2015

The Association of Lead with Cataracts and Vision-Related Problems in Perimenopausal Women

Imogene Drakes
Walden University

Walden University

College of Health Sciences

This is to certify that the doctoral dissertation by

Imogene Drakes

has been found to be complete and satisfactory in all respects,
and that any and all revisions required by
the review committee have been made.

Review Committee
Dr. Diana Naser, Committee Chairperson, Public Health Faculty
Dr. Raymond Thron, Committee Member, Public Health Faculty
Dr. Michael Dunn, University Reviewer, Public Health Faculty

Chief Academic Officer
Eric Riedel, Ph.D.

Walden University
2014

Abstract

The Association of Lead with Cataracts and Vision-Related Problems in Perimenopausal Women

by

Imogene Audrine Walcott-Drakes

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

December 2014

Abstract

Around the world, women are subject to an earlier incidence of cataracts, have a higher risk for cataracts, and also have a higher risk for other vision-related problems than men. Previous research has indicated an association between endogenous lead stored in long bones and cataracts in men over 60 years of age; however, a similar study in women did not reveal an association. This case control study was conducted to investigate whether perimenopausal mobilization of endogenous lead serves as a possible causative factor for women's generalized vision issues and cataract incidence in particular. Secondary data were gathered from 1,416 women aged 40 to 55 years of age from the 2005-2006 and 2007-2008 National Health and Nutrition Examination Surveys. Variables of interest included vision-related issues, cataract surgeries, bone density data, blood lead levels, and markers of lead mobilization. The results of the logistic regression analysis in the absence of confounders (*OR* = 1.50, 95% CI [1.08, 2.09]) indicated that endogenous lead is a possible causative factor for the low-level vision problems women experience during their perimenopausal years. Chi-square analysis of mobilized lead was also associated with cataract surgeries, $p < .05$. This appears to be the first report of a possible association between lead and cataracts in women and highlights the need for women to be studied in the context of their biology when their clinical results differ from those of men. These results should engender positive social change initiatives to minimize women's perimenopausal exposure to endogenous lead. Recommendations for further research include a case control study, which includes plasma lead levels, and a longitudinal study.

The Association of Lead with Cataracts and Vision-Related Problems in Perimenopausal Women

by

Imogene Audrine Walcott-Drakes

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

December 2014

Dedication

Give God the glory.

Great things He has done… (F. Crosby, 1875)

This dissertation is dedicated to my sons, Atsu and Attakuma, and to my mother, Elaine Louise, who with unconditional love continue to ensure I never lack emotional support. This dissertation is also dedicated to my father, Sydney, for his confidence in me. To my departed grandparents – Thomas, Ellen Elizabeth, James, and Martha Hilda – I am proud that I descended from you. You will always be remembered for the assurance you gave to me and for your humor in times of stress. To the memory of Ina Daniels and her love for me, I also dedicate this dissertation.

Acknowledgments

I especially thank Dr. Diane Naser, my very supportive Chair; Dr. Raymond Thron, my Dissertation Supervisory Committee Member; and Dr. Michael Dunn, my University Research Reviewer for guiding me through the dissertation phase of my journey. To Dr. Edward Leib of the University of Vermont Health Network, Dr. Seifried, Dr. Kennedy, Dr. Barkley, Dr. Jaeckel, Dr. Margaritis, Dr. Tschida, Mr. Derrick Wright, and the UVHN at CVPH Library Staff mainly Mrs. Chris and Mr. Stan Ransom many thanks for your assistance or for your advice.

Thanks to the many educators, family, and friends who helped along the way. A special thanks to Mrs. Myrna Norton-Sturge, my nursery school teacher; to the memory of Mr. Herman Hubbard who endured my demonstration of “a pinch of spice” while I was in kindergarten and who, in spite of that demonstration, always supported my academic efforts; to Elementary School Teachers – Mrs. Thomas, Mrs. King, and Mr. Ramdeen; to the many teachers of the Bishops’ High School, Georgetown who helped me grow from socks to stockings and expand my knowledge of the world; and to the memory of Dr. George Walcott, former Vice-Chancellor of the University of Guyana whose words, seared into my consciousness, spurred me on towards this terminal degree. I especially thank Dr. E. James Ebose, Dr. Debra Mayer-Quezada, Ms. Susan Schnall, Mr. Edwin Best, and my cousins Messieurs Conrad and Woolford Walcott for believing in me.

Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction to the Study

Preface

Cataracts are the principal cause of blindness in the world (World Health Organization, 2006) and the leading cause of vision loss in the United States of America (Centers for Disease Control and Prevention [CDC], 2013d). The American Optometric Association (2004) stated that more than 50 percent of the people over the age of 65 have some degree of cataract development. Schaumberg et al. (2004) found an association between the lifetime storage of lead in long bones and the incidence of cataracts in men who were over 60 years of age. Women have a higher risk for cataracts and other vision-related problems than men (Congdon et al., 2004; World Health Organization, 2013); however, no comparable study to Schaumberg et al. (2004) has been previously conducted on a population of women. This study was designed to address this research gap and investigate a potential cause of the phenomenon of earlier cataracts in women, potentially leading to initiatives that would help both genders.

Introduction

This research study investigated potential links between lead released in women's bodies during perimenopausal years and the earlier appearance of cataracts and other vision-related issues in women compared to men. This study examined several secondary datasets for variable data on vision and lead. The secondary datasets from the 2005 – 2006 and 2007 – 2008 National Health and Nutrition Examination Surveys (NHANES) were chosen because these datasets contain data on vision issues, cataract surgeries, lead levels, bone density data, menopause status, smoking and other covariates associated with

cataracts. These continuous NHANES datasets were sampled to be representative of the population of the United States. However, the Centers for Disease Control and Prevention oversampled some sub-groups in order to ensure that bias due to small sample size was minimized (Centers for Disease Control and Prevention, 2014b). The NHANES datasets contain data on blood lead levels, biological markers; bone density measurements; eye examinations excluding examinations for cataracts and cataract surgeries; and responses to questionnaires on osteoporosis, prescription drug use, socio-economic factors, and demographics.

Cataract surgeries were not used as the major criterion for assessing vision-related problems. One reason for this decision is that gradable cataracts can take years to develop (Brown et al., 1999); the length of time it takes cataracts to mature put these measurements outside the study scope. Another reason that cataract studies were not used as a major criterion is the American Optometric Association's (2004) advice to eye care specialists that cataract surgeries are indicated only when the presence of the lens opacities interferes with patients' routine activities. The recommendation is not based on the grade of the cataract and thus there is no standard criterion for the grade of cataract that warrants or requires cataract surgery. A third reason is that Caucasians have cataract surgery at a rate 2.8 times higher than that of African Americans (West et al., 1998). Using the presence of cataract surgeries as the only criterion for assessing the incidence of cataracts in a population sample could therefore lead to underestimating the incidence of cataracts in the non-Caucasian U.S. population to a significant degree. This led to several study design considerations such as including data from responses to vision-

related questions as well as data from the results of direct clinical examinations. The intention of this approach was to minimize bias and to determine whether there was a possible association between mobilized lead and early cataractogenesis and other vision-related problems in perimenopausal women.

Background

This section of the chapter contains information on cataracts in the general population and the reason for the premise for this research, which is that endogenous lead is a possible causative factor for cataracts in perimenopausal women. The main types of cataracts are depicted, information on possible mechanisms for injury to the eye lenses by lead are laid out, and sources of lead in the environment and entry into and storage in the compartments of the body are also explained. The section ends with discussions on the phenomenon of lead mobilization in perimenopausal women, the known deleterious effects of endogenous lead, the postulated pathway for damage to the eye lenses by mobilized lead, and the gap in knowledge that needed to be explored. The next subsection contains information on the reason for this dissertation study and the nature of the cataracts that can lead to a decrease in vison or even complete loss of vision to an individual.

Description of Cataracts and Their Impact on Individuals

Cataracts can interfere with daily activities and if left untreated may lead to blindness (American Optometric Association, 2004; World Health Organization, 2006). The only treatment for cataracts is to have surgery. Not everyone has access to surgery, and if they do; there is still an element of risk to having the surgery since complications

can result (Taylor, 2002; West et al., 1998). The majority of humans will develop some form of cataract if they live long enough (Taylor, 2002). If knowledge about cataractogenesis is increased, then steps could be taken to delay the onset of cataracts in individuals until they are no longer needed and prolong quality of life years for individuals. The goal of this dissertation is to add to the knowledge about cataracts so that quality of life years for all individuals can be extended.

Cataracts are opacities of the eye lenses which limit vision. Eye lens opacities may be caused by birth defects (congenital), trauma, or as a consequence of aging (American Optometric Association, 2014). The term "cataract" refers to how the opacities appear to run over the lenses and cloud them in a way that is characteristic of waterfalls (United Nations Environment Programme, 2006). There are three main forms of cataract: nuclear, cortical, and subcapsular. In nuclear cataracts, the center of the lenses gradually becomes opaque and the nucleus of the lens changes from clear to yellow and sometimes to brown. Cortical cataracts radiate in "spokes" from the periphery of the lens and surround the nuclei of the lenses. A Posterior subcapsular cataract develops at the back of the lens. Subcapsular cataracts may develop quickly in some patients. The main types of cataract are shown in Figures 1 – 3 below:

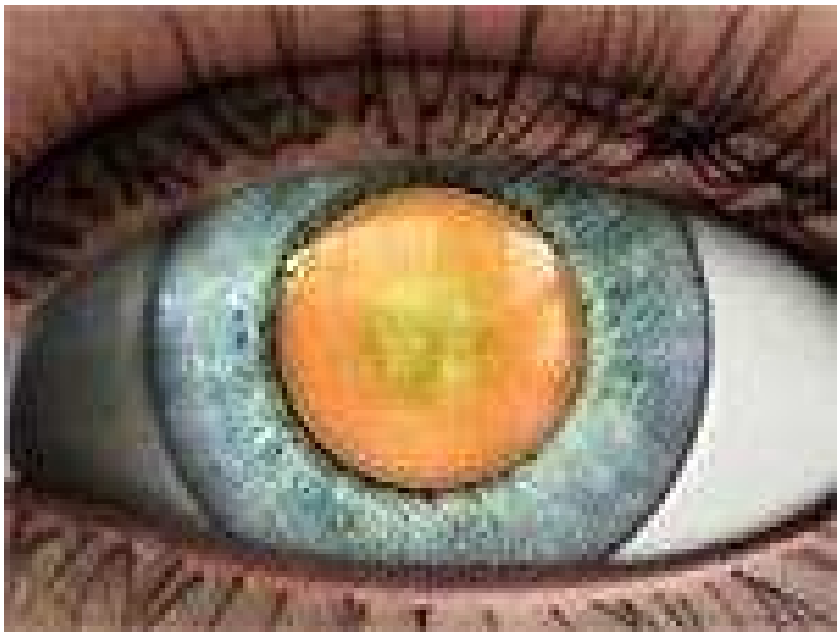

Figure 1. Illustration of a Nuclear Cataract. Adapted from “Cataract” by American Optometric Association, 2014. Retrieved from http://www.aoa.org/patients-and-public/eye-and-vision-problems/glossary-of-eye-and-vision-conditions/cataract?sso=y. Copyright 2014 by Eyemaginations. Reprinted with permission.

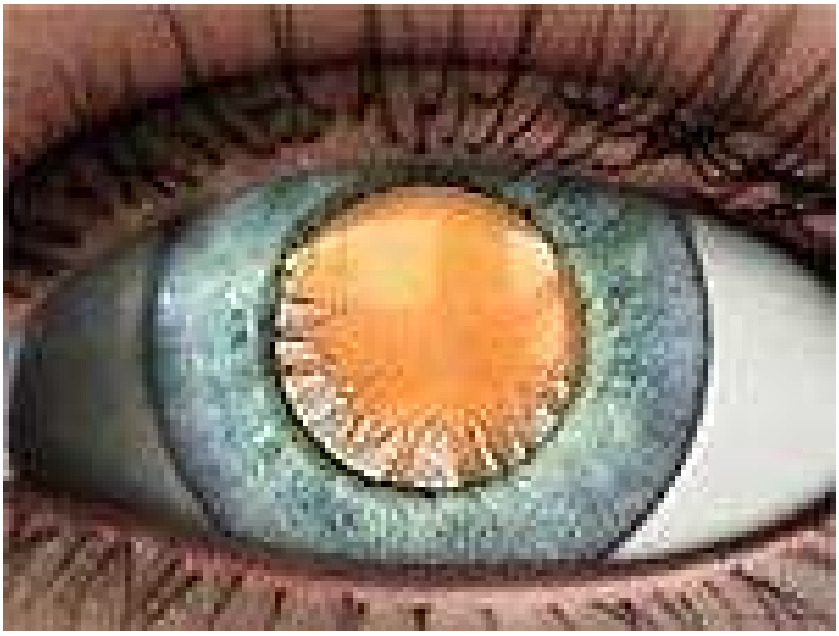

Figure 2. Illustration of a Cortical Cataract. Adapted from “Cataract” by American Optometric Association, 2014. Retrieved from http://www.aoa.org/patients-and-public/eye-and-vision-problems/glossary-of-eye-and-vision-conditions/cataract?sso=y. Copyright 2014 by Eyemaginations. Reprinted with permission.

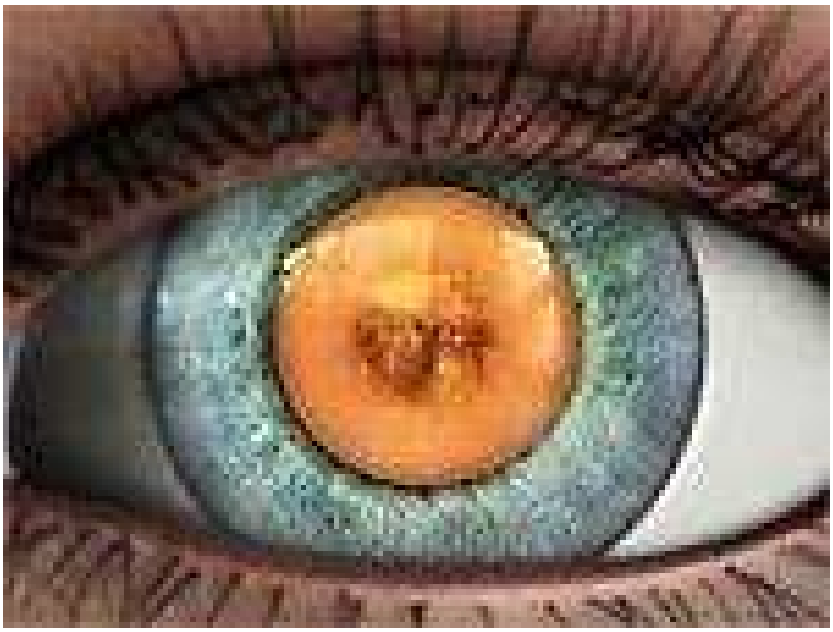

Figure 3. Illustration of a Subcapsular Cataract. Adapted from "Cataract" by American Optometric Association, 2014. Retrieved from http://www.aoa.org/patients-and-public/eye-and-vision-problems/glossary-of-eye-and-vision-conditions/cataract?sso=y. Copyright 2014 by Eyemaginations. Reprinted with permission.

Postsubcapsular (PSC) cataracts affect vision more than the other types of cataracts (McCarty et al., 2000). Although cortical opacities are reported as the most prevalent type of age-related lens change, the type of cataract most frequently responsible for the decision of patients to undergo cataract surgery is either a PSC cataract (Kanthan et al., 2008; McCarty et al., 2000) or a mixed type of opacity with a nuclear-posterior subcapsular component (Belpoliti et al., 1995). Caucasians are significantly more likely to have nuclear opacities and posterior subcapsular (PSC) opacities and African Americans are more likely to have cortical cataracts (Delcourt et al., 2000; West, 2000). This phenomenon correlates with the observation that Caucasians are more likely than non-Caucasians to have surgeries for cataracts (West et al., 1998).

Lead as a Possible Causative Factor for Age-Related Cataracts

This dissertation research is about the association of lead with cataractogenesis in perimenopausal women. It is important to review how lead from the environment can become incorporated in the body and build up over time in a manner that would lead to cataractogenesis. The premise for this dissertation study is compiled from three main hypotheses: First, lead has been linked to several health disorders and, despite well-documented toxic effects on the human body; lead continues to be employed in a variety of industrial uses (Tokar et al., 2013). Second, lead is ingested in small amounts in food or inhaled in dust particles throughout life (Rabinowitz et al., 1976). Lastly, after ingestion, some lead is compartmentalized in the various tissues of the body, but most of it is excreted. However, the half-life for lead in bone compartments is very long and lead can build up in those bone compartments over time (Rabinowitz et al., 1976). Analysis of data in an epidemiological study revealed an association between lead in long bones and cataract formation in men older than 60 years of age (Schaumberg et al. 2004). This pathway: occupational exposure or continuous incidental exposures to small amounts of lead and sequestration in the bones over a lifetime is the premise for this dissertation study.

Previous analysis of human eye lenses demonstrated the presence of lead in cataractous lenses but did not identify significant amounts of lead in clear human lenses (Cekic, 1998; Shukla et al., 1998). Lead was also found in the cataractous lenses of smokers when the cataractous lenses were analyzed directly for lead content (Mosad et al., 2010). However, the lead content of non-cataractous lenses was estimated based on

the blood lead levels of the participants who were not diagnosed as having cataracts (Mosad et al., 2010). Mosad et al. concluded that non-smokers did not have significant levels of lead in their lenses. The researchers postulated that an oxidative mechanism was responsible for the increased incidence of cataracts observed in smokers around the world since the smokers in the study who had cataracts also had low levels of vitamin C, which is an antioxidant (Mosad et al., 2010). The reported association between lead and cataracts in Mosad et al.'s study lends credence to the main premise for this research, which is that endogenous lead is a possible causative factor for cataracts in perimenopausal women.

Lead and the General Population

Significant efforts in the United States have been made to reduce lead and other toxic burdens in the environment over the last several decades. Many of these efforts are the result of the geochemist Dr. Claire Patterson's presentation on the harmful effects of lead in the environment to the U.S. Congress in 1966 (Needleman, 2000; Tepper & Levin, 1975). Patterson's efforts led to the passage of the Clean Air Act in 1970 (Callendar & Van Metre, 1997). The Act included a ban on the use of leaded gasoline, and a general reduction in other sources of lead such as stack emissions, paints, and solders (Callendar & Van Metre, 1997). Consequently, there has been a drastic reduction in lead air emissions and a corresponding decrease in ambient lead since this legislation took effect (Environmental Protection Agency, 1995). The decrease in ambient air lead levels has led to a decrease in the blood lead levels of the U.S. population by 78% from 1978 to 1991 (Pirkle et al., 1994).

Not all lead exposure comes from active pollution. Chillrud et al. (1999) stated that the environmental lead burden in New York City is the result of residues from past municipal incineration and not from residues of leaded gasoline use (Chillrud et al., 1999). The Environmental Protection Agency (EPA) has reported that, decades after the passage of the Clean Air Act, the lead levels in the soil, of industrial and non-industrial locations in some U.S. cities are still very high (EPA, 2001). The EPA also stated that the U.S. population is still exposed to environmental lead although there is no ubiquitous exposure as occurred before the regulations of the Clean Air Act became effective (EPA, 2001). This situation is also compounded by other factors such as the immigration of families with unknown blood lead levels to the U.S., the importation of some foods and toys that may contain high levels of lead, and the maintaining of customs associated with exposure to relatively high levels of lead (Abadin, 2007; CDC, 1998; CDC, 2002; CDC, 2013b; Center for Food Safety and Applied Nutrition, 2005). Expectant mothers and children are routinely tested for elevated blood lead levels but there is no similar program for the rest of the population. Therefore, the percentage of people who may have levels of lead in their bodies that are inconsistent with good health is unknown. The purpose of this study was to find out whether perimenopausal women who participated in the NHANES surveys have a higher risk for incidence of cataracts or vision-related issues based on their levels of mobilized endogenous lead: A demonstrated higher risk for this sample of women would mean that perimenopausal women should be added to the segment of the population who are routinely checked for elevated blood lead levels.

The continual ingestion of small amounts of lead in food and the inhalation of dust particles polluted with lead are sources of lead exposure for the general population (Brown & Margolis, 2012; Rabinowitz et al., 1976). A meta-review of X-ray fluorescence studies for lead in various U.S. survey respondents revealed wide variations in blood lead levels which are illustrated in Table 1 (Ambrose et al., 2000). Based on the review report of Abadin et al. (2007), I believe that exposure to lead and storage of lead by the human body lead will continue into the near and far future.

