Awareness Of Increased Risk For Heart Disease And Cardiovascular Risk Factors In Women With Systemic Lupus Erythematosus

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AWARENESS OF INCREASED RISK FOR HEART DISEASE AND CARDIOVASCULAR RISK FACTORS IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

by

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ABSTRACT

Women with systemic lupus erythematosus (SLE) develop cardiovascular disease (CVD) earlier and at a more accelerated rate compared to women without SLE. Many women with SLE are unaware of their increased risk despite years spent in the health care system, thus giving the atherogenic process time to accrue damage. Research has not explained fully why women with SLE are unaware of their increased risk for CVD or why awareness does not correspond to risk-educing behaviors. Stage theories of behavior like the Precaution Adoption Process Model (PAPM) propose that health behavior change proceeds through qualitatively different stages, and people at one stage face similar barriers before they can progress to the next. The Common Sense Model (CSM), a self-regulatory model of health behavior, explains the emotional and cognitive processes involved in progression from one stage to the next and the formation of a personal risk/illness representation. Combining the PAPM and CSM helps understand the relationship between risk perception and adoption of risk reducing behaviors. The specific aims of this study were to assess in women with SLE: (1) general knowledge of heart disease compared to women without SLE; (2) awareness of increased CVD risk and CVD risk factors; and (3) personal and healthcare system factors that influence awareness of increased CVD risk and adoption of risk reducing behaviors. Sixty women with SLE, 18 years of age or older, were recruited to participate in this descriptive study. Data included demographic information, self-report questionnaires (perceived CVD risk, CVD risk factors, depression, physical activity), body measures (height, weight, waist circumference, blood pressure), and blood samples for physiologic markers of traditional and novel CVD risk factors (glucose, insulin, lipoprotein lipids, creatinine, C-reactive protein, homocysteine, antiphospholipid antibodies). The Beck

Depression Inventory-Primary Care and the Physical Activity Disability Survey were used to determine depression and activity level respectively. General knowledge of heart disease was assessed using the American Heart Association (AHA) National Survey on women's awareness of heart disease. Logistic regression was used to categorize participants into subgroups according to perceived risk and identify important factors that influenced their PAPM stage categorization. Women with SLE in this study were more aware of women's leading cause of death than United States women who responded to the 2006 AHA survey (73% v 57%), but fewer than 25% perceived themselves at increased CVD risk. Age was a significant predictor ($p=0.05$) for awareness of increased risk; younger age correlated with increased awareness. Most women received information about heart disease from public media. On average, women had 4 CVD risk factors, but they perceived they had only 2. The number of perceived risk factors predicted adoption of risk reducing behaviors ($p=0.03$). Women in this study with SLE underestimated their CVD risk factors and did not personalize their increased CVD risk. Healthcare providers' identification and discussion of CVD risk factors in women with SLE may enhance their risk awareness and the adoption of risk reducing behaviors. This information may contribute to the development of stage-matched interventions, a potentially more effective and efficient approach than a generic program of risk-reduction, especially in individuals with SLE who face the additional burden of a chronic illness.

I dedicate this dissertation to

my daughter, Rachel Lara, who was the inspiration for this work;

my husband, Irwin, who supported me throughout the process;

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

CHAPTER ONE: INTRODUCTION

Cardiovascular disease (CVD) occurs prematurely and at an accelerated rate in individuals with systemic lupus erythematosus (SLE), an autoimmune disease that affects women and minorities disproportionately.[1] Some investigators now consider SLE to be an independent risk factor for heart disease equivalent to diabetes in the degree of increased CVD risk it confers.[2-4]

Research suggests that many women with SLE are unaware of their increased risk despite years spent in the healthcare system.[5] A lack of awareness delays the adoption of risk reducing interventions and gives the atherogenic process time to accrue damage. The limited research on awareness of increased CVD risk in individuals with SLE has failed to explain adequately why a lack of awareness exists or why awareness does not correspond to risk-reducing behaviors.[5-7]

A common assumption of almost all theories of health behavior is that perception of personal risk increases the likelihood of precaution adoption.[8, 9] Stage theories of behavior postulate that health behavior change proceeds through qualitatively different stages, and people at one stage face similar barriers before they can progress to the next.[10] The Precaution Adoption Process Model (PAPM) is unique from other stage theories in that it distinguishes individuals who are unaware of risks from those who are aware but have not actively considered risk-reducing behaviors.[11] The Common Sense Model, a self-regulatory model of health behavior, complements the PAPM by explaining the emotional and cognitive processes involved in movement from one stage to the next and the formation of a personal risk/illness representation.[12]

Identification of factors that effect people's movement from one stage to the next can be useful in developing stage-matched interventions, a potentially more effective approach than a generic program of risk-reduction, especially in individuals with SLE who face the additional burden of a chronic illness.

Specific Aims

The specific aims of this study were to:

1. Assess the general knowledge of heart disease in women with SLE compared to women without SLE;
2. Identify awareness of increased CVD risk and CVD risk factors in women with SLE;
3. Determine whether personal and healthcare system factors influence awareness of increased CVD risk and adoption of risk reducing behaviors.

The research questions are:

1. What is the perception of personal CVD risk and risk factors in women with SLE?
2. What is the knowledge of the leading cause of death in women, CVD risk factors, and risk reducing behaviors in women with SLE?
3. What personal and healthcare system characteristics distinguish women with SLE in one stage of the Precaution Adoption Process Model from those in different stages?

Theoretical Framework

Perception of risk as a determinant for the adoption of risk-reducing behaviors is a fundamental feature of models of health behavior. Many theories assume that the probability of action is an algebraic function of an individual's beliefs, experiences, and attributes that places

the individual on a continuum of action likelihood.[9, 13-16] No changes occur during the adoption of risk-reducing behaviors except the values of the variables in the equation. Other health behavior theorists contend that a single prediction rule does not adequately represent reactions to health risks.[17-19] Instead, they describe reactions to health risks in terms of a series of cognitive stages that are qualitatively distinct from one another. Individuals face different barriers and demonstrate different behaviors at different stages. As a result, the importance of the variables in precaution adoption changes from one stage to another.[11]

Stage theories propose that relatively small differences exist among individuals in the same stage and relatively large differences occur between individuals in different stages.[11] The Precaution Adoption Process Model (PAPM) is a stage model that has been used to analyze a variety of health behaviors and presumes like other health behavior models that perceptions of high personal risk increase the likelihood of precaution adoption.[20-23] It identifies seven distinct stages in recognizing, adopting and maintaining a change in behavior that reduces risk.

Stage 1 describes a state in which the individual is unaware of a health risk or a protective behavior. This stage of unawareness is unique to the PAPM and distinguishes between individuals who know nothing about the threat and those who have thought about the threat and concluded that the risk does not pertain to them. Information about and personal experience with the risk determine movement to stage 2. In stage 2, individuals are aware of the risk but not personally engaged. They do not perceive personal susceptibility to the risk even though they recognize the significance of the risk to others. In order to move to stage 3 and beyond, individuals must identify with the health risk. Knowledge of the health risk and its risk factors, personal experience with the health risk, and information about peers' risk status play a role in determining movement.

The PAPM does not provide a fixed set of variables that differentiate between stages or affect movement from one stage to another. It also does not completely describe the role emotions play in influencing behavior, the psychological processes used for coping within the stages, or the effect of social and environmental factors on behavior change throughout the stages as do self-regulatory models of health behavior.[24] Incorporating the variables of self-regulatory models into the PAPM could allow for more accurate differentiation between stages.

Self-regulatory models are based on the common theory that cognitive and emotional factors contribute significantly to health behaviors.[25] Feedback loops are an important component in these models with goals serving as reference values for determining the success of the individual's efforts. Leventhal put forth the Common Sense Model of Illness Representations (CSM), a self-regulatory theory, to understand the processes by which people make sense of their illnesses.[26] The CSM hypothesizes that people form "common sense" representations when faced with illness-related information that constitutes a health threat. The individual processes concrete and abstract information from all sources in two largely independent but parallel processing systems, cognitive and emotional.[27] Heuristics serve in the interpretation of the meaning of the information. Some heuristics serve to determine the meaning of a risk while others may be more useful for deciding upon a course of action.[28] Knowledge about the risk, which is derived from somatic changes, direct observations, discussions with others, and public media among other sources, is one factor that plays a role in forming an illness representation as well as determining movement from Stage 1 to subsequent stages in the PAPM.[29] The formation of a risk/illness representation is the first step in developing a coping strategy or adopting precautionary behaviors to manage or reduce the risk.[29]

Illness representations are identified by five dimensions: 1) *identity* refers to the label for the threat and its symptoms; 2) *timeline* is the expected and/or perceived onset and duration of the risk/illness both with and without effective treatment; 3) *cause* reflects the perceived single or complex set of events that are responsible for the risk/illness onset; 4) *consequences* are the expected and/or perceived physical/functional, personal, social and economic factors impacted by the risk/illness; and 5) *control* refers to the expectation that a specific risk or illness can be cured or controlled by the body's own defenses and/or in conjunction with healthcare provider interventions and the actual outcomes of the interventions on specific features of the risk or illness.[30]

The CSM complements and informs the PAPM. The PAPM focuses on what people decide to do or not to do while the CMS describes the processes leading to those decisions. Combining the two models helps to understand the relationship between risk perception and adoption of risk reducing behaviors, which in turn provides a basis for the development of more robust educational interventions and the criteria for evaluating their effectiveness (Figure 1.1).

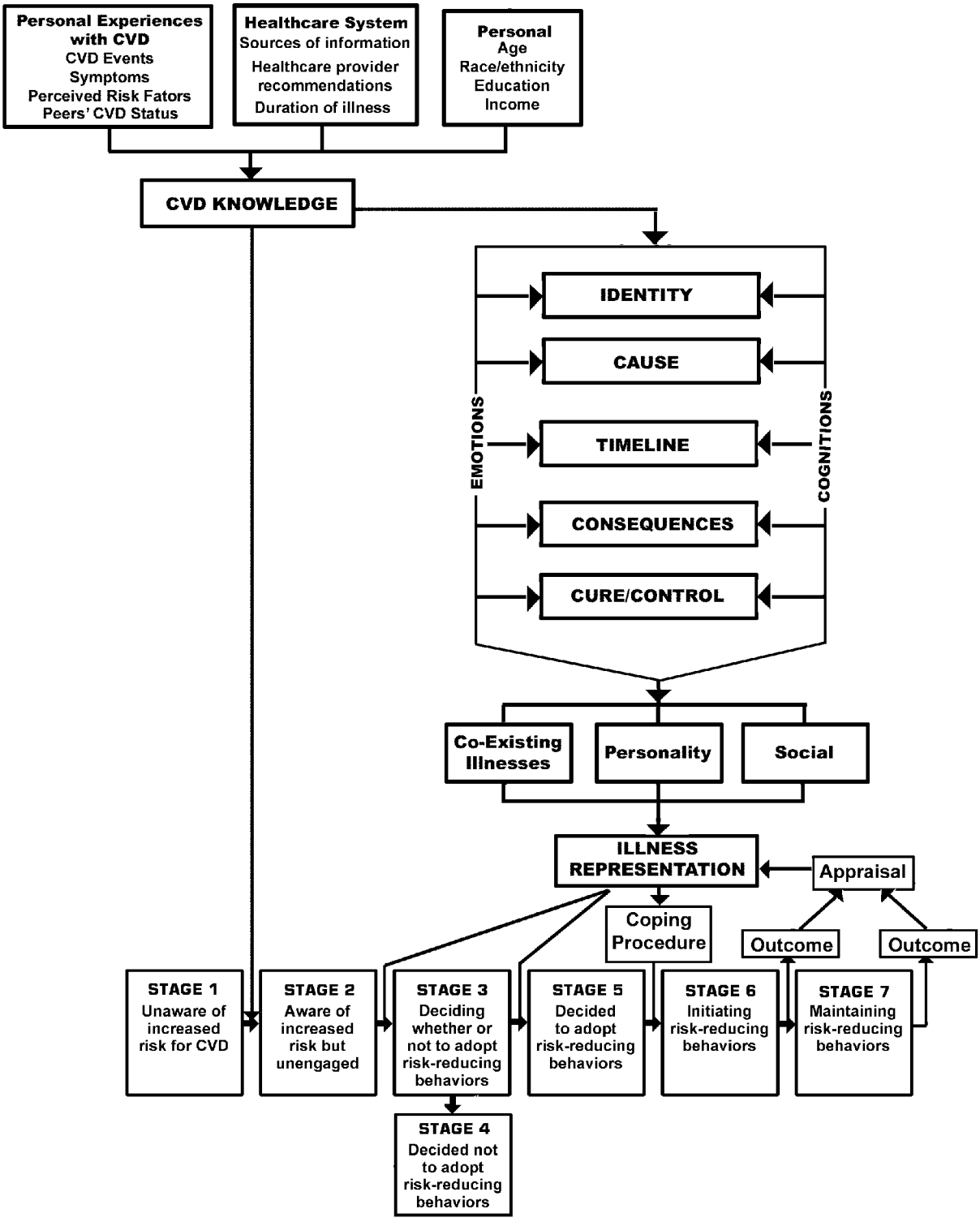

Figure 1.1: Conceptual Framework for Assessing Awareness of Increased Cardiovascular Risk

Cardiovascular Disease and Systemic Lupus Erythematosus

With early diagnosis and current therapies, the majority of individuals in the United States (US) with SLE without major organ damage achieve a near normal life span.[31] Increased survival, however, begets chronic disease-associated morbidity and/or disability, not the least of which is CVD, the most common cause of death in people with SLE who survive the acute complications of the disease.[32]

Atherosclerosis is recognized now as a chronic inflammatory disease of the vascular wall. Inflammation plays a major role not only in the development of atherosclerotic lesions but also in the destabilization and rupture of plaques.[33] During periods of inflammation, including autoimmune responses, inflammatory cells release pro-inflammatory cytokines that initiate the atherosclerotic process. Frequently, the result is premature and accelerated atherosclerosis in patients with systemic autoimmune diseases that is not fully accounted for by traditional cardiovascular risk factors.[34] The mechanisms associated with premature and accelerated CVD in SLE will be discussed in Chapter One.

Awareness of Cardiovascular Disease Risk

Accurate perception of CVD risk in women with SLE is a crucial first step in adopting risk-reducing behaviors. Women with SLE, who are under the care of a health professional, might be expected to demonstrate an increased knowledge about heart disease risks and preventive behaviors. However, the limited research that assesses awareness of increased CVD risk and risk-reducing behaviors in individuals with SLE has found that the typical patient with SLE did not consider him or herself to be at a high risk for the development of coronary artery

disease.[5] Awareness of increased CVD risk and risk factors in women with SLE will be discussed in Chapter One.

Research Project

Preliminary Study

Following IRB approval and prior to undertaking this dissertation research project, a pilot study was conducted involving 5 women with SLE. The pilot study participants were recruited from the North Orlando/Winter Park lupus support group and were not included in the main project's sample. All five participants in the pilot study were white and one of them was also Hispanic. Despite a fair number of African American support group members, none were interested in participating in the pilot study. Although there may have been some bias due to previous interactions with the support group by the investigator, the objective of the pilot study was to work out logistics before proceeding with the larger project. A lack of awareness of increased CVD risk and risk factors was apparent in preliminary analysis of the data collected from the 5 women in the pilot study and validated the merits of the research project.

Main Project

Sixty women with SLE were recruited for the study from June 2007 until August 2008. Difficulty recruiting minorities continued in the main project and is discussed in Chapter Four. The findings from the study are reported in Chapter Three.

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CHAPTER TWO: LITERATURE REVIEW

Abstract

Women with systemic lupus erythematosus (SLE) develop cardiovascular disease (CVD) earlier and at a more accelerated rate compared to women without SLE. SLE patients have a 7-10-fold increased risk of CVD that is especially pronounced in younger women whose excess risk for myocardial infarction may be >50-fold compared to non-SLE controls. Chronic inflammation and the immune dysregulation in SLE contribute to the prematurity and acceleration of atherosclerosis in these patients. Inflammation is involved in initiation of the endothelial response to injury, from formation of the atherosclerotic lesion to rupture of the fibrous cap. Factors such as endothelial dysfunction, pro-inflammatory high-density lipoprotein, complement activation, and antiphospholipid antibodies as well as a higher incidence of traditional risk factors in SLE contribute to atherogenesis. An understanding of these mechanisms provides opportunities for targeted management of risk factors. The effectiveness of CVD risk management strategies can be enhanced by educating women with SLE about the increased CVD risk that SLE confers. Many women with SLE are unaware of their increased risk despite years spent in the health care system, thus giving the atherogenic process time to accrue damage. Research has not explained fully why women with SLE are unaware of their increased risk for CVD or why awareness does not correspond to risk-educing behaviors. Studies that investigate personal and healthcare system factors and how they contribute to awareness of CVD risk stand to inform both educational and treatment interventions.

Part A: Mechanisms of Premature and Accelerated Atherosclerosis in Systemic Lupus Erythematosus

Over the past three decades, survival rates in systemic lupus erythematosus (SLE), a chronic autoimmune disease, have substantially improved particularly in the early course of SLE due to a trend in decreased deaths from infection and renal disease.[1] However, a similar decrease in deaths due to cardiovascular disease (CVD) has not been observed. As a consequence, heart disease has emerged as the most common cause of death among SLE patients with disease duration greater than five years.[2]

The burden of CVD in people with SLE is excessive, and its prevalence is substantially disproportionate compared to that in the general population. Women with SLE age 35 to 44 years have 50-times the risk of fatal vascular events compared with non-SLE matched controls[3]; women with lupus age 18 to 44 years are more than 2-times likely to be hospitalized for myocardial infarction, over 3-times as likely to develop congestive heart failure, and 2-times as likely to have a cerebrovascular accident (CVA) than non-SLE women.[4] Women with SLE also exhibit an increased incidence of subclinical atherosclerosis.[5]

Although a higher frequency of traditional CVD risk factors has been reported in lupus patients, it does not fully account for the increased CVD risk.[6] Some investigators now consider SLE to be an independent risk factor for heart disease equivalent to diabetes in the degree of increased CVD risk it confers.[6-8]

Inflammation, SLE and Atherosclerosis

The cellular interactions in the development of atherosclerosis are fundamentally the same as those in chronic inflammatory diseases.[9,10] Various stimuli have been implicated as

causes of inflammation related to atherosclerosis including but not exclusive to low-density lipoprotein (LDL) modified by advanced glycosylation end-products produced in diabetes, shear stress, free radicals from cigarette smoking, genetic alterations, elevated homocysteine levels, infectious agents, and immune complexes (ICs).[11]

Leukocytes do not normally adhere well to vascular endothelial cells. However, during periods of inflammation, pro-inflammatory cytokines stimulate vascular endothelial cells (EC) to express adhesion proteins on their surfaces.[12, 13] These adhesion proteins attract platelets, monocytes and T cells. Adherent platelets then secrete potent inflammatory mediators and chemokines that recruit more platelets as well as monocytes.[14] Inflammation also stimulates the production of reactive oxygen species (ROS) in the intima. ROS are highly active molecules such as free radicals, superoxide, hydrogen peroxide, and hypochlorous acid, that kill pathogens.[10]

Low-density lipoprotein (LDL) is the major plasma lipid carrier.[15] It circulates in the plasma while a portion of it crosses into the subendothelial space from where it can return to the plasma. In its native state, LDL is non-atherogenic. The exact mechanism of LDL oxidation and its relevance to the pathogenesis of atherosclerosis remains under investigation.[10, 16] It is speculated that ROS may oxidize LDL (oxLDL) in the subendothelial space where macrophages phagocytize oxLDL.[17] This internalization of LDL results in the formation of foam cells that herald the onset of atherosclerosis with the appearance of fatty streaks in the intima and the eventual evolution of the atheromatous plaque.[9]

Meanwhile, T cells join macrophages in the arterial intima and mount T helper-1 responses that promote secretion of pro-inflammatory cytokines and growth factors that stimulate migration and proliferation of smooth muscle cells to the intima. The activated

macrophages and endothelial cells release fibrinogenic mediators that form the fibrous cap, a collagenous extracellular matrix that surrounds the atherosclerotic lesion.[11] The integrity of the fibrous cap depends upon the balance between synthesis and degradation of the extracellular matrix of the cap. Collagen breakdown, as well as buildup, appears to depend on macrophages. Activated macrophages express proteolytic enzymes that degrade and thin the fibrous cap, rendering it vulnerable to rupture.[18] After the plaque ruptures, macrophages produce procoagulant tissue factor, which triggers thrombosis.[9] Thereupon, the central role of inflammation from initiation through development to rupture of the atherosclerotic plaque and subsequent thrombus formation becomes evident.

Endothelial Dysfunction

Endothelial dysfunction precedes the development of atherosclerosis. Inflammatory stimuli activate EC to express adhesion molecules that initiate the atherosclerotic process described above. Local inflammatory mediators also cause EC apoptosis.[19] Vascular injury stimulates EC cells to produce vascular endothelial growth factor, a potent angiogenic molecule, which in turn stimulates mobilization of endothelial progenitor cells (EPC) to sites of vascular injury where they develop into mature ECs.[20] Repair of vascular damage then takes place, which is critical in the prevention of atherosclerosis.

In SLE, the endothelium is chronically exposed to inflammatory stimuli, such as interferon-alpha (IFN-α). Recently, research by Denny et al[21] revealed IFN-α as a promoter of abnormal vascular repair in SLE by activating apoptosis of cells concerned with blood vessel function.[21] In vitro studies revealed that normal EC anti-angiogenic properties were restored when IFN-α was blocked in cultured cells, an effect observed only in the cells from SLE patients

that had shown abnormal EC function. This effect was not seen when other cytokines were blocked. These investigators proposed that this imbalance between EC damage and repair mediated by IFN-α might be a major mechanism of premature atherosclerosis of SLE. This hypothesis is supported by other studies that have shown low EPC numbers correlated with higher rates of CVD events.[22, 23]

Pro-inflammatory High-Density Lipoproteins

High-density lipoproteins (HDLs) are a highly heterogeneous class of lipoproteins that under healthy conditions are anti-inflammatory and atheroprotective.[24-26] HDL has been long recognized as atheroprotective by virtue of its role in reverse transport of cholesterol from macrophages in the arterial wall to the liver.[27] Murine studies suggest HDL also plays an important role in triglyceride metabolism.[28, 29] In addition, HDLs perform functions unrelated to lipid transport that protect against atherosclerosis. HDL inhibits ROS that oxidize LDL;[30] it suppresses expression of endothelial adhesion molecules, monocyte chemotactic protein-1 (MCP-1), and platelet activating factor; and it possibly stimulates production of endothelial nitric oxide.[31] These understandings correspond with epidemiological studies that show an inverse relationship between low HDL levels and atherosclerosis.[32-34]

During the acute phase response, HDL can convert to a pro-inflammatory state that promotes oxidation of LDL and reduces many of HDL's protective actions.[35] Under certain inflammatory conditions, such as SLE, the acute phase response becomes chronic, and the persistent presence of dysfunctional pro-inflammatory HDL (piHDL) may be a mechanism for increased atherosclerosis in SLE.[36] McMahon et al found that 50% of women (n=171) with SLE had piHDL compared to 7% of healthy controls (n=85).[37] Multivariate analysis including

traditional and SLE risk factors revealed that piHDL and higher levels of LDL were the only significant factors for plaque development.

