THE ASSOCIATION BETWEEN MENOPAUSE STATUS, AGE, AND CHOLESTEROL: THE HILO WOMEN'S HEALTH STUDY

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By:

Nichole J. M. Rahberg

Thesis Committee:

Alan Katz, Chairperson
Eric Hurwitz
Daniel Brown

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Abstract

Cardiovascular diseases (CVDs) are the number one killer worldwide, in the United States, and in the state of Hawai'i. Women's risk for CVDs increases after menopause, partially due to changing cholesterol levels. The Hilo Women's Health Study seeks to advance knowledge of women going through the menopausal transition in the multiethnic population of Hilo, Hawai'i, including Asian Americans, Native Hawaiians, and Pacific Islanders. The two phase, cross-sectional study obtained information on 189 women from the ages of 45 to 55. Menopausal status was divided into premenopause, perimenopause, and postmenopause, and regressed on total cholesterol, HDL-C, LDL-C, triglycerides, and the triglyceride to HDL-C ratio. After adjusting for potential confounders, menopause status was significantly associated with total cholesterol and LDL-C. However, ethnicity was significantly associated with all of the cholesterol measures. Conversely, age was not found to be associated with any of the measures.

Table of Contents

List of Tables

List of Figures

Chapter 1

Introduction

Cardiovascular diseases (CVDs) are the leading cause of death worldwide. Atherosclerosis disease, which includes coronary heart disease and stroke, make up the vast majority of CVD fatalities. In 2012, the World Health Organization [WHO] (2014) estimated 17.5 million deaths worldwide as the result of CVDs, with the majority resulting from coronary heart disease (7.4 million) or stroke (6.7 million). A similar trend can be seen in the United States: In 2008, heart disease was the leading cause of death, accounting for 25% of total fatalities. For women, heart disease was also the leading killer, accounting for 24.5% of all deaths. Among Asian American and Pacific Islander women, heart disease was the second highest cause of death from the ages of 35 to 64, and the highest cause of death from 65 years of age and older. Heart disease did not become the second highest cause of death for European American and American Indian or Alaskan Native women until between the ages of 45 and 54, but became number one from 65 years of age. Strokes were the fourth leading cause of fatalities, comprising 5.4% of the total deaths that year. However, when compared by sex, 6.5% of the fatalities in women were due to strokes, making them the third leading cause of death for women (Heron, 2012).

The state of Hawai’i follows a similar pattern to the world and United States, with CVDs as the number one cause of death in the state. The Hawaii State Department of Health (2011) reported that in 2009, CVDs resulted in 32% of fatalities, with 73% of those from heart disease and 21% from stroke. When using age adjusted rates, Hawai’i County had the highest coronary heart disease mortality rates (93.4 deaths per 100,000) and the second highest stroke mortality rates (42.7 deaths per 100,000). Native Hawaiian women had the highest coronary heart disease mortality rates (79.6 deaths per 100,000) and second highest stroke mortality rates (37.7 deaths per 100,000) when compared to Filipino, Japanese, and European American women.

Due to such high numbers of death, health care professionals routinely assess patients’ risk for CVDs. Risks for CVDs include abnormal lipid profiles, high blood pressure, being categorized as overweight or obese, lack of physical activity, an unhealthy diet, socioeconomic status, age, gender, and stress (Mendis et al., 2011). Doctors routinely test patients' total cholesterol, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and triglycerides. According to the National Institutes of Health, NIH, (2005), total cholesterol should be lower than 200 mg/dL, HDL-C, often referred to as "good" cholesterol, should be greater than 40 mg/dL, LDL-C, also known as "bad" cholesterol, should be less than 100 mg/dL, and triglycerides should be less than 150 mg/dL.

Recently, the triglyceride to HDL-C ratio has also been looked at as an important predictor of CVD. Based on the guidelines of normal triglyceride and HDL-C levels, a desirable triglyceride to HDL-C ratio would fall below 3.75 (Da Luz, Cesena, Favarato, & Cerqueira, 2005). Among women with suspected myocardial ischemia, the ratio was a significant predictor of all-cause mortality (Bittner et al., 2009). Similarly, among men with heart disease risk factors, such as a high LDL-C, their risk for heart disease was lowered when having low triglycerides and high HDL-C Jeppesen, Hein, Suadicani, & Gyntelberg, 2001).

Patients are often educated and screened for factors that can lead to unsatisfactory cholesterol levels. Risks include age, diabetes, an unhealthy diet, being categorized as overweight or obese, lack of physical activity, and family history (Center for Disease Control [CDC], 2010). NIH (2005) also includes gender, cigarette smoking, and high blood pressure as risk factors. Ethnicity (López, Rice, Weddle, & Rahill, 2008), socioeconomic status (Winkleby, Kraemer, Ahn, & Varady, 1998), stress (Evolahti, Hultcrantz, & Collins, 2009), and alcohol (National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2002) have also been shown to be associated with cholesterol. Women have an additional risk factor, menopause, which makes their situation unique (National Heart, Lung, Blood Institute & North American Association for the Study of Obesity, 2000). Multiple studies have assessed the relationship between menopause status and cholesterol.

Chapter 2

Literature Review

2.1 Menopause

Menopause is characterized by the cessation of periods for over twelve months. Generally, a woman does not realize she has transitioned through menopause until she is postmenopausal. The average age for natural menopause is 51, but the change can occur at any age due to surgery, radiation, medicine, autoimmune diseases, or premature ovarian failure (National Institute on Aging, 2008). Age at menopause has been found to be associated with ethnicity (Bromberger et al., 1997; Henderson, Bernstein, Henderson, Kolonel, & Pike, 2008), BMI (Henderson et al., 2008; Li et al., 2012), alcohol (Gold et al., 2013; Torgerson, Thomas, Campbell, & Reid, 1997), smoking (Dorjgochoo et al., 2008; Henderson et al., 2008; Li et al., 2012), physical activity (Dorjgochoo et al., 2008; Gold et al., 2013), socioeconomic status (Li et al., 2012; Gold et al., 2013), and stress (Bromberger et al., 1997; Cassou, Mandereau, Aegerter, Touranchet, & Derriennic, 2007).

Researchers use a variety of methods to determine a woman's menopause status. Not all researchers utilize the same guidelines, and despite similarly defined categories, subtle differences have the potential to impact results and cause confusion when interpreting or comparing studies (Sherman, 2005). For example, Pasquali et al. (1997) used a combination of hormones, menstrual cycle regularity, and symptoms to categorize women by menopausal status. Premenopausal women had normal menstrual cycles or had cycles for at least ten months out of the year, and did not have menopausal symptoms. Perimenopausal women had at least one period within the prior six months or experienced menopausal symptoms. Lastly, postmenopausal women experienced amenorrhea for at least one year, including surgically induced, and produced low oestradiol and high follicle-stimulating hormone (FSH).

In contrast, Matthews et al. (2009) divided menopause status into three segments based on changes in FSH throughout the menopausal transition. FSH levels increase throughout the menopausal transition before maintaining a steady level in postmenopause (Sievert, 2006). Matthews et al. (2009) considered segment one to be greater than one year before the final menstrual period, segment two was considered within one year before and after the final menstrual period, and segment three was considered more than one year after the final menstrual period. In an attempt to standardize menopause status, the Stages of Reproductive Aging Workshop (STRAW) set guidelines to assist researchers (Sherman, 2005).

2.2 Menopause Status and Cholesterol

Regardless of when a woman experiences the transition, changes in lipids are associated with menopause, and consequently, increased risk of CVDs. Up until menopause, women tend to experience less risk than men for CVDs. Although risk increases for postmenopausal women when compared to premenopausal women, there tends to be higher incidence of CVDs for those who go through the transition at younger ages (Kannel, Hjortland, McNamara, & Gordon, 1976). The majority of studies conducted on cholesterol and menopause status include total cholesterol, HDL-C, LDL-C, and triglycerides, as those are most often tested by health care providers due to their relationship with CVDs (Hall, Collins, Csemiczky, and Landgren, 2002; Pasquali et al., 1997). Biologically, there is plausibility for the total cholesterol and LDL cholesterol levels being higher in postmenopausal women. Estrogen has been found to maintain lower levels of LDL and higher levels of HDL (Guetta & Cannon, 1996).

Multiple studies have found a significant association between menopause status and total cholesterol. In general, postmenopausal women have higher levels than premenopausal (Peters et al., 1999; Schaefer et al., 1994) and perimenopausal women (Pasquali et al., 1997). Using data from the Study of Women's Health Across the Nation (SWAN), Derby et al. (2009) tested the association of cholesterol with five menopause status categories rather than three: premenopause, early perimenopause, late perimenopause, early postmenopause, and late postmenopause. Menopause status was associated with total cholesterol, with late perimenopause and early postmenopause having the highest mean total cholesterol values. Also using the SWAN study data, Matthews et al. (2009) observed that the largest increases in total cholesterol were found within one year before and after the final menstrual period.

Some researchers have observed a relationship between menopause status and HDL-C. Hall et al. (2002) noted that HDL-C was significantly higher among perimenopausal women. Similarly, Derby et al. (2009) observe a significant association between menopause status and HDL-C. Women in late perimenopause experienced the highest mean HDL-C levels before steadily decreasing. Matthews et al. (2009) found that levels rose dramatically more than one year before the final menstrual period, rose slightly within one year before and after the final menstrual period, and then began steadily declining more than a year after the final menstrual period. In contrast, HDL-C was not significantly associated with menopause status in some studies (Pasquali et al, 1997; Peters et al., 1999; Schaefer et al., 1994).

With regards to the relationship between menopause status and LDL-C, Peters et al. (1999) found that postmenopausal women had higher levels than premenopausal women. Additionally, Hall et al. (2002) observed that postmenopausal women had significantly higher LDL-C than both premenopausal and perimenopausal women. Menopause status was also significantly associated with LDL-C in the SWAN study. Late perimenopausal and early postmenopausal women experienced the highest mean levels (Derby et al., 2009). Similarly to total cholesterol, increases in LDL-C were greatest within one year before and after the final menstrual period (Matthews et al., 2009). In contrast, Pasquali et al. (1997) did not find a significant relationship between menopause status and LDL-C.

Triglycerides are often found not to be associated with menopause status (Hall et al., 2002; Matthews et al., 2009; Peters et al., 1999) yet interestingly, Derby et al. (2009) observed a significant relationship between triglycerides and menopause status among women in the SWAN study. The relationship was similar to total cholesterol and LDL-C in that the highest mean levels were during late perimenopause and early postmenopause.

Age has an important relationship to both cholesterol and menopause status (Matthews et al., 2009). Derby et al. (2009) and Hall et al. (2002) suggested that both menopause and age have similar impacts on cholesterol. In addition to a combined model with menopause status and age, some researchers also create separate models for age and menopause. When Pasquali et al. (1997) removed menopause status from their regression, age became significantly associated with total cholesterol. They also found a relationship between HDL-C and age, despite menopause status remaining in the model. In the SWAN study, triglyceride levels were shown to be associated with ageing rather than the menopausal transition (Matthews et al., 2009).

