 0 indicates never smoked and PKYRS1C is pack years of cigarette smoking). If cig1c=1, which indicates a former smoker, then pack years of cigarette smoking was calculated as (age quit smoking-age began smoking)* (average number of cigarettes per day/20). If cig1c=2, which indicates a current smoker, then pack years of cigarette smoking was calculated as (age- age began smoking)* (average number of cigarettes per day/20).

Alcohol use:

This is a computed categorical variable with 3 categories. It was coded as 0=never, if the person had never consumed alcoholic beverages (alcohol1=0) as determined from the personal history questionnaire. This variable was coded as 1=former, if the person had replied yes to ever consuming alcohol beverages and no to currently using alcohol. It was coded as 2=current if the person had replied yes to currently using alcohol.

Years of Alcohol use:

This is continuous variable representing the number of years drinking alcohol for both current and former alcohol users. The information was obtained from the personal history

questionnaire.

Number of drinks per week:

This is a continuous variable representing the number of drinks per week for current and former drinkers. This information was obtained from the personal history questionnaire.

Reported total physical activity hours per day:

This is a computed summary variable representing the total hours per day of physical activity. It was calculated using information from the physical activity form/questionnaire.

Social Variables:

This domain of variables includes the neighborhood social cohesion score, neighborhood problems score and number of years lived in the neighborhood.

Neighborhood social cohesion score:

This variable is a computed continuous variable representing the sum of scores to five questions which measure neighborhood social cohesion. Sample questions included “Close knit neighborhood, People willing to help their neighbors, People in neighborhood don’t get along, People in neighborhood can be trusted and People in neighborhood do not share the same values”. Scores were assigned from 1 for strongly agree to 5 for strongly disagree. The minimum possible score was 5 and the maximum possible score was 25. Two week test–retest reliabilities were 0.91 for neighborhood problems and 0.90 for neighborhood social cohesion .

Neighborhood problems:

This variable is a computed continuous variable representing the sum of scores to 7 questions. Sample questions included "Excessive noise in neighborhood, Heavy traffic or speeding cars in neighborhood, Lack of adequate food shopping in neighborhood, Lack of parks/playgrounds in neighborhood, Trash and litter problem in neighborhood, Poor sidewalks in neighborhood, Violence problem in neighborhood". Scores were assigned from 4 for a very serious problem to 1 for not really a problem. The minimum possible score was 7 and the maximum possible score was 28.

Number of years lived in the neighborhood:

This is a continuous variable computed as the total of months and years lived in the neighborhood.

Analyses Protocol:

Methods for Specific Aim1:

1) To identify behavioral, psychological, social, demographic and clinical predictors of sub-clinical cardiovascular disease in the MESA dataset with bivariate and multivariate analyses which explain variance in sub clinical disease beyond that explained by the traditional risk measures used by previous researchers.

Step 1: Descriptive Analysis

We will conduct descriptive analyses of the data and examine the distribution of the risk and protective factors identified in the literature.

Step 2: Correlations

We will conduct bivariate analyses (chi square tests, point biserial correlations and T tests) to examine the relationships between the different clinical, behavioral, psychological and social variables detailed in the independent measures above and the dependent subclinical measure of CVD (carotid artery stenosis). We will look at each set of variables separately and examine correlations between the predictor variables and the dependent variables as well as looking for correlations between the predictor variables.

Step 3: Regression Analysis

We will run 5 separate regression models for each set of risk factors and the outcome variable.. We will use logistic regression for our categorical outcome variables to determine which independent variables best serve as predictors of sub-clinical CVD. We will examine the parameter estimates and significance levels to determine which variables are the best predictors of subclinical CVD. We will refine the model so that it contains those variables which explain the greatest variance in the outcome measures from the different independent measures available to us above and beyond the variance explained by the established risk factors.

Regression Equation:

Carotid artery stenosis is the outcome variable for the regression model. A detailed list of the predictor variables can be found in table appendix c

For Outcome Variable carotid artery stenosis, we employ logistic regression using the equation below

Carotid artery stenosis = logit(z)

Where $z = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \cdots + \beta_k x_k,$

Where z is the outcome variable-carotid artery stenosis (yes/no) and represents the presence or absence of any degree of stenosis. The logit transformation is defined as $1/(1+e^{-z})$:

And x_1, x_2, x_3…….x_k are predictor variables such as age, race etc.