Upregulation of CD40 and CD40 Ligand

CD40-ligand (CD40L) is a protein on the surface of several cells, including T cells, B cells, macrophages, platelets, endothelial cells, and vascular smooth muscle cells that binds to its receptor CD40, a protein expressed on the surface of mature B cells.[38] The binding of CD40L on the T cell with CD40 on the B cell is the mechanism by which T cells directly induce B cell activation required for antigen specific immune responses.[39] Normally, T cell expression of CD40L is fleeting, therefore limiting B cell activation. However, in SLE, T cell activation is increased and prolonged, which likely contributes to the immune dysfunction in SLE.[40] Upregulation of CD40-CD40L ligation triggers inflammatory and thrombotic processes essential to atherogenesis that have been described previously. CD40-CD40L binding also induces macrophages to synthesize and secret enzymes that weaken the fibrous cap of the atherosclerotic lesion, thus facilitating plaque rupture.[41] Higher levels of circulating CD40L are associated with atherosclerosis.[42,43,44] Although studies thus far do not have enough power to establish upregulation of CD40L as a cause for CVD, it is another aberration shared by SLE and atherosclerosis.

Activation of the Complement System

Complements are blood proteins, called such because they "complement" the antigen binding function of antibodies.[39] The bound antigen and its antibody are referred to as an immune complex (IC). Complement proteins remain functionally inactive until foreign microbes,

or self-antigens and autoimmune complexes in the case of SLE, activate them. Once activated, the complement system begins a cascade of enzymatic reactions that facilitate non-inflammatory uptake by phagocytes.[45] Complement C3 and C4 binding marks the IC so it can be bound by circulating cells, especially erythrocytes, and delivered to the liver or spleen where it is degraded.[46] Unbound or soluble complement-derived fragments, namely C3b and C4b, also bind to the IC, which prevents aggregation of the IC into an insoluble complex.

Individuals with SLE are frequently deficient in complement, particularly C3 and C4, because of genetic and/or acquired factors, as when complement is increasingly consumed during periods of heightened disease activity.[46] Decreased levels of C3 and C4 may not allow adequate binding of C3 and C4 fragments to the IC, thus preventing the formation of soluble ICs and impairing their delivery to phagocytes. If the ICs are not cleared, they tend to enlarge by aggregation and precipitate in the basement membrane of small blood vessels and cause organ damage, especially in the kidneys.[46] Moreover, ICs upregulate adhesion molecules involved in the binding and recruiting of monocytes and T cells in atherogenesis and also can precipitate into the glomeruli resulting in nephritis and hypertension, both CVD risk factors.

C-Reactive Protein

C-reactive protein (CRP) is an acute phase protein synthesized in the liver in response to inflammation and is widely used as an inflammatory marker in rheumatologic disorders. Moreover, numerous studies have established it as a predictor of CVD in the general population, particularly in women.[47-50] When both CRP and LDL levels are elevated, the risk for developing CVD is increased ninefold.[51]

CRP activates the complement system, and it has been suggested that it may have a protective effect in autoimmune disorders, since it can bind the cellular debris of apoptic cells. However, in contrast to other rheumatic diseases, CRP is a poor acute phase responder in SLE flares.[52, 53] Investigators have located gene polymorphisms associated with lower CRP levels on a locus linked to SLE. It is hypothesized that defective clearance of autogenic material may contribute to SLE pathogenesis. Markedly elevated CRP levels are found in SLE patients with infections but otherwise are only moderately elevated, even in those patients with very active disease.[54] It is speculated that the inappropriate CRP response in SLE may favor its use as a marker of CVD risk since usually only infections can raise serum CRP levels.[55]

Antiphospholipid Antibodies

Antiphospholipid antibodies (aPLs) are the leading cause of acquired hypercoagulability in the general population.[56] They are a group of heterogeneous antibodies that include anticardiolipin antibody (aCL) and lupus anticoagulant (LA) and can occur naturally in the general population in association with infections, malignancies and aging. They also can be a manifestation of an autoimmune disorder, such as SLE. Approximately 30% of SLE patients have aPLs, and about half of them will develop antiphospholipid syndrome (APS), a disorder characterized by the presence of aPLs plus the occurrence of a thrombotic event.[57] Antiphospholipid antibodies in the presence of an autoimmune disease, such as SLE, at least double the risk of thrombosis.[58]

The term antiphospholipid antibody is misleading because most aPLs do not recognize phospholipids directly, but instead recognize phospholipid-binding proteins, such as beta-2-glycoportein 1 (β_2GP1).[59] β_2GP1 is a plasma protein that inhibits platelet aggregation, activates

platelet prothrombinase, and is involved in both pro- and anti-coagulant activities of the coagulation pathway.[60]

The coagulation system is unable to differentiate between a ruptured blood vessel and endothelial cells activated by inflammatory cytokines. It will initiate the coagulation cascade under both circumstances, which leads to thrombus formation. When the thrombus forms as a result of inflammation, the result can be phlebitis, myocardial infarction or stroke depending upon its location. In order to prevent this potentially lethal phenomenon, endothelial cells secrete potent antagonists of platelet activation. In addition, plasma contains several coagulation inhibitors as well as fibrinolytics to dissolve the thrombus.[61]

Normally, β_2GP1 binds to oxLDL and forms a complex resistant to uptake by macrophages, thus providing some degree of protection against atherosclerosis. However, in SLE and other autoimmune disorders, aCL targets β_2GP1 to form anti-β_2GP1 antibodies. When anti-β_2GP1 antibodies bind to oxLDL-β_2GP1 complexes, it facilitates macrophage uptake leading to increased foam cell formation.[62, 63]

Anti-β_2GP1 antibodies also bind to platelets. This induces production of thromboxane, activation of platelets, and enhanced expression of platelet membrane glycoproteins, especially glycoprotein IIb/IIIa and GPIIIa. The net result is platelet aggregation and thrombosis.[64]

Lupus Dyslipidemia

Hyperlipidemia (elevated total cholesterol, LDL, and triglycerides) is a well-established CVD risk factor in the general population as well as in individuals with SLE. Several studies have shown a “lupus pattern” of dyslipidemia that is characterized by high levels of

lipoprotein(a), very low-density lipoprotein, and triglycerides (TG), and low levels of HDL. SLE disease activity appears to enhance these alterations.[65]

One reason for these lipid abnormalities in SLE may be due to an accumulation of chylomicrons. Chylomicrons are the triglyceride-rich lipoproteins that transport dietary lipids absorbed from the intestines. Chylomicrons are broken down by the enzyme lipoprotein lipase (LPL). LPL is bound to endothelial surfaces and is downregulated by inflammatory cytokines.[66] As a consequence, individuals with SLE have decreased lipolysis and slowed chylomicron removal leading to increased levels of TG.[67] Studies also have demonstrated anti-LPL antibodies in SLE.[68] Although hyperlipidemia is a CVD risk factor, it is the interplay between blood lipids and chronic inflammation that likely contributes to increased atherosclerosis in SLE.

Homocysteine

Homocysteine is a sulfur amino acid formed by the liver during the metabolism of methionine, an essential amino acid derived from animal proteins. Dietary deficiencies of vitamin B6, folic acid and vitamin B12 can dysregulate methionine metabolism and lead to hyperhomocsyteinemia.[69] Homocysteine is prothrombotic, decreases the availability of the vasodilator nitric oxide, enhances EC apoptosis, and combines with LDL to form foam cells in vascular walls.[70-107] Epidemiological studies support an association between elevated homocysteine levels and an increased risk for atherothrombosis.[71] High homocysteine levels in SLE have been linked to CVD and independently related to progression of atherosclerosis.[72,73]

Severe hyperhomocysteinemia is rare. Mild hyperhomocysteinemia occurs in about 5-7% of the general population, while a large prospective study revealed elevated homocysteine levels in 15% of patients with SLE.[74, 75,76] This is likely due to several factors. Persistent inflammation

heightens DNA synthesis of immune cells, which in turn increases vitamin consumption.[77] Decreased glomerular filtration, a common feature of SLE, is linked with elevated homocysteine for reasons that remain unclear.[78] Methotrexate is an immunosuppressive drug commonly used in SLE. It interferes with folate metabolism as well as causes gastrointestinal toxicity that can impair vitamin absorption.[79]

Folate and B vitamins are known to decrease homocysteine levels, but research has failed to show a reduction in vascular events with vitamin therapy.[80-82] However, it has been suggested that high homocysteine levels may have a synergistic effect with other CVD risk factors and thus cause more damage in SLE patients than in non-SLE.[73]

Corticosteroid Therapy

Corticosteroids are the mainstay of SLE therapy, and it is widely assumed that they worsen metabolic conditions, such as insulin resistance, hyperlipidemia, obesity and hypertension, that contribute to CVD.[83] Several studies have examined the contribution of corticosteroid therapy to the development of atherosclerosis in SLE with inconclusive results because of the difficulty in sorting out the effects of disease activity that require steroid therapy from the effects of steroids themselves on atherosclerosis as well as the anti-inflammatory effects of steroids.

A recent study found that SLE patients with carotid plaque had been treated with less total steroid dose than those without plaque, suggesting controlling inflammation reduces CVD risk.[5] In an earlier study, prednisolone doses <10 mg/day did not show an adverse effect upon lipids while doses ≥10 mg/day increased TG with a corresponding increase in vascular disease.[84] Other investigators also have found a dose-dependent or cumulative dose effect of steroids on

CVD risk factors.[8, 85, 86] Additionally, research has shown that the most ill SLE patients who require the highest doses of corticosteroids are not necessarily the ones at the greatest risk for CVD, but instead cumulative dose and long-term duration of corticosteroid treatment predict increased risk.[87, 88] The reason for the increased risk was attributed to steroid-induced increases in traditional CVD risk factors, such as hypertension, increased cholesterol and weight gain. Most recently, Karp et al showed that higher corticosteroid dose in the past year was associated with significantly higher blood pressure, total cholesterol, HDL, LDL, triglycerides, body mass index and blood glucose.[89] A dosage increase of 10 mg was associated with approximately a 16% increase in estimated risk for CVD event over the following two years, whereas an increase in disease activity (6-point increase in the Systemic Lupus Erythematosus Disease Activity score) was associated with only a 5% CVD risk increase.

Renal Impairment

Although about one-third individuals with SLE develop lupus nephritis, histological evidence of lupus nephritis is present in most SLE patients, even if they do not have symptoms of renal disease.[90] A history of renal disease or elevated serum creatinine is associated with early atherosclerosis in SLE.[86, 91] Even renal impairment categorized as "mild" is associated with CVD events.[92] Nephrotic syndrome and excess proteinuria are associated with hyperlipidemia and prothrombotic risk, which may contribute to the development of atheroscelrosis.[93] Likewise, parathyroid hormone, endothelin-1, and circulating calcium are elevated in patients with renal failure and contribute to vascular thickening. Hence, cardiovascular disease in SLE patients with renal impairment is likely multifactorial in origin.[94, 95]

Insulin Resistance

Insulin resistance (IR) has been studied as a possible risk factor for CVD in the general population. It is one of a cluster of factors that determines the presence of the metabolic syndrome, which is associated with an increased CVD risk as well as the development of type 2 diabetes, particularly in women.[86, 96] SLE patients have a higher risk of IR and abnormal insulin secretion than age-matched healthy controls.[97, 98] Several inflammatory markers are associated with IR.[99, 100] Furthermore, non-diabetic SLE patients have demonstrated insulin resistance unrelated to obesity or steroid use.[101] It is thought that in inflammatory diseases, such as SLE, oxidative stress, and insulin resistance enhance one another.[102]

Depression

A high prevalence of depression exists among SLE patients that is likely multifactorial in etiology.[103-105] An association between depression and inflammation has been demonstrated, but it is unclear whether inflammation induces depression or depression induces inflammation.[106-108] Most recently, the cytokines tissue necrosis factor-alpha (TNF-α) and interferon-gamma (IFN-γ) were shown in murine studies to activate indoleamine 2,3 deoxygenase, a pivotal mediator of inflammation-induced depression.[109] In addition, cerebrovascular endothelial injury due to inflammation has been suggested as a possible mechanism for mood disorders in SLE. Endothelial injury increases blood-brain-barrier permeability, which gives pathogenic auto-antibodies access into the brain, an area usually protected from harmful immune-response effects.[110]

Prospective studies have shown that depression significantly predicts the risk for the first CVD event, independent of other traditional risk factors, especially in women.[111-113] A 3-year

study of older, healthy adults found that increased levels of depressive symptoms at baseline were associated with changes in carotid intima thickness.[114] Depression also has been associated with increased risk for atherosclerotic progression following bypass surgery.[115] Moreover, in a cohort of women without baseline CVD, depressive symptoms were associated with a higher risk of fatal cardiac events.[116] SLE women with depression but without previous CVD history were more than twice as likely to have coronary artery calcification compared to healthy non-SLE controls, a finding attenuated by adiposity.[117] The authors hypothesized that depression may influence lifestyle choices, such as poor diet and decreased physical activity, that contribute to weight gain, or conversely, elevated BMI may cause decreased activity and depression.

Sedentary Lifestyle

Physical inactivity is a well-documented risk factor for CVD. One mechanism by which exercise may reduce CVD risk is through downregulation of TNF-α and CRP.[118, 119] A sedentary lifestyle tends to be more prevalent in women with SLE than their non-SLE counterparts.[7] This is most likely due to the reduced muscle strength and exercise capacity, more fatigue, and greater disability in these women compared to sedentary controls.[120] One study showed that 78% of women with mild SLE demonstrated on treadmill testing insufficient aerobic capacity to carry out normal activities of daily living for more than short periods of time.[121] This significantly reduces their ability to engage in physically active lifestyle that includes regular exercise.

Earlier Menopause

Approximately 15-30% of women with SLE experience menopause 3-4 years earlier than women without SLE.[7, 122] Disease factors and immunosuppressive drugs, such as

methotrexate and cyclophosphamide, used to treat SLE contribute to premature ovarian failure.[123-125]

A recent meta-analysis showed a modest effect of younger age at menopause on CVD risk.[126] The effect was more pronounced for women with an artificial menopause, such as those who have oophorectomies or experience premature ovarian failure due to chemotherapy. Menopause causes an estrogen deficiency that induces metabolic and hemodynamic changes that may accelerate atherosclerosis.[127] Research suggests that for every year before age 50 that menopause begins, there is an associated 2% risk increase for heart disease.[128] It should be noted, however, that the impact of menopause and the ensuing loss of estrogen on CVD risk remains controversial. Some researchers suggest that it is not menopause that adversely affects cardiovascular risk, but instead CVD risk factors determine age at menopause, either by inducing ischemic changes in the ovaries or directly effecting the endocrine system.[129] In such a scenario, the increased risk for CVD in women with SLE possibly could be predicted by age at menopause.

Part B: Awareness of Increased CVD Risk in Women with SLE

Women with SLE who are under the care of a healthcare provider for a chronic disorder that confers a considerable burden in regards to CVD risk might be expected to have more opportunities to receive health information and lifestyle recommendations and therefore demonstrate an increased knowledge about heart disease risks and preventive behaviors. However, the limited research that assesses awareness of increased CVD risk and risk-reducing behaviors in women with SLE suggests they are unaware of their increased CVD risk.[122, 130, 131]

This lack of awareness has significant clinical implications since accurate perception of CVD risk is a crucial first step in adopting risk-reducing behaviors.

Several studies have examined knowledge of CVD in women in general, the most prominent of which is the American Heart Association (AHA) surveys conducted from 1997to 2006.[132-136] The most recent survey of women's knowledge of heart disease by the AHA in July 2006 showed that awareness of CVD as the leading killer of women had increased from 30% in 1997 to 57% in 2006 ($p<0.05$).[132] No studies to date have examined general knowledge about heart disease in individuals with SLE.

Factors Affecting Awareness

Several factors, both personal and related to the healthcare system, likely affect CVD risk awareness in women with SLE. Nonetheless, few studies have evaluated the contribution that such factors make to knowledge about heart disease in women in general, let alone women with SLE.

Age

SLE affects people of all ages, although symptoms most often appear between the age of 15 and 40 years. In one study of ethnically diverse women without SLE or a history of CVD, older age was a significant predictor of coronary artery disease (CAD) risk perception.[137] According to the Kaiser Women's Health Survey, a nationally representative telephone survey of 2,766 women in the US age 18 and older, cholesterol screening rates in women increased with age from 49% in ages 18-44 years to 76% in women age 65 years and older.[138] However, other studies have found the opposite or shown no relationship between age and CVD knowledge

level.[137, 139] One study revealed that older women failed to see themselves at risk for CAD even though they had risk factors or health problems that predisposed them to CAD.[140] A recent study found that younger SLE patients were 4.2 times more likely than older patients to recognize SLE as a CVD risk factor.[131]

Gender

SLE occurs more commonly in women with a gender distribution of 9:1 (female: male).[141] Despite a substantial increase in awareness of heart disease as the leading cause of death by US women,[132] women in general continue to perceive heart disease as a man's disease, even when they have a significant family history of CAD.[142, 143] Moreover, a recent Canadian study showed that women who actually had heart disease continued to perceive CAD as a man's disease.[144] General knowledge about heart disease, including heart disease as the leading cause of death in women, has not been assessed in women with SLE.

Race/Ethnicity

SLE affects minorities disproportionately in numbers and with more severe clinical manifestations.[145] The incidence of SLE is 2-3 times higher in African American women than in non-Hispanic whites.[141] Results of a survey conducted by the Lupus Foundation of America (LFA) indicated that just as many if not more Hispanic individuals have SLE than African Americans.[146] It is believed that other minorities such as Asians and native Americans also may be affected disproportionately by SLE,[141] but no reliable statistics exist to confirm this possibility.

Socioeconomic factors may be more likely to affect CVD risk awareness in minority women with SLE than their white counterparts.[147] Greater numbers of minorities live below the poverty line, which often translates into lower levels of education, decreased access to health care and lack of health insurance.[148, 149] The Institute of Medicine reported that almost half of American adults have a problem understanding and implementing health information, with the problem greatest among Hispanics (50%), African Americans (40%), and Asians (33%).[150]

Income

The Kaiser Women's Health Survey reported that one third of low-income women (≤$29,552/year for a family of 3 in 2004) had delayed or forgone health care in the past year, a rate 2.5 times higher than that of higher income women.[138] Family income also influenced site of care. Low-income women were twice as likely as higher income women to have used clinics, health centers and emergency rooms for routine care. Women with Medicaid reported financial barriers to receiving care suggesting that co-payments of any size may be an obstacle for low-income women. In addition, low-income women were four times as likely than higher income women to have transportation problems that interfered with obtaining care.

A study conducted to determine the impact of income on disease activity in a multiethnic cohort of people with SLE revealed that those with lower incomes tended to be younger, female, non-white, less educated, unmarried, less likely to have health insurance, and more likely to live below the poverty line.[151] These women also tended to have more disease activity, more illness-related behaviors, less social support, and lower levels of self-reported mental functioning.

Education

The AHA survey in 2005 reported that women with a college degree were more likely to be aware of CVD as the leading cause of death compared to women who had completed some college or less.[152] While other studies likewise have reported the predictive power of women's education level to their knowledge about CVD and its risk factors, [153-156] some studies have not found such a relationship.[157] The relationship between educational level and awareness of CVD risk or knowledge about heart disease has not been examined in women with SLE.

Duration of Illness

The longer an individual has a chronic illness, the more time the disease has to disrupt physiological and psychosocial functioning.[158] On the other hand, it seems logical that the longer an individual has a chronic illness such as SLE, the more time he or she will spend in the healthcare system and therefore have more opportunities to receive health information and lifestyle recommendations from healthcare providers. Investigators have examined "time since diagnosis" as a predictor of patients' knowledge in diabetic and breast cancer populations with equivocal results.[159-162] Thus far, only Petri and colleagues have looked at the relationship between duration of illness and knowledge of CVD risk factors in patients with SLE and found no correlation.[122]

Health Insurance

Cost or lack of health insurance can affect access to care, which includes preventive screenings and self-management of chronic conditions.[163, 164] Minority women aged 45-64 without health insurance who participated in a community survey were significantly less likely to receive Papanicolaou tests and mammograms than insured women. In general, the uninsured

women also received little counseling on healthy behaviors and delayed or went without care because they could not afford it.[165] The Kaiser Women's Health Survey reported similar results.[138] Nearly 60% of uninsured women delayed or went without care because they could not afford it and 20% did not fill prescriptions because of the cost. Uninsured women in fair or poor health fared worse. Forty percent of them could not afford to fill their prescriptions. One-third reported that they were not able to see a specialist when they needed one.[166] Uninsured women or women with Medicaid were more likely than privately insured women to obtain routine care at hospitals, clinics or health centers and less likely to receive care at a doctor's office.[166]

Sources of Information about Heart Disease

Women who participated in the AHA surveys indicated television and magazines were their leading sources of information about heart disease. The AHA survey in 2006 showed a significant positive correlation between women's awareness of CVD as the leading cause of death and having seen, heard or read information on heart disease in the past 12 months.[132] Less than half (46%) of the women reported discussing heart disease with their doctor.

Support groups for individuals with SLE or SLE-specific web sites and publications may provide information on heart disease. However, these potential sources of information about CVD risk factors and risk reducing behaviors have not been investigated.

Healthcare Provider Recommendations

In a cohort of people with SLE, only 19% of the patients with a serum cholesterol level greater than 200mg/dl had been instructed by a health professional to reduce dietary cholesterol; only 2% had received prescriptions for lipid lowering medications, and just16% had received

information on a low cholesterol diet.[122] The investigators suggested that physicians caring for patients with SLE perceived SLE disease activity as the greatest threat to health, not CVD. Motivation to monitor and treat CVD risk factors therefore may have been less.

According to the 2005 AHA survey, the most common reason given for not speaking to a physician about CVD risk within the past year was that the doctor did not bring up the subject. Recently, investigators found that 58% of SLE patients did not recall receiving counseling about CVD, yet those who did receive counseling regarding CVD were 2.3 times more likely to perceive SLE as a CVD risk factor.[131] One study showed that women with access to a nurse practitioner demonstrated significantly higher CVD knowledge than those with access to physicians only.[154] This finding highlights the nurse practitioner's distinguishing role in providing health education to patients.[167]

Implications for Healthcare Professionals

The National Heart, Lung, and Blood Institute recently announced that the number of deaths from heart disease in American women has decreased from 1 in 3 to 1 in 4 based on 2005 data.[168] Unfortunately, a similar decline has not been observed in women with SLE. Aggressive measures to prevent heart disease in SLE patients may improve overall survival rates for this high-risk group. The premature and accelerated development of atherosclerosis in SLE is a complicated, multifactorial process that in turn provides many targets for treatment.