2.3 Ethnicity

Ethnic health disparities are of growing interest in the United States. The Hawaii State Department of Health (2011) reported that in 2009, the prevalence of high cholesterol was highest among Japanese adults (45.9%) and second highest among Native Hawaiians (37.7%). According to the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (2002), African American and

European American women had similar levels of LDL-C and HDL-C, while European American women had higher levels of triglycerides than African Americans. However, Hispanics had lower HDL-C and higher triglycerides.

In a study using 2001 and 2002 data from the National Health and Nutrition Examination Survey (NHANES), a relationship between HDL-C and ethnicity was observed. Non-Hispanic African American women were associated with having normal HDL-C levels, while Hispanics were associated with having unsatisfactory HDL-C levels (López et al., 2008). Among participants in the SWAN study, Japanese women had higher levels of HDL-C than African American women (Matthews et al., 2005).

2.4 Potential Confounders

BMI, a relationship between weight and height, is one of the most frequently used determinants of body fat. People are classified as overweight if their BMI ranges from 25 to 29.9 kg/m^2, and obese with a measure of 30 kg/m^2 or greater. Despite the controversy based on misclassification of individuals with large muscle mass as overweight or obese, the majority of people are properly categorized. Overweight and obese individuals have an increased risk of high cholesterol levels often related to diet and a lack of physical activity (National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2002). BMI has most notably been associated with triglycerides in which higher BMI resulted in higher triglyceride levels (Hall et al., 2002).

The Framingham Offspring Study collected data on men and women, aged 19 to 78 years, over a period of three years. BMI and total cholesterol, LDL-C, and triglycerides shared a positive linear association and BMI and HDL-C shared a negative linear association after adjusting for age in women. When dividing age into five categories, the number of overweight women increased across the age groups, with the percentage of those overweight tripling in the 50 to 59 years old category when compared to those younger than 30 years (Lamon-Fava, Wilson, & Schaefer, 1996). Similar results between BMI and cholesterol have been reported in other studies for total cholesterol (Pasquali et al., 1997), HDL-C (Hall et al., 2002; Pasquali et al., 1997), LDL-C (Pasquali et al., 1997), and triglycerides (Hall et al., 2002). However, Hall et al. (2002) did not observe a significant relationship between BMI and total cholesterol levels when analyzing the data using multiple regression.

The NIH (2005) lists blood pressure as a risk factor for LDL-C. In general, hypertension and unsatisfactory cholesterol levels are frequently found together (National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2002). Data analyzed from the Framingham Offspring Study indicated a positive association between blood pressure and LDL-C (Schaefer et al., 1994). In a study completed in Sweden, baseline analysis revealed an increase in systolic blood pressure was associated with an increase in total cholesterol, LDL-C, and triglycerides in women (Evolahti et al., 2009).

Alcohol shares a unique relationship with cholesterol: The WHO lists low to moderate alcohol usage as beneficial to HDL-C, but heavy usage as harmful (Mendis et al., 2002). Likewise, the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (2002) mentions moderate alcohol as potentially beneficial for HDL-C, but heavy usage as a risk factor for high triglycerides. For women 50 years of age and older, alcohol consumption offers a protective effect against low HDL-C (López et al., 2008). A study completed on women 30 years of age and older in the UK observed that total cholesterol decreased as average alcohol per week increased, except for those consuming 22 or more drinks. Additionally, HDL-C increased as average alcohol per week increased up to 15-21 drinks per week. No associations were observed with LDL-C or triglycerides (Nanchahal, Ashton, & Wood, 2000).

Unlike alcohol, tobacco's relationship is straightforward: tobacco negatively impacts cholesterol levels. National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (2002) lists smoking cigarettes as a risk factor for elevated LDL-C and triglycerides, as well as low HDL-C. For women 50 years of age and older, being a nonsmokers offers a protective effect against low HDL-C (López et al., 2008). While Evolahti et al. (2009) did not observe an association between smoking and HDL-C in women, they did find that smokers were associated with having higher total cholesterol and triglycerides at follow-up.

Physical activity is associated with raising HDL-C and lowering LDL-C and triglycerides (National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2002). López et al. (2008) observed a protective effect on HDL-C in physically active women 50 years of age and older. Among sedentary, obese, postmenopausal women, an intervention of resistance exercises over 12 weeks resulted in significant differences in cholesterol between the control and exercise groups. Initially, cholesterol levels were not significantly different between the two groups. Following the intervention, however, total cholesterol and LDL-C were significantly lower in the exercise group and significantly lower than pre-intervention levels (Wooten et al., 2011).

Socioeconomic status is often measured and analyzed using reported educational level or income (Mueller & Parcel, 1981). Winkleby et al. (1998) used education as a measure of scocioeconomic status when analyzing data from the NHANES III and observed a significant, positive association between non-HDL-C and education. However, some researchers have incorporated a subjective variable of socioeconomic status that allows the participants to rank themselves based on their perception of multiple socioeconomic measures. The English Longitudinal Study of Ageing analyzed the association between subjective socioeconomic status and health indicators among men and women 52 years of age and older. The authors observed an association between HDL-C and subjective socioeconomic status among women (Demakakos, Nazroo, Breeze, & Marmot, 2008).

Although not officially listed as a risk factor for abnormal cholesterol levels, stress has been linked to health. Job satisfaction (Brown, James, & Mills, 2006; Reza, Sievert, Rahberg, Morrison, & Brown, 2012) and life satisfaction (James, Baker, Jenner, & Harrison, 1987; Reza et al., 2012) have both been used as measures of stress in research. A study published on women reported that at follow-up, they observed an association between having control at work and a higher HDL-C, lower LDL-C to HDL-C ratio, and lower total cholesterol to HDL-C ratio. Conversely, higher job strain was associated with a higher LDL-C to HDL-C ratio and total cholesterol to HDL-C ratio at follow-up (Evolahti et al., 2009).

2.5 Hilo Women's Health Study

The Hilo Women's Health Study seeks to advance the knowledge of women going through the menopausal transition in the multiethnic population of Hilo. Based on the increased risks associated with postmenopausal status, such as high cholesterol, women who are going through the menopausal transition deserve special attention. The county of Hawai'i has the second highest prevalence of high cholesterol in the state (39.8%) and the overall state prevalence of women with high cholesterol is 36.3% (Hawaii State Department of Health, 2011).

To my knowledge, no study in Hilo has been done that focuses on this transitional period in women.

The National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (2002) reported that there was limited information on Asian and Pacific Islanders when they published their third report on cholesterol. Hilo's population provides an opportunity to provide the literature with more information on ethnic differences, specifically Asian Americans, Native Hawaiians, and Pacific Islanders. The year 2000 census reported 148,677 residents on the island of Hawai'i. Of those who reported one ethnicity, 26.7% were Asian American, 31.5% were European American, and 11.2% were Native Hawaiian or Pacific Islander. Of the 28.4% who listed two or more ethnicities, 19.8% were part Native Hawaiian or Pacific Islander (Department of Business, Economic Development & Tourism, n.d.).

This thesis focuses on the association between cholesterol levels, menopause status, and age among multiethnic women residing in Hilo, Hawai'i. I hypothesize that separately, both menopause status and age will be significantly associated with cholesterol levels, but when combined into one model, only menopause status will be significantly associated. Additionally, I hypothesize that postmenopausal women will have a higher mean total cholesterol, LDL-C, triglyceride, and triglyceride to HDL-C ratio, as well as a lower mean HDL-C, when compared to premenopausal and perimenopausal women.

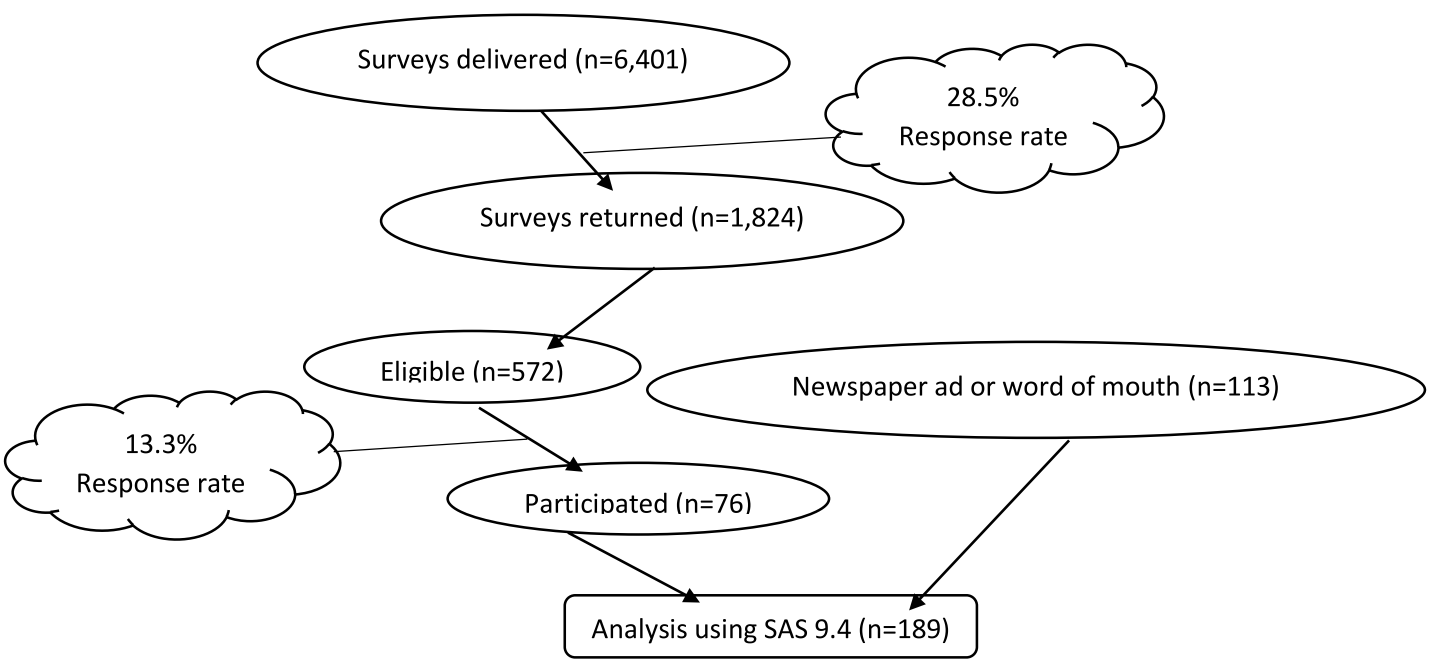
Chapter 3

Methodology

3.1 Participants

The Hilo Women's Health Study was a two phase, cross-sectional study that took place in the multiethnic population of Hilo, Hawai'i from 2005 to 2008 (Brown, Sievert, Morrison, Rahberg, & Reza, 2011). The first phase of the study consisted of mailing survey packets using a random number generator to select homes with the use of tax map keys for the Hilo district. Women 19 years of age or older were asked to participate. Of the 6,401 surveys delivered, 1,824 were returned, garnering a 28.5% response rate (Sievert et al., 2007). Women who were between the ages of 45 and 55 (n=572) were eligible to participate in the second phase of the study. Seventy-six agreed to participate in the current study, resulting in a 13.3% response rate. The remainder of the participants (n=113) were recruited from a newspaper ad or through word of mouth (Figure 3.1). Women who had diabetes, used blood pressure medication, cholesterol medication, hormone therapy, or birth control pills, or who had undergone a hysterectomy or oophorectomy were ineligible to participate (Brown et al., 2011).