Chapter 5: Results

Outcome Variable:

Recoded maximal carotid artery stenosis

The outcome variable used in the study is maximum carotid stenosis, the original variable had 5 categories: 0- no lesion 3927/6814 or 57.6% of the same, 1 indicated 1-24% lesion had 1914/6814 or 28.1%, 2 or 25-49% of the lesion consisting of 824/6814 or 12.1%, 3 indicating 50-74% lesion had 30/6814 or 4 % of the sample, 4 representing 75-99% of the lesion had 16/6814 or 2% and 5 indicating 100% lesion with 5 out of 6814 or 1% of the sample. There were 98 cases with missing values for this variable representing 1.4% of the sample. This variable was recoded into two categories, 0 and 1, 0 indicating no stenosis was the same as the 0 in the original variable. The other categories 1-5 have been collapsed into 1 category indicating any degree of stenosis. Pl ease refer table 1 for the descriptives of the outcome variables

Table 1A: Distribution of original outcome variable in the sample

Maximal Carotid Artery Stenosis	Frequency	Percent
No lesion	3927	57.6
1: 1-24 %	1914	28.1
2: 25-49%	824	12.1
3. 50-74%	30	.4
4: 75-99%	16	.2
5: 100%	5	.1

Table 1B: Distribution of Recoded Outcome Variable in the sample

	Frequency	Percent
No Carotid Artery Stenosis	3927	58.47%
Any degree of carotid stenosis	2789	41.53%

Demographic Variables:

Race: Of the total sample of 6814, 2624 were white comprising 38.5% of the sample, 1893 were Black comprising 27.8% of the sample, 1493 were Hispanic comprising 21.9% of the sample and 804 were Chinese comprising 11.8% of the sample.

Age: The age distribution of the sample was as follows, 1947 or 28.6% were between 45-54, 1885 or 27.7% were between 55 and 64, 2017 or 29.6 % were between 65 and 74 and 965 or 14.2% were between 75 and 84.

Gender: Of the total sample, 3601 or 52.8% were female and 3213 or 47.2% were male.

Education: The original education variable was distributed as follows 71 or 1% of the sample had no schooling, 678 or 10% were schooled through grades 1-8, 476 or 7% were schooled through grades 9-11, 1236 or 18.1% had completed high school/GED, 1109 or 16.3% had some college but no degree, 488 or 7.2% had a technical school certificate, 340 or 5% had an associate degree, 1171 or 17.2% had a bachelors degree and 1222 or 17.9% had completed graduate or professional school. The original variable was recoded into two categories no schooling or grades 1-8 had 749 or 11% of the sample and any other education had 6042 or 89% of the sample and 23 or 0.3% were missing information for this variable.

Socioeconomic Status: The socioeconomic status variable was more or less evenly distributed in the sample. 157 of 2.3% of the sample had annual incomes less than 5000, 254 or 3.7% had

income between 5000 and 7999, 357 or 5.2% had income between 8000 and 11999, 468 or 6.9% had income between 12,000 and 15, 999, 324 or 4.8% of the sample had income between 16,000 and 19,999, 500 or 7.3 % of the sample had income between 20,000 and 24,999, 391 or 5.7% of the sample had income between 25,000 and 29,999, 468 or 6.9% of the sample had incomes between 30,000 and 34,999, 390 or 5.7% of the sample had incomes between 35,000 and 35,999, 643 or 9.4% of the sample had incomes between 40,000 and 49,999, 1111 or 16.3% had incomes between 50,000 and 74,999 , 598 or 8.8% of the sample had incomes between 75,000 and 99,999 and 880 or 12.9% of the sample had incomes greater than 100,000. Although this variable is a categorical variable with several categories, for the purposes of these analyses we will treat it as a continuous variable

Insurance Status: In the total sample, 609 or 9% had no insurance of any kind and 6183 or 91% of the sample had some type of insurance, while 22 or 0.3% of the sample were missing information on this variable