First and foremost, healthcare providers and patients need information about the increased risk for atherosclerosis in SLE. Despite knowledge since the 1970s that SLE is associated with premature and accelerated atherosclerosis, studies have shown that SLE patients

still are not receiving adequate education on CVD risk prevention.[131, 169] Indeed, those patients who did receive counseling were the ones most likely to recognize SLE as a CVD risk factor.[131]

A recent study reported that the incidence of not only traditional but also novel CVD risk factors increases within the first three years after onset of SLE.[170] This suggests that SLE patients need immediate identification and management of risk factors. Despite having a higher number of individual risk factors, the Framingham Risk score underestimates CVD risk in SLE women.[7, 171] Therefore, healthcare providers should consider extending their risk assessment beyond traditional techniques. Findings from large studies suggest using coronary calcium score along with the Framingham Risk score but substituting the Framingham age value with the age value determined by the coronary calcium score.[172-174]

The excess CVD risk beyond traditional risk factors should not be misconstrued to mean that preventive measures have little impact on the development of CVD in SLE.[175] Both traditional and non-traditional modifiable risk factors should be aggressively treated according to guidelines with special attention directed at hypertension, obesity and smoking.[176] The American Heart Association and American College of Cardiology recommend achieving LDL levels <100 mg/dL for all patients with coronary heart disease (CHD) or CHD equivalents, such as diabetes.[177] Many researchers consider SLE patients in this group. Research supports the efficacy of HMG-CoA reductase inhibitors (statins) in reducing the risk of cardiac events through their cholesterol-lowering capabilities as well as their pleiotropic effect of immunomodulation.[178] This would appear to make statins the ideal drug for SLE patients, however, clinical trials have shown statins to be minimally effective if at all in reducing atherosclerosis or disease activity in the SLE population.[179-182] In addition, liver and muscle toxicities associated with statins appear increased in SLE patients.[182] Therefore, it is important to identify those SLE patients who would benefit

from preventive treatment with statins.[183] Liver function should be monitored on a regular basis for the duration of stain therapy in SLE patients because of the increased toxicity encountered in these patients.

SLE disease control is important in reducing CVD risk since this reduces inflammation. While corticosteroids remain the primary medication for this purpose, they should be maintained at their minimum therapeutic dose. Medications that can reduce corticosteroid dose, such as mycophenolate mofetil, hydroxychloroquine, and dehydroepiandrosterone, can be started along with steroids to minimize CVD damage.[184] Several new therapies directed at specific pathophysiologic pathways are under investigation and/or in development that could spare SLE patients the harmful side effects of steroids.[185]

Early recognition of impaired renal function can lead to better treatment and reduced CVD risk. Although no practice guidelines exist yet, early findings on the use of ACE inhibitors in SLE show they may delay the development of renal involvement and are associated with decreased SLE disease activity.[186] Limited research suggests that flaxseed may be renoprotective in individuals with lupus nephritis and warrants further investigation.[187, 188]

Other measures may provide additional benefits without doing harm. Even though research has failed to show a reduction in vascular events with vitamin therapy, folic acid plus B vitamins may be worthwhile in SLE patients.[81] Both low-dose aspirin and hydroxychloroquine have been useful in primary prevention against thrombosis in SLE patients with aPLs.[189] Studies have shown that calorie restricted diets and moderate exercise improve insulin resistance and lower CRP levels even in non-obese individuals.[190-192]

A national study by the AHA regarding physician awareness of CVD prevention guidelines revealed that risk level assignment drove recommendations for lifestyle

interventions.[152] Moreover, physicians were more likely to assign women to lower risk categories than men with similar risk profiles. Studies have shown that healthcare providers fall short in identifying and treating risk factors in women with SLE despite recommendations to aggressively manage this high risk group.[4-130, 193, 194] Healthcare providers who lack knowledge of the relationship between SLE and CVD may underestimate CVD risk in women with SLE, with greater delays in suggesting or implementing risk-reducing interventions.[195, 196]

Research Implications

An extensive review of studies examining knowledge, attitudes and beliefs about heart disease revealed that there is no consistent operational definition for these concepts.[197] In addition, researchers were inconsistent in their choice of traditional CVD risk factors and questions about attitudes and beliefs concerning heart disease. This hinders comparison among studies investigating knowledge of heart disease and thus limits generalizability of findings. Consensus of risk factors, such as those identified by the AHA, may enhance comparison of findings.

No single instrument exists that accurately measures heart disease knowledge in non-medical women. Of the few instruments available that do measure CVD knowledge, many use terminology that may be unfamiliar to non-medical individuals.[154] In the aforementioned literature review, the researchers discovered that few investigators reported instrument development or psychometrics properties of their tools.[197] The development of new tools will help expand the knowledge that thus far has been derived from the AHA national surveys. In addition, individualizing tools to assess CVD knowledge in high-risk populations such as women

with SLE, will assist in the development of more robust educational interventions and the criteria for evaluating their effectiveness.

Education, race/ethnicity and income are highly correlated, thus it is difficult to determine the actual contribution each makes to awareness of CVD risk. Inclusion of these variables in studies investigating knowledge about heart disease will provide insights into factors that influence risk awareness and adoption of risk reducing behaviors. Such insights can help focus educational interventions toward populations where the need is greatest.

Conclusion

Although long-term survival has improved in SLE, healthcare providers have the opportunity to challenge that statistic with early intervention to prevent CVD. The first step is understanding the mechanisms of premature and accelerated atherosclerosis in SLE, some of which are unique, and the opportunities they provide for targeted management of risk factors. The entire spectrum of SLE patients stands to benefit by delaying the onset/and or progression of atherosclerosis, with early intervention in mild cases potentially yielding the greatest long-term results.

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CHAPTER THREE: FINDINGS

Abstract

Women with systemic lupus erythematosus (SLE) display a 7- to 10-fold increased risk for cardiovascular disease (CVD) compared to non-SLE controls, yet many are unaware of this risk despite years spent in the healthcare system. It is not clear why they lack awareness of increased CVD risk or which factors influence awareness. The purpose of this study was to assess in women with SLE: general CVD knowledge compared to women without SLE; perceived CVD risk; association between clinically identified and perceived CVD risk factors; and factors that influenced CVD risk awareness and adoption of risk reducing behaviors. Questionnaires, interviews and clinical assessments, including fasting blood specimens, were used to collect data from 60 women with SLE (45±15 years old, 12% African-American, 14% Hispanic) on: demographics; general CVD knowledge (American Heart Association [AHA] National Survey of women's awareness of heart disease); perceived CVD risk; perceived CVD risk factors; actual CVD risk factors; risk reducing behaviors; and healthcare provider counseling. Logistic regression identified factors that influenced risk awareness and adoption of risk reducing behaviors. Women with SLE in this study were more aware of women's leading cause of death than US women who responded to the 2006 AHA survey (73% v 57%), but fewer than 25% perceived themselves at increased CVD risk. Age was a significant predictor ($p=0.05$) for awareness of increased risk; younger age correlated with increased awareness. Most women received information about heart disease from public media. On average, women had 4 CVD risk factors, but they perceived they had only 2. The number of perceived risk factors predicted adoption of risk reducing behaviors ($p=0.03$). Women in this study with SLE underestimated

their CVD risk factors and did not personalize their increased CVD risk. Healthcare providers' identification and discussion of CVD risk factors in women with SLE may enhance their risk awareness and the adoption of risk reducing behaviors.

Background and Significance

Twenty-year survival rates in patients with systemic lupus erythematosus (SLE) in North America are now estimated at 78%.[1] This improvement in survival over the past three decades, particularly in the early course of SLE, is due to a trend in decreased deaths from infection and renal disease.[2] However, a similar decrease in deaths due to cardiovascular disease (CVD) has not been observed. Research has shown a 50-times greater risk of fatal vascular events in premenopausal women with SLE[3] as well as an overall increased prevalence of coronary atherosclerosis[4] and a high burden of subclinical CVD compared with non-SLE matched controls.[5-8] After adjusting for Framingham risk factors, individuals with SLE demonstrate a 7- to 10-fold increase risk for CVD and cerebrovascular accidents compared to healthy controls.[9] As a consequence, heart disease has emerged as the most common cause of death among SLE patients with disease duration greater than five years.[10] Some investigators now consider SLE to be an independent risk factor for heart disease equivalent to diabetes in the degree of increased CVD risk it confers.[11-14]

Almost all theories of health behavior posit that accurate perception of risk is a crucial first step in adopting risk-reducing behaviors.[15, 16] Stage theories of behavior postulate that health behavior change proceeds through qualitatively different stages.[17] The Precaution Adoption Process Model is unique from other stage theories in that it distinguishes individuals who are unaware of risks from those who are aware but have not actively considered risk-reducing behaviors.[18] The Common Sense Model, a self-regulatory model of health behavior, describes the emotional and cognitive processes involved in progression from one stage to the next and the formation of a personal risk/illness representation.[19] Together the Precaution Adoption Process

Model and Common Sense Model help explain the relationship between risk perception and adoption of risk reducing behaviors.

Women with SLE who are under the care of a healthcare provider for a chronic disorder might be expected to have more opportunities to receive health information and lifestyle recommendations and therefore demonstrate an increased knowledge about heart disease risks and preventive behaviors. There is limited research that assesses awareness of increased CVD risk and risk-reducing behaviors in women with SLE, and what is available suggests they are unaware of their increased CVD risk.[20-22]

Several studies have examined knowledge of CVD in women in general, the most prominent of which is the American Heart Association (AHA) national telephone surveys of over 1,000 women in the United States (US) conducted from 1997 to 2006.[23-27] The most recent AHA survey of women's knowledge of heart disease showed that awareness of CVD as the leading cause of death for women had increased from 30% in 1997 to 57% in 2006 ($p<0.001$).[27] No studies to date have examined general knowledge about heart disease in individuals with SLE.

Petri and colleagues examined the prevalence and recognition of cardiovascular risk factors and the practice of preventive behaviors by patients in the Johns Hopkins Lupus Cohort.[21] Despite a high prevalence of CVD risk factors in this cohort, the average patient with SLE did not consider him or herself to be at a high risk for the development of coronary artery disease. Limited research exists on how demographic characteristics, such as age, race, income, education, and duration of lupus as well as healthcare system factors like insurance status and healthcare provider recommendations may influence risk awareness. Most recently, research

revealed that physician counseling regarding CVD risk in SLE had a significant impact on patients' perception of personal increased CVD risk.[22]

The purpose of this study was to examine in women with SLE: (1) general knowledge of heart disease compared to women without SLE; (2) perceived CVD risk; (3) the association between clinically identified CVD risk factors and perceived risk factors; and (4) personal and healthcare system factors that influenced awareness of increased CVD risk and adoption of risk reducing behaviors.

Methods

Participants

Sixty participants were recruited from central Florida through public media, the Greater Florida Chapter of the Lupus Foundation of America (LFA) website and newsletter, and healthcare provider referrals. Eligibility requirements were female, age 18 years or older, SLE diagnosed by a healthcare provider at least 6 months prior to enrollment, not pregnant, not receiving treatment for cancer, and English speaking. Only women were recruited because of the considerably higher incidence of SLE in females compared to males (9:1)[28] and the subsequent difficulty in making comparisons across sexes in a study of this size. Women who were pregnant or receiving treatment for cancer were excluded since these conditions can alter blood lipids. SLE diagnosis was made according to classification criteria of the American College of Rheumatology (ACR)[29] and confirmed through medical records and/or a checklist of ACR SLE criteria mailed to and completed by the participant's healthcare provider.

Measures

Demographic and Healthcare System Information

Participants completed a self-administered questionnaire that requested data on personal (age, race/ethnicity, socioeconomic status, education, and medical history) and healthcare system (health insurance and duration of SLE) factors. Information regarding healthcare provider counseling and recommendations about heart disease was obtained during interview.

General CVD Knowledge

The AHA gave permission for use of its national survey of women's awareness of heart disease for use in this study. The approach to data collection used in the AHA telephone surveys was replicated as closely as possible in this study by using an interview format. Open-ended questions were asked regarding the leading cause of death in women, CVD risk factors, warning signs for heart attack and stroke, and ways to prevent CVD. Participants also responded to general statements on CVD and stroke risk, sources of information about heart disease, and healthy blood lipids, glucose, and blood pressure levels. Statements regarding understanding of heart disease and preventive behaviors used a 4-point Likert scale (strongly agree to strongly disagree) for responses. Information on reliability and validity of the survey was not provided or reported in published articles on AHA survey results. Nonetheless, the survey has been used repeatedly by the AHA from 1997 to 2006 with weighted responses in order to provide a nationally representative sample matched most recently to the March 2005 Current Population Survey for region of the country, age, race/ethnicity, income, and household size.[30] Additional

random digit dialing of Hispanic and black women was used to supplement the core sample in all of the AHA surveys.

Perceived CVD Risk

There are four essential aspects of risk perception that should be included when measuring risk perception: who is at risk, for what risk, over what time period, and what is the individual's own behavior or intent.[31] People may or may not factor in changes in behavior they anticipate making in the future when answering questions of perceived risk. As an example, one woman may believe her risk for developing heart disease is low because she plans to eat a low fat diet and exercise next week, even though she does not engage in those behaviors today. Another woman may think that her risk of developing heart disease in the coming year is low because she does not know that her diabetes is a risk factor for heart disease. The two women in this example believe their risk is low but most likely have different levels of interest in adopting preventive behaviors. Therefore, perceived risk of heart disease was assessed during the interview with the following questions:

(Absolute) "If you do not make any changes in your diet, smoking or exercise habits, what do you think are your chances of developing heart disease sometime in the future?" Answer options were: 50-50, lower or higher.

(Relative) "If you do not any make changes in your diet, smoking or exercise habits, what do you think are your chances of developing heart disease sometime in the future compared to other women without lupus?" Answer options were: the same, lower or higher.

Actual CVD Risk Factors

Established CVD risk factors (age, family history, tobacco use, dyslipidemia, hypertension, diabetes, obesity, depression, inactive lifestyle) as well as novel risk factors found more commonly in SLE patients (insulin resistance, elevated levels of homocysteine and high sensitivity C-reactive protein, impaired renal function, corticosteroid therapy, and antiphospholipid antibodies) were assessed. National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, Adult Treatment Panel III, (NCEP ATP III) guidelines[32] and recommendations by the AHA and American College of Cardiology (ACC)[33] for blood pressure, and serum lipids were used as cut-points for undesirable levels of total cholesterol (≥ 200mg/dL), high- (< 50 mg/dL) and low-density lipoprotein (≥ 130 mg/dL), and blood pressure (systolic BP ≥ 140 mmHG and/or diastolic ≥ 90 mmHg). The AHA and ACC recognize both body mass index (BMI) and waist circumference (WC) as indicators of obesity.[33] Participants with a BMI ≥30 and /or WC > 88cm were considered obese. Diagnosis of diabetes was determined using fasting glucose levels (≥126 mg/dl) recommended by the American Diabetes Association for diagnosis of diabetes in non-pregnant adults.[34] Homocysteine levels ≥12 umol/L[35, 36] and high sensitivity C-reactive protein (hsCRP) >3.0 mg/dL were considered risk factors.[37-41]

Information on age, family history of heart disease, and tobacco use was obtained on the general information questionnaire. Age was reported in years, and age ≥ 65 years was considered as a risk factor.[33] Based on research that showed inflammatory markers related to smoking returned to baseline levels 5 years after smoking cessation, a history of tobacco use within the past 5 years was considered to be a risk factor.[42] A family history was considered positive for heart disease if a biological parent or sibling experienced a cardiac event before age 55 years in male relatives and age 65 years in female relatives.[42]

Depression was measured using the Beck Depression Inventory for Primary Care (BDI-PC). The BDI-PC is a screening instrument for depression designed to minimize the effects of medical problems by focusing on symptoms of sadness, pessimism, past failures, loss of pleasure, self-dislike, self-criticalness and suicidal ideations.[43] Its 7 items are drawn from the Beck Depression Inventory-II that assesses criteria for the Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition diagnosis of major depression. The item statements relate to the way the participant has felt for the past two weeks. The Cronbach alpha for the BDI-PC has ranged from 0.85-0.88 in family practice outpatients. Scores ≥6 were shown to have 83% sensitivity and 95% specificity for distinguishing between patients with and without major depressive disorder.[44] Thus, scores ≥6 were considered positive for depression.

The Physical Activity and Disability Survey (PADS), which was designed to assess activity level in adults with disabilities and chronic illnesses, was used to assess activity level in these women.[45] Factor analysis has confirmed 4 subscales: 1) household activity; 2) time indoors; 3) exercise; and 4) leisure time physical activity with Cronbach's alphas of 0.70, 0.77, 0.67, and 0.74 respectively. Test-retest reliability over a 1-week interval ranged from 0.78 –0.99. The self-reported activity information from the PADS was evaluated to determine if the participant met the minimum activity recommendations by the AHA and American College of Sports Medicine (ACSM) to maintain health.[46, 47] If the women did not engage in moderate intensity aerobic activity for at least 30 minutes on 5 days each week, they were considered to have an inactive lifestyle as a CVD risk factor.

The homeostatic model assessment (HOMA) was used to calculate insulin resistance. HOMA values > 2.5 μU/mL were considered positive for insulin resistance as a risk factor for CVD.[48]

Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) Study equation as a reflection of renal function. eGFR < 60 mL/min/m^2 was considered a risk factor for CVD

Antiphospholipid antibodies were measured using recommended standardized beta2 glycoprotein I-dependent ELISA.[49] Lupus anticoagulant was measured by coagulation time with diluted thromboplastin and cepahlin kaolin activated time. The presence of 2 or more elevated antibody titers (anticardiolipin IgG, anticardiolipin IgM, or lupus anticoagulant) was considered a risk factor.[50]

Information on corticosteroid therapy was obtained on the general information survey. Current prednisone therapy >10mg/day for 3 months or longer was considered a risk factor.[37]

Perceived CVD Risk Factors

An open-ended question on perceived personal risk factors for CVD was asked during the interview.

Precaution Adoption Process Model Stages

The Precaution Adoption Process Model identifies 7 distinct stages in recognizing, adopting and maintaining a change in behavior that reduces risk.[51] Stage 1 describes a state in which the individual is unaware of a health risk. This stage of unawareness is unique to the Precaution Adoption Process Model and distinguishes between individuals who know nothing about the threat and those who have thought about the threat and concluded that the risk does not pertain to them. Information about and personal experience with the risk determine movement to stage 2 where individuals are aware of the risk but not personally engaged. They do not perceive

personal susceptibility to the risk even though they recognize the significance of the risk to others.[52] In order to move to stage 3 and beyond, individuals must identify with the health risk, make decisions regarding the adoption of risk reducing behaviors, and ultimately engage in preventive behaviors. A list of 7 statements that corresponded to the 7 stages of the Precaution Adoption Process Model and specific to CVD was provided during the interview (Table 3.1).

Table 3.1
Precaution Adoption Process Model Stage Items

STAGE 1: I don't think I'm at greater risk of getting heart disease than any other woman.

STAGE 2: I know I am at risk for heart disease but I haven't thought much about it.

STAGE 3: I am thinking about changing my behaviors to decrease my chances for getting heart disease, but I haven't made up my mind if it is something I want to do.

STAGE 4: I have thought about changing some of my behaviors to decrease my chances for getting heart disease but I have decided against it.

STAGE 5: I have decided to change some of my behaviors to decrease my chances for getting heart disease, but I have not started doing them yet.

STAGE 6: I have recently changed some of my behaviors within the last month to decrease my chances for getting heart disease.

STAGE 7: I have made changes in my behavior to decrease my chances for getting heart disease for at least 6 months.

Procedure

The University of Central Florida Institutional Review Board (IRB) gave approval for the study. A general information questionnaire was mailed to participants who were asked to bring the completed questionnaire to the data collection meeting. Information on demographics, family history, tobacco use, medical history, and health insurance status as well as responses to the BDI-PC and PADS was obtained on the general information form.

The remainder of the data collection occurred during a face-to-face meeting between the participant and the investigator. All participants had height, weight, WC, and blood pressure measured. Fasting blood samples were collected for lipid profiles, glucose, insulin, creatinine, homocysteine, C-reactive protein, and antiphospholipid antibodies. Upon completion of clinical assessment and blood draw, the AHA survey was administered in an interview format. Participants also were asked questions regarding their perceived CVD risk and risk factors, and healthcare provider recommendations. They chose the statement on the 7-item Precaution Adoption Process Model stage list that best described their level of risk awareness and adoption of risk-reducing behaviors.

In order to prevent bias in responses regarding perception of CVD risk, participants were told that the name of the research project was the Lupus and Risk Awareness (LARA) Study and informed that its purpose was to assess risks for co-occurring medical conditions in patients with lupus. Heart disease was not specifically mentioned. The IRB approved this approach. At the conclusion of the face-to-face meeting, participants were told that the main objective of the study was to assess CVD risk.

Within 2 weeks following completion of their data collection, participants received a personalized CVD risk profile including laboratory results and recommendations for preventive behaviors to modify risk factors. They also were given a telephone number to contact the principal investigator if they had questions about their results.

Statistical Analyses

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) v.11.0 (Chicago, IL). Descriptive statistics were calculated to characterize the

sample and provide summary data. Logistic regression models were used to evaluate the effect of age, race/ethnicity, education, health insurance, duration of SLE, and healthcare provider recommendations on awareness of increased CVD risk. Regression models also were used to determine the effect of age, race/ethnicity, education, duration of SLE, number of perceived CVD risk factors, and healthcare provider recommendations in distinguishing women in one stage of the Precaution Adoption Process Model from those in different stages. Education was used to represent socioeconomic status (SES). The findings of a recent large, prospective study suggested that education is a robust measure of SES compared to other measures such as occupation and income since it varies little in adulthood and can be measured with less error than other measurements of SES.[53] Responses of the study's participants to the AHA survey were compared descriptively to published responses to the 2006 AHA national survey by US women, who served as the control group for drawing conclusions on the level of general knowledge of CVD in women with SLE. Statistical significance for inclusion as a predictor in all models was set at $p<0.05$. CVD risk factors were assessed as present if they met the following criteria: total cholesterol ≥ 200mg/dL, high-density lipoprotein < 50 mg/dL, low-density lipoprotein ≥ 130 mg/dL, blood pressure systolic BP ≥ 140 mmHG and/or diastolic ≥ 90 mmHg, BMI ≥30 or WC > 88cm, fasting glucose ≥126 mg/dL, homocysteine >12 umol/L, hsCRP >3.0 mg/dL, BDI-PI score ≥6, moderately intense aerobic activity <30 minutes on 5 days/week, HOMA value for insulin resistance > 2.5 μU/mL, eGFR < 60 mL/min/m^2, presence of 2 or more elevated antiphospholipid antibody titers, prednisone therapy >10mg/day for 3 months or longer, age ≥ 65 years, tobacco use within the past five years, and parent or sibling with history of cardiac event.