Table 1

Tibia Lead in a Cross-section of the U.S. Population

Group	Tibia lead, μg/g bone mineral
Suburban teens	4
Women of childbearing age	10
Adults with history of childhood lead	22
Age-matched controls	5
65 year-old males	22
Active lead workers	21
Retired lead workers	32
Lead factory office workers	8
Unexposed controls	4
Lead workers	25
Unexposed controls	10
Lead workers	48
Lead workers	41

Note. Adapted from "Bone Lead Concentrations Assessed by In Vivo X-ray Fluorescence" by Ambrose et al., 2000, *Clinical Chemistry*, *46*(8 Pt 1), p. 1171-1178.

Lead and Perimenopausal Women

Researchers have been aware of the phenomenon of lead mobilization in perimenopausal and postmenopausal women for a few decades: Previous studies performed on data from the National Health and Nutrition Examination Survey (NHANES) revealed that women begin to lose bone mass due to bone demineralization during the perimenopausal years (Symanski & Hertz-Picciotto, 1995). The 1995 study of Symanski and Hertz-Picciotto validated previous reports of perimenopausal bone depletion by Harmon and Talbert (1985). Examination of the NHANES data also revealed that postmenopausal women and smokers had higher levels of blood lead than any other group (Silbergeld et al., 1988). There appeared to be additive effects for women who were both smokers and perimenopausal (Symanski & Hertz-Picciotto, 1995). Analysis of the data also revealed a decrease in blood lead levels in the postmenopausal years as the rate of bone demineralization decreased; women in the early postmenopausal years had significantly higher levels of blood lead than women in the later postmenopausal years (Silbergeld et al., 1988; Symanski & Hertz-Picciotto, 1995). High blood lead levels post osteoporosis and post menopause were negatively associated with degree of parity (Silbergeld et al., 1988). This finding correlated with earlier work which showed that lead was leached from the bone during metabolic states such as pregnancy, lactation, and osteoporosis or osteopenia (Silbergeld et al., 1988).

Depending on their location in the world, women may experience menopause during the fifth or sixth decade of life: Women in developed countries generally experience menopause around 49.3 to 51.5 years of age (Bromberger et al., 1997; Do et

al., 1998; Frommer, 1964). The median age range for menopause for women in the United States is 51.2 years (Reynolds & Obermeyer, 2005). Bone loss begins to occur in the menopausal years (Harmon & Talbert, 1985; Weyermann & Brenner (1998), but depending on heredity and estrogen status, low bone mass may begin in the premenopausal years (Armamento-Villareal et al., 1992).The women who were the focus for this dissertation study were either in the perimenopausal years or in the first few years after menopause. By choosing women who were aged 40 to 55 years for the study, I hoped to study those women who were most at risk for bone depletion and lead mobilization and therefore more at risk for vision issues according to the hypothesis for this study.

Postulated Mechanism for Mobilization of Lead Post Menopause

Researchers have conducted studies to elucidate a mechanism for the bone demineralization or osteopenia, which occurs during the menopausal transition: Possible hypotheses have included a decrease in the release of parathyroid hormone which regulates bone mineralization following a reduction in estrogen levels, decreased absorption of calcium from the intestine, and impaired activation to the precursors of vitamin D (Cumming et al., 1985; Riggs & Melton, 1984). In 2006, Weitzman and Pacifici proposed that osteopenia resulting from reduced estrogen levels is the end product of many complex processes. Some of the processes involve an increase in interleukin-7, decreases in transforming growth factor-beta and insulin-like growth factor, amplification of T-cell activation, and suppression of the bone-forming osteoblasts (Weitzmann & Pacifici, 2006). Researches have reported that significant bone mineral

depletion occurs during the first two to four years or four to eight years after the menses cease (Riggs et al., 2002; Ruegsegger et al., 1984). Concomitant with the bone demineralization in the middle years of life is the release of lead from the bone to the bloodstream (Symanski & Hertz-Picciotto, 1996).

Deleterious Effects of Endogenous Lead

The Normative Aging Study is a longitudinal study of the health of veterans affiliated with the Department of Veteran Affairs. Investigators of the Normative Aging study found that that endogenous lead is associated with age-related diseases such as hypertension and renal dysfunction (Hu et al., 1996). The investigators hypothesized that lead could also be implicated in other age-related diseases (Hu et al., 1996). Women are more likely to experience more rapid bone demineralization than men during the perimenopausal period (Harmon & Talbert, 1985). The risk for damage by lead to internal organs increases as a result of the rapid demineralization (Gulson et al., 1995; Hu & Hernandez-Avila, 2002; Korrick et al., 1999; Nash et al., 2003; Nash et al., 2004; Rothenberg et al., 2002). Nash et al. (2003) also reported that lead mobilized during bone demineralization is associated with deleterious effects such as hypertension. The reports of the disease-causing effect of endogenous lead lend credence to the hypothesis for this study that lead is a possible causative factor for cataracts in women.

Lead as a Possible Cause for Earlier Cataractogenesis in Postmenopausal Women

Investigators of age-related cataractogenesis in twins found that the environment plays a considerable role in the development of cataracts (Hammond et al., 2000). After Schaumberg et al. (2004) reported an association between endogenous lead and cataracts;

Neal et al. (2005) verified that lead can cause opacities in lenses. However, the mechanism by which lead can damage the eyes is not singular: Theories for the mechanism of damage to the lens by lead include glutathione metabolism, changes in redox status, imbalance in calcium homeostasis, and modification of the lens protein (Park et al., unpublished). The synopsis of the theories is that lead can damage the eye lenses by one or a combination of several mechanisms.

The hypothesis for this study is that the pathway by which endogenous lead can damage the eye lenses of postmenopausal or perimenopausal women is linear: Postmenopausal women are subject to increased bone turnover (Hellekson, 2002) with a resulting loss of bone mass and likely mobilization of lead stores (Hernandez-Avila et al., 2000; Silbergeld et al., 1988; Symanski & Hertz-Picciotto; 1995). In 2009, investigators reported that high levels of bone turnover markers are significant predictors of blood lead levels (Machida et al. 2009). Analysis of the study revealed that perimenopausal women, who, on average, have the highest rate of bone turnover, have higher blood lead levels than other groups of women (Machida et al., 2009). This series of phenomena – menopausal transition, bone loss, lead mobilization, and eventual deleterious effects on internal metabolic processes – was hypothesized as a sequential pathway for damage to the eye lenses by lead in postmenopausal and perimenopausal women.

Investigators of one epidemiological study reported results that appear to support the hypothesis that lead damages eye lenses: Analysis of the results showed an inverse relationship (OR=0.25) between the prevalence of cataracts and drinking milk (Miglior et al., 1994). The reason for this belief is milk is a major source of calcium in

the diet and increased intake of calcium results in decreased absorption of lead because of competition (Bruening et al., 1999; Weyermann & Brenner, 1998). Therefore, a possible explanation for the observed inverse relationship between drinking milk and cataracts is that individuals who have a diet high in calcium have lower sequestration of lead in the bones than individuals who are exposed to the same amount of environmental lead but do not have calcium-rich diets. Consequently, decreased sequestration of lead in the bodies of individuals who drink lots of milk leads to decreased risk for lead-induced damage to the lenses of the eyes.

Conversely, women who are undergoing the menopausal transition with high levels of bone resorption have higher possible exposure to endogenous lead than women who are not at the same phase of the life cycle. If the effects of the mobilized lead are not reduced by chelation or competition from calcium, then the possibility exists that the lead could have deleterious effects on the lens of the eyes as it does to other tissues and organs of the body. Thus, the inverse relationship between drinking milk and cataracts gives credence to the hypothesis that the perimenopausal mobilization of endogenous lead may be the cause of the higher risk for cataracts in women.

The summary of information that supports the hypothesis that endogenous lead may be a causative factor for the earlier cataractogenesis and higher risk for vision-related problems in women worldwide is three-fold. First, the National Institutes of Health (2000) issued a consensus statement that both men and women experience osteoporosis in their later years but that men do so at least a decade after women (Hellekson, 2002). Second, previous investigators have shown that post-menopausal

women experience a rise in blood lead level as the bones begin to demineralize (Hernandez-Avila et al., 2000; Silbergeld et al., 1988; Symanski & Hertz-Picciotto, 1995). Third, meta-review of data on cataracts revealed that women generally experience cataracts significantly earlier than men do (Congdon et al., 2004). This sequence of events lines up in a pattern that would fit damage to the lens by endogenous lead released from the bones due to demineralization or osteoporosis during the menopausal transition. A simplified timeline of the relevant information regarding menopause, osteopenia, and maturation of cataracts that can lead to surgery is shown in Figure 4.

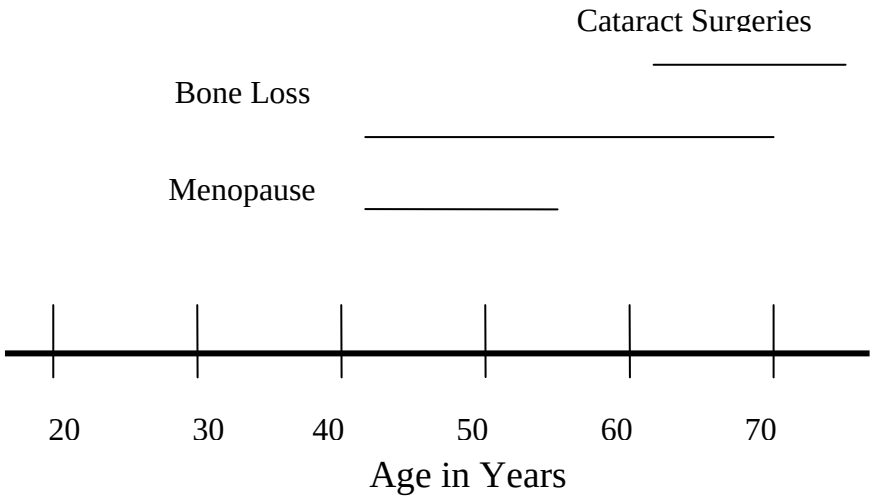

Figure 4. A visualization of the temporal sequence of events described in the study.

The purpose of this research was to explore the gap between the beginning of perimenopausal bone turnover and the manifestation of cataracts and other vision-related problems. The goal was to determine if lead is a possible causative factor for the early appearance of vision-related problems in women. The results of this study add to the pool

of knowledge regarding cataracts and other age-related eye diseases in postmenopausal women.

Gaps in Knowledge Addressed by this Study

It is not well understood how cataracts are formed or the reason that women have a higher prevalence of cataracts and show clinical vision-related symptoms earlier than men. A meta-review showed that females (depending on ethnicity) surpass or exceed males in the prevalence of cataracts during the perimenopausal years (Condgon et al., 2004). However, exogenous estrogen does not directly confer protection on the lens against cataracts (Kanthan et al., 2010). More research needed to be conducted to reveal the causative factor for the higher prevalence of cataracts in women as women enter the postmenopausal years.

Examination of the results of many studies revealed the greater prevalence of cataracts in women (Jonasson & Thordarson, 1987; Klein et al., 2003; Leske et al., 2010). However, every type of cataract may not always lead to early cataract surgery (Belpoliti et al., 1995). Bone lead is mobilized when osteoporosis occurs in post-menopausal women (Hernandez-Avila et al., 2000; Silbergeld et al., 1988; Symanski et al., 1995); cataracts also occur in the post-menopausal years. This study was conducted because I believed analysis of a study that links the various phenomena associated with lead and cataracts could reveal the reason for the higher prevalence of cataracts and other vision-related problems in postmenopausal women. In addition, the study was not confined to analysis of data on cataract surgeries. This study included the analysis of data on generic vision issues since not all types of cataracts lead to early cataract surgery and not all

individuals who need cataract surgery are generally able to do so (Taylor, 2002; West et al., 1998).

Statement of the Problem

The purpose of this research study was to focus on the problem of the earlier appearance of cataracts and other vision-related problems in women. I conducted the research because of my belief that the phenomenon was related to the increased bone turnover and release of endogenous lead that occurs after and during the perimenopausal period. Selected data on biomarkers in the sample of women aged 40 to 55 years who participated in the 2005-2008 National Health and Nutrition Examination Surveys were analyzed. Based on the results of the analysis, it is my belief that public health officials could use the information to engender change and lessen the incidence of cataractogenesis in perimenopausal women.

According to the World Health Organization (2013), women have a higher risk for vision-related problems. There are numerous published reports regarding the higher prevalence of cataracts in women than in men. Jonasson and Thordarson (1987), Leske et al. (2000), Mukesh et al. (2006), and Resnikoff et al. (2004) on behalf of the World Health Organization, are a few of the authors who reported that women have a higher risk for cataracts. A meta-review of cataract research revealed that cataractogenesis generally occurs earlier in women than in men (Congdon et al., 2004). Except for age, known causes of cataracts include asthma, (Delcourt et al., 2000), cooking with biomass fuels (Mishra et al., 1999), glucocorticoids (Cumming & Mitchell, 1999; Stanford University, 2003), radiation (Gragoudas et al., 1995), smoking (Christen et al., 2000, McCarty et al.,

1999), and ultraviolet light (Hollows & Moran, 1992). However, examination of the literature has not revealed that any of the above causes are definitely connected with women worldwide.

The expectation is that women will continue to have longer lifespans and therefore women will also have the potential for longer exposure to visual impairment problems if the causes of visual impairment are left untreated (WHO, 2013). On the other hand, cataract surgeries are not without risk (Centers for Disease Control and Prevention, 2007). Cataracts have also been associated with a higher risk for mortality (Hennis et al., 2001; Knudtson et al., 2006; West et al., 2000). Based on the foregoing, there is a need for studies to elucidate the reason for the phenomenon of earlier and higher risk for cataracts and other vision-related problems in the female gender.

Purpose of the Study

The purpose of this research was to determine if there is any association between the release of lead during perimenopausal bone demineralization and the early incidence of cataracts and other vision-related issues in women. The method was quantitative. The main independent variables were cataract surgeries and vision issues. Mobilized lead was the dependent variable. The data on the variables were obtained from the National Health and Nutrition Examination Surveys website at www.cdc.gov/nchs/nhanes.htm.

Research Question(s) and Hypotheses

The research questions and hypotheses that relate to the purpose of the study were as follows:

RQ_1 What is the relationship between the incidence of cataracts and elevated blood lead levels in perimenopausal women when there is evidence of bone turnover?

$H1_0$ There is no significant relationship between the incidence of cataracts and elevated blood levels in perimenopausal women when there is evidence of bone turnover.

$H1_A$ There is a significant relationship between the incidence of cataracts and elevated blood levels in perimenopausal women when there is evidence of bone turnover.

RQ2 What is the relationship between elevated blood lead levels and general vision problems in perimenopausal women?

$H2_0$ There is no significant relationship between elevated blood lead levels and general vision problems in perimenopausal women.

$H2_A$ There is a significant relationship between elevated blood levels and general vision problems in perimenopausal women.

RQ3 Is evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization (elevated blood lead levels and evidence of bone demineralization) significantly different from the incidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization?

$H3_0$ Evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization (elevated blood lead levels and evidence of bone demineralization) is not significantly different

from the incidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization.

$H3_A$ Evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization (elevated blood lead levels and evidence of bone demineralization) is significantly different from the incidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization.

RQ4 Is the evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization when the data are controlled for age?

$H4_0$ Evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization is not significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization when the data are controlled for age.

$H4_A$ Evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization is significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization when the data are controlled for age.

Theoretical and/or Conceptual Framework for the Study

The main hypothesis for this study is that there is a significant relationship between the incidence of cataracts and elevated blood levels in perimenopausal women when there is evidence of bone turnover. The theoretical and conceptual frameworks for this research study were synthesized from the social cognitive theory (SCT) and the results of various epidemiological and other peer-reviewed studies performed in the past 50 years. Information gauged from this research study can be associated with the various components of SCT which are psychological determinants of behavior, environmental factors, moral detachment, observational learning, and self-regulation (McAlister et al., 2008). The results of clinical studies in the past century revealed that lead is stored in compartments of the body (Rabinowitz et al., 1976). The stores of lead may be mobilized from bones due to various stressors (Hernandez-Avila et al., 2000; Silbergeld et al., 1988; Symanski & Hertz-Picciotto, 1995). The mobilized lead can have deleterious effects on the body including the lens of the eyes (Schaumberg et al., 2004). A flowchart illustration of the scientific premise for the study is shown in Figure 5.

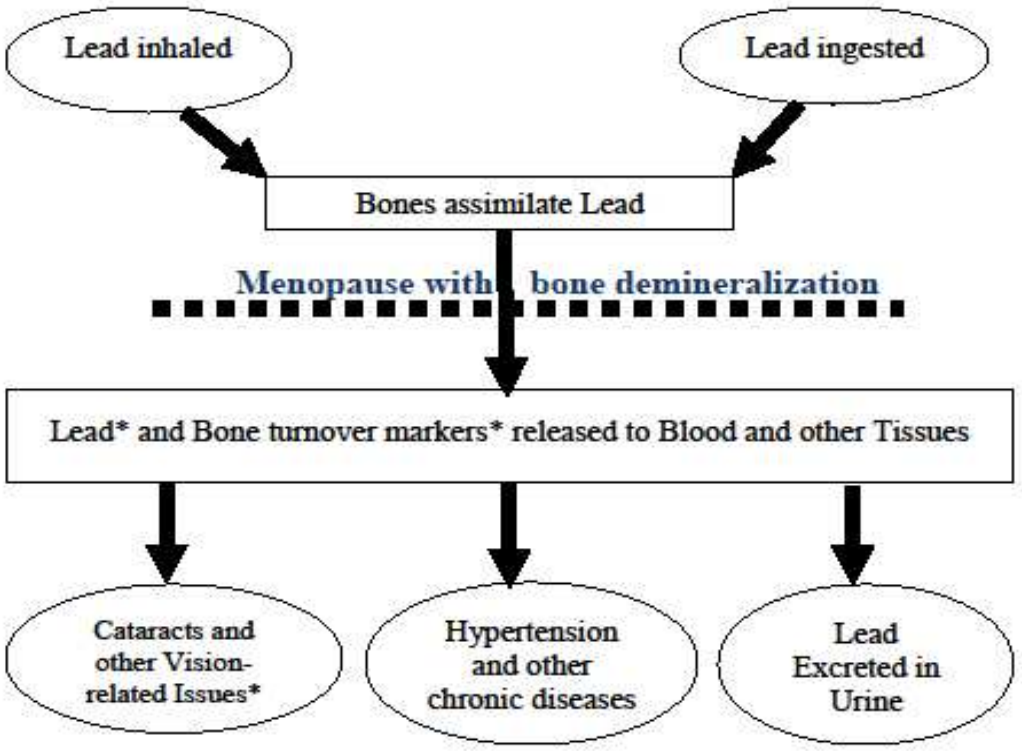

Figure 5. Flowchart Illustration of Framework for Study of Endogenous Lead and Cataracts in Perimenopausal Women.

Nature of the Study

The nature of this study was a quantitative method to investigate whether endogenous lead is a possible cause for cataractogenesis or other vision-related problems in perimenopausal women. This epidemiological study was a case control study. The research participants were perimenopausal women aged 40-55 years who participated in the National Health and Nutrition Examination Survey (NHANES) during the years 2005-2008. The sample for the NHANES was selected to represent the U.S. population by age range (Centers for Disease Control and Prevention, 2014a). However, some

groups were deliberately oversampled to ensure the statistics produced from the surveys are reliable. The groups that were oversampled included African Americans, Asians, Hispanics, and persons older than 60 years. Thus, the expectation is that the sample of women aged 40-55 years contained ethnic and racial groups that were overrepresented when compared to the composition of the U.S. population.

Cataractogenesis has many causative factors. Therefore, in order to address known confounders, prescription drugs, age at last menstruation, ever nursed children, smoking status, and other factors were included in the analysis. Variables that were analyzed included blood lead levels, the presence or absence of osteopenia, blood turnover markers, and the presence or absence of cataracts and other vision-related problems. Operational definitions that were used in the study are shown below.

Operational Definitions

Alkaline Phosphatase. An enzyme associated with the metabolism of bone and lipid transport in the intestine (Panteghini & Bais, 2014).

Calcium: Calcium is the fifth most common element in the body and the most prevalent cation. The skeleton contains about 99% of the calcium in the body (Panteghini & Bais, 2014).

Cataract: Clouding of the lens that reduces vision (Merriam-Webster, 2014).

Glaucoma: An eye disease characterized by increased pressure within the eyeball that results in damage to the optic disk and a gradual loss of vision (Merriam-Webster, 2014).

Macular degeneration: Gradual loss of the central vision. It usually affects the elderly in both eyes. Bleeding fluid leakage may occur in some forms (Merriam-Webster, 2014).