Table 2A: Distribution of Demographic categorical variables in the sample

Demographic Variables	N
Race: Total Sample	6814 (100%)
White	2624 (38.5%)
Black	1893 (27.8%)
Hispanic	1493 (21.9%)
Chinese	804 (11.8%)
Age: Total Sample	6814 (100%)
45-54	1947(28.6%)
55-64	1885(27.7%)
65-74	2017(29.6%)
75-84	965(14.2%)
Gender: Total Sample	6814 (100%)
Female	3601(52.8%)
Male	3213 (47.2%)
Education : No schooling	71 (1%)
Grades 1-8	678 (10%)
Grades 9-11	476 (7%)
Completed high school/GED	1236 (18.1%)
Some college but no degree	1109 (16.3%)
Technical School certificate	488 (7.2%)
Associate Degree	340 (5%)
Bachelors degree	1171 (17.2%)
Graduate or professional school	1222 (17.9%)
Education Recoded	6814
0: No schooling or grades 1-8	
1: Grades 9-11, Completed high school/GED, Some college but no degree, Technical School certificate, Associate Degree, achelors degree, Graduate or professional school	749 (11%) 6042 (89%)
9: Missing	23 (0.3%)
Socio economic Status	
<$5000	157 (2.3%)
$5,000-$7,999	254 (3.7%)
$8,000-$11,999	357 (5.2%)
$12,000-$15,999	468 (6.9%)
$16,000-$19,999	324 (4.8%)
$20,000-$24,999	500 (7.3%)
$25,000-$29,999	391 (5.7%)
$30,000-$34,999	468 (6.9%)
$35,000-$39,999	390 (5.7%)
$40,000-$49,999	643 (9.4%)
$50,000-$74,999	1111 (16.3%)
$75,000-$99,999	598 (8.8%)
>$100,000	880 (12.9%)
No Insurance	6792
No	6183 (91%)
Yes	609 (9%)
Missing	22 (0.3%)

Distribution of Categorical Demographic Variables by Outcome:

Please refer to table 2B

Gender: The distribution of demographic variables was further broken down by the outcome variable. 2174 of the sample were female and had no stenosis and 1366 had carotid artery stenosis, 1753 were male and had no stenosis and 1423 were male and had some degree of stenosis.

Race: Within the race category, 1393 were white with no stenosis and 1197 were white with some degree of carotid artery stenosis, 592 were asian with no stenosis and 208 were Asian wth some degree of of carotid artery stenosis, 1045 were black with no stenosis and 809 were black with some degree of carotid artery stenosis. 1045 people were black with no stenosis and 809 were black with carotid artery stenosis. 897 were Hispanic with no stenosis and 575 were Hispanic with some degree of carotid artery stenosis.

Socioeconomic Status: Among those earning less than 5,000-89 had no stenosis and 66 had some stenosis, Among those with incomes between 5,000 and 7,999, 125 had no stenosis and 123 had some stenosis. Among those with incomes between 8000 and 11999, 185 had no stenosis and 164 had some degree of stenosis. Among those with incomes between 12000 and 15999, 257 had no stenosis and 206 had no stenosis. Among those with incomes between 16000 and 19999, 169 had no stenosis and 148 had some stenosis. Among those earning between 20000 and 24,999, 267 had some stenosis and 223 had no degree of stenosis. Among those earning between

$25,000-$29,999, 225, had no stenosis and 157 had some degree of stenosis. Among those with incomes between 30,000 and 34,999, 266 had no stenosis and 196 had some degree of stenosis. Among those with incomes between 35,000 and 39,999, 219 had no stenosis and 168 had some stenosis. Among those with incomes between 40,000 and 49,999, 349 had no stenosis and 288 had some stenosis. Among those with incomes between 50,000 and 74,999, 710, had no stenosis and 390 had some stenosis. Among those with incomes between 75,000 and 99,999, 370 had no stenosis and 223 had some stenosis. Among those with incomes greater than 100,000, 592 had no stenosis and 276 had some stenosis.

Education: Among those who had no schooling 36 had no carotid artery stenosis and 33 had some degree of stenosis. Out of the persons that had schooling to grades 1-8, 382 had no stenosis and 282 had some degree of stenosis. Among those with schooling to grades 9-11, 243 had no stenosis and 223 had some degree of stenosis. Among those who had completed high school/GED, 641 had no stenosis and 578 had some degree of stenosis. Among those who had some college but no degree, 617 had no stenosis and 474 had some degree of stenosis. Among those who had a technical school certificate, 274 had no stenosis and 208 had some degree of stenosis. Among those with an associates degree 200 had no stenosis and 131 had some degree of stenosis. Among those with a Bachelors degree 740 had no stenosis and 420 had some degree of stenosis. Among those with graduate or professional school 787 had no stenosis and 426 had some degree of stenosis

Insurance: Among the people with no insurance 399 had no stenosis and 197 had some degree of

stenosis. Among those with health insurance 3521 had no stenosis and 2579 had some degree of stenosis.