Results

Participants

Sixty participants were enrolled in the study over the course of 11 months. The ACR developed criteria for SLE diagnosis in order to standardize heterogeneity for lupus research studies.[29] To satisfy ACR criteria for SLE diagnosis, a patient must meet at least 4 of 11 criteria. In this study SLE diagnosis was confirmed by physician-completed ACR SLE criteria checklists for 35 participants. Checklists returned on an additional 15 participants showed that they fulfilled 3 of the 11 ACR criteria, and the women reported that they had been told by their healthcare provider that they had SLE. Six participants provided personal copies of medical records that confirmed diagnosis. No checklists or medical records were obtained for four of the participants. Their medical history, current medications, and laboratory data obtained during the study was reviewed by the investigator, a nurse practitioner, who confirmed the presence of at least two of the 11 ACR criteria. These four women had been told by their healthcare provider that they had SLE, and they perceived themselves as SLE patients as did the 15 participants who met 3 of 11 ACR criteria according to physician-completed checklists. Since this was a descriptive study examining risk perception, they were included in the sample. Ages ranged from 19 to 80 years, and over 25% were minority women. The average duration since SLE diagnosis was $\pm$8 years. The vast majority had attained an educational level beyond high school (Table 3.2).

Table 3.2
Sample Characteristics

N = 60 women with SLE	N	Percent
Age, years	44.8±14.5	
Race		
White	44	73%
Black	7	12%
Hispanic	8	14%
Other	1	<1%
Years since SLE diagnosis	8.2±8.3	
Education, years	14±1.9	

General CVD knowledge

A comparison of awareness of the leading cause of death among women by race/ethnic group between the study group and respondents to the 2006 AHA national survey[26] is presented in Table 3.3. Overall, nearly three-quarters of the women in the study correctly identified heart disease as the leading cause of death for women compared to just over half of the respondents to the AHA survey. While white women were significantly more likely to correctly identify heart disease as the leading cause of death compared to black and Hispanic women in the AHA survey, the opposite was found in this study. More black and Hispanic women were aware of the leading cause of death for women than white women, although the difference was not statistically significant. When comparing awareness of leading cause of death by age groups, a greater percentage of the SLE participants identified heart disease as the leading cause of death compared to AHA respondents across all age groups except for 45-65 year olds (Table 3.4). When asked to identify the leading cause of death for women with SLE, 20% of the women in the study stated heart disease. Knowledge of heart attack and stroke symptoms was similar in both the SLE and AHA groups (Table 3.5). In the study group, 22% of the women considered

themselves well or very well informed about heart disease compared to 42% of the respondents to the 2006 AHA survey.

Table 3.3
Comparison of Awareness of Leading Cause of Death Among Women by Race/Ethnic Group

Response (unaided)	AHA All	SLE All	AHA White	SLE White	AHA Black	SLE Black	AHA Hispanic	SLE Hispanic
Breast cancer, %	12	7	10	7	19	17	14	0
Cancer (general), %	22	8	19	11	26	0	33	12
Heart disease/heart attack, %	57	73	62	70	38	83	34	88
Other, %	7	3	5	5	14	0	12	0

Table 3. 4
Comparison of Awareness of Leading Cause of Death Among Women by Age Group

Response (unaided)	SLE* 19-24	AHA 25-34	SLE 25-34	AHA 35-44	SLE 35-44	AHA 45-64	SLE 45-64	AHA* ≥65
Breast cancer, %	10	7	7	7	13	17	6	0
Cancer (general), %	20	8	8	11	13	0	6	12
Heart disease/heart attack, %	50	73	78	70	74	83	76	88
Other, %	20	3	7	5	0	0	12	0

* No similar age group for comparison

Table 3.5
Perception of Symptoms of Heart Attack and Stroke

Response (unaided)	AHA	SLE	Response (unaided)	AHA	SLE
Heart attack			Stroke		
Chest pain %	62	72	Speech difficulties	32	43
Pain: neck, shoulder, arm%	56	72	Vision dimming/loss	16	18
Chest tightness %	15	5	Headache	24	23
Shortness of breath %	40	37	Weakness/numbness	42	50
Nausea %	15	13	Dizziness	17	13
Fatigue %	7	10			

The women in the study recalled unaided an average of three risk factors for heart disease, while 92% recognized all major risks factors when they were read from the list on the AHA survey (aided). Likewise, 98% recognized major preventive strategies read from the list on the AHA survey (aided). These finings are similar to those of the respondents to the AHA survey. The majority (77%) of the women in the study had seen, heard or read information about heart disease in the past 12 months as had 80% of the women who responded to the AHA survey. The most common source of information about heart disease for both the SLE and AHA women was public media (Table 3.6). Very few of the women who belonged to a lupus support group reported the group as a source of information on heart disease.

Table 3.6
Sources of Information about Heart Disease

Response	AHA	SLE
Had seen, heard or read information about heart disease in the past 12 months %	80	77
Had seen, heard or read information about the red dress symbol %	29	50
Sources of information about heart disease		
Magazines %	41	23
Television %	32	27
Healthcare provider %	28	30
Newspapers %	21	13
Internet %	11	23
Lupus support group %	N/A	10

Perceived CVD risk

Nearly 20% of the women placed themselves in stage 1 of the Precaution Adoption Process Model, which indicates they did not perceive themselves at increased risk for heart disease (Figure 3.1). Just over 20% placed themselves in stage 2, which acknowledges risk but does not give much thought to it. This placement corresponds to the participants' answers about

relative and absolute CVD risk (Table 3.7). Two-thirds saw themselves at greater risk for heart disease when compared to women without SLE (relative risk), but approximately the same number did not perceive an increase in their own absolute CVD risk. In logistic regression, age was the only significant predictor (p=.049) of awareness of increased CVD risk in women with SLE with younger age associated with increased awareness.

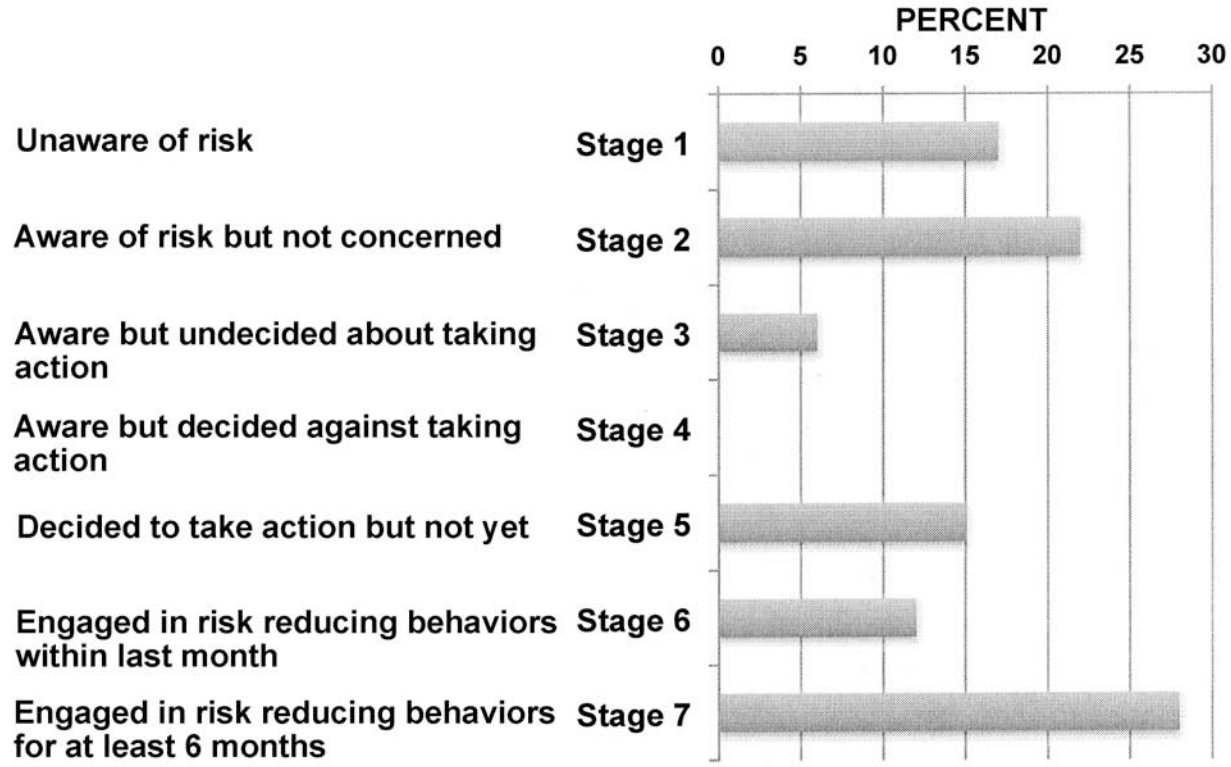

Figure 3.1: Categorization of Participants According to Precaution Adoption Process Model Stage

Table 3.7.
Perception of Absolute and Relative Risk for Cardiovascular Disease

Perceived Risk	Response	All	White	Black	Hispanic
(Absolute) "If you do not make any changes in your diet, smoking or exercise habits, what do you think are your chances of developing heart disease sometime in the future?"	Low %	47	41	50	63
	50-50 %	29	37	17	0
	High %	23	22	17	30
	Don't know %	<1	0	16	8
(Relative) "If you do not any make changes in your diet, smoking or exercise habits, what do you think are your chances of developing heart disease sometime in the future compared to other women without lupus?"	Lower %	14	9	17	38
	The same %	17	20	16	0
	Higher %	66	66	67	62
	Don't know %	3	5	0	0

CVD Risk Factors

Clinical assessment revealed that women in the study had an average of 3 major CVD risk factors (SLE excluded): dyslipidemia, hypertension, diabetes, family history, smoking, inactive lifestyle, obesity, and depression (Figure 3.2). When novel risk factors more commonly found in SLE such as elevated homocysteine level, elevated hs-CRP, corticosteroid therapy, impaired renal function, insulin resistance, and antiphospholipid antibodies were factored in, the average number of risk factors rose to 4. The most commonly identified risk factor was inactive lifestyle (60%) followed by low HDL (35%), obesity (30%) and elevated hs-CRP (29%). Of the participants with elevated hs-CRP levels (.3mg/dL), four had levels >10mg/dL, which are often associated with acute infection or inflammation. Removal of the four 4 participants with hs-CRP values >10mg/dL from analysis resulted in elevated hs-CRP as a risk factor in 26% of the

women. The prevalence of risk factors in the women in this study was similar to those reported in other lupus cohorts.[11,21]

On average, participants reported 2 personal CVD risk factors. The most commonly self-identified risk factor was inactive lifestyle, which was reported by 33% of the participants. Four participants identified novel risk factors related to SLE. One listed prednisone and the other three, two of whom had been diagnosed with antiphospholipid syndrome, reported antiphospholipid antibodies.

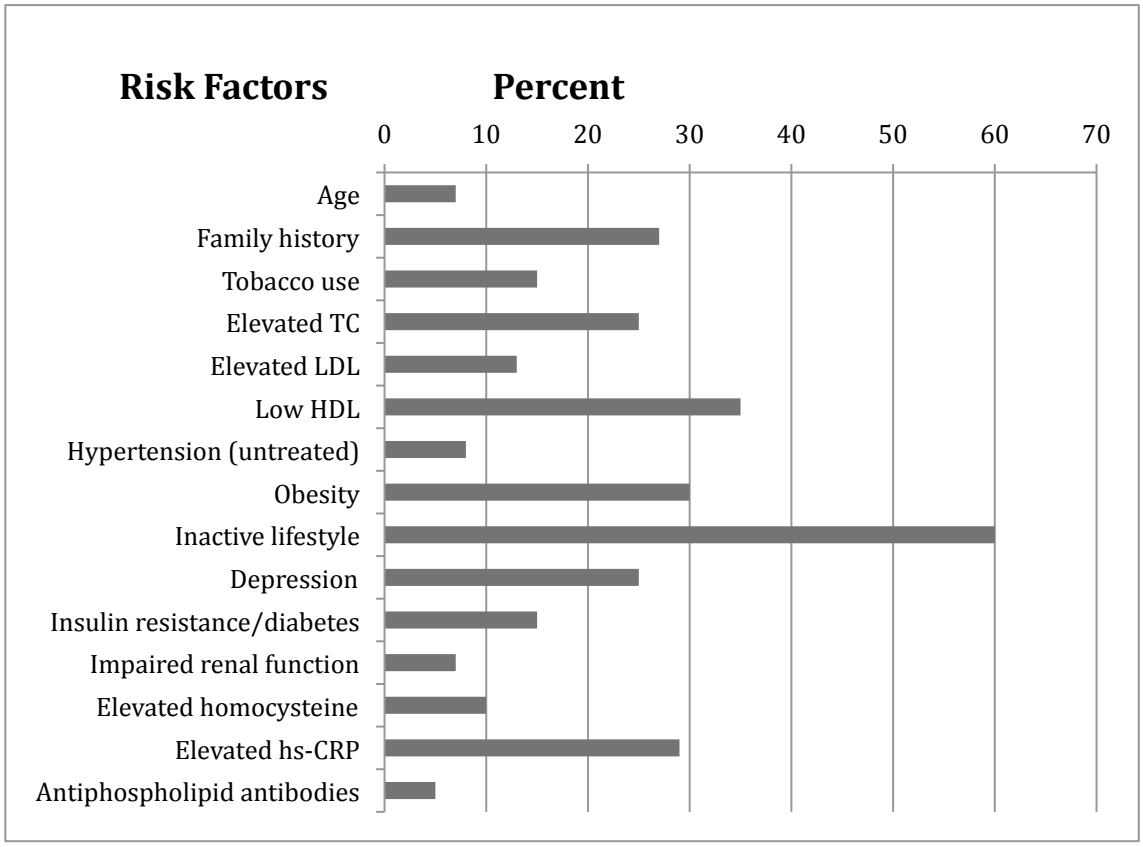

Figure 3.2: Prevalence of Cardiovascular Risk Factors in Study Women

The number of perceived risk factors was a significant predictor (p=0.028) for Precaution Adoption Process Model stage placement, with a higher number of perceived risk factors associated with progressing stages. Although 98% of the women in the study were able to identify major preventive strategies for CVD on the AHA survey, just 40% placed themselves in stage 6 or 7 of the Precaution Adoption Process Model, which indicates engagement in risk reducing behaviors. Nearly half of the women not engaged in risk-reducing behaviors reported fatigue and stress as primary reasons for not doing so. Work and lack of motivation were other reasons that were given but to a much lesser extent.

Healthcare Provider Recommendations

All of the participants thought there was something they could do to prevent heart disease compared to 86% of the respondents to the AHA survey, and 80% were comfortable talking to their doctor about prevention and treatment options. Slightly over one-third of the women in the study recalled receiving some counseling about heart disease and preventive behaviors by their healthcare provider compared to 46% of the AHA survey respondents. Of the 21 women in the study who reported receiving counseling, only 8 stated they were told that SLE confers increased risk for CVD. When women who reported not receiving counseling about heart disease were asked why they thought their healthcare provider had not discussed it with them, almost a third said it was because their provider did not see them at risk (Figure 3.3). An almost equal number stated it was because they did not bring up the subject with their provider. Participants who received counseling reported rheumatologists, cardiologists, primary care physicians, and nurse practitioners equally as providing information on heart disease.

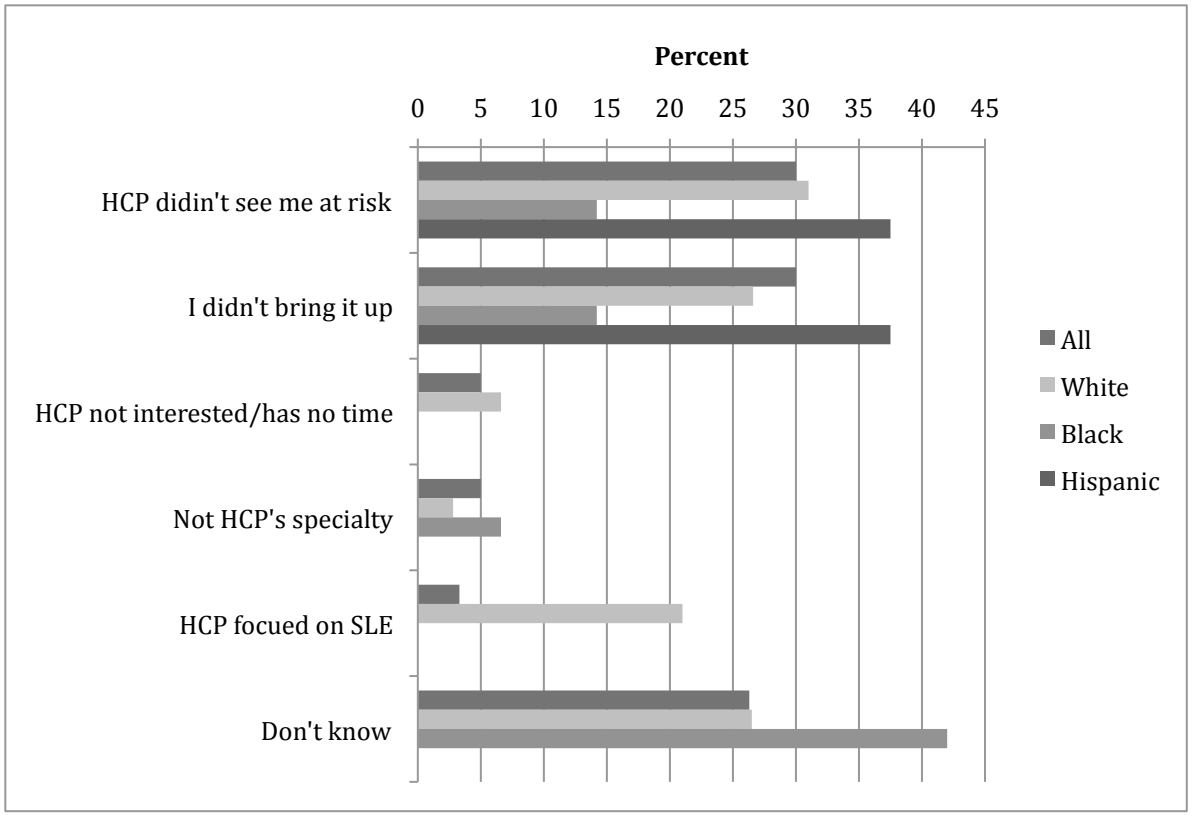

Figure 3.3: Perceptions of Why Healthcare Provider (HCP) Did Not Discuss Heart Disease

Discussion

Women with SLE in this study were equally if not more knowledgeable about the leading cause of death for all women, CVD risk factors, and risk-reducing behaviors when compared to US women who responded to the 2006 AHA national survey despite the fact only 22% considered themselves well or very well informed about heart disease compared to 42% of the AHA respondents. Even though they knew heart disease was the leading cause of death for all women, only 20% of the women in this study could identify the leading cause of death for women with SLE. The participants' knowledge of heart attack and stroke symptoms was alarmingly lacking, similar to that of respondents to the AHA survey. It is important to note that

this study and the AHA survey included only English-speaking women. Minority women are less likely to speak English and more likely to have lower SES.[54] Thus, women of lower SES, who were represented by data on level of education, may not have been adequately represented in this study. This sampling disparity may have resulted in an overestimation of knowledge about the leading cause of death in women, although education level was not a significant predictor of CVD risk awareness.

Contrary to the findings of the AHA survey,[26] there were no significant gaps in awareness of leading cause of death across racial/ethnic groups among women in this study. Since only 16 of the 60 women in this study belonged to minorities, it may have limited the power to detect differences among racial and ethnic groups. Nevertheless, minority women have a higher incidence of CVD in general,[55] and those with SLE frequently accrue more disease-related organ damage than their white counterparts.[56] Consequently, healthcare providers may have recognized their increased risk and provided them with more information about heart disease than non-minority women.

The majority of the women in this study had not personalized their increased risk for CVD related to SLE. Although 66% of the women perceived themselves at a higher relative risk for CVD compared to women without SLE, just 23% of them translated it into an increased absolute risk. Even though increased SLE disease activity or the presence of a flare (SLE exacerbation) were not exclusion criteria, selection of women with less severe SLE may have occurred unintentionally, since those who were not feeling well may have deemed participation too much of a burden. Thus, perception of CVD risk may not be as high in a "healthier" population and limits to generalization are warranted.

The women in this study underestimated their number of CVD risk factors and did not identify novel risk factors more commonly found in SLE. One-third of the participants perceived inactive lifestyle as a personal CVD risk factor. This is not surprising given the reduced muscle strength and exercise capacity, more fatigue, and greater disability in women with SLE compared to sedentary controls.[57] The number of perceived risk factors was a significant predictor for the Precaution Adoption Process Model stage into which a participant was categorized, with an increasing number of perceived risk factors associated with progressing stages that are characterized by the adoption of risk-reducing behaviors. While physiologic markers for risk factors were measured only once and a response bias may have been present in self-reported data for medical history, depression, activity level, and tobacco use as well as in verbalization of risk reducing behaviors, the relationship between perceived risk factors and progressing stages of the Precaution Adoption Process Model warrants further investigation and suggests that one way to improve the adoption of preventive strategies is to educate patients about their personal CVD risks factors.

The Common Sense Model complements the Precaution Adoption Process Model by explaining the emotional and cognitive processes involved in movement from one stage to the next and the formation of a personal risk/illness representation.[19] According to the Common Sense Model individuals form cognitive representations, or perceptions of their risk or illness condition, that influence their selection of coping strategies, which in turn impact health outcomes. As such, a failure to incorporate heart disease risk into one's risk/illness representation may preclude the adoption of preventive behaviors that could reduce that risk. Information about personal risk factors may be what women with SLE need to incorporate increased CVD risk into their risk/illness representation.

The only statistically significant predictor of awareness of increased CVD risk was age. Not surprisingly, women ages 45 and older were counseled on heart disease at more than twice the rate as those younger (19% vs. 7%, p=0.035). The increase in counseling may have represented healthcare providers' recognition of increasing rates of heart disease in older individuals rather than increased CVD risk in SLE. However, less than a third of women 45 years of age and older in this study perceived themselves at increased risk for CVD. This finding contradicts research that showed a significant correlation between healthcare provider counseling and awareness of CVD risk in SLE patients.[22] While healthcare providers may be discussing heart disease with older women with SLE, they may not be emphasizing the increased risk their SLE confers.

Younger women with SLE in this study were getting the message about heart disease as the leading cause of death for all women but not from their healthcare providers. This concurs with findings in a study of college students in the general population where 88% reported that no physician had discussed heart disease with them in the past year, yet they had received information about other diseases.[58] Although all women with SLE are at increased risk for CVD, younger women have the greatest increase in risk compared to non-SLE women.[4] It is even more critical that younger women with SLE engage in preventive behaviors since they stand to gain the greatest survival benefits.

The majority of women in this study reported that they received their information about heart disease primarily from public media, such as magazines, television, newspapers, and the Internet. Recent research suggested that the message about increased CVD risk in SLE and preventive behaviors may have greater impact when delivered by a healthcare provider.[22] Lupus patients who are fatigued or experiencing a flare may not hear or assimilate the advice of their

healthcare provider. Thus, the message may have to be repeated several times before women incorporate it into their risk/illness representation.

All of the women in this study believed that something could be done to prevent CVD, and the overwhelming majority indicated they were comfortable talking with their provider about preventive treatment options. Nevertheless, a substantial number of participants believed they were not counseled about heart disease because their healthcare provider did not see them at risk or they did not bring up the topic with their provider. Thus, it would seem that healthcare providers need to take advantage of this receptive audience and introduce and reintroduce the topic of increased CVD risk and preventive behaviors.