Menopause: The permanent cessation of menstruation due to ovarian failure (Panteghini & Bais, 2014).

Osteopenia: Osteoclastic (bone resorption) activity that supersedes osteoblastic (bone building) activity can lead to osteopenia or bone demineralization (Panteghini& Bais, 2014).

Osteoporosis: Disease characterized by a loss in bone density that can result from remodeling imbalance during the first few years after menopause (Panteghini & Bais, 2014).

Perimenopause: The period around the onset of menopause that may be characterized by several physical signs such as menstrual irregularity and hot flashes (Merriam-Webster, 2014).

Retinopathy: Noninflammatory disorders of the retina that may lead to blindness (Merriam-Webster, 2014).

Total Bilirubin: Bilirubin is a pigment derived from old red blood cells. Increased levels of bilirubin are seen in liver disorders of the liver. Testing for total bilirubin (the sum of direct and indirect bilirubin) is a method that is transferable among clinical laboratories (Panteghini & Bais, 2014).

Assumptions

The phenomenon of earlier vision-related problems in women is worldwide (World Health Organization, 2013). Therefore, no efforts were made to reweight the sample population studied for this research study to ensure that the sample of women is representative of the U.S. women. The assumption was that ethnic composition of the

sample did not matter because all women are at risk. Other implicit assumptions were that the instruments used in the National Health and Nutrition Examination Surveys of 2005-2006 and 2007-2008 gave accurate results and the recall of the participants was not biased. NHANES surveys are sampled to be representative of the United States population. However, some groups were deliberately oversampled in order to reduce potential bias due to low numbers.

Scope and Delimitations

The sample population for this study was derived from the participants of the National Health and Nutrition Examination Survey during the years 2005 to 2008. A delimitating factor for this research was that the sample population was restricted to women aged 40 to 55 years, the perimenopausal years, and the years when there is a greater likelihood that endogenous lead is mobilized (Machida et al. 2009). Information gained from the study should be generalizable to women everywhere in the time period studied since the phenomenon of earlier cataractogenesis and general vision problems in women is worldwide (Congdon et al., 2004; World Health Organization, 2013).

Limitations

The major assumption of this research study was that earlier cataracts and other vision-related problems are a consequence of demineralization of the long bones after menopause; this may not necessarily be so. Other limitations were the inherent limitation of each quantitative clinical laboratory assay that was included in the study and the completeness of the data at baseline. Quantitative laboratory assays have some degree of imprecision and bias. However, this limitation is generally acceptable once the degree of

bias or imprecision is within the limits specified by the Clinical Laboratory Improvement Act (CLIA). The Division of Laboratory Sciences, National Center for Environmental Health performed the laboratory tests for the National Health and Nutrition Examination Survey (Centers for Disease Control and Prevention, 2014,b). Information on the methods is available at the National Health and Nutrition Examination Survey website at www.cdc.gov/nchs/nhanes/nhanes_questionnaires.htm.

A study on cataracts should include adjustments for known confounders such as diabetes, use of steroids, and high exposure to ultra violet light. The presence of these confounders could limit the power of the study. Unknown confounders may cause an inaccurate interpretation of the study. Significant bias in the data was not expected since the data was collected by a computerized questionnaire, and the laboratories that performed the analyses are CLIA-certified laboratories (Centers for Disease Control and Prevention, 2014b).

Significance

Implications for Change in Care of Perimenopausal Women

Social change involves providing timely solutions to pressing problems in our contemporary society (Walden University, 2013). Hypotheses that relate to tangible efforts that can be taken to engender positive social changes have implications for positive social change (Walden University, n.d.). The hypothesis of this research was that evidence of vision-related issues in perimenopausal women with evidence of bone lead mobilization would significantly differ from evidence of vision-related problems in women with no evidence of bone lead mobilization. The research was undertaken

because of the belief that if the results of this research showed that lead can be implicated in the early vision-problems of women; then positive steps would be taken to improve the quality of life for women in their later years. One of the steps that could be taken is the modification of the standard of care for women to include testing for and chelation of mobilized lead while women are in their perimenopausal years.

Implications for Wider Societal Change

Based on the results of the Visual Impairment Study, the majority of individuals will develop cataractous lenses if they live enough years (Taylor, 2002). Therefore this epidemiological study could be used to advance knowledge regarding cataracts or other vision-related problems that would be of benefit to both genders. Increased knowledge about cataractogenesis would help individuals to make lifestyle changes to improve care of the natural lenses. Increased knowledge would also enable public health officials to advocate for perimenopausal care that would result in the delay of cataract surgeries until those surgeries are no longer necessary for many individuals. A delay in the need for surgery would mean an increase in the quality of life years. On the macroeconomic scale, delays in the need for cataract surgeries could have positive social implications for countries. Many of the healthcare dollars spent on cataract surgeries could be spent on other worthwhile social projects such as education or the building or rebuilding of roads, bridges, and railways. Thus, the results of this study could be used to advocate for positive social change that benefits individuals as well as society.

The Importance and Health Relevance of the Proposed Study

Women are living longer than men and the needs of many aging women are not being satisfactorily addressed (Laskar, 2011). If women's health issues are not addressed in a timely manner, the economic burden will be very significant (Laskar, 2011). The major aim of this study was to close the gap on one important eye health issue for women. The results of this research could be used to benefit both genders since there is a growing need to decrease the incidence of cataracts and other vision-related problems in the U.S. population that is aging as well as increasing.

The United States Census Bureau estimated that the percentage of the population that is sixty-five years of age and above will increase from 12% (2000 census) to about 20% in the year 2050 (United States Census Bureau, 2013). During that time period, the proportion of the working population to those over 65 years of age is expected to shrink (United States Census Bureau, 2013). The demand for cataract surgeries falls mainly in the over 65 age group which is composed mainly of retirees (National Eye Institute & Prevent Blindness America, 2002). As of 2002, the cost of cataract surgeries to Medicare was more than 3.4 billion dollars each year (National Eye Institute & Prevent Blindness America, 2002). Therefore, a decrease in the demand for cataract surgeries could reduce the economic burden on the working population who fund the Medicare budget through taxes. The aim of this research was to elucidate whether lead can be considered a possible causative factor for cataractogenesis or other vision-related issues in perimenopausal women. A demonstrated association between lead and vision-related issues could lead to steps that can be taken to reduce the lead burden at this critical period

in life so that cataract surgeries and other eye care may be delayed to the point where they will not be needed for some individuals.

Summary

Lead is present everywhere in the environment and is stored in the long bones over an individual's lifetime. Schaumberg et al. (2004) conducted a case control study and concluded that there was an association between lead sequestered in long bones and the incidence of cataracts in men. No similar study was performed for women at that time. A literature review revealed that women had a higher risk for cataracts and other problems associated with vision. It is possible that the higher risk for cataracts and other vision-related issues correlates with the female phenomenon of menopause. The purpose of this study was to investigate whether there is any possible association between perimenopausal activation of endogenous lead and vision-related problems in women.

Chapter 2: Literature Review

Introduction

The landmark study by Schaumberg et al. (2004) reported an association between lead in the long bones of men over 60 years old and the presence of cataracts in those men. The men were considered to have cataracts if they had cataract surgery within a year of bone lead measurements or if their lens opacities from eye examinations were graded at 3+ or greater on a 4-point grading scale. At the time this topic was first researched, no comparable study had been performed on women. Data was lacking despite a 2013 report by the World Health Organization that women all over the world have a greater risk for vision-related problems than men. Literature review on cataracts in women led to literature review on menopause. Additional research revealed that the menopausal transition was also marked by a precipitous increase in bone demineralization and release of lead to the blood stream. Thus, I developed the hypothesis that the biological phenomenon of menopause was related to the higher and earlier risk of cataracts seen in women. The risk was greater because bone lead was mobilized to the blood stream and circulated to the eye lenses as well as the other soft tissues where damage occurred.

This dissertation study was designed to bridge the gap in the literature regarding vision issues and cataractogenesis in women; the main focus being lead as a possible causative factor. The study was specifically designed to investigate potential links between cataracts in perimenopausal women and the mobilization of lead during bone demineralization. The theoretical foundation for this research was that individuals and

public health officials would be willing to make the necessary changes once there was some evidence that menopause and lead mobilization were linked to cataracts in women. Literature review was focused on cataracts, menopause, osteoporosis, lead mobilization and vision issues. The results of the review are listed under the subsections Cataracts and Their Impact on Individuals, Lead as a Possible Causative Factor for Age-Related Cataracts, Lead and the General Population, Lead and Perimenopausal Women, and the Mechanism for Perimenopausal Mobilization of Lead. Other subsections are Possible Causes for Earlier Cataractogenesis in Postmenopausal Women, Non-Reproductive Factors Associated with Cataractogenesis, Lead as a Possible Cause for Earlier Cataractogenesis in Postmenopausal Women, Lead and other Vision-Related Problems, and information on the variables used from the National Health and Nutrition Examination Survey (NHANES)

Literature Search Strategy

A time period of five years was used to conduct a current literature search to determine whether the gap in the literature remained. Literature sources consisted of peer-reviewed as well as non-peer-reviewed articles. In order to determine whether any progress had been made to connect the phenomenon of cataracts and lead in older men and the occurrence of cataracts and other vision-related problems in women, a literature search was conducted of the following databases: Expanded Web of Science, Nursing & Allied Health Source, MEDLINE with Full Text, Health & Medical Complete, PubMed, Science Direct, NHS Economic Evaluation Database Annual Reviews, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE)

Evidence-Based Resources from the Joanna Briggs Institute, Health Technology Assessments, LEXIS NEXIS, CINAHL Plus with Full Text, and Science Citation Index. Google Scholar and the ProQuest Theses & Dissertations and Walden University dissertation databases were also used in the literature search process.

The key terms and combinations of terms used in the search included: women, lead, bone, blood, and cataracts; women lead, bone, and blood; osteoporosis, women, and bone lead; women, blood and lead; bone lead and cataracts; blood lead and cataracts; osteoporosis and cataracts; and women and cataracts. The total number of abstracts cursorily reviewed from the Expanded Web of Science and other databases was 3,794. The abstracts chosen for further review based on appropriateness for this dissertation research totaled 124. The literature review identified many recent studies regarding bone demineralization, endogenous lead, and cataracts or other vision-related problems. However, very few studies connected all three health conditions.

Theoretical Foundation

The theoretical foundation for this study used social cognitive theory (SCT). SCT was first conceived by Miller and Dollard in 1941 and developed by Rotter in 1954 (McAlister et al., 2008). According to McAlister et al. (2008), the key components of SCT are psychological determinants of behavior, environmental factors, observational learning, self-regulation, and moral detachment. SCT has also been used to engender changes that led to the prevention or management of infectious or chronic diseases (McAlister et al., 2008).

Social cognitive theory (SCT) is especially applicable to this research because the information gleaned from this study should be used as necessary to change personal behavior and reduce debilitation that could be caused by the chronic disease of cataracts. The reasoning is as follows: the five components of SCT are evident in this research. People generally want to experience good health. Lead is an environmental toxicant that is ubiquitous in the environment. The results of this study could indicate there is a significant relationship between mobilized lead and cataracts or mobilized lead and early vision-related issues in perimenopausal women. If the results of the study indicate there is significant association, individuals who learn of the association would have no moral hindrance to limiting their exposure to lead or mitigating the effects if the risks are apparent. Social awareness should be the realization that continuous health monitoring in the perimenopausal years is critical to continued good health in later years. Finally, the social response to a study that demonstrates an association between lead and vision-related problems should be an augmentation in the protocol for wellness-checks of perimenopausal women.

An alternate theoretical construct considered for this study was the theory of reasoned action (TRA). According to Montaño and Kasprzyk (2008), TRA focuses on an individual's motivation to take some form of action. Steps that would be needed to implement wellness-checks for perimenopausal women involve changes to public policy. Individuals cannot singularly make changes to public policy. TRA would have been applicable if individuals could be motivated to modify their behavior to improve their health based on the results of the study. However, TRA was discarded as a possible

theoretical construct for this study because individuals cannot change or reverse the effects of past exposure to environmental lead if adjustments are not made to the healthcare system. Similarly, individuals cannot implement measures to ensure perimenopausal women are tested for mobilized lead. Any changes that will result from this dissertation will be implemented because of public, not individual policy; SCT is more applicable than TRA.

Two other theoretical constructs, the health behavior model (HBM) and the transtheoretical model (TTM), were also considered but not found to be suitable for this study. TTM is used for intervention studies (Prochaska, Redding, & Kerry; 2008). HBM is used in intervention studies and is also used to predict actions people will take to address their individual health (Champion & Sugg Skinner, 2008). However, this dissertation study was not interventional in nature. Public policy is needed to make any changes that would be necessary based on the results of this dissertation study. Therefore, based on the foregoing, Social cognitive theory was the most applicable theoretical construct for this study.

In my opinion, social cognitive theory (SCT) has already been applied to the reduction of lead in the environment and has led to the subsequent reduction of blood lead levels in the United States. Social action led to the passage of the Clean Air Act in 1970 (Environmental Protection Agency, 2001). This in turn led to changes in personal behavior as individuals learned about the toxic effects of lead compounds and took action to reduce their exposure to the compounds of the metal (Elder, 1997; Environmental Protection Agency, 2013). Public awareness also led to changes in occupational standards

that reduced workers' exposure to lead (Centers for Disease Control and Prevention, 2013a; Occupational Safety and Health Administration, [n.d.]). These successive steps that the public and public health agencies undertook to mitigate exposure to environmental lead included psychological determinants of behavior, environmental factors, observational learning, self-regulation, and moral detachment.

The scientific premise associated with this research was derived from a combination of four hypotheses. The first is that ingested or inhaled lead is assimilated in the bones over a number of years (Abadin et al., 2007; Rabinowitz et al., 1976). The second is that women undergo demineralization of bones during the perimenopausal years (Harmon & Talbert, 1985; Weyermann & Brenner, 1998). The third hypothesis is that the demineralization of bone leads to the release of endogenous lead (Hernandez-Avila, et al., 2000; Silbergeld et al., 1988; Symanski & Hertz-Picciotto, 1995). The last hypothesis is that mobilized lead can be associated with cataractogenesis (Schaumberg et al., 2004).

The association of lead with cataracts was first highlighted in the 2004 study performed by Schaumberg et al. (2004. The investigators reported an association between elevated levels of lead in long bones and the presence of cataracts in men older than 60. There was a gap in the literature regarding the vision issues of women worldwide despite the fact that the World Health Organization reported that women are more susceptible to vision issues. I investigated the gap for a possible association between the release of endogenous lead into blood and the early appearance of cataracts or other vision-related problems in perimenopausal women.

The study population for this research was delineated as women aged 40 to 55 years in the United States. This population was selected in order to test the hypothesis that mobilized lead can lead to vision-related problems in perimenopausal women. The rationale was that elevated levels of endogenous lead occur in perimenopausal women (Hernandez-Avila et al., 2000; Silbergeld et al., 1988; Symanski & Hertz-Picciotto, 1995). Endogenous lead can also cause opacities in the lenses (Neal et al., 2005). The mechanism for the damage is through the formation of reactive oxygen species (Roy & Rossman, 1992; Stohs & Bagchi, 1995). If the previously mentioned hypothesis was correct, the expectation was that evidence of cataractogenesis or vision problems in women with evidence of released endogenous lead would be significantly different from the evidence of cataractogenesis or vision problems in women with no evidence of released endogenous lead.

A literature review was conducted to ascertain whether any recent studies had connected the earlier occurrence of cataracts and other vision-related problems in women to the perimenopausal mobilization of endogenous lead. During the review, studies were also examined for other causative factors that could confound a study on lead and early cataractogenesis in perimenopausal women. The review revealed there were many additional studies on endogenous lead and many studies on cataracts. Summaries of relevant studies are outlined below.

Literature Review Related to Key Variables and Concepts

Cataracts and Their Impact on Individuals

The main hypothesis for this research is that cataracts may be caused by endogenous lead. However, investigators conducted a study in Sweden in 2008 and concluded that possible causes of cataractogenesis included diabetes, hypertension, and waist circumference greater than 80 centimeters (Lindblad et al., 2008). For Swedish women older than 65, the risk of cataracts increased three-fold if all three symptoms of metabolic syndrome were present (Lindblad et al., 2008).

In 2010, Mares et al. (2010) reported that the incidence of nuclear cataracts in women is delayed if women follow a diet that is healthy according to the U.S. Healthy Eating Index 1995 (HEI-95) score. Previously, other investigators published the results of a prospective 10-year study which indicated that more than 70 percent of Australians over the age of 49 have some form of cataracts (Kanthan et al., 2008). The results of the study also indicated women had a significantly higher risk for nuclear and cortical cataracts, but not for subcapsular cataracts (Kanthan et al., 2008).

Researchers of two of the recent studies reviewed specifically addressed women's vision-related problems: The results of one study indicated that gender and reproductive hormones influenced the dynamics of the aqueous humor, the lacrimal glands, blinking and eyelids, corneal anatomy, the crystalline nature of the lenses and cataracts, glaucoma, and other eye diseases (Wagner et al, 2008). The researchers also stated systemic diseases or conditions that were unique to women (for example, pregnancy and menopause) and certain autoimmune diseases affected conditions of the

eyes. The investigators further concluded that eye diseases should be considered in the context of gender, physical and social contexts, and the individual's stage in their life-cycle (Wagner et al, 2008). This conclusion gives plausibility for this research since the focus is on a possible causative factor for cataracts that occurs during the critical period surrounding menopause. The results of the second study confirmed the greater risk for cataracts in American women even when the data was adjusted for age (Zambelli-Weiner et al., 2012).

Lead as a Possible Causative Factor for Age-Related Cataracts

Investigators in a few recent studies focused on lead as a possible causative factor for cataracts or other vision-related problems (Mosad et al., 2010; Park et al., unpublished; Yuki et al. 2009), however, the landmark study on lead and cataracts remains the study conducted by Schaumberg et al. in 2004. Mosad et al. (2010) followed the premise of Schaumberg et al.'s study by conducting clinical research on male smokers for the presence of lead, as well as cadmium, beta carotene, and vitamins C and E, and beta carotene in blood, and extracted lenses. The researchers determined that elevated levels of lead in blood were associated with cataractous lenses of male smokers, but cadmium levels were more associated with the incidence of nuclear cataracts (Mosad et al., 20010). Park et al. (unpublished) performed bone lead studies on postmenopausal women aged 55 to 74 years and reviewed the charts of the participants for evidence of cataract surgeries. The researchers found no association between lead in bones and evidence of cataracts. However, the study by Park et al. (unpublished) did not mirror the

study by Schaumberg et al. (2004) where biomicroscopy was used for primary determination of the presence of cataracts.

Lead and the General Population

Lead was added to gasoline in the 1920s to enhance the effectiveness of gasoline as a fuel and removed after the passage of the Clean Air Act in 1973 (Get the Lead Out, 2010). Therefore, widespread exposure to toxic lead levels does not occur in contemporary times; however, there are still pockets of lead exposure in various segments of the U.S. population: American children are continually exposed to lead dust if they live in homes where older layers of lead paint have not been removed (Get the Lead Out, 2010). Other sources of lead continue to be soldering in pipes in older homes and other lead fixtures (Get the Lead Out, 2010).

A review of current articles on lead exposure revealed that hunting populations who eat wild animals killed with lead shots may be exposed to particles of the element contained in the meat (Hunt et al., 2009). Researchers concluded that this was possible after observing that the blood lead content of pigs that ate meat from deer killed in a conventional manner was significantly higher than the controls. Particularly at risk may be the 10 million hunters, hunters' family members, and other recipients of venison who use the meat to supplement their protein food supplies during the winter months (Hunt et al., 2009).

Exposure to toxic lead levels has declined. However, lead has been found to cause deleterious effects at levels that are not toxic (Get the Lead Out, 2010). The Centers for Disease Control and Prevention (CDC) updated the recommendations for

acceptable blood lead levels after studies revealed that low levels of lead can cause adverse mental and psychological effects (Centers for Disease Control and Prevention, 2012). One such study may have been an examination of data from the National Health and Nutrition Examination Survey (NHANES). The researchers of the study reported a direct dose response relationship between elevated levels of lead in the blood and panic disorder or major depression (Bouchard et al., 2009). However, there was no significant correlation between lead levels and general anxiety disorder (Bouchard et al., 2009).

The results of other studies revealed the neurotoxic effects of lead: The result of a prospective model indicated a significant relationship between gestational exposure to lead and criminal behavior in youths (Wright et al., 2008). Investigators of a clinical experiment reported that elevated levels of tibia lead were associated with the deleterious effect of reduced cognition in women aged 47 to 74 years (Weuve et al., 2009). Weuve et al. (2009) opined that women may have been underrepresented in previous studies.