Table 2B: Distribution of demographic variables by the outcome variable

Demographic variables categories	No Stenosis	Carotid Artery Stenosis
Gender	2174	1366
Female	1753	1423
Male		
Race		
White	1393	1197
Asian	592	208
Black	1045	809
Hispanic	897	575
Socioeconomic Status		
<$5000	89	66
$5,000-$7,999	125	123
$8,000-$11,999	185	164
$12,000-$15,999	257	206
$16,000-$19,999	169	148
$20,000-$24,999	267	223
$25,000-$29,999	225	157
$30,000-$34,999	266	196
$35,000-$39,999	219	168
$40,000-$49,999	349	288
$50,000-$74,999	710	390
$75,000-$99,999	370	223
>$100,000	592	276
Education		
No schooling	36	33
Grades 1-8	382	282
Grades 9-11	243	223
Completed high school/GED	641	578
Some college but no degree	617	474
Technical School certificate	274	208
Associate Degree	200	131
Bachelors degree	740	420
Graduate or professional school	787	426
Health Insurance		
No Insurance	399	197
Health Insurance	3521	2579

Table 2C: Ch Square Correlations for Demographic Variables

Chi Square Correlations	Maximal Carotid Artery Stenosis	
Age	596.138	0.000*
Gender	26.649	0.000*
Race	109.958	0.0000*
Socioeconomic Status	76.768	0.000*
Education	63.209	0.000*
Insurance	19.038	0.000*

**. Correlation is significant at the 0.01 level (2-tailed).

Chi square correlations among the demographic variables and the outcome variable were all significant at the 0.05 level. Please refer table 2C.

Regression Model for Demographic Variables:

In the first model, the demographic variables were entered as independent predictors of the outcome carotid artery stenosis. 6451 cases were included in the analyses. The categorical variables, race, age categories, health insurance, gender, education and income were dummy coded. With race, Hispanics were used as the dummy variable and with age categories, 75-84 was used as the dummy variable.

Among the demographic variables that were entered into regression equation, age, gender, race and income were significant (<0.05). Insurance status and education were not significant. Among age categories, the default against which other categories were compared was the oldest age group. As the age groups got younger people were less likely to have carotid artery stenosis. Women were more at risk for carotid artery stenosis compared to men. Among the race categories, Hispanics were used as baseline in dummy coding and the results suggest that whites were 1.5 times more likely to have carotid artery stenosis compared with Hispanics, Asians were less likely (0.4) times to have carotid artery stenosis compared with Hispanics and blacks were 1.2 times more likely to have carotid artery stenosis. Socioeconomic status was a significant

predictor. Health insurance status and education also had a significant bearing on carotid artery stenosis. The R2 for the equation was .107 (Cox and Snell) and .145 (Nagelkerke)

Please refer table 2D for results of the logisitic regression for Demographic variables

Table 2D: Regression Results for Demographic Variables

Age	B	SE (B)	B exp	Significance
1: 45-54	-1.669	.098	.187	.000
2: 55-64	-.918	.093	.398	.000
3: 65-74	-.416	.087	.658	.000
4: 75-84				
Gender				
Female				
Male	-.348	.055	.706	.000
Race				
White	.416	.081	1.516	.000
Asian	-.707	.103	.493	.000
Black	.206	.083	1.229	.013
Hispanic				
Income	-.052	.009	.949	.000
Insurance Yes No	.015	.105	1.015	.883
Education	-.047	.098	.954	.635

Clinical Variables:

Continuous Clinical Variables

The distribution of clinical variables in the sample was as follows.

Ankle Brachial Index: The mean ankle brachial index was 1.1131 with a standard deviation of .12037.

Body Mass Index: The mean body mass index was 28.33 with a standard deviation of 5.43765.

Triglycerides: The mean triglycerides were 131.59, with a standard deviation of 88.80.

LDL Cholesterol: The mean value for LDL cholesterol was 117.20 with a standard deviation of

31.463.

HDL Cholesterol: The mean value for HDL cholesterol was 50.96 with a standard deviation of 14.828.

Total Cholesterol: The mean value for total cholesterol was 194.16 with a standard deviation of 35.733.

Please refer table 3A for the distribution of continuous clinical variables.