Figure 3.1. Sample size flow diagram



3.2 Procedures

The second phase of the study consisted of two parts: a 24-hour ambulatory component and a four hour in-lab component. During the ambulatory component, the initial postal survey was administered to women who had been recruited through the newspaper or word of mouth, and readministered to women who had previously taken the survey in phase one. The survey included self-reported demographic questions such as age, ethnicity, subjective financial situation, and whether or not participants engaged in sports or exercised regularly, currently smoked, or currently drank alcoholic beverages. Participants were also asked to complete a life satisfaction and job satisfaction questionnaire, which were used as measures of stress.

Women wore an ambulatory blood pressure monitor (SpaceLabs 90217) for a 24-hour period in which readings were programmed to record blood pressure every 20 minutes during waking hours and every 30 minutes during sleeping hours. Readings were then averaged for systolic and diastolic blood pressure for use in analysis. Following the ambulatory period, a ten hour fasting blood draw was completed at Clinical Laboratories of Hawaii at participants' earliest convenience. After centrifugation, samples were sent to Northwest Lipid Metabolism and Diabetes Research Laboratories at the University of Washington for total cholesterol, LDL-C, HDL-C, and triglycerides levels (Brown et al., 2011). The triglyceride to HDL-C ratio was then computed by dividing women's triglyceride levels by their HDL-C levels. Women's current height, weight, and menopause status were collected during the in-lab component. Menopause status was determined through a questionnaire developed using guidelines from the Stages of Reproductive Aging Workshop (Sherman, 2005).

3.3 Variables

Total cholesterol, HDL-C, LDL-C, triglycerides, and the triglyceride to HDL-C ratio were used as outcome variables. Menopause status and age were the main predictors in this study. Ethnicity, BMI, systolic blood pressure average, whether participants currently drank alcohol or smoked, whether women regularly participated in sports or exercise, subjective income comfort, life satisfaction questionnaire total, and job satisfaction questionnaire total were controlled for as potential confounders. Questions were worded as yes or no questions with regards to whether or not participants currently consumed alcohol, smoked, or participated regularly in sports or exercise. All potential confounders were included in the models regardless of significance in univariate analysis based on a priori knowledge regarding their association with cholesterol and menopausal status.

Women were divided into three main menopausal groups based upon the methods used in Sherman (2005) for analysis: premenopausal, perimenopausal, and postmenopausal. Women who had menstruated within the last two months were classified as premenopausal. Participants were categorized as perimenopausal if they had not menstruated for more than two months and up to one year before they participated in the study. Women who had not menstruated in over a year were classified as postmenopausal (Sherman, 2005). Women were grouped by ethnicity into full Asian-American, full European-American, part or full Native Hawaiian and/or Pacific Islander, and other ethnicities. BMI was calculated using the equation: weight in kilograms/ (height in meters**2) (National Heart, Lung, Blood Institute & North American Association for the Study of Obesity, 2000). Although both systolic and diastolic blood pressure averages were recorded, only systolic blood pressure was used in analysis due to their high correlation ($r=0.83$, $p<0.0001$) and resulting multicollinearity problems.

A subjective socioeconomic question based on financial comfort was divided into struggling, okay, comfortable, and well-off. Due to the low amount of women reporting that they felt financially well-off (n=4), well-off and comfortable were combined into one variable. Two standardized measures of stress were utilized in this study: The life satisfaction questionnaire and the job satisfaction questionnaire. The life satisfaction questionnaire focused on changes that women wanted to make in their lives, including education, material possessions, and health, and how much the situation was bothersome on a scale of one to four. Responses were totaled, with a higher score indicating less satisfaction with their life. The job satisfaction questionnaire focused on stress in the working environment. After totaling the responses, a resulting higher score indicated less job satisfaction (Reza et al., 2012). Both the lifestyle and job questionnaires were tested for their internal consistency reliability in this study's population and were found to have a Cronbach's alpha of 0.78 and 0.83 respectively.

3.4 Analysis

Data analysis was completed using SAS 9.4. Summary statistics of participant characteristics were acquired for all variables of interest. Triglycerides and the triglyceride to HDL-C ratio were heavily skewed and therefore transformed using natural log before analysis. Mean values for total cholesterol, HDL-C, LDL-C, triglycerides, and the triglyceride to HDL-C ratio were compared for all categorical values in T-Test and ANOVA univariate analysis. Results of the T-Test were based on the pooled method unless the equality of variance was less than 0.05, in which the Satterthwaite method results were then used. Tukey's method was used for all ANOVA post-hoc tests. Although Games-Howell (GH) is the preferred method for violations of homogeneity of variances, the option was unavailable in SAS 9.4. SAS Institute Inc. (2009) indicates that Tukey's method is an acceptable substitution for the GH method. Variables that were converted for analysis were back transformed for presentation.

Five linear regression models were created to test the association of menopause status with each cholesterol variable of interest: total cholesterol, HDL-C, LDL-C, triglycerides, and triglyceride to HDL-C ratio. The first model (n=182) analyzed menopause status independently and the second model (n=161) included the potential confounders. The third model (n=179) analyzed age independently and the fourth model (n=158) included the potential confounders. The fifth, and final model, (n=158) was a combination of menopause status, age, and the potential confounders. Results are presented as log transformed for interpretation as percent changes (Vittinghoff, Shiboski, Glidden, & McCulloch, 2005).

Chapter 4

Results

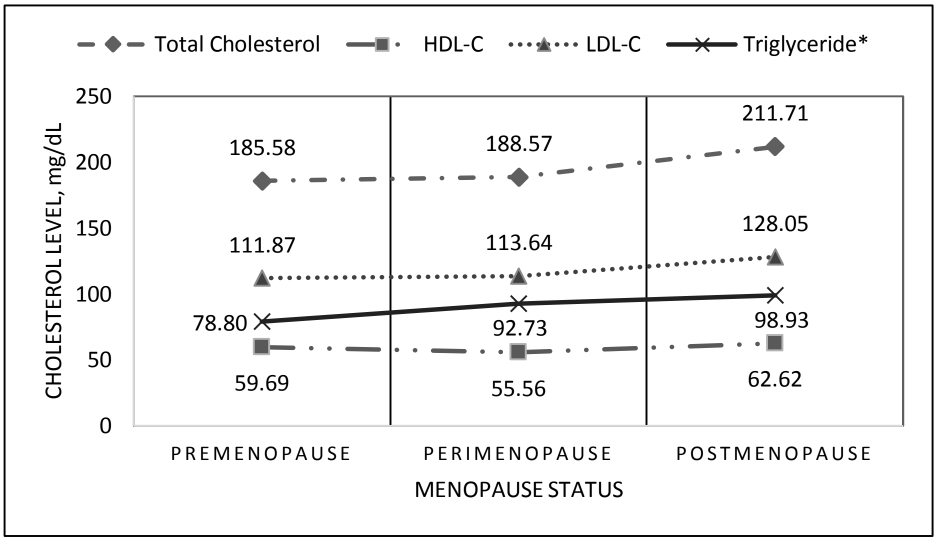
4.1 Characteristics

Means, standard deviations, sample sizes, and percent of participants' characteristics are presented in Table 4.1. Participants were found to have an average total cholesterol of 194.99 mg/dL, HDL-C of 58.73 mg/dL, LDL-C of 117.65 mg/dL, triglycerides of 103.78 mg/dL, and triglyceride to HDL-C ratio of 2.06. The majority of the participants were perimenopausal (41.18%), European American (38.10%), and felt okay with their income (42.25%). More than half of the women played sports or exercised regularly (63.24%) and currently consumed alcohol (55.68%), but less than half currently smoked (12.23%).

Almost half of the women had high total cholesterol (42.93%) and more than half had high LDL-C (72.28%). Less than a quarter of the participants had low HDL-C (9.78%), high triglycerides (14.67%), and high triglyceride to HDL-C ratio (10.87%). Of the women who were premenopausal, 25.00% had high total cholesterol, 7.69% had low HDL-C, 75.00% had high LDL-C, 11.54% had high triglycerides, and 7.69% had a high triglyceride to HDL-C ratio. With regards to women who were perimenopausal, 40.00% had high total cholesterol, 12.00% had low HDL-C, 66.67% had high LDL-C, 14.67% had high triglycerides, and 13.33% had a high triglyceride to HDL-C ratio. Of the participants in postmenopause, 61.82% had high total cholesterol, 7.27% had low HDL-C, 76.36% had high LDL-C, 16.36% had high triglycerides, and 9.09% had a high triglyceride to HDL-C ratio.

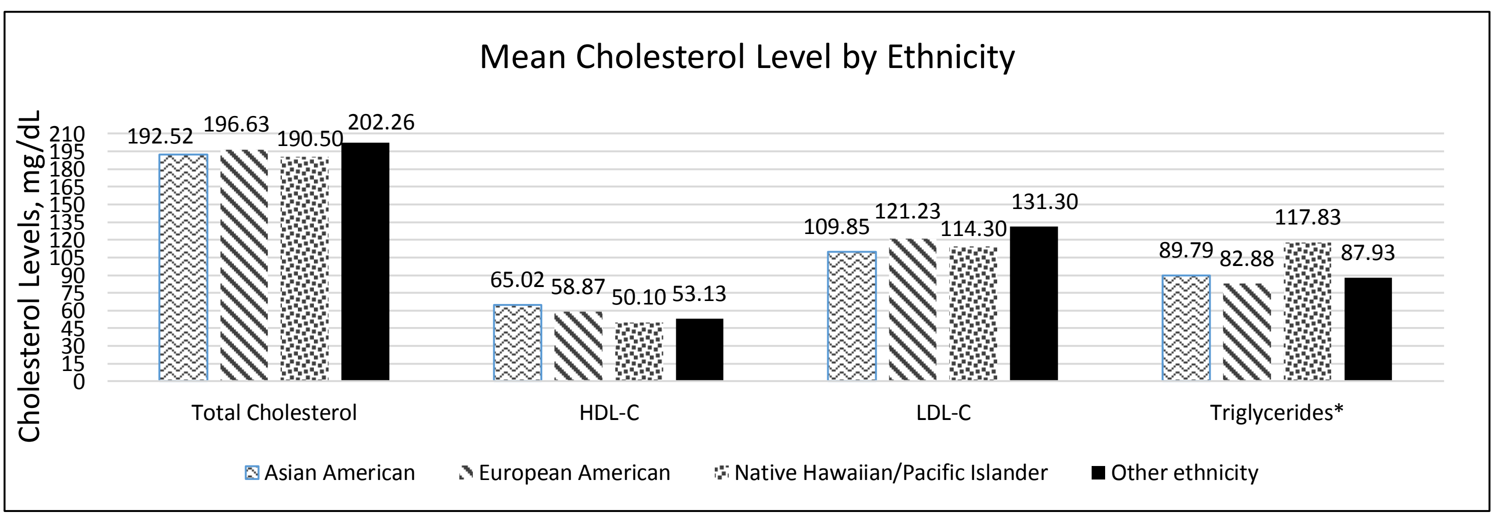
When mean cholesterol was compared by menopause status (Table 4.2), postmenopausal women had higher total cholesterol than premenopausal ($p<0.001$) and perimenopausal ($p<0.001$) women, higher HDL-C than perimenopausal women ($p<0.05$), higher LDL-C than premenopausal ($p<0.01$) and perimenopausal women ($p<0.01$), and higher triglycerides than premenopausal women ($p<0.05$). Mean cholesterol by menopause status can be visualized in Figure 4.1. Native Hawaiian and Pacific Islander women had significantly lower mean HDL-C than Asian American ($p<0.001$) and European American ($p<0.05$) women, higher mean triglycerides than European Americans ($p<0.01$), and a higher mean triglyceride to HDL-C ratio than Asian American ($p<0.01$) and European American ($p<0.01$) women. Asian American women had significantly higher HDL-C (p<0.01) and lower LDL-C (p<0.01) than other ethnicities. Mean cholesterol levels by ethnicity can be seen in Figure 4.2. Participants who currently consumed alcohol had a higher mean HDL-C and a lower mean triglyceride to HDL-C ratio when compared to those who did not drink. When current smokers were compared to non-smokers, women who smoked had higher mean triglycerides and triglyceride to HDL-C ratio. There were no significant differences between income comfort, nor those who played sports or exercised regularly.