Lead and Perimenopausal Women

The results of studies indicate that lead remains a public health concern even though there is no widespread exposure as in the period when lead compounds were added to gasoline (Get the Lead Out, 2010). The mobilization of lead during periods of bone resorption continues to be a source of exposure for women during the perimenopausal years (Silbergeld et al., 1988). To reduce bone turnover during this critical period, women may be able to benefit from a study conducted by Jehle et al. (2013) in Switzerland. Analysis of the clinical study revealed that a diet rich in potassium citrate which is found in fruits and vegetables reduced the incidence of low bone density

in Swiss women (Jehle et al., 2013). Prior to that study, Machida et al. (2009) found that evidence of bone turnover was related to blood lead levels in a sample of perimenopausal Japanese women who were farmers. Although Machida et al. (2009) stated that information on the diet of the participants was collected; no information was given regarding the diet of the women. A review of data from the NHANES datasets of 1999-2010 also revealed the additional information that women aged 45-55 years had a higher risk to exposure to endogenous lead depending on whether they had undergone natural menopause (Mendola et al., 2012).

In 2008, Khalil et al. opined that individuals who are currently seniors have had higher exposures to lead than younger individuals. Khalil et al. (2008) elaborated that the higher levels of lead to which seniors have been exposed has resulted in a higher body burden of lead than younger individuals will ever experience. The researchers also stated that additional future studies on younger individuals may be necessary in order to understand whether the leaching of lead from the bones is an occurrence that should be expected with aging. The researchers further opined the possibility exists that hormone replacement therapy (HRT) may be a way to stop the post-menopausal leaching of lead (Khalil et al., 2008).

Mechanism for Perimenopausal Mobilization of Lead

No new theory has been advanced for the mechanism of the mobilization of endogenous lead. A significant increase in the blood lead levels was found to be linked to the bone resorption and bone formation activities in pre- and postmenopausal females who participated in the NHANES surveys (Jackson et al., 2010). However, the study by

Jackson et al. (2010), was built on previous work by Rabinowitz et al. (1976) who reported that lead may be sequestered in bones for decades, Harmon and Talbert (1985) who stated women lose bone density during the perimenopausal years of life, and Silbergeld et al. (1988) who further stated that endogenous lead is released when bone is resorbed.

Recently, Nemet et al. (2013) demonstrated an association between bone resorption and cataractogenesis in a retrospective observational case-control study of 12,984 cases and 25,968 controls matched by gender. In my opinion, this study is significant because osteoporosis mobilizes lead from bone (Silbergeld et al., 1988) and lead has been found to be associated with cataracts (Schaumberg et al., 2004). However, the investigators of the study did not link lead as an intermediary component between the evidence of osteoporosis and cataracts. Instead, since calcium imbalance is linked to bone demineralization, Nemet et al. (2013) opined imbalance in calcium which occurs during osteoporosis was linked to the incidence of cataracts in this study. The strength of this community study was the large number of cases and controls that were studied. The limitation was the assumption that individuals who were not chosen to undergo surgery did not have cataracts (Nemet et al., 2013) and it has been previously demonstrated that various factors influence the decision to have cataract surgery. These factors include but are not limited to the type of cataract, the cataract patient's ability to perform routine tasks, and socioeconomic factors (American Optometric Association, 2004; Belpoliti et al., 1995; McCarty et al., 2000; West et al., 1998).

Previously, in a separate study, Miglior et al. (1984) had reported that there is an inverse relationship between calcium in the diet and the cataracts. Calcium and lead are competitors in the body (Bruening et al., 1999). Therefore the results of the studies of Nemet et al. (2013) and Miglior et al. (1984) lend credence to the hypothesis of this research that endogenous lead may be responsible for the earlier risk for cataracts observed in women.

Possible Causes for Earlier Cataractogenesis in Postmenopausal Women

A meta-review of four cohort and five case-control or cross-sectional studies indicated an overall decreased risk for cataracts in women on hormone replacement therapy (HRT) (Lai et al., 2013). Significant inverse associations were noted for both previous use and current use of HRT and nuclear cataracts. No significant associations were noted for HRT and cortical or postsubcapsular cataracts (Lai et al., 2013). These findings contradicted earlier published reports of the Blue Mountain Eye Study which indicated there was no significant association between HRT and the incidence of cataracts after the data was adjusted for age, smoking, hypertension, use of steroids, and socioeconomic status (Kanthan et al., 2010). However, there was a slight protective effect stemming from prior contraceptive use against the incidence of cortical cataracts. No other female reproductive factors such as age at menarche were either protective or contributed to the risk for cataracts in this population (Kanthan et al., 2010).

Ozcura et al. (2010) examined the effect of estrogen replacement therapy on the apoptosis of lens epithelial cells in rats. The results of the experimental investigation on apoptosis revealed that estrogen does not directly protect the lenses of the eyes (Ozcura et

al., 2010). The contradictory results of studies on estrogen and cataracts suggest the presence of a significant confounding factor associated with estrogen levels that needs to be elucidated. The construct for this research was that the confounding factor that needs to be revealed is lead that has been mobilized from demineralized bone after levels of estrogen have diminished.

Non-Reproductive Factors Associated with Cataractogenesis

Results of other recent studies revealed possible new confounders for a study on cataracts or validated the results of previous studies. In 2008, Christen et al. (2008) examined the data on vitamins C and E, risk for cataract, and dietary carotenoids in women in a prospective study. The researchers subsequently reported that 2031 cases of cataract were identified during a 10-year follow-up. The investigators also reported that higher consumption of utein/zeaxanthin and vitamin E from food and food supplements were linked with significantly decreased risks for cataract (Li et al., 2008).

Li et al. (2009) investigated whether antioxidant status and oxidative stress in older adults correlated with early cataracts. The researchers found no significant difference in the antioxidant status between the individuals with early cataract and those without. However, the level of oxidative stress was indicative of risk for cataract; the levels of isomers of 9- and 13-(Z,E)-HODE were significantly higher in the older adults who had cataracts than those who did not. The researchers also found that subsequent high performance liquid chromatography for antioxidants in the blood of 40 men and postmenopausal women (aged 50 to 70 years) revealed no significant difference in antioxidant status between the groups with and without early cataract (Li et al., 2009).

However, the level of oxidative stress was indicative of risk for cataract since isomers of 9- and 13-(Z,E)-HODE levels were significantly higher in the older adults who had cataracts than those who had no cataracts (Li, 2009).

Ciraj-Bjelac et al. (2010) performed a case control study of physicians and nurses who worked in interventional cardiology to determine the risk for radiation-induced cataract. The investigators found that 52% of the cardiologists and 45% of the nurses examined developed posterior lens opacities (Ciraj-Bjelac et al., 2010). The data were significant when cases were compared with the controls since only 9% of the controls developed posterior lens opacities (Ciraj-Bjelac et al., 2010).

Brown University published a psychopharmacology update in 2010 which showed cataracts were associated with recent use of selective serotonin reuptake inhibitors (SSRIs). SSRIs, female gender, anti-diabetic drugs or corticosteroids, and history of hypertension were associated with an increase in the incidence of cataracts (SSRI, 2010). Researchers of a population-based retrospective cohort study demonstrated that persistent statin use was significantly related to a reduced risk for cataracts for men and women aged 45 to 74 years; no reduced risk for cataracts was observed in older participants (Chodick et al., 2010).

Subsequently, examination of the results of a clinical study that incorporated the use of the Lens Opacities Classification System (LOCS) II revealed that the prevalence of cortical and postsubcapsular opacities were strongly associated with type 2 diabetes (Olafsdottir et al., 2012). Analysis of results of a literature review also published in 2012 indicated that vision loss and visual impairment correlated with age in a sample

population that was not representative of the United States (Zambelli-Weiner et al., 2012). However, it was also evident that there were racial and gender variations in acuity of vision (Zambelli-Weiner et al., 2012).

Analysis of the studies indicated that good health, intake of a nutritional diet, and reduced oxidative stress were indicators of reduced risk for cataracts. Researchers who studied healthcare workers in the interventional radiology environment found that although evidence exists that exposure to radiation can lead to increased risk for cataracts; not enough is being done to mitigate those risks.

Lead as a Possible Cause for Earlier Cataractogenesis in Postmenopausal Women

Prior to this research study, two studies were performed regarding lead as a possible cause for age-related cataracts in the elderly: Schaumberg et al. (2004) found a positive association between lead in the long bones of men aged 60 and older and the occurrence of cataracts and Park et al. (unpublished) studied women in the Boston area. The researchers of the recent study of 502 women in the Boston area could not demonstrate an association between tibia and patella lead and the occurrence of cataracts in the sample of women (Park et al., unpublished). The women in the study were aged 55 to 74 years. The authors of the unpublished conference paper concluded the hypothesis that cumulative lead exposure increases the risk for cataracts in women was not supported by the results of the study. However, the researchers also indicated that additional research on larger populations should not be ruled out (Park et al., unpublished).

Lead and other Vision-Related Problems

A prospective study was conducted on 98 male and female patients in Japan who were diagnosed with primary open-angle glaucoma and 245 controls (Yuki et al., 2009). Lead was analyzed in the hair of the participants by Inductively Coupled Plasma Mass Spectrometry (ICP-MS). Analysis of the results revealed a significant association between the lead levels in the hair of the women with primary open-angle glaucoma, especially in those women with low tension glaucoma (Yuki et al., 2009). In my view the results of the study by Yuki et al. (2009) further indicate that the earlier risk for vision-related problems seen in the female gender worldwide (WHO, 2013) may be linked to the release of endogenous lead during periods of bone demineralization.

There was no worldwide study on the possible cause of the earlier risk for vision-related problems seen in women; Congdon et al. (2004) performed a meta-review in order to determine that women around the world undergo cataractogenesis earlier than men. The largest U.S. health database believed to contain information on perimenopausal endogenous lead exposure and vision-related problems is the database of the National Health and Nutrition Examination Surveys (NHANES). The surveys are conducted by the Centers for Disease Control and Prevention. Data from the NHANES database were utilized in order to determine if there was any relationship between mobilized lead and vision-related problems in a large sample of women.

The National Health and Nutrition Examination Survey (NHANES)

NHANES is a continuous survey of a nationally representative sample of the United States non-institutionalized population (Johnson et al., 2013). Questionnaires are

administered to participants in their homes. After the questionnaires have been completed, the participants are examined in standard physical examinations, and blood and urine specimens are collected for laboratory analysis. Sampling is not random. The sampling design is complex and excludes military personnel on active duty or individuals who are under supervised care or living outside the United States (Johnson et al., 2013).

Laboratory Information from NHANES Survey

Lead. Lead is mobilized during periods of increased bone turnover, for example during pregnancy and during the perimenopausal or postmenopausal years (Silbergeld et al., 1988). Lead exhibits acute and chronic toxic effects and is reasonably considered to be a carcinogen (Agency for Toxic Substances and Disease Registry [ATSDR], 2011). Using the NHANES database, researchers have been able to show links between low blood levels of lead and cognitive and other deleterious effects (CDC, 2014a). Based on the results of research, the CDC has updated its recommendation for the upper reference level for blood lead levels in children to be 5μg/dL. The current geometric mean of blood lead levels in the U.S. population is less than two μg/dL (CDC, 2014a).

Bone Turnover Marker. Examination of clinical data revealed that bone turnover markers (BTMs) may be used to supplement bone density measurements for osteoporosis or conditions of osteopenia (Henriksen et al., 2011). One advantage of using BTMs over for bone density measurements for osteoporosis measurements in population studies is that BTMs have a high signal to noise ratio. The high sensitivity of the markers facilitates decreased time for clinical research time and smaller sample size. However, due to individual variability, BTMs are not very useful for determining an individual's

risk for osteoporosis if the BTMs are not combined with imaging studies (Henriksen et al., 2011).

Serum bone-specific alkaline phosphatase (BAP) is a bone turnover marker (BTM) that was significantly and positively associated with blood lead levels in pre- and postmenopausal women of the NHANES 1999 – 2002 Survey (Jackson et al., 2010). The segmentation of perimenopausal women in the study of the participants of the NHANES survey was considered by the researchers to be too small to be significant. The previous year, the published results of a clinical study of Japanese women farmers revealed that blood lead levels were significantly correlated with increased levels of BAP markers in perimenopausal women (Machida et al., 2009). However, bone turnover markers were not as significantly correlated with lead in women who were pre-or post-menopausal (Machida et al., 2009). The apparent difference between the two studies may have been due to the fact that segmentation by menopausal status did not occur in the same proportions for both studies.

The results of the study of the Japanese women farmers with more segmentation by menopausal status seem to correlate with the theory that women are most susceptible to bone demineralization during the perimenopausal years (Salamone et al., 1998): The high levels of blood lead and bone turnover markers (BTM) in the perimenopausal Japanese women in the study of Machida et al. (2009) correlated with the increased rate of bone resorption in perimenopausal women reported by Salamone et al. (1998). The results of the studies indicate that BTMs are a good supplement to bone density measurements for osteopenia and BTMs are also good indicators of bone lead

mobilization during the perimenopausal, years. Therefore, this secondary data analysis included alkaline phosphatase levels as the BTM.

There was a clear indication for the use of BTMs in this study. However, the criteria for menopausal status that were used in the studies were not as clear. For example, contrary to the studies of Machida et al. (2009) and Salamone et al. (1998), Ruegsegger et al., (1984) found that bone loss was most rapid in the first two to four years after the menses cease. The Japanese women (in the study by Machida et al, 2009) were considered to be perimenopausal if they were aged 49 to 55 years. In the study by Salamone et al. (1998), women were classified as perimenopausal if they reported no menses within the three months prior to their examination. Based on the two varied criteria for perimenopausal status – the average age of U.S. women at menopause and the results of the study that showed that significant demineralization can also occur in the early postmenopausal period – participants of this study were selected from the 40 to 55 years age range.

Alkaline Phosphatase (ALP). Alkaline phosphatase can be found in the majority of tissues of the body and ALP has various chemical structures which may be specific to the source of the enzyme. ALP is found in liver, bone, placenta, kidneys and intestine but the major sources are liver and bone (Panteghini & Bais, 2014). It is likely that ALP is associated with the calcification of bone as well as lipid absorption in the intestine. Liver ALP is the major structural form found in blood. However, bone ALP may have up to half the total activity of all the ALP in the blood. ALP activity is also age and gender-dependent (Panteghini & Bais, 2014). Females aged 20 to 50 years of age

have an ALP reference interval of 42 to 98 U/L. Females older than 60 years have a reference interval of 53 to 141 U/L but ALP levels may vary with fasting status. Serum ALP levels are useful in the treatment of hepatobiliary disease and bone disease (Panteghini & Bais, 2014). Since ALP levels are also associated with hepatobiliary obstruction (Panteghini & Bais, 2014), participants with elevated ALP levels as well as elevated total bilirubin levels were not counted as positive in an intermediary variable for elevated enzymes. This technique was used to increase the likelihood the elevated ALP values used in the study were associated with increased osteoclastic activity.

NHANES Clinical Information

Bone Density Measurements. More than 50 percent of fractures occur in individuals with low bone mass (National Osteoporosis Foundation [NOF], 2013). The NHANES datasets of 2005 to 2008 contain data on fractures and bone density that were utilized in this study on bone demineralization and its association with lead and cataracts in perimenopausal women. Mean values and standard deviations of bone density measurements were used to assess the participants' level of osteopenia.

The World Health Organization developed a Fracture Risk Assessment Tool (FRAX) to assist physicians to determine their patients' risk for fracture (World Health Organization Collaborating Centre for Metabolic Bone Diseases, University of Sheffield, UK, n.d.). Criteria from the FRAX tool were used to assess whether participants have osteopenia or have a high risk for osteoporosis. The criteria included the consideration of whether a parent of the participant had ever broken a hip.

Vision Examination. The 2005- 2008 NHANES vision examination datasets included data on impairment of visual awareness, lens refractive error, as well as the diminished ability to function due to visual impairment (CDC, 2014a). Participants who were blind or had eye infections at the time of the survey were excluded. The assessment of visual acuity was determined by examination with a Nidek Auto Refractor Model ARK-760 instrument and the evaluation of the prescription for any eyeglasses worn by the participants (CDC, 2014a).

Questionnaires. Participants of the 2005-2008 NHANES surveys responded to questions using a Computer-Assisted Personal Interviewing-CAPI (interviewer-administered) system (CDC, 2014a). The questions were answered prior to the physical examination and laboratory analysis sections of the surveys. The questionnaire included questions on difficulty in performing various tasks due to low vision, cataract operations, and general condition of eyesight. Vision-related questions for participants aged 40 years and older included questions on age-related macular degeneration, glaucoma, and other eye diseases (CDC, 2014a). Participants were sampled in a manner to ensure the survey was representative of the U.S. civilian population that was not institutionalized. Not all participants were required to fast prior to the blood collection for laboratory examination.

Answers to non-vision related questions in the questionnaire provided data on known confounders for cataracts as well as risk factors for osteoporosis. For examples, survey respondents were asked to provide information on medications they were taking and whether a parent had ever fractured a hip. Other pertinent data included in the

questionnaire were smoking status, age at last menstrual period, ever had a hysterectomy, age when both ovaries were removed, and number of live births.

Summary and Conclusion

Researchers have shown that the mobilization of endogenous lead has many deleterious effects on the body. Some of the effects include hypertension, cardiac diseases, loss of mental acuity, and age-related cataracts in men (Hu et al., 1996, Jain et al., 2007; Schaumberg et al., 2004). Causes of cataracts include diabetes, use of steroids, occupations that involve radiation, smoking, and exposure to ultraviolet radiation. The results of newer studies on eye diseases indicate that the female gender has a disproportionate risk for cataracts (World Health Organization, 2013). A possible reason for the phenomenon has not been highlighted. However, it is expected that the Medicare dollars spent annually on cataract surgeries will continue to increase substantially as the population ages and women continue to have longer lifetimes than men.

A review of the literature uncovered one study that was performed to determine whether there is any association between lead and cataractogenesis in women (Park et al., unpublished). The participants of the study were all postmenopausal women and an association between lead and cataracts was not demonstrated in this study. However, the researchers did not rule out the possibility that the same research carried out on a larger sample of women could produce a different result. The study of the postmenopausal Boston area women by Park et al. (unpublished) appears to be the only study performed to date to determine whether there is any association between endogenous lead and cataracts in women. However, the perimenopausal age appears to be a period during

which women are most at risk for damage from mobilized endogenous lead based on the study of Machida et al. (2009).

Significant bone loss occurs during the first two to four years after the last menstrual period (Ruegsegger et al., 1984). Since American women have an average age of 51.2 years at menopause, the women in the study conducted by Park et al. (unpublished) were older than the age at which most lead would be mobilized during bone demineralization. Therefore, it is possible that for the women in the study by Park et al. (unpublished), lead had already leached from their bones and caused damage to their lens of their eyes before the lead was excreted from their bodies. Based on the hypothesis for this study, Park et al.'s study was conducted on a group of women who were not in the age range that would yield adequate data for a study on association. This study was carried out on the data of women who were in the age range when mobilization of lead and early cataractogenesis and other vision-related problems could occur.

Women are living longer but have special health needs which include the management of the incidence of cataracts and other age-related diseases (Laskar, 2011). The purpose of this study was to close the gap on important eye health issues for women. A study performed to address the phenomenon of early cataracts and other vision-related problems in women should include the perimenopausal period – a period that is unique to women and marked by rapid bone turnover and the mobilization of endogenous lead. An effort was made to close this gap by mining the NHANES surveys for the relevant data that has been collected on women who fit the criteria needed to conduct this research.

Chapter 3: Research Method

Introduction

The purpose of this study was to determine if there was a significant association between cataracts and endogenous lead as in perimenopausal women. The design of the study was similar to the study performed by Schaumberg et al. (2004) who reported a significant association between endogenous lead and cataract in elderly men. Yuki et al., (2009) reported an association between endogenous lead and glaucoma, but the researchers did not specifically link this phenomenon to the female gender. The hypothesis for this research was that there is a relationship between vision problems and mobilization of lead in perimenopausal women who participated in the National Health and Nutrition Examination Surveys (NHANES) during the years 2005 to 2008. The datasets and codebooks were obtained from the NHANES website for surveys 2005 - 2006 and 2007 - 2008. This study employed a case control design, as suggested by Sullivan (2011).

In an effort to help close the gap in the literature, I analyzed variable data from the NHANES datasets including answers to questions on general vision, glaucoma, and cataract surgery. The clinical examination results from bone density scans, laboratory results of blood lead levels and levels of alkaline phosphatase, and bone turnover biomarkers, from these datasets were deemed for this study. Known confounders such as occupation, number of pregnancies, and number of live births could not be addressed because of a paucity of data. Since evidence of vision deterioration and evidence of bone loss were required, the variables that contributed to these two categories were combined

into new variables more suitable for this case control study. I tabulated the original and new variables for easy review.