Table 3A Distribution of continuous clinical variables

Variable	N	Mean	Std Dev
Ankle Brachial Index	6735	1.1131	.12037
Body Mass Index	6814	28.3373	5.43765
Triglycerides	6791	131.59	88.801
LDL Cholesterol	6701	117.20	31.463
HDL Cholesterol	6788	50.96	14.828
Total Cholesterol	6791	194.16	35.733

Categorical Clinical Variables:

Hypertension by JNC 7 criteria: Among the categorical clinical variables, 3756 or 55.1% of the sample did not have Hypertension by the JNC 7 criteria and 3058 or 44.9% of the sample did have hypertension.

Anti-Hypertensive Medication: 4275 or 62.7% of the sample did not take anti-hypertensive medications and 2536 or 37.2% of the sample did take anti-hypertensive medications.

Diabetes by ADA criteria: 5274 or 77.4% of the sample had normal blood sugars by the ADA criteria. 545 or 8% had impaired fasting glucose, 291 or 4.3% had untreated diabetes and 680 or 10% of the sample had treated diabetes.

Family History of Heart Attack: 3661 of 53.7% of the sample had no family history of heart attack and 2734 or 40.1% had family history of heart attack.

Please refer Table 3B & 3C for the distribution of the categorical clinical variables

Table 3B Distribution of Categorical Clinical variables

Variable	N
Hypertension by JNC 7 criteria	
No	3756 (55.1%)
Yes	3058 (44.9%)
Hypertension medication	
No	4275 (62.7%)
Yes	2536 (37.2%)
Diabetes Mellitus by ADA criteria	
Normal	5274 (77.4%)
IFG	545 (8%)
Untreated Diabetes	291 (4.3%)
Treated Diabetes	680 (10%)
Family History of Heart Attack	
No	3661 (53.7%)
Yes	2734 (40.1%)

Table 3C: Distribution of Categorical Clinical Variables by Outcome

	No carotid artery stenosis	Carotid Artery Stenosis
Hypertension by JNC 7 criteria		
No	2718	1507
Yes	1208	1280
Hypertension medication		
No	2718	1507
Yes	1208	1280
Diabetes Mellitus by ADA criteria		
Normal	3048	1884
IFG	484	432
Untreated Diabetes	93	86
Treated Diabetes	289	379
Family History of Heart Disease		
Yes	2228	1382
No	1455	1236

In the sample, among those who did not take antihypertensives 1507 had some degree of carotid artery stenosis and 2718 did not have carotid artery stenosis. Among those that took antihypertensives (2488 persons), 1280 had carotid artery stenosis and 1208 did not have carotid artery stenosis. Chi square tests between having Hypertension by the JNC 7criteria and carotid artery stenosis were significant. Out of the 3714 patents that did not have hypertension by JNC 7, 2501 did not have carotid artery stenosis and 1213 had carotid artery stenosis. Of the 3002 patients that did have hypertension, 1576 had carotid artery stenosis and 1426 did not have

carotid artery stenosis. Chi square tests between DM by ADA 2003 criteria and carotid artery stenosis were significant at the 0.05 level. Of the 4932 patients who did not have DM, 3048 did not have carotid artery stenosis and 1884 had carotid artery stenosis. Of the 916 in the sample who had indeterminate fasting glucose values, 484 did not have carotid artery stenosis and 432 had some degree of carotid artery stenosis. Of the 179 patients who had untreated DM, 93 did not have Carotid artery stenosis and 86 had some degree of carotid artery stenosis. Of the 668 persons who had treated diabetes, 289 did not have carotid artery stenosis and 379 had some degree of carotid artery stenosis.

Table3D: Chi Square Correlations for Clinical Variables

Chi Square Correlations	Maximal Carotid Artery Stenosis	
Family History of Heart Attack	37.136	0.000*
Hypertensive Medications	160.556	0.000*
Hypertension by JNC crietria	269.064	0.000*
Diabetes by ADA criteria	101.227	0.000*
Education	63.209	0.000*
Insurance	19.038	0.000*

**. Correlation is significant at the 0.01 level (2-tailed).

Table 3E: Regression results for Clinical Variables: Regression model for clinical variables

The R 2 for the model was .064 (Cox andSnell) and .087 (Nagelkerke).