Figure 4.1 Mean cholesterol level by menopause status



*Log transformed before analysis, then back transformed for presentation

Figure 4.2 Mean cholesterol level by ethnicity



*Log transformed before analysis, then back transformed for presentation

Table 4.1. Selected characteristics of participants

Characteristic (n)	Mean (SD) or n (%)
Total Cholesterol, mg/dL (184)	194.99 (32.07)
HDL Cholesterol, mg/dL (184)	58.73 (16.12)
LDL Cholesterol, mg/dL (184)	117.65 (28.00)
Triglyceride, mg/dL (184)	103.78 (63.87)
Triglyceride/HDL Ratio (184)	2.06 (1.81)
Menopause Status (187)	
Premenopausal	53 (28.34%)
Perimenopausal	77 (41.18%)
Postmenopausal	57 (30.48%)
Age, years (183)	50.46 (3.02)
Ethnicity (189)	
Asian American	60 (31.75%)
European American	72 (38.10%)
Native Hawaiian/Pacific Islander	30 (15.87%)
Other	27 (14.29%)
BMI, kg/m^2 (185)	25.64 (4.95)
Systolic Blood Pressure Average, mmHg (187)	114.05 (11.21)
Diastolic Blood Pressure Average, mmHg (187)	73.29 (7.48)
Current Drinkers (185)	103 (55.68%)
Current Smokers (188)	23 (12.23%)
Play Sports/Exercise Regularly (185)	117 (63.24%)
Income Comfort (187)	
Struggling	45 (24.06%)
Okay	79 (42.25%)
Comfortable/Well-off	63 (33.69%)
Life Satisfaction Questionnaire Total (187)	12.84 (7.57)
Job Satisfaction Questionnaire Total (179)	83.15 (12.11)

Table 4.2. Comparison of cholesterol by sample characteristics

Characteristic (n)	Mean Total Cholesterol (p-value)	Mean HDL Cholesterol (p-value)	Mean LDL Cholesterol (p-value)	Mean Triglyceride[a] (p-value)	Mean Triglyceride/HDL Ratio[a] (p-value)
Menopause Status	(<0.0001)	(0.0425)	(0.0032)	(0.0473)	(0.1317)
Premenopausal (52)	185.58***[b]	59.69	111.87**[b]	78.80*[b]	1.36
Perimenopausal (75)	188.57***[b]	55.56*[b]	113.64**[b]	92.73	1.72
Postmenopausal (55)	211.71	62.62	128.05	98.93	1.65
Ethnicity	(0.5131)	(<0.0001)	(0.0076)	(0.0116)	(0.0019)
Asian American (60)	192.52	65.02***[c]	109.85	89.79	1.42**[c]
European American (71)	196.63	58.87*[c]	121.23	82.88**[c]	1.46**[c]
Native Hawaiian/Pacific Islander (30)	190.50	50.10	114.30	117.83	2.42
Other (23)	202.26	53.13**[d]	131.30**[d]	87.93	1.69
Current Drinkers	(0.8199)	(0.0028)	(0.2970)	(0.0741)	(0.0121)
Yes (100)	194.60	61.98**	116.00	85.06	1.42*
No (80)	195.70	54.81	120.40	96.74	1.82
Current Smokers	(0.3989)	(0.0818)	(0.5474)	(0.0267)	(0.0159)
Yes (22)	200.50	53.09	121.00	113.31*	2.22*
No (161)	194.30	59.48	117.20	88.39	1.54
Play Sports/Exercise Regularly	(0.2741)	(0.1697)	(0.1431)	(0.4802)	(0.2709)
Yes (113)	192.70	59.87	115.10	89.57	1.55
No (67)	197.90	56.51	121.30	94.48	1.73
Income Comfort	(0.731)	(0.1856)	(0.6186)	(0.8170)	(0.5388)
Struggling (42)	196.21	55.12		93.51	1.75
Okay (78)	196.60	60.77	117.10	88.66	1.52
Comfortable/Well-off (62)	192.47	58.31	116.16	92.51	1.64

*p<0.05, **p<0.01, ***p<0.001.

[a]Log transformed before analysis, then back transformed for presentation

[b]Significantly different from postmenopausal women

[c]Significantly different from Native Hawaiian/Pacific Islander women

[d]Significantly different from Asian American women

4.2 Total Cholesterol

When menopause status was regressed alone on total cholesterol in Model 1 a significant linear relationship was identified, $F(2,179)=12.60$, $p<0.0001$ (Table 4.3). Premenopausal and perimenopausal women were associated with a decreased total cholesterol of 26.13 mg/dL ($p<0.001$) and 23.14 mg/dL ($p<0.001$) respectively when compared to postmenopausal women. When ethnicity, BMI, systolic blood pressure average, current alcohol intake status, current smoking status, current sport and exercise regularity, income comfort, and life and job satisfaction questionnaire totals were included as potential confounders to compute Model 2, the overall model remained significant, $F(14,146)=2.68$, $p=0.0016$. Women who were postmenopausal, of other ethnicity, and less satisfied with their job had higher total cholesterol levels. When compared to postmenopausal women, being premenopausal was associated with a 24.45 mg/dL ($p<0.001$) decrease in total cholesterol and being perimenopausal was associated with a 21.45 mg/dL ($p<0.001$) decrease in total cholesterol. When compared to Native Hawaiian and Pacific Islanders, other ethnicities had an average of 20.67 mg/dL ($p<0.05$) higher total cholesterol. A decrease in job satisfaction was associated with an increase in total cholesterol of 0.50 mg/dL ($p<0.05$).

When age was regressed alone in Model 3, age was linearly associated with total cholesterol, $F(1,177)=8.91$, $p=0.0032$. An increase in age, by years, resulted in an increase of cholesterol by 2.29 mg/dL ($p<0.01$). After the addition of the potential confounders in Model 4, age maintained a positive linear relationship with total cholesterol, although the overall model was not significant, $F(13,144)=1.78$, $p=0.0509$. Cholesterol increased by 2.22 mg/dL with a unit increase in age ($p<0.01$). In addition, a decrease in job satisfaction was associated with an increase in total cholesterol by 0.46 mg/dL ($p<0.05$).

Age and menopause status were combined with the potential confounders in Model 5, $F(15,142)=2.38$, $p=0.0044$. Menopause status, ethnicity, and job satisfaction were significantly associated with total cholesterol, but not age. When all other variables were held constant, premenopausal and perimenopausal women had a mean total cholesterol 19.31 ($p<0.05$) mg/dL and 19.09 mg/dL ($p<0.01$) lower than postmenopausal women, respectively. Other ethnicities had an 18.67 mg/dL ($p<0.05$) higher total cholesterol when compared to Native Hawaiian and Pacific Islanders. Similarly to Model 2 and Model 3, a decrease in job satisfaction ($p<0.05$) was associated with a 0.48 mg/dL increase in cholesterol.

Table 4.3. Multiple linear regression analysis summary for Total Cholesterol

	Model 1, n=182		Model 2, n=161		Model 3, n=179		Model 4, n=158		Model 5, n=158	
Characteristic	B	(95% CI)	B	(95% CI)	B	(95% CI)	B	(95% CI)	B	(95% CI)
Intercept	211.71		110.06		79.69		-17.48		66.22	
Menopause Status										
Premenopausal	-26.13***	(-37.67, -14.59)	-24.45***	(-37.04, -11.85)					-19.31*	(-34.05, -4.57)
Perimenopausal	-23.14***	(-33.73, -12.54)	-21.45***	(-32.46, -10.44)					-19.09**	(-30.89, -7.28)
Postmenopausal	ref		ref						ref	
Age, years					2.29**	(0.78, 3.81)	2.22**	(0.55, 3.89)	0.85	(-1.03, 2.73)
Ethnicity										
Asian American			7.82	(-7.22, 22.85)			7.13	(-8.51, 22.76)	5.39	(-9.94, 20.73)
European American			12.15	(-2.05, 26.35)			10.34	(-4.55, 25.23)	10.35	(-4.11, 24.80)
Native Hawaiian/Pacific Islander			ref				ref		ref	
Other			20.67*	(3.37, 37.97)			16.03	(-2.48, 34.54)	18.67*	(0.61, 36.72)
BMI, kg/m^2			0.43	(-0.61, 1.47)			0.60	(-0.48, 1.68)	0.47	(-0.59, 1.54)
Systolic Blood Pressure Average, mmHg			0.29	(-0.15, 0.72)			0.28	(-0.17, 0.73)	0.28	(-0.16, 0.72)
Current Dinkers			-1.81	(-11.37, 7.74)			-0.81	(-10.72, 9.10)	-1.37	(-10.99, 8.25)
Current Smokers			0.081	(-14.11, 14.27)			2.76	(-12.44, 17.95)	-0.024	(-15.12, 15.07)
Play Sports/Exercise Regularly			-3.06	(-13.17, 7.06)			-3.66	(-14.03, 6.71)	-3.10	(-13.33, 7.13)
Income Comfort										
Struggling			ref				ref		ref	
Okay			8.62	(-4.21, 21.44)			5.64	(-7.63, 18.91)	7.92	(-5.03, 20.86)
Comfortable/Well-off			3.49	(-10.14, 17.13)			1.84	(-12.38, 16.06)	3.08	(-10.74, 16.91)
Life Satisfaction Questionnaire Total			0.32	(-0.44, 1.09)			0.47	(-0.33, 1.26)	0.37	(-0.41, 1.14)
Job Satisfaction Questionnaire Total			0.50*	(0.091, 0.90)			0.46*	(0.040, 0.88)	0.48*	(0.079, 0.89)

*p<0.05, **p<0.01, ***p<0.001.