The research questions that are pertinent for a study on the association between lead and cataractogenesis in perimenopausal women are listed in the methodology section, along with the analytical computations chosen to address the research questions. Based on the comparative nature of this research, Chi-square analysis was included in the methodology. The methodology section of this chapter contains the outlines of steps that were followed to prepare a working dataset from the combined 2005 – 2006 and 2007 – 2008 NHANES datasets. General descriptive information about the target population – perimenopausal women – are delineated and the results of the *a priori* analysis for minimum sample size using G*Power software – 143 cases and 143 controls – are displayed for review.

Research Design and Rationale

The primary research question was, “Is evidence of cataractogenesis in perimenopausal women with evidence of bone lead mobilization (elevated blood lead levels and evidence of bone demineralization) significantly different from the incidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization?” The hypothesis of this research was that evidence of vision-related issues in perimenopausal women with evidence of bone lead mobilization is significantly different from vision-related problems in women with no evidence of bone lead mobilization. In order to determine significant difference, a case control study was necessary. The women who showed signs of mobilized lead were the

cases, and women who did not, were the controls. The list of variables that were selected from the National Health and Nutrition Examination Surveys (NHANES) is presented in Table 2 in the data collection section in this chapter. Independent variables included all variables on vision. Lead, the dependent variable, was synthesized from blood lead levels and bone mobilization markers. Known causative factors of cataractogenesis such as age, smoking, and corticosteroid use, comprised the covariables.

There were no time constraints with this choice of design since all the data were already available online. Unlike a prospective study that may require years for the data to become available, a case control study is performed at one instance in time. The data used in this study were readily available to the general public; as a result, no permission was necessary to use the data.

A case control design was suitable for this dissertation study because the same design was used for the landmark study performed by Schaumberg et al. (2004) and one of the goals of this dissertation was to extend Schaumberg et al.'s inquiry to women. In that case control study, analysis of the results revealed a significant difference between the incidences of cataracts in men who had elevated lead levels in bones and men who did not have elevated lead levels. Another reason for choosing this design is that case control studies are considered to be cost-effective epidemiological studies (D'Agata, 2005). Other advantages to using a case control design are exposure to the variable of interest may be more than once and there is no need to expend resources to follow-up cases.

There are several limitations of case control studies. These include recall or observer bias and inaccurate inference if the disease of interest is rare (D'Agata, 2005). However, observer bias was minimized in the NHANES survey from which the study data were obtained, since the respondents were allowed to enter some of their responses into a computerized program (Centers for Disease Control and Prevention, 2014a). Computerized entry of participant responses is one way to eliminate bias in data collection (Mitchell & Jolley, 2013). Inaccurate interpretation due to the rarity of the disease is not applicable in this case since cataracts and other vision related issues are not rare occurrences in the general population.

Methodology

Population

The study population comprised women, aged 40 to 55 years, who participated in the 2005-2006 and 2007-2008 National Health and Nutrition Examination Surveys. This subset was chosen from the survey respondents from those years because, based on published reports, women may undergo menopausal and perimenopausal symptoms including bone loss during this age range (Armamento-Villareal et al., 1992; Bromberger et al., 1997; Do et al., 1998; Frommer, 1964; Harmon & Talbert, 1985; Reynolds & Obermeyer, 2005; Weyermann & Brenner, 1998). The 2005-2006 and 2007-2008 surveys were chosen because only these surveys contain data on ophthalmology, bone density, and answers to questions on vision, as well as data on a bone turnover marker (alkaline phosphatase), blood lead levels, osteoporosis, and smoking. This means that the results of

this dissertation study cannot be interpreted as representative of women before or after this time period.

Sampling and Sampling Procedures

The sampling strategy for the National Health and Examination Surveys (NHANES) was multi-staged (Centers for Disease Control and Prevention, 2014a). First, individual counties of the United States were chosen, and then specific sections within those counties were chosen. Next, individual households within the sections and individuals within the households were chosen in this multi-stage method. Efforts were made to choose individuals who are representative of the major demographic groups of the United States but some small groups may have been oversampled in an effort to reduce bias (Centers for Disease Control and Prevention, 2014a).For the purpose of this dissertation study, males and non-perimenopausal females were deselected from a total of 20,497 participants of the 2005-2006 and 2007-2008 NHANES surveys leaving a total number of 1,416 participants for this research. Only the datasets that contained the variables listed in Tables 3 to 9 below were selected.

I used the SPSS software program to merge the datasets, sort the study population from the datasets, and analyze the variables. Based on a priori power analysis, 5 degrees of freedom, an alpha of 0.05, and an effect size of 0.3, the smallest sample for a χ^2 analysis with 80 percent power is 143 cases and 143 controls. Therefore, a sample size of 1,416 participants was adequate for this research study. The results of the a priori analysis with G*Power Software Version 3.1.6. (2013) for the minimum sample size for this study are shown below:

Table 2

Input and Results for Computation of Sample Size

Analysis	Input	Output
A priori: Compute required sample size χ^2 test Goodness-of-fit tests : Contingency tables	Effect size $\omega = 0.3$ α err prob = 0.05 Power (1-β err prob) = 0.95 Degrees of Freedom = 5	Noncentrality parameter λ=12.8700000 Critical χ^2=11.0704977 Total sample size=143 Actual power=0.8015133

Data Collection

The sample of respondents for this study was culled from the National Health and Nutrition Examination Surveys (NHANES) 2005-2006 and 2007-2008 datasets (CDC, 2014). These survey datasets were chosen because they are the only datasets that contain all the variables – ophthalmology, blood lead levels, osteoporosis, and vision – that are necessary for this study. The number of women aged 40 to 55 years of age who participated in the 2005-2006 and 2007-2008 NHANES surveys was 1,416. However, not all the women who participated in the original survey were also requested to participate in the clinical examination and laboratory sections of the surveys, resulting in incomplete data for some respondents. Examination of the baseline data revealed that 1,316 women participated in the laboratory examination for alkaline phosphatase, 1,329 women participated in the analysis for blood lead level, 1,133 women were examined for bone mineral density, 1,200 women were given an ophthalmologic examination that did not include examination for cataracts, and all 1,416 of the selected women responded to questions regarding their vision.

NHANES data dictionary. The data dictionary for the variables are shown in Table 3 - 6.

Table 3

Data Dictionary for General Variables Used in Case Control Study

CODE	LABEL
SEQN	Respondent sequence number
RIAGENDR	Gender

Table 4

Data Dictionary for Independent Variables Used in Case Control Study

CODE	LABEL
DXXNKBMD	Femoral neck BMD
DXXOSBMD	Total spine BMD
LBXBPB	Lead (ug/dL)
LBXSAPSI	Alkaline phosphatase (U/L)
LBXSTB	Bilirubin, Total
OSQ010A	Broken or fractured a hip
OSQ010B	Broken or fractured a wrist
OSQ010C	Broken or fractured spine
OSQ080	Doctor ever told any other fractures?
OSQ090A	Fracture result of severe trauma?
OSQ100A	Where fracture occurred
OSD110A	How old when fracture occurred?
OSQ060	Ever told had osteoporosis/brittle bones
OSQ070	Ever treated for osteoporosis
RHQ060	Age at last menstrual period
RHQ291	Age when had hysterectomy
RHQ332	Age when both ovaries removed

Table 5

Data Dictionary for Covariates Used in Case Control Study

CODE	LABEL
DIQ010	Doctor told you have diabetes
DIQ160	Ever told you have prediabetes
DMDBORN	Country of Birth - Recode
INDHHINC	Annual Household Income
LBXBCD	Cadmium (ug/L)
MCQ010	Ever been told you have asthma
RHQ210	Breastfed any of your children?
RIDAGEYR	Age at Screening Adjudicated - Recode
RIDRETH1	Race/Ethnicity - Recode
RXDDRUG	Generic drug
SMQ020	Smoked at least 100 cigarettes in life

Table 6

Data Dictionary for Dependent Variables Used in Case Control Study

CODE	LABEL
MCQ140	Trouble seeing even with glass/contacts
OPDUARMA	Any retinopathy, worse eye
OPDUME	Macular edema, worse eye
OPDUMACH	Macular hole, worse eye
VIQ010	Can see light
VIQ017	Blind in both eyes
VIQ031	General condition of eyesight
VIQ041	Time worrying about eyesight
VIQ051A	Difficulty reading ordinary newsprint
VIQ051B	Difficulty with up close work or chores
VIQ051C	Difficulty seeing steps/curbs-dim light
VIQ051D	Difficulty noticing objects to side
VIQ051E	Difficulty finding object on crowded shelf
VIQ056	Difficulty driving daytime-familiar place
VIQ061	Vision limits how long can do activities
VIQ071	Ever had a cataract operation
VIQ090	Ever told had glaucoma
VIQ310	Told had macular degeneration
VIQ170	Glasses or contacts worn for near test?
VIQ200	Eye surgery for cataracts?
VIQ211	Which eye(s) cataract surgery?
VIQ220	Glasses/contact lenses worn for distance

Variables. Vision variables from non-ophthalmologic examinations were combined into one composite variable, Vision status, which represented all vision issues that were not cataract surgery-related. Similarly, all variables related to loss in bone density were combined into one variable, Evidence of osteoporosis. Combining the variables in this manner facilitated the analysis of data to answer the main research question. Tables 7 and 8 illustrate how the variables were combined.

Table 7

Main Type of Variables and Levels of Measurement

Variable	Codes of Source Variables	Type of Variable	Level of Measurement	Code for New Variable
Cataracts	VIQ071; VIQ200; VIQ211	Dependent	Nominal	CATARACTS
Vision	MCQ140; OPDUARMA OPDUME; OPDUMACH; VIQ010 VIQ017; VIQ031 VIQ041; VIQ051A VIQ051B; VIQ051C VIQ051D; VIQ051E VIQ056; VIQ061 VIQ090; VIQ310 VIQ170; VIQ220	Dependent	Nominal	VISION
Alkaline Phosphatase	LBXSAPSI	Independent	Scale	ALKPHOS
Bilirubin, Total	LBXSTB	Independent	Scale	BILI
Lead in Blood	LBXBPB	Independent	Scale	LEAD
Evidence of Osteoporosis	DXXNKBMD; DXXOSBMD; OSQ010A; OSQ010B; OSQ090A; OSQ010C; OSQ080; OSQ100A; OSD110A; OSQ060; OSQ070	Independent	Scale	OSTEO

Table 8

Confounding Variables and Levels of Measurement

Variable	Codes of Source Variables	Type of Variable	Level of Measurement	Code for New Variable
Diagnosis of Diabetes	DIQ010; DIQ160	Independent	Scale	PRE-/DIABETES
Nursed Children	RHQ210	Independent	Nominal	BREASTFED
Asthma	MCQ010	Independent	Nominal	ASTHMA
Smoking Status	SMQ020	Independent	Nominal	SMOKER
Generic Drug	RXDDRUG	Independent	Nominal	DRUG
Cadmium	LBXBCD	Independent	Scale	CADMIUM
Age	RIDAGEYR	Independent	Scale	AGE
Place of Birth	DMDBORN	Independent	Nominal	BIRTH

I merged datasets (from 2005-2006 and 2007 -2008) which contained the necessary source variables. The variables that were not needed were deleted from the merged datasets. All the remaining variables were then merged into one large dataset. Participants who are female and were aged 40 to 55 years were selected from the merged dataset; the remaining participants were deleted. Variables that relate to vision and osteoporosis were then combined into the composite variables VISION and OSTEO, respectively (see Table 3). Other composite variables were DIABETES (see Table 4) and intermediate variables for elevated enzymes and mobilized lead (not shown). The new

variables were created from source variables based on appropriate threshold values. The new variables were created to ensure easier computation. SPSS software version 21.0.0 and EXCEL spreadsheets were used in the analysis.

For this research the variable RIDAGEYR, age at screening, was used to compile the research dataset. The U.S. Department of Health and Human Services (HHS) recommended analysts make decisions regarding whether to impute results for datasets missing more than 10 percent of the data for particular variables (Johnson et al., 2013). The decision was made to impute the datasets. In view of the fact that women's greater risk for vision-related problems are worldwide (WHO, 2013); adjusted weights were not used in the secondary data analysis. HHS also cautioned analysts to be aware that two assumptions are being made when data from two consecutive surveys are combined. The assumptions are that the estimates in the two time periods are the same and with regard to the interpretation, the estimate is the average of the interpretation over the period of time. The datasets used in the analyses were adjacent to each other and in my opinion the time periods were small enough that differences between the two datasets would not have been significant.

Prior to the analysis of the data, SPSS was used to impute the missing data in responses to the questionnaires, namely for responses such as "don't know" and "refused". The reason the missing values were imputed is that if missing values are not addressed in statistical determinations, biases can result (Langkamp et al., 2010). Missing data were also imputed for data missing from direct examinations and laboratory tests. Thus a complete dataset based on imputation was used for the analysis. Variables that

were included in the merged datasets to ensure more accurate imputations of the data are shown in Table 9.

Table 9

Socioeconomic Variables Included to Ensure More Accurate Imputation

Variable	Type of Variable	Level of Measurement	Source
RIDAGEYR	Independent	Scale	Age-Recode
RIDRETH1	Independent	Nominal	Race/Ethnicity - Recode
DMDBORN	Independent	Nominal	Country of Birth - Recode
DMDYRSUS	Independent	Scale	Length of Time in US
INDHHINC	Independent	Scale	Annual Household Income

After the data were imputed, the variables were recoded to a binomial format. For example, borderline responses in the table below were recoded thus: 1 (Yes) and 2 (No) were not recoded, Borderline was recoded as 1 (Yes), and Refused, Don't know and Missing were deleted and imputed using the demographic data. The table that explains the recoded and imputed data is shown below:

Table 10

Questionnaire Values Recoded or Imputed

Code or Value	Value Description	Recoded Value
1	Yes	Yes
2	No	No
3	Borderline	1
7/77	Refused	Imputed
9/99	Don't know	Imputed
.	Missing	Imputed

Data Analysis Plan

Research questions. This investigation focused on whether lead mobilized from bones is positively linked with vision problems in women of perimenopausal age. Cases of elevated alkaline phosphatase without concomitant increase in total bilirubin levels were recorded as cases with evidence of bone turnover. Cases with evidence of bone turnover with elevated lead levels were recorded as evidence of bone lead mobilization. Therefore, survey participants with elevated levels of lead and elevated levels of alkaline phosphatase without elevated levels of total bilirubin were classified as participants with evidence of bone lead mobilization. The research questions were:

RQ1: What is the relationship between the incidence of cataracts and elevated blood lead levels in perimenopausal women when there is evidence of bone turnover?

RQ2: What is the relationship between elevated blood lead levels when there is evidence of bone turnover and general vision problems in perimenopausal women?

RQ3: Is evidence of cataractogenesis in perimenopausal women with evidence of bone lead mobilization (elevated blood lead levels and evidence of bone demineralization) significantly different from the incidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization?

RQ4-: Is the evidence of cataractogenesis in perimenopausal women with evidence of bone lead mobilization significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization when the data are controlled for age?

Research hypotheses. The null and alternative hypotheses for this study were as follows:

$H_0$1: There is no significant relationship between evidence of cataracts and elevated blood levels in perimenopausal women when there is evidence of bone turnover.

$H_1$1: There is a significant relationship between the evidence of cataracts and elevated blood levels in perimenopausal women when there is evidence of bone turnover.

$H_0$2: There is no significant relationship between elevated blood lead levels and general vision problems in perimenopausal women.

$H_1$2: There is a significant relationship between elevated blood levels and general vision problems in perimenopausal women.

$H_0$3: Evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization (elevated blood lead levels and evidence of bone demineralization) is not significantly different from the incidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization

$H_1$3: Evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization (elevated blood lead levels and evidence of bone demineralization) is significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization

$H_0$4: Evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization is not different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization when the data are controlled for age.

$H_1$4: Evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization is different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization when the data are controlled for age.

Analytical computations. SPSS Software (Release 21.0.0.0) was used to perform the analysis. The computations for each research question were performed as follows:

RQ1: What is the relationship between the evidence of cataracts and elevated blood lead levels in perimenopausal women when there is evidence of bone turnover?

Logistic regression with evidence of cataracts as the dependent variable.

RQ2: What is the relationship between elevated blood lead levels and general vision problems in perimenopausal women?

Logistic regression with evidence of general vision problems as the dependent variable.

RQ3: Is evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization (elevated blood lead levels and evidence of bone demineralization) significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization?

Chi-square analysis between the cases and the controls. The analysis was performed using the following equation:

$$\chi^2 = \sum \frac{(O-E)^2}{E}$$

Where $\chi 2$ equals= chi-square, O equals the observed value and E equals the expected value.

RQ4: Is the evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization when the data are controlled for age?

Stepwise logistic regression was performed to determine the contribution of possible confounding factors such as smoking status, age, use of steroids, menopause status, and ever nursed children. Significance for the Chi-square and logistic regression analysis was determined by an alpha value of less than 0.05 (Wolverton, 2009). If the alpha value was less than 0.05, the null hypotheses were rejected.

Threats to Validity

Known external threats to the validity of this study included cadmium and exposure to environmental tobacco smoke. Known confounding variables included in the NHANES datasets were included in the logistic regression analysis. Stepwise regression analysis was performed in order to determine if lead (the independent variable of interest) was significantly associated with cataractogenesis in perimenopausal females once the known mediating variables were addressed.

Possible internal threats to validity included the slow maturation of cataracts to a stage that was gradable and sufficiently mature to warrant surgery. Other internal threats were missing or incorrectly recorded data. Validity that is threatened by the slow maturation of cataracts was addressed by the use of data on responses about difficulty with vision. If the data had not been recorded correctly for some participants, the

probability that other variables for those participants would also be skewed in a manner to bias the data would also be very small.

Ethical Procedures

There were no issues of privacy or personal harm which needed to be addressed by informed consent: Secondary datasets from the National Health and Nutrition Examination Surveys were used for this study and are publicly available on the Centers for Disease and Prevention's website at http://www.cdc.gov/nchs/nhanes.htm. The datasets used for this study were previously de-identified, did not contain any personally identifiable information, and can be downloaded by any individual from the section entitled "Questionnaires, datasets, and related documentation". The data were password-protected and they are being stored on an Iomega external hard drive which will be kept for a period of seven years. Results of the research will be published in the first peer-reviewed journal that accepts a completed article version of the study. The research study was submitted to the Walden University Institutional Review Board (IRB) prior to data analysis.

Summary

This chapter described the methodology that was prepared to answer four research questions about a possible association between mobilized lead in perimenopausal women and cataracts. The study had a case control study design. The cases were women who showed evidence of mobilized lead; the controls were women who did not. Data from the National Health and Nutritional Surveys of 2005 to 2006 and 2007 to 2008 were mined for information on possible bone demineralization and release

of endogenous lead in perimenopausal women. Individuals with elevated levels of lead and evidence of bone demineralization (cases) were compared with individuals without both characteristics to determine if there is a difference in cataractogenesis or vision-related problems. An overview of planned data analysis for this secondary dataset was provided.

Chapter 4: Results

Introduction

The results of the analyses showed that there is an association between mobilized lead and vision issues in perimenopausal women. The association was derived by Chi-square analysis of cataract surgeries and logistic regression of vision issues with lead. The former method is similar to the method used by Schaumberg et al. in the 2004 case control study of elderly men and cataracts, which yielded a positive result for the association. The latter method mirrored the method used by Park et al. (2013) who reported no association between cataract surgeries and lead when confounders were included in the analysis. This dissertation study is the first known report of an association between endogenous lead and vision issues in perimenopausal women.

The purpose of this research was to determine whether there is any association between the perimenopausal release of lead due to bone demineralization and the early incidence of cataracts and other vision-related issues in women.

The research questions and hypotheses for this study were as follows:

RQ_1: What is the relationship between the incidence of cataracts and elevated blood lead levels in perimenopausal women when there is evidence of bone turnover?

$H1_0$: There is no significant relationship between the incidence of cataracts and elevated blood levels in perimenopausal women when there is evidence of bone turnover.

$H1_A$: There is a significant relationship between the incidence of cataracts and elevated blood levels in perimenopausal women when there is evidence of bone turnover.

RQ2: What is the relationship between elevated blood lead levels and general vision problems in perimenopausal women?

$H2_0$: There is no significant relationship between elevated blood lead levels and general vision problems in perimenopausal women.

$H2_A$: There is a significant relationship between elevated blood levels and general vision problems in perimenopausal women.

RQ3: Is evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization (elevated blood lead levels and evidence of bone demineralization) significantly different from the incidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization?