	B	S.E	Exp (B)	Sig
Diabetes by 2003 ADA criteria				
Normal				
IFG	-.572	.095	.564	.000
Untreated DM	-.342	.113	.711	.003
Treated DM	-.225	.188	.799	.232
HTN by JNC VI				
No				
Yes	-.649	.077	.522	.000
Family History of Heart Attack				
No				
Yes	-.264	.055	.768	.000
Antihypertensive medication				
No				
Yes	-.033	.079	.967	.676
LDL cholesterol	.034	.091	1.034	.711
HDL Cholesterol	.026	.091	1.026	.778
Total cholesterol	-.030	.091	.971	.742
Triglycerides	.006	.018	1.006	.722
BM Index	-.009	.005	.991	.106
AB Index	-1.959	.243	.141	.000

In the regression analysis, having no diabetes was considered the baseline. Compared to this group, persons with impaired fasting glucose and untreated diabetes were significantly related to having maximal carotid artery stenosis where as the group with treated diabetes was not significant, Having a family history of a heart attack was a significant predictor of the outcome as was having hypertension by the JNC criteria. Among the continuous clinical variables, only the AB Index was a significant predictor of the outcome.

Psychological Variables

The distribution of psychological variables in the sample is as follows.

Spielberger Trait Anger Scale: The mean value for the Spielberger trait anger scale was 14.75 (range from 10-30) and a standard deviation of 3.66.

Chronic Burden Scale: The mean value for the Chronic burden scale was 1.09 (range 0-5) and standard deviation of 1.16.

Center for Epidemiologic Studies-Depression Scale: The mean value for the Center for Epidemiologic Studies-Depression scale was 7.58 (range 0-53) and a standard deviation of 7.59.

Emotional Social Support Index: The mean value for the Emotional Social Support Index was 24.17 with a range of (6-30) and a standard deviation of 5.278.

Perceived Discrimination over a Lifetime: The mean value for the perceived discrimination over a lifetime was .74 (range 0-6) and a standard deviation of 1.079.

Everyday Hassles Scale: The mean value for everyday hassles was 14.47 (range for 9-54) and a standard deviation of 6.011.

Spielberger Trait Anxiety Scale: The mean value for the Spielberger Trait Anxiety Scale was 15.89 with a range from 10-37 and a standard deviation of 4.51.

Table 4A with Distribution of Psychological variables (continuous scales)

Variable	N	Mean	Std Dev	Range
Spielberger Trait Anger Scale	6782	14.7467	3.65813	10-30
Chronic Burden Scale > 6 months	6683	1.09	1.162	0-5
Center For Epidemiologic Studies-Depression scale	6778	7.58	7.591	0-53
Emotional Social Support Index	6768	24.17	5.278	6-30
Perceived Discrimination Lifetime	6695	.74	1.079	0-6
Everyday Hassles	6743	14.47	6.011	9-54
Spielberger Trait Anxiety Scale	6775	15.89	4.512	10-37

Regression Results for Psychological variables: The regression model showed that spielberger trait anger scale, and the everyday hassles scale were significant predictors of carotid artery stenosis at the 0.05 level. The chronic burden scale, center for epidemiologic depression scale, emotional social support index and spielberger trait anxiety scale were not significant predictors. Please refer Table 4B below for results of the regression model

Table 4B: Regression Results for Psychological Variables

Predictor Variable	B	S.E (B)	B exp	Sig
Spielberger Trait Anger Scale	-.017	.008	.983	.030
Chronic Burdens >6 months	-.009	.025	.991	.721
Center for Epidemiologic studies Depression scale	.006	.005	1.006	.183
Emotional Social Support index	-.005	.005	.995	.391
Everyday hassles	-.023	.005	.978	.000
Spielberger trait anxiety scale	-.009	.098	.991	.242
Perceived discrimination over a lifetime	-.026	.026	.974	.321

The Cox and Snell R Square for the model was .007 and the Nagelkerke R Square was .010

Social Variables:

Distribution of Social Variables in the Data: The distribution of social variables was as follows

Neighborhood Social Cohesion Scare: The mean value for the Neighborhood Social Cohesion score was 17.53 with a range from 5-25 and a standard deviation of 2.895.

Neighborhood Problems Score: The mean value for the neighborhood problems score was 10.41 with a range from 7-28 and a standard deviation of 3.373.

Length of Time Lived in Neighborhood: The mean length of time lived in the neighborhood was 18.79 years with a range from 8-81 years and a standard deviation of 14.31.