Model 1: Adj R^2 = 0.1137; F(2,179) = 12.60, p <0.0001; Model 2: Adj R^2 = 0.1283; F(14,146) = 2.68, p = 0.0016; Model 3: Adj R^2 = 0.0425; F(1,177) = 8.91, p = 0.0032;
Model 4: Adj R^2 = 0.0609; F(13,144) = 1.78, p = 0.0509; Model 5: Adj R^2 = 0.1163; F(15,142) = 2.38, p = 0.0044

4.3 HDL-C

A significant linear relationship between HDL-C and menopause status was identified in Model 1, $F(2,179)=3.21$, $p=0.0425$, as shown in Table 4.4. On average, perimenopausal women had an HDL-C 7.06 mg/dL ($p<0.05$) lower than postmenopausal women. After incorporating the potential confounders into the regression for Model 2, $F(14,146)=6.47$, $p<0.0001$, both premenopausal and perimenopausal women were associated with significantly lower HDL-C than postmenopausal women. Premenopausal women and perimenopausal women were linked with 7.48 mg/dL ($p<0.05$) and 5.84 mg/dL ($p<0.05$) decreases, respectively. Ethnicity, BMI, alcohol consumption, and reported income comfort were also related to HDL-C levels. Native Hawaiians and Pacific Islanders were found to have an average HDL-C 9.41 mg/dL ($p<0.01$) lower than Asian Americans. A unit increase in BMI decreased "good" cholesterol by 1.18 mg/dL ($p<0.001$). In contrast, women who consumed alcohol had an average 6.67 mg/dL ($p<0.01$) higher HDL-C level when compared to those who did not drink alcohol. Women who were okay with their income had 'good' cholesterol levels 6.12 mg/dL ($p<0.05$) higher than those who felt they were struggling.

When age alone was regressed in Model 3, $F(1,177)=4.85$, $p=0.0289$, there was a positive linear relationship with HDL-C. Levels increased by 0.88 mg/dL ($p<0.05$) for a yearly increase in age. The relationship between age and HDL-C remained significant upon the addition of potential confounders in Model 4, $F(13,144)=6.74$, $p<0.0001$. A yearly increase in age was associated with a 1.01 mg/dL ($p<0.01$) rise in "good" cholesterol. Ethnicity, BMI, and alcohol intake were again associated with HDL-C. Asian Americans had an average HDL-C level 10.12 mg/dL ($p<0.01$) higher when compared to Native Hawaiian and Pacific Islanders. A 1.06 mg/dL decrease was associated with a unit increase in BMI ($p<0.001$) and current alcohol drinkers had an average HDL-C 7.21 mg/dL ($p<0.01$) higher than those who abstained.

Both menopause status and age were no longer significantly associated with HDL-C when combined with the potential confounders in Model 5, $F(15,142)=6.08$, $p<0.0001$. However, ethnicity, BMI, and alcohol intake maintained their relationship. Native Hawaiian and Pacific Islanders had an average HDL-C 9.79 mg/dL ($p<0.01$) lower than Asian Americans. An increase in BMI was associated with an average decrease of 1.10 mg/dL ($p<0.001$). Compared to women who did not currently drink alcohol, current drinkers had an average HDL-C that was 7.08 mg/dL ($p<0.01$) higher.

Table 4.4. Multiple linear regression analysis summary for HDL Cholesterol

Characteristic	Model 1, n=182 B	Model 1 (95% CI)	Model 2, n=161 B	Model 2 (95% CI)	Model 3, n=179 B	Model 3 (95% CI)	Model 4, n=158 B	Model 4 (95% CI)	Model 5, n=158 B	Model 5 (95% CI)
Intercept	62.62		95.45		14.45		40.69		61.71	
Menopause Status										
Premenopausal	-2.93	(-9.00, 3.15)	-7.48*	(-13.22, -1.75)					-4.96	(-11.75, 1.82)
Perimenopausal	-7.06*	(-12.64, -1.48)	-5.84*	(-10.86, -0.83)					-4.41	(-9.84, 1.03)
Postmenopausal	ref		ref						ref	
Age, years					0.88*	(0.092, 1.66)	1.01**	(0.26, 1.75)	0.66	(-0.20, 1.53)
Ethnicity										
Asian American			9.41**	(2.56, 16.25)			10.12**	(3.12, 17.12)	9.79**	(2.73, 16.85)
European American			5.08	(-1.38, 11.54)			4.75	(-1.92, 11.42)	4.77	(-1.89, 11.42)
Native Hawaiian/Pacific Islander			ref				ref		ref	
Other			1.41	(-6.46, 9.29)			-0.19	(-8.48, 8.11)	0.48	(-7.83, 8.79)
BMI, kg/m^2			-1.18***	(-1.66, -0.71)			-1.06***	(-1.55, -0.58)	-1.10***	(-1.59, -0.61)
Systolic Blood Pressure Average, mmHg			-0.11	(-0.31, 0.084)			-0.13	(-0.33, 0.074)	-0.13	(-0.33, 0.076)
Current Dinkers			6.67**	(2.32, 11.02)			7.21**	(2.77, 11.65)	7.08**	(2.65, 11.51)
Current Smokers			-5.10	(-11.57, 1.36)			-3.98	(-10.79, 2.82)	-4.76	(-11.71, 2.19)
Play Sports/Exercise Regularly			0.72	(-3.88, 5.33)			0.33	(-4.32, 4.97)	0.39	(-4.32, 5.09)
Income Comfort										
Struggling			ref				ref		ref	
Okay			6.12*	(0.28, 11.96)			4.96	(-0.99, 10.90)	5.50	(-0.45, 11.46)
Comfortable/Well-off			-0.69	(-6.89, 5.52)			-1.60	(-7.97, 4.77)	-1.33	(-7.69, 5.04)
Life Satisfaction Questionnaire Total			0.12	(-0.23, 0.46)			0.14	(-0.22, 0.49)	0.11	(-0.24, 0.47)
Job Satisfaction Questionnaire Total			-0.011	(-0.19, 0.17)			-0.029	(-0.22, 0.16)	-0.023	(-0.21, 0.16)

*p<0.05, **p<0.01, ***p<0.001.

Model 1: Adj R^2 = 0.0239; F(2,179) = 3.21, p=0.0425; Model 2: Adj R^2 = 0.3238; F(14,146) = 6.47, p < 0.0001; Model 3: Adj R^2 = 0.0212; F(1,177) = 4.85, p = 0.0289; Model 4: Adj R^2 = 0.3222; F(13,144) = 6.74, p < 0.0001; Model 5: Adj R^2 = 0.3267; F(15,142) = 6.08, p < 0.0001

4.4 LDL-C

Menopause status produced a significant linear relationship, F(2,179)=5.94, p=0.0032, when regressed on LDL-C for Model 1 (Table 4.5). Both premenopausal and perimenopausal women were associated with decreased LDL-C, 16.19 mg/dL (p<0.01) and 14.41 mg/dL (p<0.01) respectively, when compared to postmenopausal women. After controlling for confounding in Model 2, F(14, 146)=3.30, p<0.0001, premenopausal women had an average LDL-C 14.18 mg/dL (p<0.05) lower than postmenopausal women and perimenopausal women had an average LDL-C 15.63 mg/dL (p<0.01) lower than postmenopausal women. Ethnicity, BMI, and job satisfaction also shared a relationship with LDL-C. European American women were associated with having an increase in LDL-C of 12.84 mg/dL (p<0.05) and other ethnicities with having an increase of 23.92 mg/dL (p<0.01) when compared to Native Hawaiian and Pacific Islander women. A unit increase in BMI was associated with a 0.95 mg/dL (p<0.05) increase in cholesterol, whereas a decrease in job satisfaction resulted in a 0.45 mg/dL (p<0.05) increase.

Age was significantly associated with an increase in "bad" cholesterol when regressed alone in Model 3, F(1,177)=6.68, p=0.0105. A yearly increase in age was associated with an LDL-C increase of 1.76 mg/dL (p<0.05). When potential confounders were added to create Model 4, F(13,144)=2.90, p=0.0009, age, ethnicity, BMI, and job satisfaction were associated with higher cholesterol. When all other variables were held constant, an increase in age was associated with a 1.50 mg/dL (p<0.05) increase. Other ethnicities had an average LDL-C 20.58 mg/dL (p<0.05) higher than Native Hawaiian and Pacific Islander women. A unit increase in BMI was associated with a rise in 'bad' cholesterol of 1.02 mg/dL (p<0.05), and a unit decrease in job satisfaction was associated with an increase of 0.43 mg/dL (p<0.05).

When menopause status, age, and potential confounders were combined in Model 5, F(15,142)=3.04, p=0.0003, age and premenopausal status were no longer associated with LDL-C. Women who were postmenopausal had an average 'bad' cholesterol 13.71 mg/dL (p<0.05) higher than perimenopausal women. Native Hawaiian and Pacific Islanders were associated with having an average LDL-C 21.98 mg/dL (p<0.01) lower than other ethnicities. An increase in BMI was associated with a 1.00 mg/dL (p<0.05) increase in cholesterol, and a decrease in job satisfaction was associated with 0.45 (p<0.05) mg/dL increase.

Table 4.5. Multiple linear regression analysis summary for LDL Cholesterol

Characteristic	Model 1, n=182		Model 2, n=161		Model 3, n=179		Model 4, n=158		Model 5, n=158	
	B	(95% CI)	B	(95% CI)	B	(95% CI)	B	(95% CI)	B	(95% CI)
Intercept	128.05		35.72		29.07		-48.80		-2.69	
Menopause Status										
Premenopausal	-16.19**	(-26.64, -5.74)	-14.18*	(-25.28, -3.08)					-9.68	(-22.71, 3.36)
Perimenopausal	-14.41**	(-24.00, -4.83)	-15.63**	(-25.34, -5.93)					-13.71*	(-24.15, -3.27)
Postmenopausal	ref		ref						ref	
Age, years					1.76*	(0.42, 3.10)	1.50*	(0.046, 2.96)	0.77	(-0.89, 2.43)
Ethnicity										
Asian American			1.35	(-11.90, 14.60)			1.15	(-12.48, 14.77)	-0.69	(-14.25, 12.87)
European American			12.84*	(0.33, 25.36)			11.18	(-1.81, 24.16)	11.06	(-1.72, 23.85)
Native Hawaiian/Pacific Islander			ref				ref		ref	
Other			23.92**	(8.67, 39.17)			20.58*	(4.44, 36.71)	21.98**	(6.01, 37.95)
BMI, kg/m^2			0.95*	(0.029, 1.86)			1.02*	(0.084, 1.97)	1.00*	(0.055, 1.94)
Systolic Blood Pressure Average, mmHg			0.24	(-0.14, 0.62)			0.23	(-0.16, 0.63)	0.22	(-0.17, 0.61)
Current Dinkers			-5.06	(-13.48, 3.36)			-4.23	(-12.87, 4.41)	-4.60	(-13.11, 3.91)
Current Smokers			-1.16	(-13.66, 11.35)			0.40	(-12.85, 13.65)	-0.50	(-13.85, 12.85)
Play Sports/Exercise Regularly			-3.74	(-12.66, 5.17)			-4.58	(-13.62, 4.46)	-3.60	(-12.64, 5.45)
Income Comfort										
Struggling			ref				ref		ref	
Okay			1.23	(-10.08, 12.53)			-0.86	(-12.43, 10.71)	0.60	(-10.85, 12.05)
Comfortable/Well-off			1.42	(-10.59, 13.43)			0.21	(-12.18, 12.61)	1.21	(-11.02, 13.43)
Life Satisfaction Questionnaire Total			-0.057	(-0.73, 0.61)			0.021	(-0.67, 0.71)	-0.027	(-0.71, 0.66)
Job Satisfaction Questionnaire Total			0.45*	(0.098, 0.81)			0.43*	(0.064, 0.79)	0.45*	(0.087, 0.80)

*p<0.05, **p<0.01, ***p<0.001.