$H3_0$: Evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization (elevated blood lead levels and evidence of bone demineralization) is not significantly different from the incidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization.

$H3_A$: Evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization (elevated blood lead levels and evidence of bone demineralization) is significantly different from the incidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization.

RQ4: Is the evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization when the data are controlled for age?

$H4_0$: Evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization is not significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization when the data are controlled for age.

$H4_A$: Evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization is significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization when the data are controlled for age.

This chapter contains information about the characteristics of the participants of the sample, univariate statistics, histograms, and bar charts as appropriate. The results section contains the data that illustrates the association between mobilized lead and cataract surgeries, and elevated lead and vision issues. The results are displayed in tabular form with footnotes highlighting additional information. In the summary section, results are compared against each of the research questions in turn and an evaluation is made regarding whether the null hypothesis can be rejected.

Data Collection

I analyzed the responses and examination results of selected participants of the National Health and Nutrition Examination Surveys (NHANES) during the years 2005 - 2006 and 2007-2008. I retrieved SAS datasets on demographics, clinical data, bone density measurements, and laboratory results from the NHANES website and imported the data using SPSS version 21.0. Using SPSS, I selected cases for all female participants aged 40 to 55 years and merged the datasets for the two survey periods. SPSS and Excel software were used to separate, combine, and compute variables as necessary to answer the research questions. A total of 1,416 cases were selected and analyzed for this research.

The original plan for this case control study included the imputation of missing data for responses to questionnaires. The plan did not include the imputation of laboratory data or any other direct measurements but I discovered that the datasets for bone density measurements did not have sufficient data to complete the study. However, the Centers for Disease Control and Prevention (CDC) had already determined that bone density data for the years 2005 to 2006 were inadequate and had released imputed datasets subsequent to the release of the original datasets (CDC, 2013c). Since it was necessary to impute direct bone density data, the plan for this study was changed to include the imputation of laboratory and other direct clinical measurements. Thus, all 1,416 participants of the selected age group were included in every analysis. The laboratory data imputed were total bilirubin, alkaline phosphatase, blood lead levels, and cadmium levels. Missing responses to the vison, osteoporosis, general medical, diabetes,

and prescription medicine questionnaires were also imputed using general demographic data such as age, income level, and country of birth. Imputation of the data may bias the results towards the null and at best is an approximation of the missing data points in the analysis.

Baseline Statistics

Descriptive Statistics

The age distribution of the selected participants was not significantly different from U.S. population estimates for the same age group. This was determined by comparing the age distribution of the participants selected for this study alongside the age distribution of women counted in the 2010 United States census (see Figure 6). Comparative census data were retrieved from census.gov (United States Census Bureau, 2014).

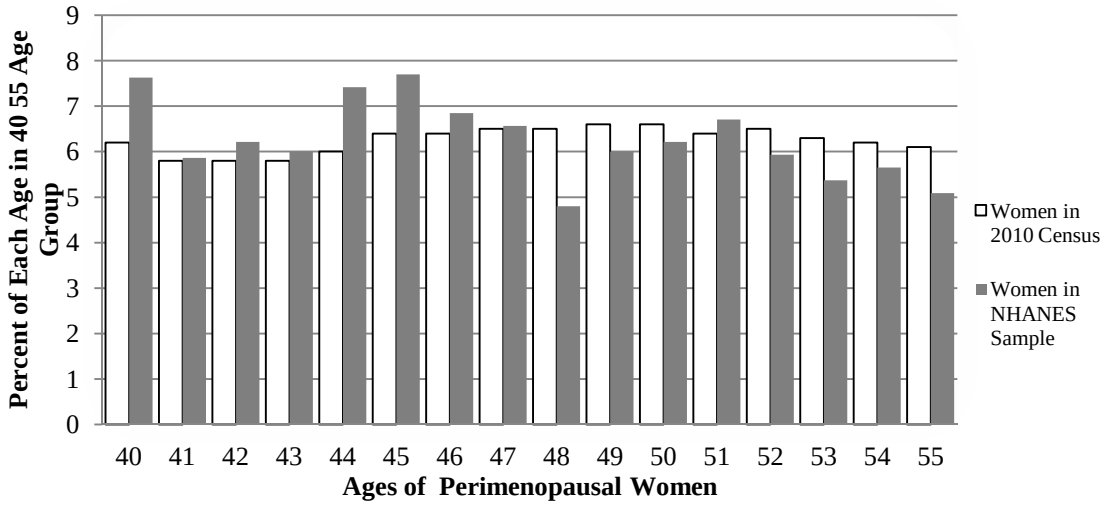

Figure 6. Bar chart of Percentages of age of Perimenopausal Participants in 2005-2008 National Health and Nutrition Examination Surveys and women in the US 2010 census.

Demographic Data

Analysis of the baseline data shows that the mean age of the participants in the 40 to 55 years age group was 47.16. The standard deviation was 4.555 and the total number of participants in the sample was 1,416. The participants were then grouped into three age categories to facilitate logistic regression analysis. The categorization of age was used to determine if there was any significant association between mobilized lead and vision issues in perimenopausal women when age was included as a confounder. A bar chart of the categorized age distribution is shown in Figure 7 below.

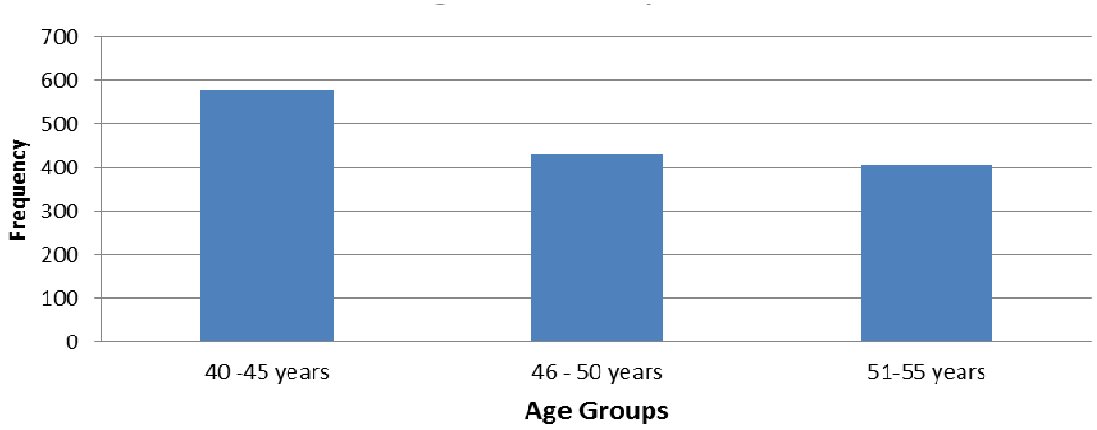

Figure 7. Barcharts of Participants Categorized Into 3 Age Groups

Cooking with biomass fuels is an activity of low-income households in India and a possible causative factor for cataracts for women who live in India (Mishra et al., 1999). Mexican-Americans have a high risk for cataracts (Broman et al., 2005). Based on these reports, place of birth was added to the regression analysis as a possible

confounding factor for cataracts and general vision problems. Descriptive analysis of the data revealed that approximately three-quarters of the women in the age group 40 to 55 years were born in the United States, 11.2 percent were born in Mexico, and the remainder was born elsewhere. Table 11 shows the classification of places of birth recorded in the National Health and Nutrition Examination Surveys (NHANES). Table 12 shows how the participants were reclassified (born in the U.S.A. or Born elsewhere) in order to answer the research questions.

Table 11

Place of Birth of Perimenopausal Women in the 2005-2008 NHANES Surveys

Country of Birth	Frequency	Percent
Born in 50 US States or Washington, DC	1066	75.3
Born in Mexico	159	11.2
Born Elsewhere	60	4.2
Born in Other Spanish Speaking Country	78	5.5
Born in Other Non-Spanish Speaking Country	53	3.7
Total	1416	100.0

Table 12

Place of Birth of Perimenopausal Women Recoded

Location of Birth	Frequency	Percent
Born in the USA	1066	75.3
Born Elsewhere	350	24.7
Total	1416	100.0

Ethnicity was examined in this study because of previous reports suggesting significant differences related to ethnic background: Non-Hispanic Whites are more likely to have cataract surgeries than African Americans (West et al., 1998); African American women under the age of 70 years have a higher prevalence of cataracts than their non-Hispanic White counterparts (Congdon et al., 2004). Income levels have been negatively associated with high blood lead levels and vision issues (Klein and Klein, 2013; Lee et al., 2005; Zambelli-Weiner et al., 2012). Therefore, income levels were also included in this study. Tables of race/ethnicity and income levels (Tables 13 to 16) are displayed below as well as the corresponding reclassified groups computed for ease of analysis.

Table 13

Race/Ethnicity Breakdowns in the Original Data

Race or Ethnicity	Frequency	Percent
Mexican American	259	18.3
Other Hispanic	112	7.9
Non-Hispanic White	641	45.3
Non-Hispanic Black	339	23.9
Other Race - Including Multi-Racial	65	4.6
Total	1416	100.0

Table 14

Reclassified Race/Ethnicity Breakdowns

[Recoded Race or Ethnicity]	Frequency	Percent
Non-Hispanic White	641	45.3
Hispanic/Mexican Hispanic	371	26.2
Non-Hispanic Black	339	23.9
Other Race	65	4.6
Total	1416	100.0

Table 15

Annual Household Incomes Breakdowns in the Original Data

Income Levels	Frequency	Percent
$ 0 to $ 4,999	27	1.9
$ 5,000 to $ 9,999	54	3.8
$10,000 to $14,999	91	6.4
$15,000 to $19,999	80	5.6
$20,000 to $24,999	109	7.7
$25,000 to $34,999	151	10.7
$35,000 to $44,999	113	8.0
$45,000 to $54,999	108	7.6
$55,000 to $64,999	89	6.3
$65,000 to $74,999	98	6.9
$75,000 and Over	201	14.2
Over $20,000	33	2.3
Under $20,000	4	0.3
$75,000 to $99,999	91	6.4
$100,000 and Over	124	8.8
Refused	12	0.8
Don't know	15	1.1
Missing	16	1.1
Total	1416	100.0

Table 16

Reclassified Annual Household Incomes for the Study Population

Reclassified Income Levels	Frequency	Percent
Less than $20,000	250	17.7
$20,000 - $74,999	707	49.9
$75,000 and over	416	29.4
Missing	43	3.0
Total	1416	100.0

Responses to Questionnaires

Diabetes, asthma, selective serotonin resorption inhibitors (SSRIs), glucocorticosteroids, cigarette smoking, and breast-feeding were included as covariates in the regression analyses. The baseline data were retrieved from the medical, prescription medication, smoking, and reproductive questionnaires of National Health and Nutrition Examination Surveys. Descriptive statistics on diabetes, asthma, smoking, and the use of glucocorticoids and selective serotonin reuptake inhibitors are included in this report to provide information on the proportion of these confounders relative to the total sample. The majority of the participants were not diabetic or prediabetic, nor were they asthmatic. Of the women who responded for each of the respective questions, more than half had breastfed their children, 45 percent had smoked at least 100 cigarettes, and 18 percent had taken a selective serotonin reuptake inhibitor or glucocorticoid. The descriptive statistics on the covariates are shown in Figure 8 and 9 and in Tables 17 to 19.

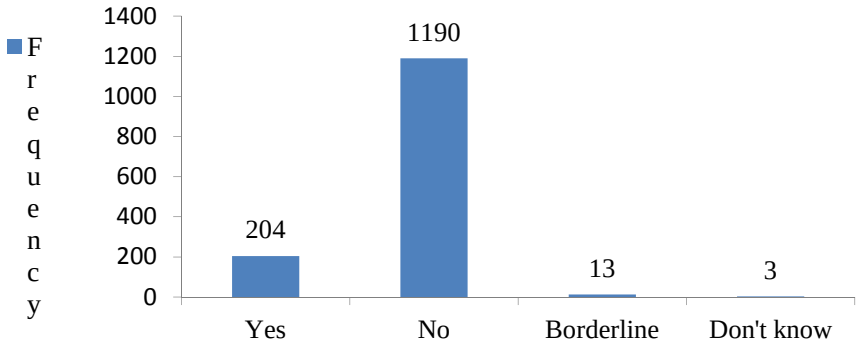

Figure 8. Barchart of Diabetes and Prediabetes Breakdowns in the Original Data

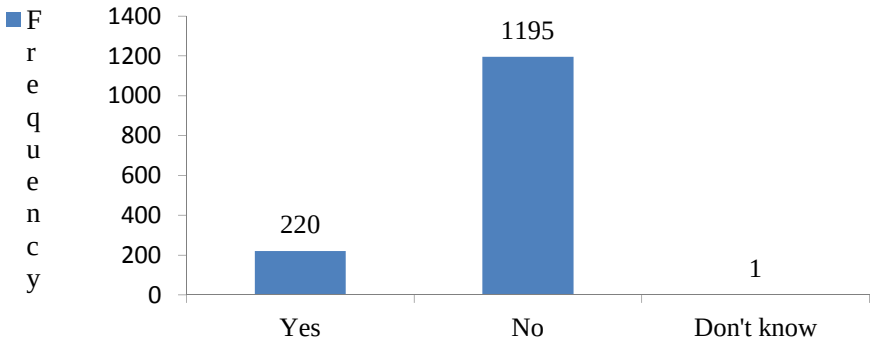

Figure 9. Barchart of Asthma Breakdowns in the Original Data

Table 17

Breastfeeding History Breakdowns in the Original Data

Responses	Frequency	Percent
Yes	641	45.3
No	464	32.8
Total	1105	78.0
Missing	311	22.0
Total	1416	100.0

Table 18

Participants Who Smoked at Least 100 Cigarettes in Their Lifetime

Responses	Frequency	Percent
Yes	634	44.8
No	782	55.2
Total	1416	100.0

Table 19

SSRI or Glucocorticoid Use Breakdowns in the Original Data

Responses	Frequency	Percent
Yes	252	17.8
No	1153	81.4
Refused	6	.4
Don't Know	4	.3
Total	1415	99.9
Missing	1	.1
Total	1416	100.0

Selective Serotonin Reuptake Inhibitors (SSRIs) and Glucocorticoid drugs were included based on the classifications listed on the websites of the Food and Drug Administration (2014) and the National Institutes of Health (2014). The SSRIs identified in this study were citalopram, escitalopram, fluoxetine, paroxetine, and sertraline. The corticosteroids identified were beclomethasone, budesonide, clobetasol, cortisone, dexamethasone, desoximetasone, fludrocortisone, flunisolide, fluocinonide, fluticasone, hydrocortisone, mometasone, prednisone, prednisolone, and triamcinolone.

General Vision Issues

Baseline data from responses to questions on the NHANES vision questionnaire were used to compile the variable General Vision Issues that did not contain any information on cataract surgeries. General Vision Issues also did not contain any information on any other diagnosed diseases. Summaries from the responses that comprise General Vision Issues are shown in Tables 20 to 29.

Table 20

Trouble Seeing Even With Glasses/Contacts Baseline Data

Responses	Frequency	Percent
Yes	375	26.5
No	1040	73.4
Don't know	1	0.1
Total	1416	100.0

Table 21

General Condition of Eyesight Breakdowns in the Original Data

Responses	Frequency	Percent
Excellent	368	26.0
Good	730	51.6
Fair	253	17.9
Poor	48	3.4
Very Poor	15	1.1
Don't know	2	0.1
Total	1416	100.0

Table 22

Time Worrying About Eyesight Breakdowns in the Original Data

Responses	Frequency	Percent
None of the time	675	47.7
A little of the time	324	22.9
Some of the time	245	17.3
Most of the time	82	5.8
All of the time	90	6.4
Total	1416	100.0

Table 23

Difficulty Reading Ordinary Newsprint Breakdowns in the Original Data

Responses	Frequency	Percent
No difficulty	944	66.7
A little difficulty	290	20.5
Moderate difficulty	113	8.0
Extreme difficulty	48	3.4
Unable to do because of eyesight	12	0.8
Does not do this for other reasons	8	0.6
Don't know	1	0.1
Total	1416	100.0

Table 24

Difficulty with Up Close Work or Chores Breakdowns in the Original Data

Responses	Frequency	Percent
No difficulty	1017	71.8
A little difficulty	275	19.4
Moderate difficulty	89	6.3
Extreme difficulty	24	1.7
Unable to do because of eyesight	6	0.4
Does not do this for other reasons	5	0.4
Total	1416	100.0

Table 25

Difficulty Seeing Steps/Curbs-Dim Light Breakdowns in the Original Data

Responses	Frequency	Percent
No difficulty	1086	76.7
A little difficulty	199	14.1
Moderate difficulty	77	5.4
Extreme difficulty	35	2.5
Unable to do because of eyesight	5	0.4
Does not do this for other reasons	13	0.9
Don't know	1	0.1
Total	1416	100.0

Table 26

Difficulty Noticing Objects to Side Breakdowns in the Original Data

Responses	Frequency	Percent
No difficulty	1231	86.9
A little difficulty	121	8.5
Moderate difficulty	39	2.8
Extreme difficulty	19	1.3
Unable to do because of eyesight	4	0.3
Does not do this for other reasons	2	0.1
Total	1416	100.0

Table 27

Difficulty Finding Object on Crowded Shelf Breakdowns in the Original Data

Responses	Frequency	Percent
No difficulty	1220	86.2
A little difficulty	145	10.2
Moderate difficulty	36	2.5
Extreme difficulty	11	0.8
Unable to do because of eyesight	2	0.1
Does not do this for other reasons	1	0.1
Don't know	1	0.1
Total	1416	100.0

Table 28

Difficulty Driving Daytime – Familiar Place Breakdowns in the Original Data

Responses	Frequency	Percent
No difficulty	1204	85.0
A little difficulty	51	3.6
Moderate difficulty	11	0.8
Extreme difficulty	3	0.2
Unable to do because of eyesight	7	0.5
Does not do this for other reasons	37	2.6
Refused	103	7.3
Total	1416	100.0

Table 29

Vision Limits How Long can do Activities Breakdowns in the Original Data

Responses	Frequency	Percent
None of the time	1237	87.4
A little of the time	102	7.2
Some of the time	56	4.0
Most of the time	14	1.0
All of the time	7	0.5
Total	1416	100.0

Cataract Surgeries

The data on cataract surgeries, a dependent variable for the logistic regression analysis in this dissertation research study, are summarized in Table 30 below.

Table 30

Ever had a Cataract Operation Breakdowns in the Original Data

Responses	Frequency	Percent
Yes	13	0.9
No	1403	99.1
Total	1416	100.0

Specific Non-Cataract Diseases

Specific diseases with known etiologies were added to the nonspecific General Vision Issues variable in order to create a complete vision issues variable named All Vision Issues. The baseline summary statistics of specific diseases recorded on vision questionnaires are shown in Tables 31 and 32. Vision issues due to refractive errors – the need for glasses for distance and near glasses – were also included in the dependent variable General Vision Issues. The baseline descriptive statistics for responses on refractive errors are displayed in Tables 33 and 34.

Table 31

Ever Told had Glaucoma Breakdowns in the Original Data

Responses	Frequency	Percent
Yes	30	2.1
No	1379	97.4
Total	1409	99.5
Missing	7	0.5
Total	1416	100.0

Table 32

Told had Macular Degeneration Breakdowns in the Original Data

Responses	Frequency	Percent
Yes	13	0.9
No	1396	98.6
Missing	7	0.5
Total	1416	100.0

Table 33

Glasses or Contacts for Near Test Breakdowns in the Original Data

Responses	Frequency	Percent
Glasses	291	20.6
Contacts	20	1.4
Both glasses and contact lenses	5	0.4
Subtotal	316	22.3
Missing	1100	77.7
Total	1416	100.0

Table 34

Glasses/Contact Lenses worn for Distance Breakdowns in the Original Data

Responses	Frequency	Percent
Yes	619	43.7
No	684	48.3
Don't know	1	0.1
Missing	112	7.9
Total	1416	100.0

Clinical Examination Data

Unbiased clinical examination data should provide accurate information on the state of survey respondents' health. The Centers for Disease Control and Prevention provided information on the training of the observers and the steps taken to minimize observer bias in the collection of clinical data for the National Health and Nutrition Examination Surveys of 2005-2006 and 2007 -2008 (Centers for Disease Control and Prevention, 2014a). Ophthalmologic data were utilized to supplement the data derived from questionnaires on vision. Bone density examination data were used to supplement the data culled from responses to questions on the osteoporosis questionnaire.

Ophthalmologic Examinations.