Please refer table 5A for the distribution of the Social Variables in the data

Table 5A Distribution of Social Variables (Scores)

Variable	N	Mean	Std Dev	Range
Neighborhood social Cohesion Score	6765	17.53	2.895	5-25
Neighborhood Problems Score	6729	10.41	3.373	7-28
Length of time lived in neighborhood	6769	18.7936	14.31160	.08-81

Regression Results for Social Variables: Of the social variables, only the length of time people had lived in the neighborhood was a significant predictor of the outcome variable at the 0.05 level. For every one unit increase in length of time lived in neighborhood, the likelihood of carotid artery stenosis increased by 1.02. The R2 for the social variables model was .021 (Cox and Snell) and .028 (Nagelkerke). Please refer to Table 5B for the Regression Results for Social

Table 5B for Regression results among Social variables

	B	S.E (B)	B Exp	Sig
Neighborhood social Cohesion Score	.017	.009	1.018	.060
Neighborhood Problems Score	-.013	.008	.987	.119
Length of time lived in neighborhood	.020	.002	1.020	.000

Behavioral Variables:

Distribution of Continuous Behavioral Variables in the Sample:

The distribution of behavioral variables in the sample is as follows.

Total Physical Activity: The mean number of total physical activity hours per day was 12.6 with a range from 0-82 and a standard deviation of 5.9.

Pack Years of Cigarette Smoking: The mean pack years of cigarette smoking was 11.4 with a range from 0-640 and a standard deviation of 22.3.

Years Drinking Alcohol: The mean number of years drinking alcohol was 31.7 with a range from 0-68 and a standard deviation of 16.

Drinks per Week: The mean number of drinks per week was 5 with a range from 0-99 and a

standard deviation of 9.3.

Distribution of Categorical behavioral variables in the Sample:

Cigarette Smoking: 3418 persons had never smoked a cigarette (50.2%), 2487 persons were former smokers (36.5%) and 887 were current smokers (13%).

Alcohol Consumption: Of the sample 1726 or 25.3% of the sample did not consume alcohol, whereas 3749 persons or 55% of the sample consumed alcohol.

Please refer Table 6A and B for Distribution of continuous and categorical behavioral variables

Table 6A Distribution of Continuous Behavioral Variables

Variable	N	Mean	Std Dev	Range
Number of total physical activity hours per day	6795	12.5965	5.86933	0-82.10
Pack years of cigarette smoking	6720	11.3978	22.25225	0-640
Number of years drinking alcohol	5332	31.73	15.98	0-68
Number of drinks per week	5353	5.07	9.292	0-99

Table 6B Distribution of Categorical Behavioral Variables

Variable	N
Cigarette smoking status	
Never	3418 (50.2%)
Former	2487 (36.5%)
Current	887 (13%)
Current alcohol consumption	
No	1726 (25.3%)
Yes	3749 (55%)

Distribution of Categorical Behavioral variables by the Outcome Variable:

Of the 1369 persons who had never used alcohol, 859 did not have carotid artery stenosis, where as 510, did have some degree of carotid artery stenosis. OF the 1599 persons who were former smokers 891 did not have carotid artery stenosis whereas 708 had some degree of carotid artery stenosis . Of the 3702 persons who are current smokers, 2157 did not have carotid artery stenosis whereas 1545 had some degree of carotid artery stenosis. Of the 3375 persons who had never smoked 2176 had no carotid artery stenosis whereas 1199 has some degree of stenosis Of the 2449 former smokers, 1291 had no carotid artery stenosis, whereas 1158 had some degree of stenosis. Of the 872 current smokers, 453 had no stenosis, whereas 419 had some degree of stenosis. Of the 5161 persons who did not take an aspirin on at least 3 days of the week, 3158 did not have carotid artery stenosis and 2003 had some degree of stenosis. Of the 1273 persons that did take an aspirin on at least 3 days of the week, 603 had no stenosis and 670 had some degree of stenosis. Please refer table 6C for the Distribution of Categorical Behavioral Variables in the sample

Table 6C: Distribution of categorical behavioral variables by Outcome

	No Stenosis	Carotid artery stenosis
Alcohol Use		
Never	859	510
Former	891	708
Current	2157	1545
Cigarette Smoking		
Never	2176	1199
Former	1291	1158
Current	453	419
Current aspirin use		
No	3158	2003
Yes	603	670

Regression Model for Behavioral Variables:

The R square for the model with behavioral variables was .066(Cox and Snell) and .089 (Nagelkerke). Of the variables entered into the model, the number of hours of physical activity per day had a significant effect on the outcome. For every one hour of physical activity per day increment, the likelihood of carotid artery stenosis went down by .98. Alcohol use also had a significant effect on the outcome. Current alcohol users were 1.825 times more likely to have carotid artery stenosis and former alcohol users where 13.65 times more likely to have carotid artery stenosis as opposed to people who never used alcohol. The number of drinks of alcohol per week was not significant. The number of years of drinking alcohol was a significant predictor. With every one year increment in alcohol drinking, the likelihood of carotid artery stenosis increased by 1.03. Pack years of cigarette smoking was a significant predictor and for every additional pack year of cigarette smoking, the likelihood of carotid artery stenosis increased by 1.01. Only cigarette smoking had a significant effect on carotid artery stenosis. Please refer table 6D for results of the Regression Model

Table 6D: Regression Model for Behavioral Variables

Predictor	B	S.E (B)	B (exp)	Sig
Physical Activity hours per day	-.020	.005	.980	.000
Alcohol User				
Never				
Former	2.614	.828	13.648	.002
Current	.602	.078	1.825	.000
Number of drinks per week	-.001	.003	.999	.843
Years of alcohol consumption	.029	.002	1.029	.000
Pack Year of cigarettes	.011	.002	1.011	.000
Cigarette smoking				
Never				
Former	-.139	.088	.871	.117
Current	-1.161	.143	.313	.000

Chapter 6: Discussion

Among the demographic variables, age categories were a significant predictor. The likelihood of carotid artery stenosis increases with age. This is in keeping with prior research. Among the racial subgroups, our analyses confirms prior research in that compared with Asians and Hispanics, Blacks and Whites are more likely to have carotid artery stenosis. Income and Insurance status were also significant predictors of carotid artery stenosis. However, marital status and education did not have significant effect on carotid artery stenosis. Among the clinical variables, our research showed that cholesterol levels did not have significant effect on carotid artery stenosis. This would require further investigation as we know high LDL and low HDL to impact coronary artery disease. Whether these become significant predictors at the level of clinically manifest disease but do not impact subclinical processes within the body, would need further investigation. Further it is possible that cholesterol levels have a greater impact on coronary artery stenosis than on carotid artery stenosis. This would favor the explanation that these values impact clinical disease more so than subclinical disease. Whether cholesterol levels need to be followed in patient's without known coronary artery disease is a broader policy question that could arise as a result of this finding. Having untreated diabetes was a significant predictor of the outcome. This is important since carotid artery stenosis is not used clinically as a marker for progression of diabetes. In clinical practice, the progression of diabetes is monitored by blood tests for nephropathy with a micro albumin/creatinine ratio, and retinopathy with an opthalmoscopic exam , glycosylated hemoglobin and neuropathy with a physical exam. This finding could suggest that carotid Doppler ultra sonography be another test to monitor

progression of diabetes. Hypertension was found to be a significant predictor however being on anti-hypertensive medication was not a significant predictor. There could be several explanations for this finding including length of time on anti-hypertensives and degree of blood pressure control achieved as well as appropriateness of therapy.

Among the psychological variables, only the Spielberger trait anger scale and everyday hassles scale were significant predictors of carotid artery stenosis. Interestingly the Spielberger anxiety scale was not a significant predictor, nor was the chronic burden scale or center for epidemiologic studies scale for depression. This could suggest that the body's mechanisms for short term stress such as one experiences with anger or daily hassles trigger a cascade of events which effects carotid artery stenosis as opposed to anxiety or chronic burden or depression which tend to be more long term insults.

Among the social variables, only the length of time the person had lived in a neighborhood seemed to be a significant predictor of carotid artery stenosis. There is not much research or clinical focus on the effect of social or neighborhood factors on subclinical cardiovascular disease, hence further research is necessary to understand this finding.

Among the behavioral variables the number of hours of physical activity was a significant predictor of CVD. This is in keeping with previous research.

Chapter 7: Conclusions and Policy Implications:

Our research supports most of the previously known findings with regards to the risk of developing carotid artery stenosis. We learn, through these analyses of some new factors that can be targeted to decrease risk. More so, we learn that we can impact risk and measure the impact of individual factor disease progression even before clinical disease begins. This research has policy implications for this very reason. Clinical practice today is focused on identifying and targeting risk factors, but we have to wait till clinical disease occurs to determine the impact our interventions or lack thereof have on the disease process. Now, we can measure subclinical disease and look at factors which impact subclinical disease even before clinical disease occurs. Also, this research shows us that there are factors other than those typically dealt with in the clinician's office which can be addressed to decrease or modify the risk for atherosclerotic cardiovascular diseases

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