Model 1: Adj $R^2 = 0.0517$; $F(2,179) = 5.94$, $p=0.0032$; Model 2: Adj $R^2 = 0.1676$; $F(14,146) = 3.30$, $p < 0.0001$; Model 3: Adj $R^2 = 0.0309$; $F(1,177) = 6.68$, $p = 0.0105$;
Model 4: Adj $R^2 = 0.1357$; $F(13,144) = 2.90$, $p = 0.0009$; Model 5: Adj $R^2 = 0.1633$; $F(15,142) = 3.04$, $p = 0.0003$

4.5 Triglycerides

Menopause status was significantly associated with triglycerides when regressed alone in Model 1, $F(2,179)=3.10$, $p=0.0473$ (Table 4.6). Women who were premenopausal had triglycerides that were 20.35% ($p<0.05$) lower than postmenopausal women. When potential confounders were included in analysis for Model 2, menopause status was no longer associated with triglycerides, $F(14,146)=4.55$, $p<0.0001$. Instead, ethnicity, BMI, systolic blood pressure average, and life satisfaction questionnaire total were significantly related to triglycerides. European Americans had triglyceride levels 18.81% ($p<0.05$) lower than Native Hawaiian and Pacific Islanders. For a unit increase in BMI ($p<0.001$) and systolic blood pressure average ($p<0.05$), triglycerides increased 3.21% and 0.80% respectively. Triglycerides were also observed to increase by 1.13% for a decrease in life satisfaction ($p<0.05$) when all other variables were held constant.

Age was not significantly associated with triglyceride levels when regressed alone in Model 3, $F(1,177)=0.72$, $p=0.3974$, nor was the model significant. Age remained unassociated with triglycerides even after adjustment for potential confounders in Model 4, $F(13,144)=4.87$, $p<0.0001$. Similar to Model 2, ethnicity, BMI, systolic blood pressure average, and life satisfaction questionnaire total were significantly associated with triglycerides. Native Hawaiian and Pacific Islanders had levels 19.24% higher than European Americans ($p<0.05$). Increased changes in triglycerides of 3.12% and 0.83% were observed for a unit increase in BMI ($p<0.001$) and a unit increase in systolic blood pressure average ($p<0.05$), respectively. For a decrease in life satisfaction, triglyceride levels increased by 1.18% ($p<0.05$).

When all variables were combined in Model 5, $F(15,142)=4.27$, $p<0.0001$, neither menopause status nor age were significantly associated with triglycerides. When compared to Native Hawaiians and Pacific Islanders, European Americans had triglycerides that were 19.04% ($p<0.05$) lower. A unit increase in BMI was associated with an increased change of 2.96% ($p<0.001$), while an increase in systolic blood pressure average resulted in an increased change of 0.86% ($p<0.01$). Unlike Models 2 and 4, the life satisfaction questionnaire total was no longer significantly associated with triglycerides.

Table 4.6. Multiple linear regression analysis summary for Triglyceride[a]

Characteristic	Model 1, n=182 B	Model 1 (95% CI)	Model 2, n=161 B	Model 2 (95% CI)	Model 3, n=179 B	Model 3 (95% CI)	Model 4, n=158 B	Model 4 (95% CI)	Model 5, n=158 B	Model 5 (95% CI)
Intercept[b]	98.93		13.11		154.27		19.27		27.88	
Menopause Status										
Premenopausal	-20.35*	(-33.88, -4.05)	-6.38	(-21.94, 12.27)					-9.97	(-27.38, 11.61)
Perimenopausal	-6.27	(-20.99, 11.19)	0.50	(-14.26, 17.80)					-1.77	(-17.30, 16.68)
Postmenopausal	ref		ref						ref	
Age, years					-1.03	(-3.40, 1.39)	-0.84	(-3.15, 1.53)	-1.46	(-4.13, 1.27)
Ethnicity										
Asian American			-4.54	(-23.15, 18.57)			-8.44	(-26.55, 14.14)	-7.47	(-26.01, 15.72)
European American			-18.81*	(-33.85, -0.35)			-19.24*	(-34.53, -0.37)	-19.04*	(-34.42, -0.049)
Native Hawaiian/Pacific Islander			ref				ref		ref	
Other			-15.86	(-34.44, 7.99)			-16.68	(-35.82, 8.17)	-15.62	(-35.14, 9.79)
BMI, kg/m^2			3.21***	(1.68, 4.78)			3.12***	(1.56, 4.70)	2.96***	(1.38, 4.57)
Systolic Blood Pressure Average, mmHg			0.80*	(0.17, 1.43)			0.83*	(0.19, 1.47)	0.86**	(0.21, 1.51)
Current Dinkers			-9.54	(-21.19, 3.83)			-10.64	(-22.29, 2.76)	-10.74	(-22.42, 2.70)
Current Smokers			16.93	(-4.72, 43.49)			18.39	(-4.44, 46.67)	15.42	(-7.38, 43.83)
Play Sports/Exercise Regularly			2.95	(-11.03, 19.12)			4.95	(-9.33, 21.47)	3.74	(-10.63, 20.43)
Income Comfort										
Struggling			ref				ref		ref	
Okay			2.82	(-14.55, 23.72)			3.28	(-14.34, 24.53)	3.87	(-13.99, 25.45)
Comfortable/Well-off			15.86	(-4.82, 41.03)			17.16	(-4.12, 43.17)	17.04	(-4.32, 43.18)
Life Satisfaction Questionnaire Total			1.13*	(0.021, 2.24)			1.18*	(0.051, 2.32)	1.12	(-0.016, 2.27)
Job Satisfaction Questionnaire Total			0.18	(-0.40, 0.77)			0.19	(-0.39, 0.79)	0.20	(-0.39, 0.79)

*p<0.05, **p<0.01, ***p<0.001

[a]Transformed before analysis, then transformed back for presentation as percent change

[b]Transformed before analysis, then transformed back for presentation

Model 1: Adj R^2 = 0.0227; F(2,179) = 3.10, p=0.0473; Model 2: Adj R^2 = 0.2368; F(14,146) = 4.55, p < 0.0001; Model 3: Adj R^2 = -0.0016; F(1,177) = 0.72, p = 0.3974; Model 4: Adj R^2 = 0.2425; F(13,144) = 4.87, p < 0.0001; Model 5: Adj R^2 = 0.2379; F(15,142) = 4.27, p < 0.0001

4.6 Triglyceride to HDL-C Ratio

When menopause status was regressed alone on the triglyceride to HDL-C ratio in Model 1, F(2,179)=2.05, p=0.1317, neither menopause status nor the model were significant (Table 4.7). The relationship remained unrelated after controlling for potential confounders in Model 2, F(14,146)=6.35, p<0.0001. Ethnicity, BMI, systolic blood pressure average, and alcohol were significantly associated with the ratio. European Americans had triglyceride to HDL-C ratios on average 24.85% (p<0.05) lower than Native Hawaiian and Pacific Islanders. For a unit increase in BMI and systolic blood pressure average, the triglyceride to HDL-C ratio had an observed increased change of 5.41% (p<0.001) and 1.04% (p<0.05) respectively. The ratio was 18.81% (p<0.05) lower among women who consumed alcohol when compared to those who did not currently drink.

Age was not significantly associated with the triglyceride to HDL-C ratio when regressed alone in Model 3, F(1,177)=2.28, p=0.1325, nor was the model significant. Age remained unassociated with the ratio even after adjustment for potential confounders in Model 4, F(13,144)=7.03, p<0.0001. However, ethnicity, BMI, systolic blood pressure average, and alcohol consumption were significantly associated with the ratio. On average, Native Hawaiian and Pacific Islanders had a ratio 24.89% (p<0.05) higher European Americans. Increased changes of 5.09% and 1.09% were observed for a unit increase in BMI (p<0.001) and a unit increase in systolic blood pressure average (p<0.05), respectively. Women who consumed alcohol had a triglyceride to HDL-C ratio 20.45% (p<0.05) lower than those who abstained from alcohol.

Neither menopause status nor age were significantly associated with the triglyceride to HDL-C ratio when all variables were combined in Model 5, F(15,142)=6.06, p<0.0001. Similarly to Models 2 and 3, ethnicity, BMI, systolic blood pressure average, and alcohol consumption were significantly associated with the ratio. When compared to Native Hawaiians and Pacific Islanders, European Americans had a triglyceride to HDL-C ratio that was 24.73% (p<0.05) lower, on average. A unit increase in BMI was associated with an increased change of 5.00% (p<0.001) and an increase in systolic blood pressure average resulted in an increased change of 1.11% (p<0.01). The triglyceride to HDL-C ratio was 20.38% (p<0.01) lower among women who consumed alcohol when compared to those who did not currently drink.