A survey of 500 randomly selected US physicians showed a high prevalence of awareness of NCEP ATP III (89%) and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) (86%) guidelines among respondents.[59, 60] Yet, only 64% of the physicians were aware of the more recently published AHA Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women. Less than half of the physicians correctly categorized a patient's risk level and the majority reported a much lower rate of incorporation of guidelines into practice. Furthermore, risk level assignment drove recommendations for lifestyle interventions, and physicians were more likely to assign women to lower risk categories than men with similar risk profiles.

Investigators have called for aggressive management of CVD risk factors in SLE patients. The AHA Evidence-Based Guidelines for Cardiovascular Disease Prevention in Women as well as the NCEP ATP III and JNC 7 guidelines could be valuable tools to help practitioners identify CVD risk factors and make treatment recommendations for women with SLE.

Conclusion

While the number of deaths from heart disease in US women has decreased from 1 in 3 to 1 in 4 from 2003 to 2005,[61] a similar decline has not been observed in women with SLE. A recent study reported that the incidence of CVD risk factors increased within the first three years after the onset of SLE.[62] Although traditional CVD risk factors do not fully account for the increased CVD risk in lupus,[9] aggressive treatment of modifiable risk factors, especially early in disease onset, potentially may improve overall survival rates for this high-risk group. The first beneficial step healthcare providers should consider in that direction is to insure that their SLE patients are aware of their increased risk for CVD. Identification and discussion of the patient's traditional CVD risk factors as well as those more commonly related to SLE, may be a helpful place to start. Given the complexities of treating lupus, the fatigue and disability that plague many of its sufferers, and the detrimental effects of corticosteroids on CVD risk factors, efforts to engage lupus patients in risk reducing strategies is a daunting clinical challenge but certainly one more than worth the effort.

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CHAPTER FOUR: METHODOLOGY

Abstract

SLE is a chronic autoimmune disease with serious sequelae. The development of new treatments relies upon studies with large enough sample sizes to provide adequate power to uncover significant findings. Recruitment of SLE patients for research studies poses serious challenges for investigators. The infrequency of SLE limits the pool of patients from which to recruit. The lack of a biomarker or definitive diagnostic test for SLE often requires burdensome procedures to confirm a diagnosis of SLE. Women and minorities, both traditionally difficult groups to recruit for research studies, are disproportionately affected by SLE. This necessitates their inclusion in research in order for findings to be generalizable. Healthcare providers, who can be influential in patients' decisions to enroll in studies, are often protective of their SLE patients and hesitant to recommend enrollment. Careful planning can help overcome these challenges and favorably impact recruitment goals.

Introduction

Recruitment of participants frequently is the most challenging aspect of research. Failure to meet recruitment goals can compromise power, consume resources, delay study commencement, and reduce validity if eligibility criteria are broadened to increase numbers. Recruitment is perhaps even more challenging in studies involving patients with systemic lupus erythematosus (SLE). This difficulty may contribute to fact that the Food and Drug Administration (FDA) has not approved a drug specifically for lupus in 50 years.[1]

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that occurs more commonly in women, especially during their reproductive years. It has a gender distribution of 9:1 (female: male) and relative infrequency in the general population with minorities affected disproportionately.[2] A systematic review of 94 randomized controlled trials of lupus studies published between 1971 and 2002 found the average sample size at 28 with only 7.5% of the studies adequately powered.[3] Recently, a feasibility study for a clinical trial of atherosclerosis prevention strategies in SLE patients was terminated early because of poor enrollment.[4]

The reasons for difficulty in recruiting lupus patients are many, among which are the infrequency of SLE, rigid eligibility requirements, difficulty reaching women and minorities, and reluctance of healthcare providers to refer their patients for research studies.

Eligibility Requirements

SLE is a chronic, relapsing disorder with unpredictable manifestations that often vary within the same patient as well as from patient to patient. Unlike many diseases, SLE has no single test or biomarker to confirm diagnosis. The American College of Rheumatology (ACR) developed a set of criteria to operationalize the definition of SLE and establish eligibility for

epidemiologic studies and clinical trials. The intent of the ACR criteria is not to diagnose SLE in individual patients but to insure standardization of heterogeneity for research purposes. The origins of the revised 1982 ACR criteria for classification of SLE and its 1997 update have been discussed at length elsewhere.[5-7]

To satisfy ACR criteria, a patient must meet at least 4 of 11 criteria (Table 4.1), either serially or simultaneously, during any interval of observation. Subsets exist within 5 of the criteria. For example, the criterion, serositis, can be satisfied with a diagnosis of either pleuritis or pericarditis. From a mathematical standpoint, it would be possible to enroll 2,249 patients who meet the minimum combination of 4 criteria before any two of them presented with identical symptoms (see Appendix A).

Table 4.1
American College of Rheumatology Criteria for Systemic Lupus Erythematosus Diagnosis

CRITERION	DEFINITION
1. Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds
2. Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
3. Photosensitivity	Skin rash as a result of unusual reaction to sunlight by patient history or physician observation
4. Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by physician
5. Arthritis	Nonerosive arthritis involving 2 or more peripheral joints, characterized by tenderness, swelling or effusion
6. Serositis	a. Pleuritis—convincing history of pleuritic pain or rub herd by a physician or evidence of pleural effusion OR b. Pericarditis—documented by EKG or rub or evidence of pericardial effusion
7. Renal disorder	a. Persistent proteinuria greater than 0,5 grams per day or greater than 3+ if quantitation not performed OR b. Cellular casts—may be red cell, hemoglobin, granular, tubular, or mixed
8. Neurologic disorder	a. Seizures—in the absence of offending drugs or known metabolic derangements, e.g., uremia, ketoacidosis, or electrolyte imbalance OR b. Psychosis—in the absence of offending drugs or known metabolic derangements, e.g., uremia, ketoacidosis,or electrolyte imbalance
9. Hematologic disorder	a. Hemolytic anemia with reticulocytosis OR b. Leukopenia—less than 4,000/mm^3 OR c. Lymphopenia—less than 1,500/ mm^3 in the absence of offending drugs OR d. Thrombocytopenia—less than 100,000/ mm^3 in the absence of offending drugs
10. Immunologic disorder	a. Anti-DNA: antibody to native DNA in abnormal titer OR b. Anti-Sm: presence of antibody to Sm nuclear antigen OR c. Positive finding of antiphospholipid antibodies based on 1) an abnormal serum level of IgG or IgM anticardiolipin antibodies, 2) a positive test result for lupus anticoagulant using a standard method, or 3) a false-positive serologic test for syphilis known to be positive for at least 6 months and confirmed by Treponema pallidum immobilization or fluorescent treponemal antibody absorption test
11. Antinuclear antibody	An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time and in the absence of drugs known to be associated with "drug-induced lupus" syndrome

Controversy exists over the use of the ACR criteria for clinical trials. Some criteria, such as photosensitivity, are subjective and require the skills of trained clinicians to determine whether they are lupus-related or due to a concomitant condition. Varying sensitivity and

specificity exist for the different criteria with critics claiming ACR criteria may exclude nearly half of SLE patients.[7-10] The ACR criteria were developed using data from primarily Caucasian patients who differ in manifestations from other ethnic groups and in whom validation of the criteria has been limited.[11-15] The results of several studies indicate that anywhere from 3-69% of clinically diagnosed SLE patients do not fulfill ACR criteria, thereby excluding from research those patients whose disease is early in its onset or serious but limited in the number of organs involved. [1, 3, 4, 12-14] Equally disconcerting is the fact that patients with other rheumatic diseases, such as rheumatoid arthritis and antiphospholipid syndrome, may not have SLE but fulfill criteria because of an overlap in manifestations.[16, 17] These factors not only reduce the number of SLE patients eligible for clinical trials but also may limit the generalizability of study results and create selection bias.[8, 18]

Although the ACR SLE criteria have inherent limitations, they have helped maintain a standard of heterogeneity for clinical trials and continue to be the gold standard for eligibility to participate in such studies.[7] As a consequence, determining if participants meet criteria becomes a burden during recruitment for several reasons. First, as previously mentioned, many SLE patients cannot meet the criteria, which limits the already small pool of SLE patients from which to draw the sample. Second, obtaining medical records to corroborate SLE criteria requires satisfaction of additional HIPPA regulations as well as the time and cooperation of the participant's healthcare provider. Third, it is time consuming and costly to clinically determine the presence of criteria where no previous medical records exist or the records are unobtainable. The problem is even more pronounced in large epidemiologic studies where it is not feasible to clinically examine participants because of cost and logistics.

Investigators have proposed alternative methods of SLE classification for research purposes. Some researchers have suggested that a weighted classification system may identify a broader range of potential participants without specificity suffering.[18-20] Costenbader, Karlson, Lang and Mandl[18] devised the Boston Weighted Criteria that includes antiphospholipid antibodies, anti-ß$_2$-glycoportien antibodies, and World Health Organization renal disease classifications, while it decreases the importance given to photosensitivity and oral ulcers. This system had a sensitivity of 93% and specificity of 69% compared to that of the ACR criteria of 84% and 77% respectively. The researchers who developed the Boston Criteria estimate that it would provide 7% more patients eligible for SLE clinical trials than the ACR criteria, not an inconsequential number given the limited number of SLE patients. The Boston Weighted Criteria has been independently validated by another study.[21]

Researchers have examined the accuracy of self-reported SLE diagnoses,[22, 23] but there is concern that such cases are over-reported.[24] This is due in part to varying presentations between patients, overlapping of symptoms among autoimmune disorders, and the evolution of symptoms over time. Nonetheless, accuracy may be improved by collecting additional information regarding symptoms and treatments of SLE. Researchers examined data collected from 53,322 participants in the Black Women's Health Study, including a lupus screening questionnaire and questions about lupus diagnosis and medications.[22] In all, 609 participants reported a diagnosis of SLE, and 339 gave consent for record review. Of those providing consent, medical records and/or physician checklists were obtained for 251, and 59% fulfilled ACR criteria. However, physician checklists alone confirmed 77% of cases compared to only 25% using just chart review. While self-reported diagnosis along with a physician criteria checklist could identify a larger number of potential SLE cases, the authors pointed out that 44% of the women with self-

reported SLE diagnosis did not give consent for record review and the physician return rate of the checklists was poor (43%). Another study reported similar findings.[25] Further investigation is needed to determine if adding information such as medications, recent healthcare provider contacts, and the use of rheumatology services could improve the accuracy of self-report SLE diagnosis.

Investigators have suggested that lupus studies include the complete spectrum of SLE patients seen in clinical practice with the inclusion of patients who do not meet criteria but have been diagnosed with SLE by rheumatologists, the caveat being that researchers clearly describe the patient's clinical manifestations.[7] Detailed descriptions of patient characteristics permit the reader to judge a study's participants. Smith and Shmerling[7] offered a standardized format for doing so that shows frequencies and number of each criterion. In studies that include both patients who meet criteria and those who do not, results could be analyzed separately with and without those not meeting criteria to determine the effect on findings. The authors cautioned that these alternatives might not be appropriate for some studies, such as ones that evaluate potentially toxic therapies.

Other researchers have proposed that ACR criteria not be used as minimum inclusion criteria for lupus studies.[26] Instead, they recommended that trials treat ACR criteria as covariates rather than as the only eligibility criteria, with the study question determining the eligibility criteria. Such methodology could reduce the risk of a minority of seriously ill patients determining the rate of clinical events in trials where the sample population has diverse baseline symptomology.[27]

Not all questions about lupus are best answered by randomized clinical trials. Careful consideration of the research question will not only direct study design but also determine eligibility criteria.

Efficacy trials are meant to determine if an intervention works under ideal conditions. Participants are selected on the basis of narrow eligibility criteria that will show the largest effect between treatment groups. This is accomplished by selecting participants using eligibility criteria that minimize within-subject differences and maximize between group differences.[28] This process favors selection of participants with more severe symptoms since participants with mild disease are less likely to demonstrate change. If a large portion of the participants in an efficacy trial have mild disease, the effect on those with more serious disease will not be evident unless the study is adequately powered. Increasing power requires increasing sample size. Using ACR criteria for eligibility serves the purpose of efficacy trials.

Effectiveness studies address the question of whether or not an intervention will work in the real world, and often their findings are the most useful to clinicians. Since results from effectiveness trials are meant to be more generalizable, the study population should reflect a broader range of symptoms and/or severity.[29] Participants in this type of lupus study may not necessarily meet ACR criteria, thus allowing access to a larger pool of potential participants. However, investigators should keep in mind that broadening eligibility criteria may improve study feasibility, but it also runs the risk of not being able to answer the research question. Often disease activity indices are used as endpoints in lupus studies. A broad spectrum of SLE patients with a wide baseline of symptoms may make it difficult to select a primary endpoint or show treatment benefits.[30]

Qualitative research questions tend to be broad with a focus on the human experience. For example, a qualitative study may explore differences in coping strategies among young women newly diagnosed with lupus. An endpoint of qualitative research is descriptive data that leads to an understanding of the human experience.[29] Although not bound by some of the statistical constraints of randomized clinical trials, qualitative studies still have eligibility requirements that are determined by their research question. As such, qualitative researchers face some of the same concerns as quantitative researchers regarding SLE diagnosis confirmation. However, since efficacy or effectiveness are not usual study endpoints, qualitative researchers may choose less stringent eligibility criteria than the ACR's, thereby yielding a larger population for recruitment.

Infrequency of SLE

Perhaps the greatest challenge for lupus researchers is the limited number of patients with the disease from which to derive an adequately sized sample. Currently, no nationally representative figure exists for the prevalence of SLE in the United States (US). Estimates of prevalence rates of SLE in the US display a ten-fold difference ranging from 15 to 124 per 100,000 persons and vary depending upon definition of SLE diagnosis, sampling method, and geographic and racial diversity.[31-34] Most recently, researchers used hospitalization data to estimate SLE prevalence and derived similar prevalence rates, although these figures unlikely captured mild cases of SLE.[35] The most generous estimation of SLE prevalence, using a prevalence rate of 124 per 100,0000 and 2000 US census data, is approximately 130,000 adult women age ≥ 18 years.[33, 36] Some researchers consider such estimates a lower boundary of actual

SLE incidence since they do not include undiagnosed cases.[34] There also is some evidence to suggest a rise in SLE incidence that may reflect improved survival as well as earlier diagnosis.[37]

SLE is even more infrequent in the male population with a 9:1 female: male ratio. During childhood, the gender ratio (female to male) is 2:1, it then jumps to 12:1 during a woman's reproductive years (ages 15 to 45), and drops to 3:1 after age 50.[38-40] The numbers are even smaller in pediatric SLE where the incidence is estimated at 0.6 per 100,000 children <18 years of age.[41, 42]

In contrast to these results, the largest estimate of 1.5 million individuals with SLE in the US was derived from a 1995 national telephone survey of 2,982 respondents by the Lupus Foundation of America that relied upon self-reported diagnosis.[43] Many researchers do not consider this figure helpful since no attempt was made to confirm if the diagnosis met ACR SLE criteria.[24]

Another telephone survey of 4,034 women conducted to identify SLE patients yielded a prevalence rate of 372 cases per 100,000 persons.[41] However, when the medical records of the self-reported cases were examined for ACR SLE criteria, the prevalence rate dropped to 124 per 100,000. Other studies have suggested that prevalence of suspected SLE may equal that of definite cases.[9, 10, 31] Those studies as well as the LFA and Hochberg et al surveys represent the number of individuals who consider themselves to be SLE patients and who seek healthcare for SLE-related issues, and thus may be candidates for some research.[34]

Given the relative infrequency of SLE in the general population, investigators may need more than one recruitment strategy. One potential source of participants is patient registries. These are administrative organizations often associated with an academic institution that collect data from patients whom they follow over time with repeated monitoring and are more likely to

reflect real life conditions for patients. Several well-designed lupus registries exist that contain large numbers of SLE patients, most notably LUpus in MInorities, NAture versus nurture (LUMINA),[44] Toronto Lupus Databank,[45] and the Johns Hopkins Lupus Cohort.[46] The Centers for Disease Control is currently funding the development of 2 registries in Georgia and Michigan.[47] The majority of registry patients are likely already to have met ACR criteria since academic medical centers, such as Johns Hopkins where 93% of its cohort meets criteria, often attract more severe or atypical cases.[48] Findings from these registries have changed the way lupus is diagnosed and managed.[49] They provide ideal sources for selection of patients not only for randomized controlled trials (RCT) but also observational studies. Some registries are not specific to lupus but still contain a significant number of lupus patients such as the American Rhuematism Medical Information System (ARAMIS) database[50] and the National Center for Health Statistics.[51] However, these registries may not have sufficient information to determine if patients meet ACR SLE criteria. The data in most registries is accessible only by investigators associated with the administrative organization, most often a medical school. Access to government-administered registries, however, such as the National Center for Health Statistics, is not restricted.

Researchers often can identify potential participants in healthcare practices and medical institutions using IRB-approved mechanisms such as direct referral by the healthcare provider or posting IRB-approved advertisements. This requires enlisting the cooperation of the healthcare provider or agency, which is discussed later. Targeting practices that treat SLE patients should extend beyond rheumatologists to those subspecialties that manage the co-morbidities of SLE, such as cardiology, nephrology and dermatology.

Many lupus patients belong to support groups around the country. The LFA is the world's largest non-profit organization for lupus patients with nearly 300 chapters and support groups in 32 states.[52] Other lupus organizations in the country also have their own support groups for adults as well as children.[53, 54] These organizations can provide a starting point for recruitment. Most are willing to inform members of lupus studies via e-mail or newsletters. The LFA provides a list of active studies on its website that includes contact information for individuals interested in participating.[55]

Over one billion people worldwide access the Internet.[56] An Internet search will reveal several support groups available online as well as lupus listservs and bulletin boards. Listservs most often require a subscription, and gatekeepers for some forums may not allow posting of announcements without review. Recruitment of geographically distant and/or remote participants will not suit some studies. Additionally, issues of authenticity exist. Nonetheless, 56 participants were recently recruited for a qualitative study of lupus patients using the Internet, with 23 of them completing data collection.[57] Another study used banner advertisements to successfully recruit for an in Internet-based HIV prevention trial.[58] As attractive as Internet recruitment may appear, it requires considerable planning and investment of resources, but it may be worth the effort.[59]

Media strategies such as paid advertisements in newspapers and public transportation, public service announcements, free classified ads in community and university newspapers, fliers, and posters, can reach large numbers of people but may not be cost effective when recruiting lupus patients whose numbers in the community are small. More effective may be efforts to advertise in geographic areas with significant minority populations, particularly

African Americans and Hispanics who are disproportionately affected by SLE. Likewise, participation in health fairs in those communities may provide an additional recruitment contact.

Researchers can use their professional status to make contacts in the medical community by: contacting other area researchers who are conducting lupus studies to see if they are willing to share information about new studies with their participants; joining professional organizations for healthcare providers who care for patients with rheumatic disorders as well as those who treat the complications of lupus; and joining the local chapter of a lupus foundation, attending its support group meetings, and offering services as a guest speaker. This is where an investigator will meet lupus patients and their healthcare providers.

Referrals by Healthcare Providers

A significantly positive correlation exists between healthcare provider recommendations and a patient's decision to participate in research studies.[60-64] Nonetheless, healthcare providers may not refer their patients to studies for many reasons: an unwillingness to lose control over their patient's care, a belief that standard therapy is the best, unawareness of research studies, the additional administrative burden a study may entail, unfavorable prior research experiences, distrust of the researchers or institutions conducting the trials, and fear of criticism of their practice by researchers to their patients.[63, 65-67] Others may not refer for reasons as simple as time pressures and forgetfulness.[68] About 80% of patients referred by rheumatologists are accurately diagnosed.[69] This substantially eases the burden of confirming SLE diagnosis and as such is an appealing recruitment venue. Thus, it is worth the effort to engage healthcare providers in that endeavor.

First and foremost, healthcare providers need information regarding research studies so that they understand the protocol, its benefits and risks, and the expected endpoints. Printed literature can be informative if it makes it past the front desk of a clinic or physician's office, but often face-to-face encounters are more effective. Investigators can present information about the study at professional meetings and community forums and sponsor information sessions for providers as well as their staff.

Investigators can relieve healthcare providers' fears about disrupting the existing patient-doctor relationship by: assuring them that their patients will be referred back to their care if it will be taken over by the research team during the study; establishing a collaborative relationship that keeps them updated about the study and their patients' progress; sharing results of diagnostic tests and patient care notes; if referred patients are not eligible, explaining why in a letter to the referring provider; and never questioning or criticizing the provider's care to his or her patient. [67]

Administrative burdens can be relieved by: providing members of the research team to review records, gather data, and perform other secretarial tasks related to the study as much as HIPAA regulations will allow; providing information packets for distribution to potential participants; placing posters or flyers in waiting rooms with websites or telephone numbers where patients can get more information about the study; preparing and providing recruitment letters including stamped envelopes for the provider to mail out; and designing study protocols that eliminate unnecessary office visits, diagnostic tests or hospitalizations. Physicians will not want to place any additional financial burdens upon their patients or provide the manpower to file insurance claims for diagnostic studies used by the research study but not deemed necessary for patient care.[70]

Reaching Women and Minorities

SLE preferentially affects vulnerable populations–women of reproductive age, minorities, and lower socioeconomic groups–not only in numbers but also disease severity. Studies that attempted to estimate the prevalence of SLE showed a 3 to 4 times higher frequency in African Americans than in the non-Hispanic white population in the US.[31-35, 38] Hispanics, Native Americans, and Asians also displayed an increased incidence of SLE compared to non-Hispanic whites, but there is insufficient data to make reliable estimates of prevalence rates in these groups. The LFA survey, which relied on self-reported diagnosis, found that SLE affected Hispanic women as much if not more than African American women.[43] Many SLE patients also have lower socioeconomic status not only because of the disproportionate number of minorities with the disease but also due to the disability that SLE can confer. In one study, the rate of work disability at 5 years of SLE disease duration was reported at 25% for African Americans, 19% for Hispanics from Texas, and 18% for Caucasians.[71]

Recruiting women, minorities and vulnerable populations for research studies continues to be a challenge.[72, 73] Nonetheless, given the increased incidence of SLE in African Americans and Hispanics, it is essential that extra effort be made to include them in representative numbers in lupus studies so that findings are generalizable.