Data from the 2005 to 2008 National Health and Nutrition Examination Surveys did not include ophthalmologic examinations for cataracts; responses to questions on cataract surgeries were used to analyze the relationship between cataracts and mobilized lead. The results of the clinical examinations for retinopathy and macular edema were assessed and coded based on standardized criteria (Centers for Disease Control and

Prevention, 2014a). The data from the ophthalmologic examinations (shown in Tables 35 to 37) are included in the variable All Vision Issues.

Table 35

Any Retinopathy, Worse Eye Breakdowns in the Original Data

Responses	Frequency	Percent
No	1119	79.0
Yes	81	5.7
Subtotal	1200	84.7
Missing	216	15.3
Total	1416	100.0

Table 36

Macular Edema, Worse Eye Breakdowns in the Original Data

Responses	Frequency	Percent
No	1184	83.6
Yes or Questionable	3	0.2
Yes, but not Clinically Significant Macular Edema	3	0.2
Yes, Clinically Significant Macular Edema	8	0.6
Other	1	0.1
Subtotal	1199	84.7
Missing	217	15.3
Total	1416	100.0

Table 37

Macular Hole, Worse Eye Breakdowns in the Original Data

Responses	Frequency	Percent
No	1198	84.6
Questionable	2	0.1
Subtotal	1200	84.7
Missing	216	15.3
Total	1416	100.0

Bone Density Measurements

Femoral neck and spine bone mineral density measurements were used to code for the osteoporosis variable. Respondents with either femoral neck or total spine bone mineral density (BMD) measurement two standard deviations below the mean were coded osteoporotic as well as post-menopausal women with either bone measurement one standard deviation below the mean. The statistics for BMD measurements for the sample population are shown in Table 38.

Table 38

Femoral Neck BMD and Total Spine BMD statistics

Statistic	Femoral neck BMD Statistic	Total spine BMD
Mean	0.8287	1.0376
Std. Deviation	.13204	.14117
Minimum	0.48	0.60
Maximum	1.46	1.72
Range	0.98	1.11

Laboratory Data

Lead was an independent variable in this study. Descriptive statistics of lead levels from this sample population were used to determine elevated versus non-elevated levels of lead. The reference range for total bilirubin is 0.3 to 1.2 mg/dL (Centers for Disease Control and Prevention, 2014a). The reference range for alkaline phosphatase in adult females aged 40 to 45 years is 37 U/L to 98 U/L (Mayo Clinic, 2014). This reference range was used since the 40 to 45 years age group was the reference group in the logistic regression analyses. Elevated alkaline phosphatase levels (greater than 98 U/L) levels without elevated levels of total bilirubin (greater than 1.2 mg/dL) and evidence of osteoporosis were used to code elevated lead levels as mobilized lead. Cadmium was analyzed as a covariate in the logistic regression analyses. Data on lead, total bilirubin, alkaline phosphatase, and cadmium levels of the sample population are shown in Table 39.

Table 39

Total Bilirubin, Blood Alkaline Phosphatase, Cadmium, and Lead Levels

Statistic		Lead (ug/dL)	Total bilirubin (mg/dL)	Alkaline phosphatase (U/L)	Cadmium (ug/L)
N	Valid	1329	1317	1316	1329
	Missing	87	99	100	87
Mean		1.529	0.637	70.68	0.636
Median		1.250	0.600	67.00	0.410
Std. Deviation		1.0224	.2475	23.402	.6646
Range		7.99	2.50	209	5.86
Minimum		0.28	0.10	26	0.14
Maximum		8.27	2.60	235	6.00

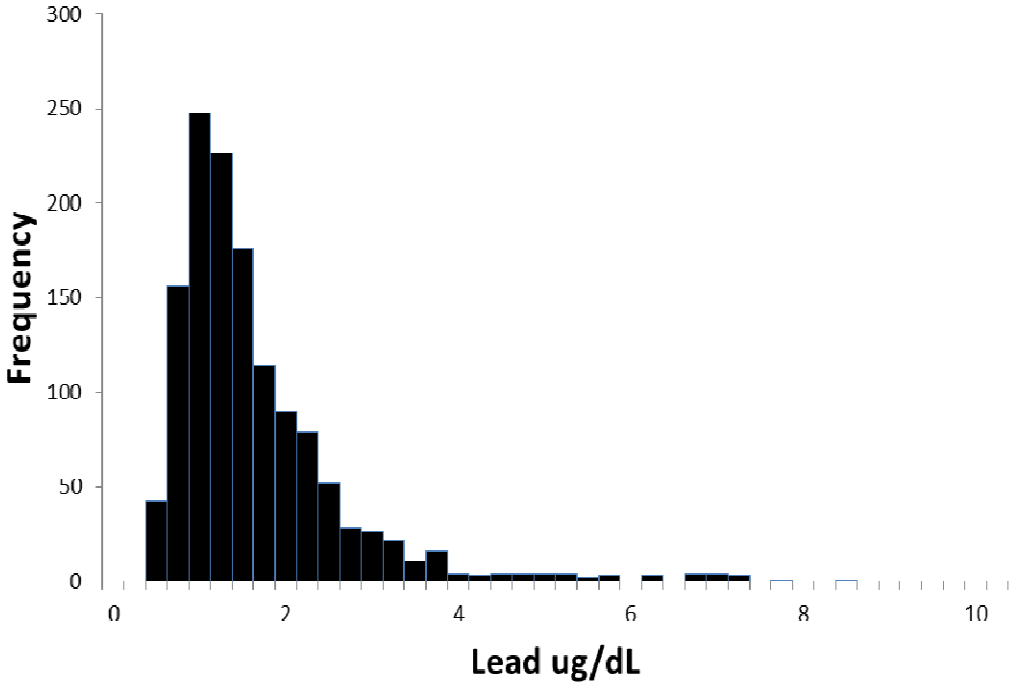

Figure 10. Histogram of Blood Lead Levels
Note: Mean = 1.53, Median = 1.25, N = 1329.

The histogram for lead shown in Figure 10 is not normally distributed and the distribution is skewed to the right (kurtosis = 9.34). The Centers for Disease Control and Prevention (2014a) stated that the geometric mean for lead in the population is currently below 2 µg/dL. The descriptive statistics for this segment of the population support that statement. Therefore, current central parameters were evaluated for the cut point for this study. The mean is higher than the median. Since the distribution is right-skewed, the median of 1.25 ug/dL, not the mean, was chosen as the cut point for the determination of elevated lead.

Preparation of the Data

Missing data were imputed using demographic data such as age, country of birth, and ethnic characteristics. The data were coded in binary form (1= Yes, 0 = No) except for age, ethnicity, income, and blood lead status. The variable Mobilized Lead was created in a series of steps. First an intermediate variable, OSTEO, was coded based on bone density measurements two standard deviations below the mean for women who were not postmenopausal and one standard deviation below the mean for postmenopausal women. A separate intermediate variable, EL_ALK, was created for cases with elevated alkaline phosphatase levels without corresponding elevation in total bilirubin. Cases with OSTEO = 1 or EL_ALK = 1 or both and with lead levels above the median value (1.25 µg/dL) were coded as Mobilized Lead. Cases with lead levels above the median value of 1.25 µg/dL but without any evidence of osteoporosis (OSTEO = 0) or elevated alkaline phosphatase levels without elevated levels of total bilirubin (EL-ALK = 0) were coded as Elevated Lead. All other cases were coded No Lead. Thus the lead variable was comprised of three dummy variables – No Lead, Elevated Lead, and Mobilized Lead.

Results of Analyses

The results of the analyses were compared with the null and alternative hypotheses of each research question. A decision was made regarding whether the null hypothesis could be rejected or not based on the criteria of $p < .05$ and an odds ratio greater than one. All results of all variables for each model of the stepwise logistic regression analyses are not recorded in this chapter. For ease of interpretation, the most significant result of the most significant dummy variable is recorded in each table, as well

as the result of the constant in the final model. However, the most significant results for Elevated Lead and Mobilized Lead are all recorded for every regression analysis. The research questions and conclusions follow:

RQ1: What is the relationship between the incidence of cataracts and elevated blood lead levels in perimenopausal women when there is evidence of bone turnover?

Logistic Regression with Evidence of Cataracts as the Dependent Variable

The Enter logistic method forces all the variables for the possible equation into one block and SPSS calculates the parameter estimates for the variables in that block (Field, 2009). The Forward Regression method may result in a type II error (Field, 2009). Therefore, based on the foregoing and the small number of cataract cases (13), the Wald Backward Stepwise Regression was used to determine any possible relationship between elevated or mobilized lead and the likelihood of cataract surgery. The coding for the regression analysis is shown in Table 40 and the results are shown in Table 41.

Table 40

Categorical Coding for Lead

Variable	Frequency	Parameter coding (1)	(2)
No Elevated Lead	683	.000	.000
Elevated Lead	523	1.000	.000
Mobilized Lead	210	.000	1.000

Table 41

Result of Regression Analysis between Mobilized Lead and Cataract Surgeries

Variable	B	S.E.	Sig.	Odds Ratio	95% C.I.for Odds Ratio	
					Lower	Upper
Elevated Lead	-.246	.733	.738	.782	.186	3.288
Mobilized Lead	1.196	.637	.061	3.307	.948	11.537
Constant	-4.910	.449	.000	.007		

Note: R^2 = .003 (Cox & Snell), .032 (Nagelkerke). Model χ^2 =4.498, p =.11.

The results showed that the contribution of the variable Mobilized Lead could not be significantly distinguished from 0. Thus, the model could not predict whether any participant would have a cataract surgery based on the presence of elevated lead and evidence of bone turnover.

RQ2: What is the relationship between elevated blood lead levels and general vision problems in perimenopausal women?

Logistic Regression with Evidence of General Vision Problems as the Dependent Variable

The results of the analysis for the second research question are shown in Table 42 below.

Table 42

Result of Logistic Regression between Mobilized Lead and General Vision Issues

Variables in the Equation	B	S.E.	Sig.	Odds Ratio	95% C.I.for Odds Ratio	
					Lower	Upper
Mobilized			.011			
Elevated Lead	.314	.126	.013	1.368	1.069	1.752
Mobilized Lead	.408	.167	.015	1.504	1.084	2.088
Constant	-.975	.086	.000	.377		

Note: R^2 = .01 (Cox & Snell), .01 (Nagelkerke). Model χ^2 =9.06, p =.01.

The results in Table 38 indicate that the model can be used to predict whether a participant may have general vision issues based on the presence of elevated lead and evidence of bone turnover ($p<0.05$). However, the Cox, Snell, and Nagelkerke R square values are low and introduction of the variables into the regression analysis does not improve the number of cases correctly predicted by the null model: The number of cases correctly predicted by the null model and the full model was exactly 68.9 per cent.

RQ3-: Is evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization (elevated blood lead levels and evidence of bone demineralization) significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization?

Chi-square analysis between the cases and the controls

(a) Since there were only 13 cases of participants who had cataract surgeries, there were insufficient cases for a valid chi-square analysis. The cross-tabulation table is shown below.

Table 43

Cross Tabulation Table for Mobilized Lead and Cataract Surgeries

Category			Cataract		Total
			No	Yes	
Lead status	Mobilized	Count	205	5	210
		Expected Count	208.1	1.9	210.0
		% within Lead status	97.6%	2.4%	100.0%
		% within Cataract	14.6%	38.5%	14.8%
		% of Total	14.5%	0.4%	14.8%
		Std. Residual	-.2	2.2	
	Not mobilized	Count	1198	8	1206
		Expected Count	1194.9	11.1	1206.0
		% within Lead status	99.3%	0.7%	100.0%
		% within Cataract	85.4%	61.5%	85.2%
		% of Total	84.6%	0.6%	85.2%
		Std. Residual	.1	-.9	
Total		Count	1403	13	1416
		Expected Count	1403.0	13.0	1416.0
		% within Lead status	99.1%	0.9%	100.0%
		% within Cataract	100.0%	100.0%	100.0%
		% of Total	99.1%	0.9%	100.0%

(b) The results of Chi-square analysis between mobilized lead levels and general vision issues are shown in Tables 44 and 45. There was no significant association between incidence of vision-related issues and evidence of bone lead turnover in the sample of perimenopausal women $\chi 2 = 2.93$, $p = .09$.

Table 44

Cross-tabulation Table between Mobilized Lead and General Vision Issues

Category		VISION NO CATARACTS		
		No general vision issues	Bad vision	Total
No Evidence of Mobilized Lead	Count	841	365	1206
	Expected Count	830.4	375.6	1206.0
	% within Mobilized Lead	69.7%	30.3%	100.0%
	% within Vision No Cataracts	86.3%	82.8%	85.2%
	% of Total	59.4%	25.8%	85.2%
	Std. Residual	.4	-.5	
Evidence of Mobilized Lead	Count	134	76	210
	Expected Count	144.6	65.4	210.0
	% within Mobilized Lead	63.8%	36.2%	100.0%
	% within Vision No Cataracts	13.7%	17.2%	14.8%
	% of Total	9.5%	5.4%	14.8%
	Std. Residual	-.9	1.3	
Total	Count	975	441	1416
	Expected Count	975.0	441.0	1416.0
	% within Mobilized Lead	68.9%	31.1%	100.0%
	% within Vision No Cataracts	100.0%	100.0%	100.0%
	% of Total	68.9%	31.1%	100.0%

Table 45

Statistics for Chi-square Test Between Mobilized Lead and General Vision Issues

Statistic	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.928[a]	1	.087	.090	.053
Likelihood Ratio	2.864	1	.091	.106	.053
Fisher's Exact Test				.090	.053
N of Valid Cases	1416				

(c) There was significant association between the incidence of vision-related issues with the 13 cases of cataracts and the evidence of bone turnover in the sample of perimenopausal women: $\chi 2 = 3.45$, p (one-tailed) =.04. The cross-tabulation table is shown in Table 46 and full Chi-square result statistics are shown in Table 47.

Table 46

Cross-tabulation Table Between Mobilized Lead and General Vision Issues Combined With Cataract Surgeries

Category		VISION WITH CATARACTS INCLUDED		Total
		No General vision issues	Bad vision	
No Evidence of Mobilized Lead	Count	836	370	1206
	Expected Count	824.4	381.6	1206.0
	% within Mobilized Lead	69.3%	30.7%	100.0%
	% within Vision with Cataracts Included	86.4%	82.6%	85.2%
	% of Total	59.0%	26.1%	85.2%
	Std. Residual	.4	-.6	
Evidence of Mobilized Lead	Count	132	78	210
	Expected Count	143.6	66.4	210.0
	% within Mobilized Lead	62.9%	37.1%	100.0%
	% within Vision with Cataracts Included	13.6%	17.4%	14.8%
	% of Total	9.3%	5.5%	14.8%
	Std. Residual	-1.0	1.4	
Total	Count	968	448	1416
	Expected Count	968.0	448.0	1416.0
	% within Mobilized Lead	68.4%	31.6%	100.0%
	% within Vision with Cataracts Included	100.0%	100.0%	100.0%
	% of Total	68.4%	31.6%	100.0%

Table 47

Statistics for Chi-square test between Mobilized Lead and Cataract Surgeries with General Vision Issues

Statistic	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square*	3.454[a]	1	.063	.065	.039
Likelihood Ratio*	3.376	1	.066	.077	.039
Fisher's Exact Test*				.065	.039
N of Valid Cases	1416				

* Test significant at the one-tailed level.

Chi-square analysis of general vision issues – non-specific vision diseases including refractive errors – did not yield a significant p value. However, chi-square analysis of all vision variables combined with mobilized lead was significant (p=0.003, two-tailed; p=0.001, one-tailed). Chi-square analysis of mobilized lead and general vision issues combined with glaucoma was significant (p=0.037, two-tailed; p=0.021, one-tailed); general vision issues with macular degeneration (p=0.041, one-tailed); and general vision issues with a macular hole (p=0.024, two-tailed; p=0.013, one-tailed).

Logistic Regression including Confounding Variables

RQ4: Is the evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization when the data are controlled for age?

Stepwise logistic regression was performed to determine the contribution of known confounding factors such as smoking status, age, use of steroids, ever nursed

children, diabetes status, ethnicity, and asthma status, Additional possible confounding factors such as being born in the United States and Income level to represent socio-economic status were also added to the regression analysis. Menopause status was factored into the determination of bone demineralization and therefore the variable was omitted from the regression analysis.

Backward logistic regression was performed on the dependent variables and covariates. The parameter coding is shown in Table 48 and the results are shown in Table 49 to 51.

Table 48

Coding of Parameters

Categories		Frequency	Parameter coding		
			(1)	(2)	(3)
Rae/Ethnicity	Non-Hispanic White	633	.000	.000	.000
	Hispanic/Mexican Hispanic	366	1.000	.000	.000
	Non-Hispanic Black	335	.000	1.000	.000
	Other Race	64	.000	.000	1.000
Mobilized Lead	No Elevated Lead	676	.000	.000	
	Elevated Lead	520	1.000	.000	
	Mobilized Lead	202	.000	1.000	
Ages in 3 Groups	40 -45 years	574	.000	.000	
	46 - 50 years	424	1.000	.000	
	51-55 years	400	.000	1.000	
Income	Less than $20,000	249	.000	.000	
	$20,000 - $74,999	733	1.000	.000	
	$75,000 and over	416	.000	1.000	
Born in our out of USA	Born in the USA	1053	.000		
	Born Elsewhere	345	1.000		
Breastfed Child	Yes	827	1.000		
	No	571	.000		
SSRI or Glucocorticoid	SSRI or Glucocorticoid	1077	1.000		
	No SSRI or Glucocorticoid Medication	321	.000		
Smoked at least 100 cigarettes	Yes	624	1.000		
	No	774	.000		
Pre-diabetics/Diabetic	Yes	208	1.000		
	No	1190	.000		

Note: SSRI=Selective Serotonin Reuptake Inhibitors

Table 49

Logistic Regression Results of Cataract Surgeries and Known Confounders

Variables	B	S.E.	Sig.	Odds Ratio	95% C.I.for Odds Ratio	
					Lower	Upper
Smokers	.078	.650	.905	1.081	.302	3.865
Cadmium	-.098	.500	.844	.907	.340	2.417
Breastfed children	-.219	.599	.715	.804	.248	2.600
Mobilized Lead	.604	.703	.391	1.829	.461	7.255
Born outside the USA	.853	.901	.344	2.346	.401	13.716
Pre-diabetic/Diabetic	-1.167	1.066	.273	.311	.039	2.514
Asthma	-1.376	1.078	.202	.253	.031	2.088
Aged >50 years*	1.751	.800	.028	5.763	1.202	27.621
Ethnic	.066	.594	.911	1.068	.334	3.421
Income > $75,000	-2.132	1.111	.055	.119	.013	1.046
SSRI or corticosteroid use*	1.199	.578	.038	3.316	1.068	10.296
Constant	-4.995	.881	.000	.007		

Note: SSRI=Selective Serotonin Reuptake Inhibitors

* Significant at the 0.05 level

Note: R^2 = .023 (Cox & Snell), .229 (Nagelkerke). Model χ^2 =25.73, p =.009.

There were a small number of cataract surgeries; however, age was the variable that was most predictive regarding whether a participant would have had cataract surgery. The use of selective serotonin inhibitors or glucocorticoids was predictive of cataract surgery in this sample of women even though the sample was small. However, due to the small number of cataract surgeries, the predictive power of the model with variables was not improved over the null model.

(a) Backward Logistic Regression (LR) of 1105 cases with general vision issues and mobilized lead with various covariates yielded the following significant information:

Table 50

Logistic Regression Results for General Vision Issues

Variables	B	S.E.	Sig.	Odds Ratio	95% C.I. for Odds Ratio	
					Lower	Upper
Aged > 50 years	.110	.147	.455	1.116	.837	1.488
Asthma	.293	.164	.074	1.341	.972	1.851
Born outside the USA	-.102	.187	.584	.903	.626	1.302
Breastfed children	-.197	.126	.116	.821	.642	1.050
Cadmium*	.215	.098	.029	1.240	1.023	1.504
Hispanic/Mexican-Hispanic*	.466	.151	.002	1.593	1.184	2.144
Income>$75,000*	-1.167	.189	.000	.311	.215	.451
Mobilized Lead	.115	.179	.521	1.122	.790	1.593
Prediabetic-/Diabetic*	.356	.159	.025	1.428	1.046	1.950
Smokers*	.346	.134	.010	1.413	1.087	1.837
SSRI or corticosteroid use*	.409	.161	.011	1.505	1.098	2.064
Constant	-1.050	.190	.000	.350		

Note: SSRI=Selective Serotonin Reuptake Inhibitors

* Significant at the 0.05 level
Note: R^2 = .08 (Cox & Snell), .12 (Nagelkerke). Model χ^2 =116.84, p =.00.

Table 46 showed that mobilized lead did not contribute significantly to the model. However, the model with variables included improved the number of cases of vision issues predicted over the null model from 68.9 percent cases to 70.5 percent.