Table 4.7. Multiple linear regression analysis summary for Triglyceride to HDL Cholesterol ratio[a]

	Model 1, n=182		Model 2, n=161		Model 3, n=179		Model 4, n=158		Model 5, n=158	
Characteristic	B	(95% CI)	B	(95% CI)	B	(95% CI)	B	(95% CI)	B	(95% CI)
Intercept[b]	1.65		0.11		5.77		0.41		0.43	
Menopause Status										
Premenopausal	-17.32	(-35.86, 6.59)	5.67	(-16.52, 33.75)					-2.76	(-26.38, 28.44)
Perimenopausal	4.74	(-17.03, 32.23)	10.47	(-10.10, 35.74)					5.17	(-15.84, 31.43)
Postmenopausal			ref						ref	
Age, years					-2.50	(-5.66, 0.78)	-2.49	(-5.42, 0.52)	-2.59	(-5.99, 0.93)
Ethnicity										
Asian American			-18.11	(-38.19, 8.49)			-22.39	(-41.62, 3.19)	-21.16	(-40.98, 5.31)
European American			-24.85*	(-42.38, -1.98)			-24.89*	(-42.74, -1.48)	-24.73*	(-42.71, -1.11)
Native Hawaiian/Pacific Islander			ref				ref		ref	
Other			-18.02	(-40.69, 13.31)			-16.53	(-40.43, 16.94)	-16.34	(-40.51, 17.63)
BMI, kg/m^2			5.41***	(3.37, 7.48)			5.09***	(3.05, 7.18)	5.00***	(2.91, 7.13)
Systolic Blood Pressure Average, mmHg			1.04*	(0.22, 1.86)			1.09*	(0.26, 1.93)	1.11**	(0.28, 1.96)
Current Dinkers			-18.81*	(-32.10, -2.91)			-20.45*	(-33.60, -4.71)	-20.38*	(-33.61, -4.52)
Current Smokers			27.97	(-1.87, 66.90)			27.57	(-3.28, 68.25)	25.87	(-5.34, 67.38)
Play Sports/Exercise Regularly			1.33	(-16.14, 22.45)			4.13	(-13.79, 25.78)	2.84	(-15.22, 24.75)
Income Comfort										
Struggling			ref				ref		ref	
Okay			-5.84	(-25.93, 19.70)			-3.51	(-24.23, 22.88)	-3.78	(-24.64, 22.86)
Comfortable/Well-off			18.69	(-8.03, 53.17)			22.09	(-5.78, 58.19)	21.45	(-6.45, 57.67)
Life Satisfaction Questionnaire Total			1.00	(-0.43, 2.45)			1.03	(-0.42, 2.51)	1.02	(-0.45, 2.50)
Job Satisfaction Questionnaire Total			0.21	(-0.55, 0.97)			0.25	(-0.51, 1.02)	0.25	(-0.52, 1.02)

*p<0.05, **p<0.01, ***p<0.001

[a]Transformed before analysis, then transformed back for presentation as percent change

[b]Transformed before analysis, then transformed back for presentation

Model 1: Adj R^2 = 0.0115; F(2,179) = 2.05, p=0.1317; Model 2: Adj R^2 = 0.3188; F(14,146) = 6.35, p < 0.0001; Model 3: Adj R^2 = 0.0072; F(1,177) = 2.28, p = 0.1325;
Model 4: Adj R^2 = 0.3329; F(13,144) = 7.03, p < 0.0001; Model 5: Adj R^2 = 0.3259; F(15,142) = 6.06, p < 0.0001

Chapter 5
Discussion

The Hilo Women's Health Study provided an opportunity to delve deeper into the menopausal transition in a multicultural setting. An increased risk among postmenopausal women for CVDs raises questions about what changes in risk factors, such as cholesterol, happen throughout the menopausal transition. I hypothesized that both menopause status and age would be significantly associated with cholesterol levels, but that when combined into one model, only menopause status would remain associated. Additionally, I hypothesized that when compared to women in premenopause and perimenopause, postmenopausal women would have higher average total cholesterol, LDL-C, triglyceride, and triglyceride to HDL-C ratio levels, but a lower average HDL-C level.

Based on cholesterol guidelines produced by the NIH (2005), the average total cholesterol (194.99 mg/dL), HDL-C (58.73 mg/dL), triglyceride (103.78 mg/dL), and triglyceride to HDL-C ratio (2.06) were considered desirable. However, the average LDL-C (117.65 mg/dL) was above the recommended level. When comparing participants by menopause status, the average total cholesterol for postmenopausal women (211.71 mg/dL) was above the recommended level; however, the average for premenopausal and perimenopausal women were considered desirable. All three menopausal groups had less than desirable LDL-C levels, with postmenopausal women having the highest average LDL-C (128.05 mg/dL). All three groups had desirable HDL-C, triglyceride, and triglyceride to HDL-C ratio. Unexpectedly, postmenopausal women had the highest average HDL-C (62.62 mg/dL).

As hypothesized, both menopause status and age were significantly associated with total cholesterol when placed into separate models. When menopause status and age were combined with potential confounders, only menopause status remained associated; with postmenopausal women having higher total cholesterol concentrations than women in premenopause or perimenopause. These findings are in agreement with Hall et al. (2002), Pasquali et al. (1997), Schaefer et al. (1994), and similar to Derby et al. (2009) and Matthews et al. (2009). Ethnicity and job satisfaction were also found to have a relationship with total cholesterol. Native

Hawaiian and Pacific Islanders have a lower average total cholesterol than other ethnicities and those with less job satisfaction tend to have higher levels of cholesterol.

Contrary to initial hypotheses, despite menopause status and age having significant associations with HDL-C in separate models, neither were significantly associated with "good" cholesterol when combined into one model. Pasquali et al. (1997) also found a lack of significance between HDL-C and menopause status. However, Pasquali et al. (1997) observed an association between age and HDL-C, and Hall et al. (2002) found a relationship between menopause status and HDL-C. Despite the lack of significance in the final model, confidence intervals for premenopause (-11.75, 1.82) and perimenopause (-9.84, 1.03) indicate a relationship in which menopause status has a moderate to strong relationship with HDL-C (Rothman, 2012): Postmenopausal women had higher HDL-C values than both premenopausal and perimenopausal women. Statistical significance may have been achieved if both perimenopause and postmenopause had been divided into two groups each, as done in Derby et al. (2009).

Based on results from Derby et al. (2009) and Matthews et al. (2009), postmenopausal women may have had higher HDL-C because levels peaked in perimenopause and then began declining twelve months after the final menstrual period. Therefore, if the majority of women were in early postmenopause, their HDL-C would have just started to decline. Ethnicity, BMI, and alcohol were also important in relation to HDL-C levels. Native Hawaiian and Pacific Islanders had significantly lower "good" cholesterol in comparison to Asian Americans. High BMI resulted in decreased HDL-C, while alcohol assisted in raising levels. Although income comfort was initially associated with HDL-C, there were no associations visible when age was included in the models.

Menopause status and age were significantly associated with LDL-C in separate models, but when combined in an adjusted model, only menopause status was associated. Perimenopausal women were observed to significantly differ from postmenopausal women. Hall et al. (2002) found that both premenopausal and perimenopausal women were significantly different from postmenopausal women, while Peters et al. (1999) found that premenopausal women were different. Despite not finding a relationship between LDL-C and menopause status after adjustment, Pasquali et al. (1997) observed a negative association between oestradiol and LD-C. This further supports the idea that oestrogens, which decrease over the menopausal transition, have an impact on cholesterol (Pasquali et al., 1997). An association between LDL-C and ethnicity, BMI, and job satisfaction was also observed. Native Hawaiian and Pacific Islander women were associated with lower LDL-C compared to other ethnicities. Despite European Americans initially having significantly higher levels than Native Hawaiian and Pacific Islanders, the association disappeared with the addition of age into the models. Increases in LDL-C were associated with an increase in BMI and a decrease in job satisfaction.

Menopause status was initially associated with triglycerides, however, contrary to my initial hypothesis, no relationship was observed after being combined with age and the potential confounders. Similarly, no association was observed between triglycerides and age before or after menopause status and potential confounders were included in the model. These results were also found in Hall et al. (2002) and Peters et al. (1999). In contrast, Matthews et al (2009) observed a relationship between age and triglycerides while Derby et al. (2009) described a relationship between menopause and triglycerides. Perhaps a relationship was not found in this study because there were not two perimenopausal and two postmenopausal groupings. Ethnicity, BMI, and systolic blood pressure average had a significant relationship. Native Hawaiian and Pacific Islander women had higher triglycerides than European American women. Additionally, high measures of BMI and systolic blood pressure average were associated with increased triglyceride levels. Although life satisfaction was initially significantly related to triglyceride levels, the relationship disappeared upon the addition of both age and menopause in the model.

The triglyceride to HDL-C ratio was neither significantly associated with menopause status nor age. Based on the relationships found between menopause status and triglycerides and HDL-C, an insignificant relationship between the ratio and menopause status is plausible. However, there was an association between the ratio and ethnicity, BMI, systolic blood pressure average, and alcohol consumption. On average, Native Hawaiian and Pacific Islander women have a higher triglyceride to HDL-C ratio than European American women. Increases in the ratio were associated with both higher BMI and higher systolic blood pressure average. Women who currently ingested alcohol had an average lower triglyceride to HDL-C ratio when compared to participants who did not consume alcohol.

As with all studies, there are limitations to the Hilo Women's Health Study. Although there was an association between menopause status and cholesterol, causality could not be determined because this was a cross-sectional study. More than half of the participants in the study were not acquired through random sampling, which prevents some generalizability. Using data on the frequency of exercise, cigarettes smoked, and alcoholic beverages ingested would have been more beneficial, however the amount of missing data prevented analysis. Lastly, there are additional potential confounders that we may have missed.

Despite the limitations, there were multiple strengths to this study. A large number of ethnically diverse women were willing to participate in this important research: 31.75% were Asian American, 38.10% were European American, and 15.87% were part or full Native Hawaiian or Pacific Islander. Similar numbers were seen in the 2000 census: 26.7% were Asian American, 31.5% were European American, and 11.2% were Native Hawaiian or Pacific Islander. Of the 28.4% who listed two or more ethnicities, 19.8% were part Native Hawaiian or Pacific Islander (Department of Business, Economic Development & Tourism, n.d.). This study adds to the literature much needed information on Asian Americans and Native Hawaiian or Pacific Islanders. Overall, ethnicity was an important predictor, with all five outcome variables having an association with the ethnic groups involved in the study.

In the past, hormone replacement therapy was prescribed to women to replace the declining amounts of estrogen that are thought to protect women from the side effects of menopause. However, hormone replacement therapy has been found to increase the risk of CVDs and breast cancer (Writing Group for the Women's Health Initiative Investigators, 2002). Health care professionals currently prescribe statins as a means to control cholesterol, but as with all medications, there are unhealthy side effects. Increased emphasis on physical activity, smoking cessation, and diet needs to be addressed. Free programs and resources need to be readily available and easy to understand to help women have a healthy transition. Lastly, incorporating cultural practices, such as traditional diets, can be beneficial. The Waianae Diet Program found significant average changes among Native Hawaiians that adhered to the traditional diet, including a decrease in total cholesterol, LDL-C, and triglycerides (Shintani, Hughes, Beckham, & O'Connor, 1991).

In conclusion, menopause status was significantly associated with total cholesterol and LDL-C. The narrow age gap of 45 to 55 year olds supports the findings that menopause status, but not age, was closely associated with a woman's cholesterol profile. Despite a lack of statistical significance with some variables, that does not indicate a lack of important association, nor that there is no clinical or public health meaningfulness. These results have important public health implications for women transitioning through menopause. Women cannot change their menopause status, so there is importance in studying the association between modifiable variables associated with the menopausal transition and cholesterol levels. In addition, studying a variety of ethnicities, such as those who participated in the Hilo Women's Health Study, provide unique information to add to the research that is being conducted.

References

Bittner, V., Johnson, B. D., Zineh, I., Rogers, W. J., Vido, D., Marroquin, O. C., … Sopko, G. (2009). The TG/HDL cholesterol ratio predicts all cause mortality in women with suspected myocardial ischemia: A report from the Women's Ischemia Syndrome Evaluation (WISE). *American Heart Journal*, *157*(3), 548–555.