Several studies have identified mistrust as a barrier to research participation among African Americans that dates from the Tuskegee Syphilis Study.[74-77] In contrast, other studies indicate that African Americans are willing to participate at rates similar to non-Hispanic whites.[78-80] Recently, Gadegbeku et al examined 141 African American respondents (70 participants and 71 non-participants) to the African American Study of Kidney Disease and Hypertension Trial.[81] Both groups were similar in demographics and views on discrimination and

shared the opinion that medical research was important. Practical considerations such as health status and transportation played the greatest role in determining participation. Only 7% responded that race of the initial recruitment contact influenced their decision. When non-participants were asked what might have helped convince them to participate, more information from the research team was the most frequent response. Perception of health status has been identified as a barrier to participation in women of all ethnic groups in lupus studies as well as other chronic illnesses.[4, 61, 82, 83] Interestingly, lupus patients expressed inconsistent concerns about their health status. Some whose disease was stable were worried that the study would upset that balance, while others were willing to participate because their disease was stable.[4]

A focus group conducted by the University of Michigan with 31 African American women revealed several factors that influenced participation of African American women in the university's Women's Health Registry.[84] First, the women were not receiving information about the registry. There also was a general perception that the research benefited primarily white people and trust could develop only through community involvement of the researchers. Many women would not participate unless they saw a benefit to their own health, their community or other people of color. Compensation was an important motivator as was minority representation on the research team. Lastly, the women expressed unwillingness to participate because of time and financial constraints.

A review of 95 studies describing minority recruitment strategies showed that personalized direct mailings were effective across ethnic groups in large national prevention intervention trials, followed by referral by a friend for African Americans and Hispanics and newspaper ads and brochures for whites.[85] The review also found that community involvement by the research team was more critical to retention than initial recruitment.

There exists a prevailing opinion that it is more effective to recruit African Americans from churches, health fairs and public housing than through media sources, but a study by Meharry Medical College that compared methods used to recruit whites and blacks found differently.[81] Printed materials and radio announcements were as effective in recruiting African Americans as whites and required less time and effort than engaging community assistance, a finding found in other studies.[86, 87]

The same barriers to participation for minorities have been identified in the general population. A 2000 Harris poll of nearly 6,000 mostly non-Hispanic white cancer patients in the US found that 83% of adults thought clinical trials were important or necessary but only 3% actually enrolled in such trials.[88] Almost 85% reported that they were not aware of opportunities to participate in research studies. Among other concerns they expressed were receiving less than standard care or placebo, cost would not be covered by insurance, traveling far distances, and the amount of effort involved in the consent process. Some patients did not want to go against their healthcare provider's wishes, so if the provider did not recommend enrolling in the study, it was likely the patient would not participate. Nonetheless, the survey found that the vast majority of patients who participated in clinical trials had a positive experience.

Other marketing efforts may include focusing mailing and advertising in areas where minorities work and reside; offering to speak about lupus at civic groups, minority professional organizations and lupus support groups in those areas; and involving a member of the research team of the same ethnicity or race as the target population. Hispanic patients may have language barriers.[89] If recruitment efforts are taking place in areas where Spanish is commonly spoken, it may be beneficial to have a Spanish-speaking member on the research team. Study materials also should be in available in both Spanish and English. Many minority patients prefer minority

physicians, especially if English is not their primary language. Targeting minority healthcare providers as well as those who serve minority populations for assistance in recruiting may increase enrollment numbers.

The most critical task in recruiting is educating potential enrollees about the study. This includes not only the details of the protocol but also the purpose of the study, the benefit to the participant as well as others with lupus, and what effect participation may have upon the patient's disease. If someone expresses interest, follow-up needs to be immediate and include contact information for where additional information can be obtained and enrollment initiated.

Efforts to remove as many obstacles to enrollment as possible may include: conveniently locating recruitment and enrollment sites with easy parking, near transportation lines, and with wheelchair access; providing clear instructions in regard to appointment dates and times, driving directions, and a number to call if they have difficulty finding the site; designing time-efficient and flexible study protocols with as few demands on the participant's time as possible. In the Study of Methotrexate in Lupus Erythematosus (SMILE), investigators reduced follow up requirements without sacrificing study integrity in order to ease the burden for participants, which improved recruitment.[67] Fatigue is a common problem for SLE patients. Adjustments to data collection times to accommodate for occasions when the patient may be tired or not feeling well may remove enrollment barriers for some patients.

Monetary incentives can relieve some of the financial burden of participating in research, such as traveling expenses, babysitting, and time off from work. A Cochrane Review of 15 trials involving 33, 719 participants showed that incentives provided a benefit to recruitment.[90] There may be concern that payment represents a form of inducement, but research revealed that such

incentives did not change patients' perceptions of their risks of participating in research and the amount of payment level was less influential on poorer patients than more wealthy ones.[91]

Strategies Used in a Recent Study

A recent cross-sectional study recruited 60 women with SLE in a Southeastern metropolitan area.[92] In order to reach recruitment goals, the investigator invested considerable effort and time in the local "lupus community." She joined a local LFA support group and subsequently became a board member of the area LFA chapter. In addition to providing her expertise as speaker for several support group meetings, she assumed responsibility for organizing the annual lupus awareness seminar sponsored by the local support group and LFA chapter, including initiating the awarding of continuing education units to healthcare provider attendees.

Recruitment strategies included advertisements in a free business ad flyer mailed to area residents, notices in the LFA chapter newsletter and on its web site, paid ads in the local and university newspapers, referrals from a rheumatology nurse practitioner, word of mouth from participants, and notices posted at the city hall and in the quarterly newsletter of a predominately African American community. Almost half of the participants were recruited through the LFA chapter with the remainder primarily from ads in free business flyers, healthcare provider referral and word of mouth. The principal investigator recruited participants for the pilot study from the support group to which she belonged.

Achieving an ethnically representative sample (non-Hispanic whites, 73%; African Americans, 10%; Hispanics, 16%; others, >1%) was a challenge despite the diversity of the geographical region (non-Hispanic whites, 57%; African Americans, 14%; Hispanics, 20%).

Minority recruiting patterns were similar to non-Hispanic whites with almost half recruited through the LFA chapter. The other half of the African American participants were recruited by referrals from friends and support group members.

SLE diagnosis was confirmed by physician-completed ACR SLE criteria checklists for 35 of the 60 participants. Checklists returned on an additional 15 participants showed that they fulfilled 3 of the 11 ACR criteria, and the women reported that they had been told by their healthcare provider that they had SLE. Six participants provided personal copies of medical records that confirmed diagnosis. No checklists or medical records were obtained for four of the participants. Their medical history, current medications, and laboratory data obtained during the study were reviewed by the investigator, a nurse practitioner, who confirmed the presence of at least two of the 11 ACR criteria. These four women had been told by their healthcare provider that they had SLE, and they perceived themselves as SLE patients as did the 15 participants who met 3 of 11 ACR criteria according to physician-completed checklists. Since this was a descriptive study examining risk perception, they were included in the sample.

Seven locations were provided for data collection to address transportation challenges.[92] Four were in the offices of healthcare providers, one was in research space used by the college of nursing at a local university, another was in a hospital, and the last in the office of the area's LFA chapter. The sites were secured through contacts made by the principal investigator. Parking was convenient and free except at the hospital where valet parking was provided at no cost to the participant. The study website included detailed information about the study, its locations and contact information. Door-to-door driving directions were obtained on Mapquest® for each enrollee and mailed to them a few days before the scheduled appointment. In order to

limit time requirements, questionnaires were mailed before the scheduled appointment so that participants could complete them at home at their convenience.

Fasting was required for the study blood work. Some of the women had difficulty initiating morning activities due to pain or often slept late because of fatigue, thus scheduling was done at their convenience including weekends in some cases. Blood work was obtained first, then participants were given something to eat, and the remainder of the data were collected. This allowed data to be collected at a single meeting. Results of the blood work were shared with participants in this study and were mailed to them and their healthcare provider if they chose. Any questions about the results were discussed over the phone.

The main barriers expressed by individuals who initially expressed interest in participating but then decided not to enroll were work and travel distance. Participants who were not feeling well the day of the scheduled meeting were given the opportunity to reschedule another day. Participants were provided a nominal monetary incentive. Although some declined the incentive or indicated the incentive was not the reason for their participation, many expressed appreciation for help in covering time and travel expenses.

All administrative paperwork was handled by the investigator. The only request to participants' healthcare providers was to complete the ACR SLE criteria checklist. The request was mailed to the provider along with a stamped, addressed envelope for return of the checklist to the investigator. Approximately one-half of providers did not respond to the initial request to complete the checklist, and they were mailed a second one. Ultimately, 80% of the healthcare providers returned the checklists.

Conclusion

Achieving recruitment goals historically has been a problem in lupus research.[3, 4] This is due to a set of factors related to SLE that are unique from other disorders and include the relative infrequency of SLE and disproportionate number of affected minorities, rigid eligibility requirements, and reluctance of healthcare providers to refer patients to studies. Not all researchers are associated with institutions that have lupus patient registries, but there are several strategies that can improve recruitment results.

Printed materials and targeted advertising potentially can reach individuals across all ethnic groups and involve less time and resources than engaging community gatekeepers. The mission statement of most lupus foundations includes promoting research, and the organizations can be willing partners in recruitment through their newsletters, web sites and support groups. Healthcare providers, particularly rheumatologists, are a source of accurately diagnosed lupus patients. The providers need not only information about research opportunities for their lupus patients but also collaboration with the research team and relief from as many administrative responsibilities as possible in enrolling patients. The research question should direct eligibility requirements, and therefore in some instances may expand the available recruitment pool of SLE patients. Self-reported SLE diagnosis confirmed by physician checklists may help reduce the burden of determining ACR criteria. SLE is an unpredictable disease with flares and remissions and marked by fatigue and disability. Flexibility and accommodation are critical in enrollment and protocol design in order to provide convenience and accessibility to participants. Participation incentives may positively impact recruitment. Last but not least, educating potential participants about the study, its benefits and its potential effect upon SLE disease status may be the most useful recruitment strategy since concern about health status was identified as a major challenge to enrollment in not only lupus studies but other research as well.

The eventual discovery of an SLE biomarker may ease confirmation of disease, but lupus patients will remain a difficult group to reach for research studies given SLE's relative infrequency and disproportionate number of affected minorities. Efforts to recruit lupus patients can be time consuming and often costly but are necessary to achieve samples with adequate power. Careful planning can facilitate implementation of recruitment strategies and have a substantial positive impact on recruitment goals.

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APPENDIX A: IRB APPROVAL

University of Central Florida

Office of Research & Commercialization

March 16, 2007

Patricia Weinstein, MSN, ARNP
500 Manor Road
Maitland, FL 32751

Dear Ms. Weinstein:

With reference to your protocol #07-4298 entitled, "Awareness of Increased Risk for Heart Disease and Cardiovascular Disease Risk Factors in Women with Systemic Lupus Erythematosus" I am enclosing for your records the approved, expedited document of the UCFIRB Form you had submitted to our office. **This study was approved on 3/13/2007. The expiration date for this study will be 3/12/2008.** Should there be a need to extend this study, a Continuing Review form must be submitted to the IRB Office for review by the Chairman or full IRB at least one month prior to the expiration date. This is the responsibility of the investigator.

Please be advised that this approval is given for one year. Should there be any addendums or administrative changes to the already approved protocol, they must also be submitted to the Board through use of the Addendum/Modification Request form. Changes should not be initiated until written IRB approval is received. Adverse events should be reported to the IRB as they occur.

Should you have any questions, please do not hesitate to call me at 407-823-2901.

Please accept our best wishes for the success of your endeavors.

Cordially,

Joanne Muratori

Joanne Muratori
(FWA00000351 Exp. 5/13/07, IRB00001138)

Copies: IRB File
Karen Dennis, Ph.D., RN, FAAN

JM:jm

12201 Research Parkway • Suite 501 • Orlando, FL 32826-3246 • 407-823-3778 • Fax 407-823-3299

APPENDIX B: INFORMED CONSENT FORM

THE LARA STUDY
LUPUS AND RISK AWARENESS

RESEARCH PARTICIPANT CONSENT FORM

Investigators: Patricia Weinstein, MSN, ARNP
Doctoral student, College of Nursing, University of Central Florida

Karen E. Dennis, PhD, RN, FAAN
Professor, College of Nursing, University of Central Florida

1. Purpose of the Research

The purpose of the Lupus and Risk Awareness (LARA) Study is to study the awareness of health risks in women with systemic lupus erythematosus (SLE) and factors that may affect their awareness. We anticipate learning new information that will help in developing an educational program designed specifically for women with lupus.

2. Specific Procedures to be Used

You have been invited to participate in this research project because you are a woman 18 years of age or older who has been diagnosed by a healthcare provider with systemic lupus erythematosus.

You first will be asked to complete a questionnaire with information such as your name, address and telephone number so we can contact you during the study. You will also be asked to provide other information such as age, education, health history, and physical activity as well as some of your feelings and healthcare experiences. This information will remain anonymous. Your name or other information that may identify you will not be used on the questionnaire. You will fill out the questionnaire at your own pace at home before meeting with the principal investigator (PI), Patricia Weinstein, who is a nurse practitioner. Your completion of the questionnaire will be considered your consent to participate in that part of the study.

Next, you will meet with the PI for 2 hours or less. This meeting will take place at a location that is inconvenient for you. During this meeting, the PI will go over the steps in the study, the Consent Form, the Permission to Release Personal Health Information for Research Form, and the Authorization to Release Information Form, and answer any of your questions. You will sign this Consent Form and Permission to Release Personal Health Information for Research Form if you agree to participate in the remainder of the study. Your blood pressure, heart rate, temperature, height, weight, and waist circumference will be measured. Blood will be drawn from your arm in order to measure substances in your blood that may show that you have health risks, such as a high blood sugar. At the most, a total of 2-3 tablespoons of blood will be drawn. In order to get accurate results from your blood work, you will need to fast before the blood is drawn. This means you should not drink alcohol for 48 hours before and should not have food or drinks except for water for 12 hours before the blood is drawn. After the blood is drawn, you will be given a nutrition bar and fruit juice. The PI will then interview you and ask questions about your health knowledge. With your permission, the interview will be audiotaped. Your name will not be mentioned during the interview, so there will be no way to identify the audiotape as your conversation with the PI. If you do not wish the interview to be audiotaped, the PI will write down your responses. You also have the opportunity to have the tape erased immediately following the interview. Otherwise, the tapes will be destroyed within three years after the study is completed.

Some of your blood will be frozen and saved with just a code number. No commercial tests are available at the present to identify some blood substances that may be related to lupus, but it is expected that tests may become available in the future that will provide us with useful information about lupus. By having the stored blood, future research will be able to test theories about lupus. Eventually, such knowledge may help us to develop measures aimed at the treatment of lupus. Your stored blood sample will be linked to certain information about you, but it will not be linked to your name or any other information that might identify the sample as yours. You may choose not to have your blood sample frozen and stored. The decision not to have your blood saved will not limit or in anyway affect your eligibility to enroll in this research study.

When all laboratory results are available, they will be mailed to you. You may call the study to discuss any questions or concerns you have about the results. With your permission, a copy of your results will be mailed to your healthcare provider if you so desire.

3. Duration of Participation
The duration of your participation will be the time involved in completing the questionnaire at home, which should take less than one hour, and the time spent in the meeting with the PI, which should not exceed 2 hours.

4. Compensation
After all blood has been drawn and all information collected, you will be given $30.00 in cash to compensate for your time and travel.

5. Cost to Participate
None

6. Confidentiality
Your privacy will be protected. Your name or other identifying information will not be used. Instead, only a number will identify you. The only connection between your participation in this study and the study itself will be this signed consent form, but there will be no association between your identity and your laboratory results, your physical measurements and the information you provide on questionnaires or in the interview. Your identity will not be made a part of any published findings resulting from this study. All results will be published as group data. All personal or protected health information that we collect from you in this study including audioptapes and transcriptions made from the tapes will be destroyed within three years of the completion of the study.

The only persons who are authorized to use and/or disclose your health information are the investigators, who are listed on page one of this Research Consent Form, and the UCF Institutional Review Board. The persons who are authorized to receive this information are any healthcare providers whom you have given written permission for us to contact, the UCF Institutional Review Board or its designees, and (as allowable by law) state and federal agencies as required for their research oversight in connection with this research study. Your authorization will expire after the study is completed.

7. Potential Risks
You may feel some discomfort when your blood is drawn. There is a small chance the needle will cause bleeding, a bruise, or an infection. This is uncommon with blood withdrawals performed by personnel trained in blood drawing techniques using sterile. In this study, all blood will be drawn by either the PI, a licensed nurse practitioner or medical technologist, both of whom have extensive blood drawing experience.

This research study has been reviewed and approved by the UCF Institutional Review Board. Questions or concerns about research participants' rights may be directed to the UCF IRB office, University of Central Florida, Office of Research & Commercialization, 12201 Research Parkway, Suite 501, Orlando, FL 32826-3246. The telephone number is (407) 823-2901. If you believe you have been injured during participation in this research project, you may file a claim with UCF Environmental Health & Safety, Risk and Insurance Office, P.O. Box 163500, Orlando, FL 32816-3500 (407) 823-6300. The University of Central Florida is an agency of the State of Florida for purposes of sovereign immunity and the university's and the state's liability for personal injury or property damage is extremely limited under Florida law. Accordingly, the university's and the state's ability to compensate you for any personal injury or property damage suffered during this research project is very limited.

8. Benefits to You or Others
By taking part in this study, you will receive a risk profile that includes results from your blood work at no cost to you. You also may help us learn how to help women with lupus in the future.

9. Voluntary Nature of Participation
You do not have to participate in this research study. If you agree to participate, you can withdraw at any time without penalty. You do not have to answer any questions that you do not wish to answer when doing questionnaires or interviews.

10. Contact Information
If you have any questions about this research project, you can contact Patricia Weinstein by telephone (407-468-4476) or by e-mail (LARA@cfl.rr.com) or her supervisor, Dr. Karen Dennis, (407-823-1832 or kdennis@mail.ucf.edu).

I have had the opportunity to read this consent form and ask questions about the research project. I voluntarily agree to participate in the LARA Study, and I have received a copy of this consent form.

Please initial ONE option for A, ONE option for B and ONE option for C.

A. _____ I consent to have my interview taped.
_____ I do not consent to have my interview taped.

B. _____ I consent to have some of my blood frozen and stored for future research.
_____ I do not consent to have my blood frozen and stored for future research.

C. _____ I consent to be contacted with information about future lupus research studies.
_____ I do not consent to be contacted with information about future lupus research studies.

_____ _____ Participant's
Signature Date

_____
Participant's Name (Please print)

_____ _____
Investigator's Signature Date

THE LARA STUDY
LUPUS AND RISK AWARENESS

PERMISSION TO USE PERSONAL HEALTH INFORMATION FOR RESEARCH

1. What is the purpose of this form?

State and federal privacy laws protect the use and release of your health information. Under these laws, your health care provider cannot release your health information to the LARA research team unless you give your permission. If you decide to give your permission and to participate in the study, you must sign this form as well as the Consent Form. This form describes the different ways that the research team may use your health information for the research study. The research team will use and protect your information as described under number 6, "Confidentiality" in the attached Consent Form. If you have questions, ask a member of the research team.

2. What Personal Health Information will be released?

If you give your permission and sign this form, you are allowing the healthcare provider whom you have designated on the Authorization to Release Medical Information form to confirm your diagnosis of systemic lupus erythematosus. He/she will do this by completing a checklist of symptoms and laboratory results that is used by the American College of Rheumatology to diagnose lupus. The Personal Health Information will include your name. However, as soon as we receive the form with the information and your name on it from your health care provider, it will be coded immediately and your name removed to protect your confidentiality.

3. Do I have to give my permission for certain specific uses?

Yes. The following information will only be released if you give your specific permission by putting your initials on the line below.

____ I agree to the release of information pertaining to my diagnosis of systemic lupus erythematosus.

4. How will my Personal Health Information be used?

Your Personal Health Information may be released to these people for the following purposes:

1. To the research team for the research described in the attached Consent Form;
2. To others at the University of Central Florida who are required by law to review the research;
3. To others who are required by law to review the quality and safety of the research, including: U.S. government agencies, such as the Food and Drug Administration, the research sponsor or the sponsor's representatives, or government agencies in other countries. These organizations and their representatives may see your Personal Health Information. They may not copy or take it from your medical records unless permitted or required by law.

5. How will my Personal Health Information be used in a research report?

If you agree to be in this study, the research team may fill out a research report. The research report will **NOT** include your name, address, telephone, social security number or any other information that could identify you. The research report may include your date of birth, initials, dates you were enrolled the study, and an identification code. The research report will also include information the research team collects for the study. The research team and the research sponsor may use the research report and share it with others in the following ways:

1. To perform more research;
2. Share it with researchers in the United States or other countries;
3. Place it into research databases;
4. Use it to improve the design of future studies; or
5. Use it to publish articles or for presentations.

6. Does my permission expire?
This permission to release your Personal Health Information expires when the research ends and all required study monitoring is over. Research reports can be used forever.

7. Can I cancel my permission?
You can cancel your permission at any time. You can do this in two ways. You can write to the researcher or you can ask someone on the research team to give you a form to fill out to cancel your permission. Their contact information is on the Consent Form. If you cancel, information that was already been collected and disclosed about you may continue to be used. Also, if the law requires it, the sponsor and government agencies may continue to look at your medical records to review the quality or safety of the study.

8. Signature
You should take as much time as you need to decide whether you wish to permit the use and disclosure of your Protected Health Information for the LARA Study. Please feel free to ask questions about any parts of this form that are unclear to you.

I have read this Authorization, which describes how my Protected Health Information will be used and/or disclosed for the LARA Study. I have had the opportunity to ask, and I have received answers to, any questions I had regarding the use and disclosure of my Protected Health Information for the Research Study. I agree to the use and/or disclosure of my Protected Health Information, as described above, for the Research Study.

_____ _____ Participant's
Signature Date

_____
Participant's Name (Please print)

_____ _____
Investigator's Signature Date

APPENDIX C: HIPAA CONTINUNG EDUCATION CERTIFICATE

National Cancer Institute
U.S. National Institutes of Health | www.cancer.gov

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Human Participant Protections Education for Research Teams

Completion Certificate

This is to certify that

Patricia Weinstein

has completed the **Human Participants Protection Education for Research Teams** online course, sponsored by the National Institutes of Health (NIH), on 07/18/2006.

This course included the following:

- key historical events and current issues that impact guidelines and legislation on human participant protection in research.
- ethical principles and guidelines that should assist in resolving the ethical issues inherent in the conduct of research with human participants.
- the use of key ethical principles and federal regulations to protect human participants at various stages in the research process.
- a description of guidelines for the protection of special populations in research.
- a definition of informed consent and components necessary for a valid consent.
- a description of the role of the IRB in the research process.
- the roles, responsibilities, and interactions of federal agencies, institutions, and researchers in conducting research with human participants.

National Institutes of Health
http://www.nih.gov

APPENDIX D: GENERAL INFORMATION QUESTIONNIARE

DO NOT WRITE YOUR NAME ON THIS QUESTIONNAIRE

Directions: Please answer all of the following questions to the best of your ability using a pen or pencil. You do not have to answer any questions that make you uncomfortable or you do not understand. There are no right or wrong answers. All your responses will be kept anonymous.

1. Birthdate:_____/_____/_____ 2. Place of birth: _____
MONTH DAY YEAR

2. Please check the box next to the answers that best describe you
Race and Ethnicity
❏ Non-Hispanic White
❏ Black or African American
❏ Hispanic White
❏ Hispanic Black
❏ Asian
❏ Native American or Native Alaskan
❏ Native Hawaiian or Other Pacific Islander
❏ Some other race (describe)_____
❏ More than one race (describe) _____

If you are Hispanic or Latino, what is your country of ethnic origin?
❏ Mexico ❏ Puerto Rico ❏ Cuba ❏ Guatemala ❏ Honduras
❏ South America ❏ Other_____

If you are black, what is your country of ethnic origin?
❏ African ❏ Caribbean ❏ Other_____

3. Marital Status
❏ Never married ❏ Married ❏ Divorced ❏ Separated ❏ Widowed

4. Education
Circle the highest level of education you have completed
Grade School 7 8 9 10 11 12 College 1 2 3 4 Graduate School 1 2 3 4 5 Degree _____

5. Employment
❏ Employed ❏ Unemployed ❏ Disabled ❏ Retired
Occupation or job you had while working if you are now unemployed, disabled or retired
_____

6. Total number of people living in your household (adults and children) _____

7. Family income (combined total income earned by all working members of your family)
❏ Under $ 25,000
❏ $25,001 - $50,000
❏ $50,001 - $75,000
❏ $75,001 – 100,00
❏ $100,001 - $125,000
❏ over $125,000

8. Health insurance
❏ Uninsured ❏ Medicaid ❏ Medicare ❏ Private insurance
If private insurance, ❏ PPO ❏ HMO

Health History
9. How would you rate your current health?
❏ Excellent ❏ Good ❏ Average ❏ Fair ❏ Poor
Are you having a lupus flare now? ❏ Yes ❏ No ❏ Not sure
If you are not having a flare now, the approximate date when you last had a flare_____
MONTH & YEAR

10. List all your food and drug allergies
_____
_____

Menstrual History

11. Age when you got your first period _____ Were/are your periods regular? ❑ Yes ❑ No

    If you are menopausal, what was your age when you had your last period?_____
    Were your periods regular when you did have them? ❑ Yes ❑ No ❑ Don't remember

    Number of pregnancies _____ Number of miscarriages _____ Number of live births_____

    When you were pregnant, did your lupus ❑ get better ❑ stay the same ❑ get worse

    Did you breastfeed any of your babies? ❑ Yes ❑ No

12. Family History
    Which, if any, of your other relatives has been diagnosed with lupus?_____
    _____

    Do you know of any of your blood relatives who now have or have had in the past any of the following conditions? Check all that apply and give the relationship, for, example, maternal aunt.

    ❑ Cancer_____ ❑ Leukemia_____
    ❑ Heart Disease_____ ❑ Diabetes _____
    ❑ High Blood Pressure_____ ❑ Stroke _____
    ❑ Chronic Fatigue Syndrome_____ ❑ Goiter _____
    ❑ Sjorgen Syndrome_____ ❑ Psoriasis _____
    ❑ Rheumatoid Arthritis_____ ❑ Myasthenia Gravis _____
    ❑ Multiple Sclerosis_____ ❑ Scleroderma _____
    ❑ Crohn's Disease_____ ❑ Colitis _____
    ❑ Ankylosing Spondylitis_____

13. Did you have a parent who had heart attack before age 65 or died of heart disease before age 65?
    ❑ Yes ❑ No ❑ Don't know

14. Did you have a brother or sister who had a heart attack before age 65 or died of heart disease before age 65?
    ❑ Yes ❑ No ❑ Don't know

15. Present Medications
    List the names of any medications your are now taking including over the counter medications like aspirin, calcium, vitamins, and supplements such as herbal, natural, bioidentical or alternative remedies.

    _____
    _____
    _____
    _____
    _____
    _____
    _____
    _____

16. Past Medications

As best you can, try to remember if you have taken any of the following medications.

Mycophenol mofetil (Cellcept)

❑ Yes, I am taking it now ❑ Yes, but I am NOT taking it now ❑ No ❑ Don't know

Hydroycholorquine (Plaquenil)

❑ Yes, I am taking it now ❑ Yes, but I am NOT taking it now ❑ No ❑ Don't know

Methotrexate (Rheumatrex, Mextate)

❑ Yes, I am taking it now ❑ Yes, but I am NOT taking it now ❑ No ❑ Don't know

Azathioprine (Imuran)

❑ Yes, I am taking it now ❑ Yes, but I am NOT taking it now ❑ No ❑ Don't know

Cyclophosamide (Cytoxan)

❑ Yes, I am taking it now ❑ Yes, but I am NOT taking it now ❑ No ❑ Don't know

Steroids of any kind including prednisone, medrol and decadron

❑ Yes, I am taking it now ❑ Yes, but I am NOT taking it now ❑ No ❑ Don't know

If you can remember, about how many years all together have you taken steroids?_____

17. Place a check in the box next to the sentence that best describes your tobacco use.

❑ I have never smoked
❑ I used to smoke, but successfully quit
❑ I smoke, but not every day
❑ I smoke less than 10 cigarettes a day
❑ I smoke 10 or more cigarettes, but less than 1 pack a day
❑ I smoke 1-2 packs of cigarettes a day
❑ I smoke more than 2 packs a day

What symptoms have you experienced or are now experiencing? Check both the first and second boxes if you have experienced the symptom in the past and are experiencing it now.

18. A red rash or butterfly-shaped rash across your cheeks and nose

❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

19. Raised patches with scaling on your skin that may have caused scarring. Your doctor may have referred to it as discoid or cutaneous lupus.

❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

20. Sensitivity to the sun where your skin breaks out after being in the sun (not a sunburn)

❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

21. Sores or ulcers in your mouth and/or nose that lasted more than 2 weeks

❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

22. Achy, painful and/or swollen joints for more than 3 months

❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

23. Chest pain that gets worse when taking a breath and that lasted for more than a few days. Your doctor may have called it pleurisy or pericarditis.
❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

24. Protein or red blood cells in your urine or other kidney problems
❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

25. Seizures (fits), convulsions, delusions or hallucinations that were not caused by a drug or medical condition
❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

26. Anemia (low red blood cell count), low white blood cell count or low platelets
❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

27. Unexplained fevers over 100 degrees for more than a few days
❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

28. Fatigue that lasted for days or weeks at a time even after getting enough sleep at night
❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

29. Hair loss either all over or in patches
❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

30. Fingers and/or toes turning pale, numb or uncomfortable in the cold
❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

31. Stomach pains or indigestion that lasted longer than one day and NOT associated with a stomach virus
❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

32. Significant unexplained weight loss
❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

33. Swelling of the feet and ankles
❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

34. Shortness of breath while resting or doing something that did NOT require a lot of effort
❑ I have experienced in the past ❑ I am experiencing now ❑ I have never experienced

List any other symptoms NOT mentioned above that you have had and think are caused by your lupus.

_____

_____

_____

35. How many bladder infections do you get in a year? ❑ None ❑ 1 or 2 ❑ 3 or more

Have you had more than one bladder infection in the past? ❑ Yes ❑ No ❑ I don't know

36. Have you ever tested positive for lupus antibodies? ❑ Yes ❑ No ❑ I don't know

37. Have you ever tested positive for antiphospholipid antibodies? ❑ Yes ❑ No ❑ I don't know

38. Looking back, how old were you when you first began to notice lupus symptoms? _____

39. What was the very first symptom you remember experiencing?_____

40. How long did you wait to get medical care after you first noticed symptoms? _____

41. About how many years passed from when you first went to a doctor about your symptoms until the time you were finally diagnosed with lupus? _____

42. What kind of healthcare provider did you first go to see about your symptoms? Check one.
- ❑ General practitioner or family doctor
- ❑ Immunologists
- ❑ Nephrologist (kidney doctor)
- ❑ Pediatrician (children's doctor)
- ❑ Cardiologist (heart doctor)
- ❑ Gastroenterologist (stomach doctor)
- ❑ Internist
- ❑ Rheumatologist
- ❑ Dermatologist (skin doctor)
- ❑ Gynecologist/Obstetrician
- ❑ Pulmonologist (lung doctor)
- ❑ Nurse Practitioner
- ❑ Other specialist (describe)_____

43. Which healthcare provider made the actual diagnosis of lupus? Check one.
- ❑ General practitioner or family doctor
- ❑ Immunologists
- ❑ Nephrologist (kidney doctor)
- ❑ Pediatrician
- ❑ Cardiologist (heart doctor)
- ❑ Gastroenterologist (stomach doctor)
- ❑ Internist
- ❑ Rheumatologist
- ❑ Dermatologist (skin doctor)
- ❑ Gynecologist/Obstetrician
- ❑ Pulmonologist (lung doctor)
- ❑ Nurse Practitioner
- ❑ Other specialist (describe)_____

44. What kind of healthcare provider do you mostly see now to help you manage your lupus?
- ❑ General practitioner or family doctor
- ❑ Immunologists
- ❑ Nephrologist (kidney doctor)
- ❑ Pediatrician
- ❑ Cardiologist (heart doctor)
- ❑ Gastroenterologist (stomach doctor)
- ❑ Internist
- ❑ Rheumatologist
- ❑ Dermatologist (skin doctor)
- ❑ Gynecologist/Obstetrician
- ❑ Pulmonologist (lung doctor)
- ❑ Nurse Practitioner
- ❑ Other specialist (describe)_____

45. Did you know what lupus was when you were first diagnosed? ❑ Yes ❑ No

46. What was your main source of information about lupus when you were first diagnosed?_____

47. How would you describe your satisfaction with the care you are getting now from your healthcare providers to help you manage your lupus?
❑ Very satisfied ❑ Somewhat satisfied ❑ No opinion ❑ Somewhat dissatisfied ❑ Very dissatisfied

48. What one single thing could your healthcare provider do or change that would make you more satisfied with the care you are getting to manage your lupus? _____
_____
_____

49. Which sign or symptom of lupus MOST disrupts your daily activities and lowers your quality of life?
_____

50. What one single thing in your life has changed the most since you developed lupus?
_____
_____

51. Looking back, what is the one thing you wish you had been told when you were first diagnosed with lupus?
_____
_____

Read each group of statements carefully, then pick one statement in each group that best describes the way you have been feeling during the past two weeks, including today. Check the box beside the statement you have picked. If several statements in one group seem to apply equally well, choose the statement with the highest number beside it.

52. Sadness
- ❑ 0 I do not feel sad.
- ❑ 1 I feel sad much of the time.
- ❑ 2 I am sad all the time.
- ❑ 3 I am so sad or unhappy I can't stand it.

53. Pessimism
- ❑ 0 I am not discouraged about my future.
- ❑ 1 I feel more discouraged about my future than I used to be.
- ❑ 2 I do expect things to work out for me.
- ❑ 3 I feel my future is hopeless and will only get worse.

54. Past failure
- ❑ 0 I do not feel like a failure.
- ❑ 1 I have failed more than I should have.
- ❑ 2 As I look back, I see a lot of failures.
- ❑ 3 I feel I am a total failure as a person.

55. Self-dislike
- ❑ 0 I feel the same about myself as ever.
- ❑ 1 I have lost confidence in myself.
- ❑ 2 I am disappointed in myself.
- ❑ 3 I dislike myself.

56. Self-criticalness
- ❑ 0 I don't criticize or blame myself more than usual.
- ❑ 1 I am more critical of myself than I used to be.
- ❑ 2 I am disappointed in myself.
- ❑ 3 I blame myself for everything bad that happens.

57. Suicidal thoughts or wishes
- ❑ 0 I don't have any thoughts of killing myself.
- ❑ 1 I have thoughts of killing myself, but I would not carry them out.
- ❑ 2 I would like to kill myself.
- ❑ 3 I would kill myself if I had the chance

58. Loss of interest
- ❑ 0 I have not lost interest in other people or activities.
- ❑ 1 I am less interested in other people or things than before.
- ❑ 2 I have lost most of my interest in other people or things.
- ❑ 3 It's hard to get interested in anything.

59. How many episodes of depression that have lasted two weeks or more have you experienced over the past year?_____

60. Are you currently receiving treatment, either medication or counseling, for depression? ❑ Yes ❑ No
Have you received treatment, either medication or counseling, for depression in the past? ❑ Yes ❑ No

61. Would you consider yourself a depressed person? ❑ Yes ❑ No ❑ Don't know

62. When things get really difficult with your lupus, who is the one person you can count on most to help you out? (Describe relationship, such as mother, friend, sister, husband, doctor, etc)
_____

63. When you are having a difficult time with your lupus, what is the most helpful thing someone can do for you?_____

The following questions relate to your present physical activity level.

64. Check all the assistive devices that you currently use.
❑ Walker ❑ Braces ❑ Cane ❑ Wheelchair

65. Which describes the use of your arms? ❑ Full ❑ Partial ❑ No use

66. Which describes the use of your legs? ❑ Full ❑ Partial ❑ No use

67. Do you currently exercise? ❑ Yes ❑ No If No, skip questions 68 - 70 and go to question 71.

68. What kind of exercises do you do?
List up to 4 activities below that you do on a regular basis for the primary purpose of increasing or maintaining your fitness. **Aerobics** are done for a sustained period of time and result in an increase in your heart rate and breathing rate. Examples include walking, jogging, attending an aerobics class and bicycling. **Strength** activities include lifting weights or using elastic bands or weight training machines. **Flexibility** refers to activities that involve muscle stretching.

Type of Activity (check one)	**Activity**	**Days per Week**	**Minutes per Day**	**Months per Year**
❑Aerobic ❑Strength ❑Flexibility				
❑Aerobic ❑Strength ❑Flexibility				
❑Aerobic ❑Strength ❑Flexibility				
❑Aerobic ❑Strength ❑Flexibility				

69. Have you been exercising for more than one year or less than one year?
❏ More than one year ❏ Less than one year

70. How would you describe the average intensity of your exercise program?
❏ Light exercise: Don't sweat or breathe heavily.
❏ Moderate exercise: Breathe a little harder and may sweat.
❏ Vigorous: Breathe hard and sweat.

71. Do you engage in leisure time activity? ❏ Yes ❏ No If No, skip question 72 and go to question 73.

72. What type of activities do you do?
List up to 4 activities that you do for leisure or recreation. These activities can be done on a regular or irregular basis and may not necessarily result in sustained increases in your heart rate or breathing rate. Examples include boating, skiing, dancing and sport activities. Please indicate whether the activity is an endurance activity or a non-endurance activity. Non-endurance activities include boating, softball and horseback riding. Do not list activities here that you already listed under exercise.

Type of Activity (check one)	**Activity**	**Days per Week**	**Minutes per Day**	**Months per Year**
❏ Endurance ❏ Non-endurance				
❏ Endurance ❏ Non-endurance				
❏ Endurance ❏ Non-endurance				
❏ Endurance ❏ Non-endurance				

73. From Monday through Friday, how many waking hours a day do you usually spend inside your house?
❏ Less than 6 hours a day ❏ 6 to 10 hours a day ❏ More than 10 hours a day

74. On Saturday and Sunday, how many waking hours a day do you usually spend inside your house?
❏ Less than 6 hours a day ❏ 6 to 10 hours a day ❏ More than 10 hours a day

75. On average, how many hours a day do you sleep including naps? _____hours

76. On average, how many hours a day are you sitting or lying down, not counting sleeping? ____hours

77. Are most of your indoor household activities done by you or someone else?
❏ Done by me ❏ Done by someone else
If done by someone else, skip question 78 and go to question 79.

78. Please list up to 4 indoor household activities you do and the number of minutes a week you spend on each. Indoor household activities could be sweeping, vacuuming, washing dishes, dusting, etc.

Activity	**Minutes per Week**

79. Do you do any outdoor household activities such as gardening? ❏ Yes ❏ No
If no, skip question 80 and go to question 81.

80. Please list up to 4 outdoor household activities you do and the number of minutes a week you spend on each activity.

Activity	Days per Week	Minutes per Day	Months per Year

81. How much assistance do you need to perform activities of daily living such as dressing and bathing?
❏ No assistance ❏ Some assistance ❏ Full assistance

82. Do you currently receive physical or occupational therapy? ❏ Yes ❏ No
If no, skip questions 83 - 84 and go to question 85.

83. How many days a week do you receive therapy? _____days

84. How long does each therapy session last? _____minutes

85. Are you currently employed and/or attending school?
❏ Employed ❏ Not employed ❏ Retired ❏ Attending school
If not employed or retired, skip questions 86 - 91 and go to question 92.

86. For most of your work/school day, do you ❏ Move around ❏ Stand ❏ Sit

87. Do you climb any stairs during the work/school day? ❏ Yes ❏ No
If no, skip questions 88-89 and go to question 90.

88. How many flights of stairs do you climb? _____ flights

89. How many times a day so you climb the stairs? _____ times

90. In your transportation to and from work/school, do you get any physical activity?
❏ Yes ❏ No If no, skip question 91 and go to question 92.

91. Please list up to 4 activities job/school related physical activities you do and the number of minutes a week you spend on each activity.

Activity	Days per Week	Minutes per Day	Months per Year

92. Do you use a wheelchair? ? ❏ Yes ❏ No If no, skip questions 93 - 97 and go to question 98.

93. How many years have you used a wheelchair? _____years

94. During the time that you are awake, how much time do you spend in your wheelchair?

❑ All day ❑ Most of the day ❑ A few hours

95. What type of wheelchair do you primarily use?
❑ Manual wheelchair ❑ Powered wheelchair
If powered, skip question 96 and go to question 98.

96. Who usually pushes your wheelchair? ❑ Myself ❑ Someone else
If someone else, skip question 97 and go to question 98.

97. On average, how many minutes a day do you push your self?
❑ Less than 60 minutes ❑ 60 minutes or more

98. Do you belong to a lupus support group? ❑ Yes ❑ No

99. If yes, how long have you belonged to the support group? _____

100. How many meetings have you attended in the past year? _____

101. Do you search the Internet for information on lupus? ❑ Yes ❑ No

102. If yes, which site have you found more helpful than others?_____

103. If you have not searched the Internet for lupus information, why not?
❑ No interest ❑ No computer ❑ Internet access
❑ Other (explain) _____

104. Which way would you prefer to learn information about lupus? If you choose more than one way, indicate your first, second, etc. choice by putting a number in the box next to your choice.
❑ Internet ❑ Brochure or book ❑ Audiotape/CD ❑ Videotape/DVD
❑ Small group meeting (less than 20 people) led by a healthcare provider
❑ Small group meeting (less than 20 people) led by someone with lupus
❑ Conference or seminar (20 or more people) presented by lupus experts
❑ One-on-one meeting with a healthcare provider
❑ Other (explain) _____

Optional
If there is anything else you would like to share about having lupus, please write it below.

_____

_____

_____

_____

_____

Thank you for completing this questionnaire.

APPENDIX E: AMERICAN HEART ASSOCIATION PERMISSION FOR SURVEY USE

From: Karen Robb <karen.robb@heart.org>
Subject: **RE: AHA women's healthy survey**
Date: October 13, 2004 9:56:59 AM EDT
To: 'Patricia Weinstein' <PWeinstein@cfl.rr.com>
1 Attachment, 72.0 KB Save

Patricia,
Here is the survey. As I'm sure you will, please reference the AHA in your work. We would be very interested in a copy of your paper once completed. You may send it to my attention. Good luck.

Best Regards,
Karen

Karen Robb
Marketing Research Consultant

American Heart Association
7272 Greenville Avenue
Dallas, Texas 75231-4596
214.706.1409
214.706.5241 FAX
karen.robb@heart.org

-----Original Message-----
From: Patricia Weinstein [mailto:PWeinstein@cfl.rr.com]
Sent: Tuesday, October 12, 2004 9:58 PM
To: Karen Robb
Subject: Re: AHA women's healthy survey

Dear Ms. Robb,

I am student in the doctoral nursing program at the University of Central Florida. My area of interest is cardiovascular risk reduction in women. My dissertation work involves investigating women with co-morbidities that increase CAD risk and determining the women's awareness of their increased risk for CAD. As part of the study, I want to compare their knowledge about heart disease in general to that of women nationally. The Women's Health Survey is a survey instrument with proven reliability and could therefore provide valid comparison data. My investigation is purely for educational purposes and there will be no cost to the participants, nor is there any commercial intent or support.

Thank you for the quick response to my inquiry. I look forward to hearing from you.

Patricia Weinstein, MSN, ARNP

On Oct 12, 2004, at 2:44 PM, Karen Robb wrote:

Patricia Weinstein,

I was contacted by our contact center regarding your inquiry about the Women's Health Survey. Can you tell me a bit more about your

intended use of the survey instrument?

Thanks,

Karen

Karen Robb

Marketing Research Consultant

American Heart Association

7272 Greenville Avenue

Dallas, Texas 75231-4596

214.706.1409

214.706.5241 FAX

karen.robb@heart.org

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APPENDIX F: INTERVIEW (AHA SURVEY)

I. GENERAL AWARENESS OF WOMEN'S HEALTH ISSUES

First, I would like to ask you your views on women's health issues today.

1. What do you think is the one greatest health problem facing women today? (DO NOT READ LIST. RECORD ONLY ONE RESPONSE.)

AIDS .....-1
Alzheimer's .....-2
Breast cancer .....-3
Cancer (general) .....-4
Diabetes .....-5
Drug addiction/alcoholism .....-6
Heart disease/heart attack .....-7
Lung cancer .....-8
Osteoporosis .....-9
Smoking .....-0
Stroke .....-x
Other (SPECIFY _____) .....-y
Don't know .....-1
Refused .....-2

2. As far as you know, what is the leading cause of death for all women? (DO NOT READ LIST. RECORD ONLY ONE RESPONSE.)

Accidental death .....-1
AIDS .....-2
Alzheimer's .....-3
Breast cancer .....-4
Cancer (general) .....-5
Diabetes .....-6
Drug addiction/alcoholism .....-7
Heart disease/heart attack .....-8
Lung cancer .....-9
Osteoporosis .....-0
Smoking .....-x
Stroke .....-y
Violent crime .....-1
Other (SPECIFY _____) .....-2
Don't know .....-3
Refused .....-4

3. As far as you know, what is the leading cause of death for women with lupus?_____

4. Please tell me the extent to which you worry about getting each of the following health conditions. Do you worry a lot about this, a little, or do you not worry at all about it? (READ LIST. RANDOMIZE. RECORD ONE RESPONSE FOR EACH ITEM).

	Worry a lot		**Worry a little**	**Do not worry at all**		**(Do not read) Don't know**	**(Do not read) Refused**
a. Cancer (general)	-1	-2	-3	-4	-5		
b. Heart disease/heart attack	-1	-2	-3	-4	-5		
c. AIDS	-1	-2	-3	-4	-5		
d. Breast cancer	-1	-2	-3	-4	-5		
e. Lung cancer	-1	-2	-3	-4	-5		
f. Stroke	-1	-2	-3	-4	-5		
g. Alzheimer's	-1	-2	-3	-4	-5		
h. Diabetes	-1	-2	-3	-4	-5		
j. Osteoporosis	-1	-2	-3	-4	-5		

II. COMMUNICATIONS AND BEHAVIORS RELATED TO HEART DISEASE PREVENTION

I would now like to ask you several questions about heart disease, which includes among others, heart attack, stroke, high blood pressure and angina.