Bromberger, J. T., Matthews, K. A., Kuller, L. H., Wing, R. R., Meilahn, E. N., & Plantinga, P. (1997). Prospective study of the determinants of age at menopause. *American Journal of Epidemiology, 145*(2), 124-133.

Brown, D. E., James, G. D., & Mills, P. S. (2006). Occupational differences in job strain and physiological stress: Female nurses and school teachers in Hawaii. *Psychosomatic Medicine, 68*(4), 524-530.

Brown, D. E., Sievert, L. L., Morrison, L. A., Rahberg, N., & Reza, A. (2011). Relationship between hot flashes and ambulatory blood pressure: The Hilo Women's Health Study. *Psychosomatic Medicine*, *73*, 166-172.

Cassou, B., Mandereau, L., Aegerter, P., Touranchet, A., & Derriennic, F. (2007). Work-related factors associated with age at natural menopause in a generation of French gainfully employed women. *American Journal of Epidemiology, 166*(4), 429-438.

Center for Disease Control. (2010). Cholesterol: Risk factors. Retrieved December 14, 2014, from http://www.cdc.gov/Cholesterol/risk_factors.htm.

Da Luz, P. L., Cesena, F. H., Favarato, D., & Cerqueira, E. S. (2005). Comparison of serum lipid values in patients with coronary artery disease at <50, 50 to 59, 60 to 69, and >70 years of age. *The American Journal of Cardiology*, *96*(12), 1640-1643.

Demakakos, P., Nazroo, J., Breeze, E., & Marmot, M. (2008). Socioeconomic status and health: The role of subjective social status. *Social Science & Medicine, 67*(2), 330-340.

Department of Business, Economic Development & Tourism. (n.d.). *Hawaii state data center reports and tables (Data focused on Hawaii)*. Retrieved February 20, 2015, from http://files.hawaii.gov/dbedt/census/Folder.2005-10-13.2927/pl94-171/pltable10.pdf.

Derby, C. A., Crawford, S. L., Pasternak, R. C., Sowers, M., Sternfeld, B., & Matthews, K. A. (2009). Lipid changes during the menopause transition in relation to age and weight: The Study of Women's Health Across the Nation. *American Journal of Epidemiology, 169*(11), 1352-1361.

Dorjgochoo, T., Kallianpur, A., Gao, Y., Cai, H., Yang, G., Li, H., … Shu, X. (2008). Dietary and lifestyle predictors of age at natural menopause and reproductive span in the Shanghai Women's Health Study. *Menopause, 15*(5), 924-933.

Evolahti, A, Hultcrantz, M, & Collins, A. (2009). Psychosocial work environment and lifestyle as related to lipid profiles in perimenopausal women. *Climacteric : The Journal Of The International Menopause Society, 12*(2), 131-145.

Gold, E. B., Crawford, S. L., Avis, N. E., Crandall, C. J., Matthews, K. A., Waetjen, L. E., ... Harlow, S. D. (2013). Factors related to age at natural menopause: Longitudinal analyses from SWAN. *American Journal of Epidemiology, 178*(1), 70-83.

Guetta, V. & Cannon, R. O. III. (1996). Cardiovascular effects of estrogen and lipid-lowering therapies in postmenopausal women. *Circulation, 93*, 1928-1937.

Hawaii State Department of Health. (2011). *Hawaii's plan for the prevention of heart disease and stroke 2011-2016*. Honolulu, HI: Hawaii State Department of Health, Heart Disease and Stroke Prevention Program.

Hall, G., Collins, A., Csemiczky, G., & Landgren, B-M. (2002). Lipoproteins and BMI: a comparison between women during transition to menopause and regularly menstruating healthy women. *Maturitas*, *41*, 177-185.

Henderson, K. D., Bernstein, L., Henderson, B., Kolonel, L., & Pike, M. C. (2008). Predictors of the timing of natural menopause in the Multiethnic Cohort Study. *American Journal of Epidemiology, 167*(11), 1287-1294.

Heron, M. (2012). Deaths: Leading causes for 2008. *National Vital Statistics Reports*, *60*(6), 1-95.

James, G. D., Baker, P. T., Jenner, D. A., & Harrison, G. A. (1987). Variation in lifestyle characteristics and catecholamine excretion rates among young Western Samoan men. *Social Science & Medicine*, *25*(9), 981-986.

Jeppesen, J., Hein, H.O., Suadicani, P., & Gyntelberg, F. (2001). Low triglycerides-high high-density lipoprotein cholesterol and risk 88of ischemic heart disease. *Archives of Internal Medicine*, *161*, 361–366.

Kannel, W., Hjortland, M., McNamara, P., & Gordon, T. (1976). Menopause and risk of cardiovascular disease: The Framingham study. *Annals of Internal Medicine, 85*(4), 447-452.

Lamon-Fava, S., Wilson, P. W., & Schaefer, E. J. (1996). Impact of body mass index on coronary heart disease risk factors in men and women. The Framingham Offspring Study. *Arteriosclerosis, Thrombosis, and Vascular Biology, 16*(12), 1509-1515.

Li, L., Wu, J., Pu, D., Zhao, Y., Wan, C., Sun, L., ... Zhang, M. (2012). Factors associated with the age of natural menopause and menopausal symptoms in Chinese women. *Maturitas, 73*(4), 354-360.

López, E. P., Rice, C., Weddle, D. O., & Rahill, G. J. (2008). The relationship among cardiovascular risk factors, diet patterns, alcohol consumption, and ethnicity among women aged 50 years and older. *Journal of the American Dietetic Association, 108*(2), 248-256.

Matthews, K. A., Crawford, S. L., Chae, C. U., Everson-Rose, S. A., Sowers, M. F., Sternfeld, B., & Sutton-Tyrrell, K. (2009). Are changes in cardiovascular disease risk factors in midlife women due to chronological aging or to the menopausal transition? *Journal of the American College of Cardiology, 54*(25), 2366-2373.

Matthews, K. A., Sowers, M. F., Derby, C. A., Stein, E., Miracle-McMahill, H., Crawford, S. L., & Pasternak, R. C. (2005). Ethnic differences in cardiovascular risk factor burden among middle-aged women: Study of Women's Health Across the Nation (SWAN). *American Heart Journal, 149*(6), 1066-1073.

Mendis, S., Puska, P., & Norrving, B. (2011). *Global atlas on cardiovascular disease prevention and control*. Geneva: World Health Organization.

Mueller, C. W., & Parcel, T. L. (1981). Measures of socioeconomic status: Alternatives and recommendations. *Child Development, 52*(1), 13-30.

Nanchahal, K., Ashton, W. K., & Wood, D. A. (2000). Alcohol consumption, metabolic cardiovascular risk factors and hypertension in women. *International Journal of Epidemiology, 29*(1), 57-64.

National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. (2002). *Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III): Final report* (NIH Publication No. 01-3670). Bethesda, MD: National Cholesterol Education Program.

National Heart, Lung, Blood Institute & North American Association for the Study of Obesity. (2000). *The practical guide identification, evaluation, and treatment of overweight and obesity in adults* (NIH publication ; no. 00-4084). Bethesda, Md: National Heart, Lung, and Blood Institute.

National Institutes of Health. (2005). *High blood cholesterol: What you need to know*. Retrieved May 9, 2014, from http://www.nhlbi.nih.gov/health/public/heart/chol/wyntk.htm .

National Institute on Aging. (2008). *Menopause time for a change* (NIH Publication No. 08-6143). Bethesda, MD: National Institute on Aging, U.S. Dept. of Health and Human Services, National Institutes of Health.

Pasquali, R., Casimirri, F., Pascal, G., Tortelli, O., Morselli Labate, A. M., Bertazzo, D., . . . Virgilio Menopause Health Group. (1997). Influence of menopause on blood cholesterol levels in women: The role of body composition, fat distribution and hormonal milieu. *Journal of Internal Medicine, 241*, 195-203.

Peters, H. W., Westendorp, I. C., Hak, A. E., Grobbee, D. E., Stehouwer, C. D., Hofman, A., & Witteman, J. C. (1999). Menopausal status and risk factors for cardiovascular disease. *Journal of Internal Medicine, 246*(6), 521-528.

Reza, A., Sievert, L. L., Rahberg, N., Morrison, L. A., & Brown, D. E. (2012). Prevalence and determinants of headaches in Hawaii: The Hilo Women's Health Study. *Annals of Human Biology, 39*(4), 305-314.

Rothman, K. J. (2012). *Epidemiology: An introduction* (2nd ed.). New York: Oxford University Press.

SAS Institute Inc. (2009). *SAS/STAT 9.2 user's* guide (2nd ed.). Cary, NC: SAS Institute Inc.

Schaefer, E. J., Lamon-Fava, S., Cohn, S. D., Schaefer, M. M., Ordovas, J. M., Castelli, W. P., & Wilson, P. W. (1994). Effects of age, gender, and menopausal status on plasma low density lipoprotein cholesterol and apolipoprotein B levels in the Framingham Offspring Study. *Journal of Lipid Research, 35*(5), 779-792.

Sherman S. (2005). Defining the menopausal transition. *The American Journal of Medicine, 118*, 35-75.

Shintani, T. T., Hughes, C. K., Beckham, S., & O'Connor, H. K. (1991). Obesity and cardiovascular risk intervention through the ad libitum feeding of traditional Hawaiian diet. *American Journal of Clinical Nutrition, 53*(6), 1647S-1651S.

Sievert, L. L. (2006). *Menopause a biocultural perspective*. New Brunswick, N.J.: Rutgers University Press.

Sievert, L. L., Morrison, L. A., Reza, A. M., Brown, D. E., Kalua, E., & Tefft, H. A. (2007). Age-related differences in health complaints: The Hilo Women's Health Study. *Women & Health*, *45*(3), 31-51.

Torgerson, D. J., Thomas, R. E., Campbell, M. K., & Reid, D. M. (1997). Alcohol consumption and age of maternal menopause are associated with menopause onset. *Maturitas*, *26*(1), 21-25.

Vittinghoff, E., Shiboski, S. C., Glidden, D. V., & McCulloch, C. E. (2005). *Regression methods in biostatistics: Linear, logistic, survival, and repeated measures models*. New York, NY: Springer New York.

Winkleby, M., Kraemer, H., Ahn, D., & Varady, A. (1998). Ethnic and socioeconomic differences in cardiovascular disease risk factors: Findings for women from the Third National Health and Nutrition Examination Survey, 1988-1994. *JAMA*, *280*(4), 356-362.

Wooten, J. S., Phillips, M. D., Mitchell, J. B., Patrizi, R., Pleasant, R. N., Hein, R. M., ... Barbee, J. J. (2011). Resistance Exercise and Lipoproteins in Postmenopausal Women. *International Journal Of Sports Medicine*, *32*(1), 7-13.

World Health Organization. (2014). The top 10 causes of death. Retrieved December 2, 2014, from http://www.who.int/mediacentre/factsheets/fs310/en/.

Writing Group for the Women's Health Initiative Investigators. (2002). Risks and benefits of estrogen plus progestin in healthy postmenopausal women: Principal results from the Women's Health Initiative randomized controlled trial. *JAMA, The Journal of the American Medical Association*, *288*(3), 321-333.