1. If you do NOT make any changes in your diet, (smoking [include if reports current tobacco use]) or exercise habits, what do you think are your chances of developing heart disease sometime in the future?
   ❑ low ❑ high ❑ 50-50 ❑ don't know (DO NOT READ) ❑ Refused (DO NOT READ)

2. If you do NOT any make changes in your diet, (smoking [include if reports current tobacco use]) or exercise habits, what do you think are your chances of developing heart disease sometime in the future compared to other women who do not have lupus?
   ❑ the same ❑ higher ❑ lower ❑ don't know (DO NOT READ) ❑ Refused (DO NOT READ)

3. Which of the following statements best describes you and your feelings.
(Provide participant with printed copy of list to look over before answering)
   1. I don't think I'm at any greater risk of getting heart disease than other women my age.
   2. I know I am at risk for getting heart disease, but I really haven't thought much about it.
   3. I am thinking about changing some of my behaviors to decrease my chances for getting heart disease, but I have not made up my mind yet if it is something I want to do.
   4. I have thought about changing some of my behaviors to decrease my chances for getting heart disease, but I have decided against it.
   5. I have decided to change some of my behaviors to decrease my chances of getting heart disease, but I have not started doing any of them yet.
   6. I have recently changed some of my behaviors within the last month to decrease my chances for getting heart disease.
   7. I have made changes in my behaviors to decrease my chances for getting heart disease for at least the last 6 months.

4. Why do you think your chances are _____ (FILL IN RESPONSE TO QUESTON 1) for developing heart disease in the future?

   _____

   _____

   _____

   If thinks chances are higher, where she received this information_____

5. Have you seen, heard, or read information about heart disease within the past 12 months?

   Yes .....-1
   No.....-2
   Don't know (DO NOT READ).....-3
   Refused (DO NOT READ).....-4

IF "YES" HAVE SEEN, HEARD, OR READ INFORMATION ABOUT HEART DISEASE WITHIN PAST 12 MONTHS, ASK:

6. Where did you see, hear or read this information? (DO NOT READ LIST. RECORD ALL THAT APPLY.)

In a magazine .....-1
On the radio.....-2
In a book .....-3
On TV .....-4
Information in a brochure .....-5
Provided by physician, nurse or other healthcare professional .....-6
In a newspaper .....-7
On the Internet or World Wide Web.....-8
From a friend or relative .....-9
Library.....-0
Other (SPECIFY _____).....-1
Don't know .....-2
Refused .....-3

7. Have you seen, heard, or read information about women and heart disease within the past 12 months?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

8. Have you seen, heard, or read information about women and heart disease from the American Heart Association in the past three years?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

9. Have you seen, heard, or read information about the Red Dress symbol in the past 3 years?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

10. Have any of your healthcare providers ever discussed heart disease with you when discussing your health?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

IF ANSWERS "YES" ASK:

11. Which healthcare provider discussed heart disease with you?_____

IF ANSWERS "NO" ASK:

12. Why do you think your healthcare provider did not discuss heart disease with you?

_____
_____

13. Have any of your healthcare providers ever told you are at an increased risk for developing heart disease because of your lupus?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

IF ANSWERS "YES" ASK:

14. Which healthcare provider discussed your increased risk with you?_____

15. How informed are you about heart disease in women? Would you say you are…? (READ LIST. RECORD ONLY ONE RESPONSE.)

Very well informed.....-1
Well informed.....-2
Moderately informed .....-3
Not at all informed.....-4
Don't know (DO NOT READ).....-5
Refused (DO NOT READ).....-6

16. How informed are you about stroke or "brain attack" in women? Would you say you are…? (READ LIST. RECORD ONLY ONE RESPONSE.)

Very well informed.....-1
Well informed.....-2
Moderately informed .....-3
Not at all informed.....-4
Don't know (DO NOT READ).....-5
Refused (DO NOT READ).....-6

17. When was the last time you had your blood pressure checked? _____

18. When you had it checked last, were you told the result was normal, too high, or too low?

Normal .....-1
Too high .....-2
Too low .....-3
Don't know (DO NOT READ).....-4
Refused (DO NOT READ).....-5

19. What do you think is a healthy blood pressure level?

_____
Don't know (DO NOT READ).....-4
Refused (DO NOT READ).....-5

20. About how long ago was your cholesterol checked?_____

21. When you had it checked last, were you told the result was normal, too high, or too low? (RECORD ONLY ONE RESPONSE.)

Normal .....-1
Too high .....-2
Too low .....-3
Don't know (DO NOT READ).....-4
Refused (DO NOT READ).....-5

22. Do you know what your HDL or "good" cholesterol level is?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

23. What do you think is a healthy HDL or good cholesterol level?

_____
Don't know (DO NOT READ).....-4
Refused (DO NOT READ).....-5

24. Do you know what your LDL or "bad" cholesterol level is?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

25. What do you think is a healthy LDL or bad cholesterol level?

_____

Don't know (DO NOT READ).....-4
Refused (DO NOT READ).....-5

26. Have you been diagnosed with diabetes?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

27. About how long ago was your blood sugar checked?_____

28. When you had it checked last, were you told the result was normal, too high, or too low? (RECORD ONLY ONE RESPONSE.)

Normal .....-1
Too high.....-2
Too low .....-3
Don't know (DO NOT READ).....-4
Refused (DO NOT READ).....-5

29. Do you know what your blood glucose level is?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

30. What do you think is a healthy fasting blood sugar level?

_____

Don't know (DO NOT READ).....-4
Refused (DO NOT READ).....-5

31. Have you ever been told by your health care provider that you have heart disease?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

32. Have you ever been told by your health care provider that you had a stroke or "brain attack"?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

33. Have you ever been told by your health care provider that you are obese or overweight?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

III. SPECIFIC UNDERSTANDING OF HEART DISEASE AMONG WOMEN/ BEHAVIORS ASSOCIATED WITH PREVENTION

1. Now I would like to read you a series of statements. For each one, please tell me whether you believe the statement is true or false. (READ LIST. RANDOMIZE. RECORD ONE RESPONSE FOR EACH.)

	True	False	(Do not read) Don't know	(Do not read) Refused
a. Once men are diagnosed with heart disease, they are more likely than women to become seriously ill or die	-1	-2	-3	-4
b. The loss of estrogen is a significant contributor to the development of heart disease in women following menopause.	-1	-2	-3	-4
c. Heart disease develops gradually over many years and can easily go undetected	-1	-2	-3	-4
d. Women are less likely to get heart disease after menopause than before	-1	-2	-3	-4
e. Black women are more likely than white women to die from a heart attack or stroke	-1	-2	-3	-4
f. Hispanic women are more likely than white women to die from a heart attack or stroke	-1	-2	-3	-4
g. Men are more likely than post menopausal women to have heart attacks	-1	-2	-3	-4
h. Some forms of heart disease may result in a stroke	-1	-2	-3	-4
i. Men and women experience the same symptoms of a heart attack	-1	-2	-3	-4
j. Women are more likely than men to have unusual or atypical symptoms of a heart attack	-1	-2	-3	-4
k. In the first few hours after the onset of heart attack or stroke symptoms, treatments exist that can break up blood clots to reduce the damage	-1	-2	-3	-4

2. I am going to read you another set of statements. For each, please tell me if you agree or disagree. (READ STATEMENT.) Do you agree or disagree? Is that strongly or somewhat? (READ LIST. RANDOMIZE. RECORD ONLY ONE RESPONSE FOR EACH.)

	Agree Strongly	Agree Somewhat	Disagree Somewhat	Disagree Strongly	(Do not read) Don't know	(Do not read) Refused
a. When I think of heart disease, I most often think of someone having a heart attack and dying quickly	-1	-2	-3	-4	-5	-6
b. When I think of stroke, I most often think about someone having a long-term disease that will reduce the quality of their life	-1	-2	-3	-4	-5	-6
c. By taking estrogen replacement therapy, I can help reduce my risk for heart disease	-1	-2	-3	-4	-5	-6
d. There is nothing I can do to help prevent myself from getting heart disease	-1	-2	-3	-4	-5	-6
e. I am comfortable talking with my healthcare provider about preventive treatment options regarding my health	-1	-2	-3	-4	-5	-6
f. I am confused about how hormone therapy affects my overall health	-1	-2	-3	-4	-5	-6
g. It is important to me to learn about methods to lower my risk of heart attack and stroke	-1	-2	-3	-4	-5	-6
h. It is easy to find accurate and easy to understand information about heart disease and stroke in women	-1	-2	-3	-4	-5	-6
i. I am at low risk for a heart attack or stroke for a woman my age.	-1	-2	-3	-4	-5	-6

3. Based on what you know, what are the major causes of heart disease? (DO NOT READ LIST. RECORD ALL THAT APPLY.)

A family history of heart disease .....-1
Aging.....-2
Being overweight .....-3
Diabetes.....-4
Drinking alcohol .....-5
High blood pressure .....-6
High cholesterol .....-7
High triglycerides.....-8
Low levels of estrogen .....-9
Menopause .....-0
Not exercising .....-x
Smoking .....-y
Stress .....-1
Stroke .....-2
Your racial heritage.....-3
Other (SPECIFY _____).....-4
Don't know .....-5
Refused .....-6

4. Which risks for heart disease do you believe you personally have?

_____
_____
_____

5. Based on what you know, what warning signs do you associate with having a heart attack? (DO NOT READ LIST. RECORD ALL THAT APPLY.)

Chest pain.....-1
Fatigue.....-2
Nausea.....-3
Pain that spreads to the shoulders, neck, or arms .....-4
Shortness of breath.....-5
Tightness in the chest.....-6
Other (SPECIFY _____).....-7
Don't know .....-8
Refused .....-9

6. And again, based on what you know, what warning signs do you associate with having a stroke or "brain attack"? (DO NOT READ LIST. RECORD ALL THAT APPLY.)

Loss of/trouble talking or trouble understanding speech .....-1
Sudden dimness/loss of vision, often in one eye .....-2
Sudden, severe headache .....-3
Sudden weakness/numbness of face or limb on one side ....-4
Unexplained dizziness .....-5
Other (SPECIFY _____).....-6
Don't know .....-7
Refused .....-8

7. Do you think you would be able to tell if you were in danger of a heart attack or stroke?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

Now I would like to discuss ways to prevent heart disease.

8. Which of the following activities do you believe can prevent or reduce the risk of getting heart disease? (READ LIST. RECORD ALL THAT APPLY. RANDOMIZE.)

Quitting smoking .....-1
Getting physical exercise .....-2
Taking special vitamins like E, C or A .....-3
Losing weight.....-4
Reducing dietary cholesterol intake.....-5
Reducing stress .....-6
Taking multivitamins with folic acid.....-7
Taking hormone replacement therapy .....-8
Reducing sodium or salt in the diet.....-9
Taking Omega-3s or fish oil .....-10
Reducing animal products in your diet (such as meat, whole milk, butter and cream) .....-0
Aromatherapy .....-1
Acupuncture.....-2
Yoga.....-3
None of these (DO NOT READ).....-4
Don't know (DO NOT READ).....-5
Refused (DO NOT READ).....-6

9. Which of the following recommendations has one of your healthcare providers made to you? (READ LIST. RECORD ALL THAT APPLY.)

	Which healthcare provider?	When?
❑ Quitting smoking	_____	_____
❑ Getting physical exercise	_____	_____
❑ Losing weight	_____	_____
❑ Reducing dietary cholesterol intake	_____	_____
❑ Reducing stress	_____	_____
❑ Taking folic acid	_____	_____
❑ Taking hormone replacement therapy	_____	_____
❑ Reducing sodium or salt in the diet	_____	_____
❑ Reducing animal products in your diet (such as meat, whole milk, butter, cream)	_____	_____
❑ Taking a drug to lower cholesterol	_____	_____
❑ Taking a omega-3s or fish oil capsules	_____	_____
❑ Don't know (DO NOT READ)		
❑ Refused (DO NOT READ)		

10. Which of the following activities have you done in the past 12 months to lower your risk of heat disease? (READ LIST. RECORD ALL THAT APPLY.)

❑ Quitting smoking
❑ Getting physical exercise
❑ Losing weight
❑ Reducing dietary cholesterol intake
❑ Reducing stress
❑ Taking folic acid
❑ Reducing animal products in your diet (such as meat, whole milk, butter and cream)
❑ None of these (DO NOT READ) ❑ Don't know (DO NOT READ) ❑ Refused (DO NOT READ)

11. Is there anything else you have done to reduce your risk for heart disease?_____

12. Do you agree or disagree with the statement, "I am confident that I can successfully change my behavior"?

Agree.....-1
Disagree .....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

13. What do you see as the biggest obstacle that prevents you from taking actions to reduce your risk of heart disease? _____

14. Do you know anyone with lupus who has heart disease?

Yes .....-1
No.....-2
Don't know (DO NOT READ).....-3
Refused (DO NOT READ).....-4

15. Of the people with lupus that you know have heart disease, how do you think it has affected their lives?_____
_____
_____

IF PARTICIPANT HAS DIAGNOSED HEART DISEASE, ASK

16. How has having heart disease affected your life?_____
_____
_____

APPENDIX G: CURRICULIM VITAE

Patricia Weinstein, MSN, ARNP, PhD-c
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I. EDUCATION

Year	Degree	Institution	Area of Study
2003-present	Doctoral candidate	University of Central Florida, Orlando, FL	Nursing
2002-2003	Postgraduate	University of Central Florida, Orlando, FL	Nursing
1978-1979	Postgraduate	State University of New York, Buffalo, NY	Science Education
1975-1976	MSN	Medical College of Georgia, Augusta, GA	Adult Health Nursing
1971-1973	BSN	University of Maryland, Baltimore, MD	Nursing
1969-1971		Ohio State University, Columbus, OH	General studies

II. LICENSURE/CERTIFICATION

1984-present	Advanced Registered Nurse Practitioner, Florida
1980-1984	Registered Nurse, Missouri
1973- 1984	Registered Nurse, New York
2003-present	Certified Menopause Practitioner, North American Menopause Society
2000-present	Advanced Cardiopulmonary Life Support and Basic Life Support

III. EMPLOYMENT

ACADEMIC APPOINTMENTS

2008-	Adjunct faculty, University of Central Florida, College of Nursing
2006-2008	Online Course Facilitator, Florida Hospital College of Health Sciences, Orlando, FL
Aug – Dec 2007	Teaching Assistant, University of Central Florida, College of Nursing, Orlando, FL
2003-2006	Research Assistant, University of Central Florida, Orlando, FL
1980-1984	Assistant Professor, St. Louis Community College, Kirkwood, MO
1977-1980	Instructor, Millard Fillmore School of Nursing, Buffalo, NY

CLINICAL APPOINTMENTS

2003-2005	Staff Nurse, Cardiac Progressive Care Unit, Florida Hospital, Altamonte Springs, FL
1993	Nurse Practitioner, Camp Ramah, Palmer, MA
1983-1984	Staff Nurse, Medical Unit, Bethesda Dillworth Hospital, St. Louis, MO
1976-1977	Staff Nurse, CCU/ICU, Veterans Hospital, Buffalo, NY
1976	Staff Nurse, CCU/ICU, Doctors Hospital, Augusta, GA
1973-1976	Staff/Charge Nurse, CCU/ICU, US Army Nurse Corps, Fort Gordon, GA,
1973	Staff Nurse, Medical-Surgical Unit, Kenmore Mercy Hospital, Kenmore, NY

IV. RESEARCH

2007 –	Principal Investigator, Dissertation Research, *Assessing Awareness of Increased Risk for Heart Disease and Cardiovascular Risk Factors in Women with SLE*. Period : March 2007-March 2009. Funding: Southern Nursing Research Society Dissertation Research Grant, Florida Nurses Association Undine Sams and Friends Research Grant, Sigma Theta Tau International Nursing Honor Society Theta Epsilon Chapter, Chapter grant.
2007 –	Research assistant, *CD40 and CD40 Ligand: Key Players in Thrombosis and Targets for Thrombotic Antibodies*. Principal Investigator: Ali Amirkhosravi, PhD, Florida Hospital Institute of Translational Research. Period: September 2007-. Funding: American Heart Association grant.
2003-2006	Graduate Research Assistant, *Home vs. Center-based Weight Loss and Exercise in Menopause*. Period: April 1, 2003 – December 1, 2007. Principal Investigator: Karen Dennis, PhD, RN, FAAN, University of Central Florida, College of Nursing. Funding: NINR/NIH RO1 grant.

2004-2006 Graduate Research Assistant, *Intergenerational Physical Activity*, Period: May 1, 2003 – January 31, 2006, Principal Investigator: Karen Dennis, PhD, RN, FAAN, University of Central Florida, College of Nursing.

V. PUBLICATIONS

PEER REVIEWED

Weinstein, PK. (2006). A review of weight loss interventions delivered via the Internet. *Journal of Cardiovascular Nursing*. 21 (4):251-8.

NON-PEER REVIEWED

Weinstein, PK. (2008). Lupus and Bone Health. *Lupus Foundation of Northern California Newsletter*, 30(3), 3-7.

Weinstein, PK. (2007). Lupus and Bone Health. Greater Florida Chapter of the Lupus Foundation of America publication.

Weinstein, PK. (2006). Lupus and Fats. Greater Florida Chapter of the Lupus Foundation of America publication.

ABSTRACTS

Ali Amirkhosravi A, Meyer T, Robles-Carillo L, Davila M , Langer F, Desai H, **Weinstein P**, Amaya M, Francis JL. (2008). Mechanistic components of platelet-associated thrombosis by anti-CD40 ligand antibodies and their prevalence in patients with thrombotic autoimmune disorders. *Blood*, 112 (11), abstract 2857.

Weinstein PK, Rash E, Dunn S, Goodwin Z, Haggar L. Lowndes J, Angelopoulos T, Dennis KE. (2006). Home vs. Center-Based Weight Loss and Maintenance in Menopause. *Obesity*, Program Abstract Supplement, 14:A98, 2006 Annual Scientific Meeting of the NAASO Obesity Society, Boston, MA.

Weinstein PK, Dennis KE. (2006). Assessing the Risk for Cardiovascular Disease among "Healthy" Overweight and Obese Postmenopausal women. *Obesity*, Program Abstract Supplement, 14:A160, 2006 Annual Scientific Meeting of the NAASO Obesity Society, Boston, MA.

VI. PRESENTATIONS

REFEREED

December 2008 Mechanistic components of platelet-associated thrombosis by anti-CD40 ligand antibodies and their prevalence in patients with thrombotic autoimmune disorders, poster presentation. American Society of Hematology Annual Meeting and Exposition, San Francisco, CA.

October 2008 Awareness of increased risk for cardiovascular disease in women with systemic lupus erythematosus, poster presentation. 2008 National State of the Science Congress on Nursing Research, Washington, DC.

April 2007 Assessing Cardiovascular Disease Risk in "Healthy" Overweight an Obese Postmenopausal Women, poster presentation. Preventive Cardiovascular Nurses Association Annual Meeting, Minneapolis, MN, 3rd place winner.

October 2006 Assessing Cardiovascular Disease Risk in "Healthy" Overweight and Obese Postmenopausal Women, poster presentation. NAASO The Obesity Society 2006 Annual Scientific Meeting, Boston, MA.

October 2006 Home vs. Center-Based Weight Loss and Maintenance in Menopause, poster presentation. NAASO The Obesity Society 2006 Annual Scientific Meeting, October 2006, Boston, MA.

March 2006 Sole Mates: Intergenerational Walking Pilot Study, oral presentation, University of Central Florida Graduate Research Forum, Orlando, FL.

March 2005 Concept Development of Expectancy, poster presentation. University of Central Florida Graduate Research Forum, Orlando, FL.

February 2005 Concept Development of Expectancy, poster presentation. Southern Nursing Research Society Annual Meeting, Atlanta, GA.

NON-REFEREED

April 2007 Assessing Cardiovascular Disease Risk in "Healthy" Overweight an Obese Postmenopausal Women, oral presentation. Sigma Theta Tau International Nursing Honor Society, Theta Epsilon Chapter, 15th Annual Research Day, Winter Park, FL.

April 2005 Concept Development of Expectancy, poster presentation. Sigma Theta Tau International Nursing Honor Society, Theta Epsilon Chapter, 13th Annual Research Day, Winter Park, FL.

April 2004 Expectancy as a Middle Range Theory, oral presentation. Sigma Theta Tau International Nursing Honor Society, Theta Epsilon Chapter, 12th Annual Research Day, Winter Park, FL.

INVITED

May 2008	UCF-TV, For Your Health. *Heart Disease and Lupus*, episode 21(2008).
May 2006	*Lupus and Bone Health*. Dorough Lupus Foundation, Orlando, FL.
January 2008	*Keeping Your Bones Healthy—For Women and Men*. Orlando/Winter Park Lupus Support Group, Winter Park, FL.
July 2006	*Lupus: Why Me? Etiology of SLE*. Orlando/Winter Park Lupus Support Group, Winter Park, FL.

VII. AWARDS/GRANTS

2007	Southern Nursing Research Society Dissertation Research Grant
2007	Florida Nurses Association, Undine Sams and Friends Research Grant
2007	Sigma Theta Tau International Nursing Honor Society, Theta Epsilon Chapter, Chapter Grant for dissertation research
2005	University of Central Florida, Who's Who at UCF Scholarship
2003-2004	University of Central Florida Graduate Research Assistantship
2003-2004	University of Central Florida Graduate Merit Fellowship
1969-1973	Walter Reed Army Institute of Nursing Scholarship

VIII. PROFESSIONAL ACTIVITIES & SERVICE

PROFESSIONAL ORGANIZATIONS MEMBERSHIP

Year	**Organization**
2008-	Council for the Advancement of Nursing Science
2008-	Association for Rheumatology Health Professionals
2007-	Rheumatology Nurses Society
2007-	Epidemiology and Prevention Council, American Heart Association
2007-	Society for Women's Health Research
2007-	Organization for the Study of Sex Differences
2004-	Sigma Theta Tau International Nursing Honor Society, Theta Epsilon Chapter
2004-	Phi Kappa Phi Honor Society
2004-	Florida Nurses Association
2003-	Southern Nursing Research Society
2002-	North American Menopause Society
2000-	Preventive Cardiovascular Nurses Association
2000-2007	Cardiovascular Nursing Council, American Heart Association
1973-1980	American Association of Critical Care Nurses, founding secretary, Augusta, GA chapter

PROFESSIONAL SERVICE ACTIVITIES

Lupus Foundation of America

National

2006-	Member, National Education Committee
2007-	Chairman, Health Professionals Resources Task Force

Regional

2007–	Board Member, Greater Florida Chapter of the Lupus Foundation of America
2006–	Coordinator, Greater Florida Chapter of the Lupus Foundation of America Annual Lupus Awareness Seminar
March 1, 2007	Greater Florida Chapter representative, Lupus Advocacy Day, Washington, D.C.

Preventive Cardiovascular Nurses Association

Regional

2002-2007	Central Florida Chapter, Webmaster

Manuscript Review

2008	One article for peer-reviewed journal *Obesity*

COMMUNITY SERVICE ACTIVITIES

2007-	Shepherd's Hope Health Clinic, volunteer nurse practitioner
2007-	Russell Home for Atypical Children, volunteer nurse practitioner