Backward Logistic Regression (LR) of general vision issues with cataract operations and mobilized lead with breastfeeding, age, smoking status yielded the following significant information:

Table 51

Logistic Regression Results for General Vision Issues with Cataract Surgeries

Variables	B	S.E.	Sig.	Odds Ratio	95% C.I. for Odds Ratio	
					Lower	Upper
Aged >50 years	.067	.156	.667	1.069	.788	1.452
Asthma	.254	.164	.122	1.289	.934	1.779
Born outside the USA	-.135	.188	.473	.874	.605	1.263
Breastfed children	-.201	.125	.108	.818	.641	1.045
Cadmium*	.215	.098	.028	1.240	1.024	1.502
Hispanic/Mexican-Hispanic*	.404	.150	.007	1.497	1.116	2.009
Income $75,000 or over*	-1.213	.188	.000	.297	.206	.430
Lead> 1.10 ug/dL	.169	.138	.219	1.184	.904	1.551
Mobilized lead	.142	.177	.422	1.153	.815	1.632
Prediabetic-/Diabetic*	.356	.158	.024	1.428	1.048	1.944
Smokers*	.345	.133	.009	1.412	1.088	1.833
SSRI or corticosteroid use*	.489	.158	.002	1.630	1.197	2.220
Constant	-.924	.186	.000	.397		

Note: SSRI=Selective Serotonin Reuptake Inhibitors

*Significant at the 0.05 level
Note: R^2 = .08 (Cox & Snell), .12 (Nagelkerke). Model χ^2 =114.08, p =.00.

Backward logistic regression of all vision cases was constructed for comparison. The vision variables included were glaucoma, macular edema, macular hole, and retinopathy. The results were similar to results obtained with backward regression of general vision issues and cataract surgeries but the model's predictive ability was better with a final prediction of 71.0 percent correct over 69.8 percent predicted by the null model. The results of the logistic regression are shown in Table 52.

Table 52

Logistic Regression Results for All Vision Issues Combined

Variables	B	S.E.	Sig.	Exp(B)	95% C.I.for EXP(B)	
					Lower	Upper
Aged >50 years*	1.612	.174	.000	5.013	3.562	7.055
Asthma	.105	.185	.571	1.111	.773	1.596
Born outside the USA*	-.458	.139	.001	.633	.482	.831
Breastfed children	-.039	.135	.772	.962	.738	1.253
Cadmium	-.045	.108	.679	.956	.773	1.182
Ethnic	-.328	.302	.277	.720	.398	1.302
Income > $75,000	-.250	.189	.186	.779	.537	1.128
Lead>1.10ug/dL	.170	.140	.227	1.185	.900	1.561
Mobilized Lead	.083	.211	.694	1.087	.718	1.643
Prediabetic-/Diabetic*	.490	.191	.010	1.632	1.122	2.372
Smokers*	.318	.126	.011	1.375	1.074	1.760
SSRI or corticosteroid use*	.616	.184	.001	1.851	1.291	2.653
Constant	.135	.116	.242	1.145		

Note: SSRI=Selective Serotonin Reuptake Inhibitors

.831

Note: R^2 = .11 (Cox & Snell), .16 (Nagelkerke). Model χ^2 =165.92, p =.000.

Additional Statistical Tests

The inverse relationship between being born outside the U.S.A. and poor vision was unexpected. Therefore, Chi-square analyses were performed to test the significance of the difference in incidence of cataract surgeries and vision issues between women who were born in the USA and women who were born elsewhere. The results are shown in Table 49.

Table 53

Significance values for Chi-square analysis between Born in the U.S.A. and Vision Variables

Location of Birth	Cataract Surgeries	General Vision Issues	All Vision Issues
Born in the U.S.A. (one-tailed p value)	.138	.000	.000
Born in the U.S.A. (two-tailed p value)	.328	.000	.000

Cataract surgery cases were then classified by location of birth (U.S., Mexico, other Spanish-speaking country, or elsewhere) in order to determine where the women who had cataract surgeries were born. Classification of the cataract surgery cases by place of birth is shown in Table 54.

Table 54

Cataract Surgeries by Place of Birth

Location of Birth	Frequency	Percent of Total # Cataracts	Number born in Location	Percent born in Location
Born in 50 U.S. States or Washington, DC	8	61.5	1066	75.3
Born in Mexico	3	23.1	159	11.2
Born in Other Spanish Speaking Country	2	15.4	78	5.5
Born Elsewhere	0	0.0	113	8.0
Total	13	100.0	1416	100.0

An inverse relationship between breastfeeding and poor vision was anticipated. However, the relationship was not significant when other confounders such as smoking, age, and income were included in the logistic regression model. Therefore the association

between breastfeeding and the vision variables – cataract surgeries, general vision issues, and all vision issues – was investigated with Chi-square analysis to determine the significance of the difference in vision between women who had ever breastfed and women who had not. The results of the analyses are shown in Table 55.

Table 55

Significance Values for Chi-square Analysis Between Ever Having Breastfed and Vision Variables

Statistic	Cataract Surgeries	General Vision Issues	All Vision Issues
Breastfed a child (one-tailed p value)	.448	.006.	.002
Breastfed a child (two-tailed p value)	.779	.010	.004

Ethnicity is a nominal categorization. Individuals of Hispanic and Mexican Americans origin were found to be at risk for general vision issues and general vision issues and cataract surgeries combined. Cataract surgeries were tabulated by ethnicity to understand just how many of the cataract surgeries were attributed to Hispanic American, Mexican American and individuals of the other ethnic groups. The results of the categorization by ethnic group are shown in Table 56.

Table 56

Cataract Surgeries by Ethnic Group

Ethnic Group	Frequency	Percent	Number in Sample	% of Total Sample
Non-Hispanic White	8	62	641	45
Mexican American	3	23	259	18
Other Hispanic	2	15	112	8
Non-Hispanic Black	0	0	339	24
Other Ethnic Groups	0	0	65	5
Total	13	100	1416	100.0

Summary

Research Question One

Logistic regression of cataract cases and data on mobilization of lead in perimenopausal women in the NHANES 2005-2008 surveys did not reveal any statistically significant association between mobilized lead and cataracts (p>0.5). The odds ratio of each category of the variable Mobilized Lead included the number one. However, closer examination of the data revealed the possibility of clinical significance between lead levels above the median and the need for cataract surgeries (p=.06). The null hypothesis could not be rejected.

Research Question Two

Analysis of the data revealed an association between mobilized lead and general vision problems in perimenopausal women (p=.015) and odds ratio = 1.50 (1.08-2.09). However, the association was weak as evidenced by the small R square values and the fact that the full model did not improve on the number of cases predicted by the null

model. Although, the association is weak, based on the value of alpha and the confidence interval of the odds ratio that does not include one; the null hypothesis was rejected.

Research Question Three

There were insufficient cataract cases for a valid chi square analysis of cataract cases and mobilized lead. However, analysis of cataract cases combined with general vision problems revealed a significant difference between cases of cataracts in women with evidence of mobilized lead and women who did not have evidence of mobilized lead at the one-tailed level but not at the two-tailed level. The difference is significant because chi-square analysis of general vision problems and mobilized lead without the inclusion of cataracts did not reveal an association between the two conditions. The null hypothesis was rejected.

Research Question Four

Logistic regression analysis revealed that age and the use of selective serotonin reuptake inhibitors (SSRIs) was a significant factor in the incidence of cataract surgeries (*OR* = 5.72, $p < .05$, 95% CI [1.20, 27.34]; *OR* = 3.31, $p < .05$, 95% CI [1.01, 10.30]; respectively) but mobilized lead was not (p=.39). Besides age and SSRIs, a diagnosis of pre-diabetes/diabetes, and having the characteristics of being born in a foreign country, income above $75,000, and being Hispanic or Mexican-American heritage contributed to the models for non-specific vision issues, non-specific vision issues and cataracts and all vision issues combined. However, mobilized lead did not contribute. Therefore, the null hypothesis that mobilized lead has no association with the incidence of cataracts in perimenopausal women when age is considered could not be rejected. The null

hypothesis for an association between mobilized lead and general vision issues when age and other confounders are included in the analysis also could not be rejected.

In the next chapter, the results of the analyses for the four research questions are discussed. Confirmations or disconfirmations of the results of previous studies are reported and the limitations and generalizability of the study will also be stated. In the final section of the discussion chapter, the significance of the study and implications for social change are addressed.

Chapter 5: Discussion, Recommendations, and Conclusion

Introduction

The purpose of this study was to determine whether there is any association between lead mobilized during the perimenopausal years and the incidence of cataracts or general vision-related issues observed in women worldwide. Investigators of a 2004 study found a significant association between endogenous lead and cataracts in elderly men (Schaumberg et al., 2004). A similar study conducted in 2013 on women aged 55 to 70 years was negative for an association between lead and cataracts (Park et al., unpublished). However, literature review did not reveal any research that addressed the mobilization of lead that occurs during the perimenopausal years as a possible causative factor for the higher risk for vision issues and the higher incidence of cataracts in women. This study was conducted to help close the gap in the literature regarding a possible cause for the phenomenon of earlier incidence for cataracts and higher risk for vision issues in women seen worldwide.

This study was specifically designed to investigate the mobilization of endogenous lead in women using a younger population than Park et al.'s unpublished 2013 study. The sample for this study was drawn from women in their perimenopausal years (aged 40 to 55 years) who had participated in the National Health and Nutrition Examination Surveys during the years 2005-2006 and 2007-2008. Blood lead levels and data on vision issues and cataract surgeries were examined in order to determine whether there was any association between mobilized lead and cataracts or vision issues. Elevated

alkaline phosphatase levels without corresponding elevated levels of total bilirubin were interpreted as evidence of bone demineralization.

For this study, I used the attainment of menopause as an additional indicator that bone lead mobilization could have occurred based on the work of Ruegsegger et al. (1984) and Machida et al. (2009). The laboratory test results for total bilirubin and alkaline phosphatase, bone mineral density measurements, and self-reported age at menopause were included in the examination in order to ascertain whether elevated levels of lead were due to a possible demineralization of bone. The results of ophthalmologic examinations for retinopathy, macular degeneration, as well as responses to questionnaires on difficulty with vision or ever had cataract surgeries were used to compile the dependent variables for vision.

Key Findings

The key finding of this study was that evidence of cataractogenesis in perimenopausal women with evidence of bone lead mobilization was significantly different from evidence of cataracts in perimenopausal women with no evidence of bone lead mobilization. The significance was a derived significance because 13 cataract surgeries were insufficient for a Chi-square analysis to be performed. However, Chi-square analysis with general vison issues did not yield a significant result ($p = .090$, two-tailed; $p = .053$, one-tailed) but Chi-square analysis with the 13 cataract surgeries plus general vision issues yielded a significant result at the one-tailed level ($p = .039$).

Another important finding was that there was a relationship between elevated blood lead levels and general vision problems in perimenopausal women. Elevated lead

levels without evidence of mobilization (*OR* = 1.37, p = .13, 95% CI [1.07, 1.75]) and mobilized lead (*OR* = 1.50, p = .015, 95% CI [1.08, 2.09]) were significant contributors to the model when no confounders were included. However, the null hypothesis could not be rejected for the remaining research questions. The results are summarized in Table 57 below.

Table 57

Answers to Research Questions

Research Question	Null Hypothesis Rejected
1. Is there a relationship between the incidence of cataracts and elevated blood lead levels in perimenopausal women when there is evidence of bone turnover?	No
2. Is there a relationship between elevated blood lead levels and general vision problems in perimenopausal women?	Yes
3. Is evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization?	Yes
4. Is the evidence of cataractogenesis or general vision-related problems in perimenopausal women with evidence of bone lead mobilization significantly different from the evidence of cataracts or general vision-related problems in perimenopausal women with no evidence of bone lead mobilization when the data is controlled for age?	No

The methods used to extract the data from the National Health and Nutrition Examination datasets and prepare the data for the analyses were validated by the results of the logistic regression analyses for research question four. Many of the covariates gleaned from the literature review, such as age, smoking, and the use of corticosteroids;

were positively associated with either cataracts or general vision issues. The complete list of contributing covariates included diabetes (Lindblad et al., 2008; Olafsdottir et al., 2012), selective serotonin reuptake inhibitors and glucocorticosteroids (SSRI, 2010), age (Kanthan et al., 2008), smoking of cigarettes (McCarty et al., 1999), elevated levels of cadmium (Mosad et al., 2010), and a higher risk for vision issues if an individual were Hispanic or Mexican American (Broman et al., 2005).

Cataractogenesis is a slow process that takes years to develop (Brown et al., 1999). Therefore the finding that age increased the odds ratio for cataract surgeries (p =.028) in this sample of women validated the analysis. This finding also confirms reports of previous studies such as the report of Zambelli-Weiner et al. (2012). Other significant contributors to vision problems in this sample of women were diabetes, selective serotonin reuptake inhibitors and glucorticosteroids, smoking, elevated cadmium blood levels, and being of the Hispanic or Mexican-American ethnic group. Asthma was not found to be a significant contributor.

Covariates negatively associated with vision issues were income higher than $75,000 per year and being born outside of the United States of America. Individuals who had breastfed their children had a reduced risk for vision issues including cataract surgeries, but the reduced risk was not significant when the analysis included known predictors of poor vision such as SSRIs and glucocorticoids, smoking, diabetes, and cadmium (OR = 0.82, p = .11, 95% CI [0.64, 1.05]). The covariables that were significantly associated with cataract surgeries were SSRIs and age. Covariables that were significantly associated with general vision issues and general vision issues plus

cataract surgeries were being Hispanic-or Mexican-American, income level, a diagnosis of diabetes or prediabetes, smoking status and use of SSRIs or corticosteroids. Mobilized lead was weakly associated with general vision issues only in the absence of confounders. Age, being born outside of the U.S.A., a diabetes or prediabetes diagnosis, smoking status and SSRI or corticosteroid use were all significantly associated with all vison issues combined. The significance of the associations between the covariables, mobilized lead, and the dependent variables – cataract surgeries, general vision issues, general vision issues with cataract surgeries, and all vision issues – are graphically illustrated in Figure 11 below.

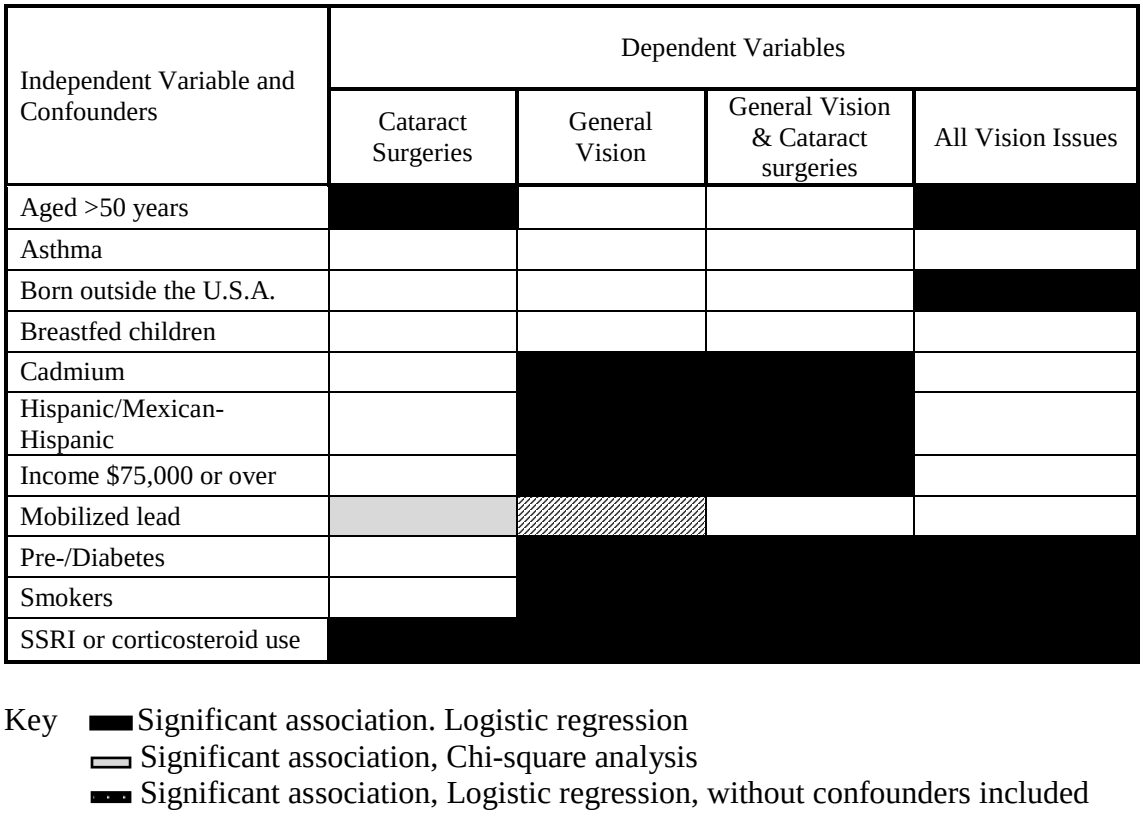

Figure 11. Graphic representation of results of logistic regression and Chi-square analyses.

Interpretation of the Findings

In Context of Previous Findings

This study extends the knowledge regarding cataracts in women and lead as a possible causative factor for cataracts. The landmark study on lead and cataracts was published by Schaumberg et al. in 2004, who only examined men older than 60 years (Schaumberg et al., 2004). In an unpublished study in 2013, Park et al. analyzed data on cataract surgeries and bone lead in women aged 55 to 70 years. The women in my dissertation study were aged 40 to 55 years. At the time of writing, this appears to be the first study regarding a possible association between lead and cataract surgeries in perimenopausal women.

The results of this study indicate that there is a significant difference in the incidence of cataract surgeries between women who have evidence of mobilized lead and women who do not. This association was deduced from the results of the Chi square analyses of mobilized lead and vision issues with cataract surgeries ($p < .05$) and mobilized lead and vision issues without cataract surgeries ($p > .05$). The level of significance was deduced with only 13 cases of cataract surgery out of a total number of 1,416 survey respondents. These Chi-square analysis results are different from the results obtained by logistic analysis between bone lead content and cataract surgeries for women aged 55 to 70 years: Park et al. (unpublished) did not find any significant association in their study. The difference in results underscores the importance of method selection for comparative study. By choosing Chi-square analysis as one of the methods for determining association between mobilized lead and cataract surgeries, I was able to

show that lead can be considered a possible causative factor for-vision issues in perimenopausal women.

Logistic regression analysis of the cases in this study yielded no significant association between mobilized lead and cataract surgeries but there was significant association between mobilized lead and vision issues in this sample of perimenopausal women. The positive coefficient for mobilized lead indicated that the relationship between mobilized lead and vision issues was direct. The significance of the relationship between lead and vision issues diminished, however, when known confounders such as age, smoking, diabetes status, selective serotonin reuptake inhibitor and corticosteroid use, ethnicity, born outside the USA, and income level were included in the analysis. Once the confounders were considered, the results of logistic regression analysis of the data matched the results obtained by Park et al. (unpublished).The similarity in results between the two studies indicates there could be a weak association between lead and cataract surgeries in Park et al.'s study that was similarly masked by the stronger covariables. On the other hand, due to the age of the women in Park et al.'s study; such an association may not exist.

A noteworthy finding in this study was that blood lead levels have continued to decline throughout the decades since the United States Congress banned lead from gasoline in 1970 (Callendar & Van Metre, 1997; Pirkle et al., 1994): The mean blood lead level in the sample of perimenopausal women during the years 2005 to 2008 was 1.50 micrograms per deciliter; lower than 2.76 micrograms per deciliter in 1994 and 1.64 micrograms per deciliter in 2002 (Muntner et al., 2005). This finding mirrors the 2009

report of decreased blood lead levels in U.S. children (Jones et al., 2009). However, this research study was conducted to determine whether there is any association between mobilized lead and cataracts and general vision problems in perimenopausal women. Therefore, data of vision issues in women with no evidence of mobilized lead was compared with data of vision issues of women with evidence of mobilized lead in order to determine if there was any significant difference. The result indicated there was a significant difference between these two groups of women (p = .039, one-tailed). This result validates the result of the case control study of Schaumberg et al. (2004). This study also extends knowledge in the discipline since the data analyzed were from perimenopausal women; a group that has not been studied for an association between lead and vision issues before.

The information gleaned from this study should be representative of the women of the perimenopausal age group during the years 2005-2008 because according to the Centers for Disease Control and Prevention (2014a), sampling techniques were used to reduce bias in the National Health and Nutrition Examination Surveys. Also, age-by-age comparison between the women in this sample and the women in United States census estimates of 2010 did not reveal any significant differences between the two groups. The minimum sample size for this case control study was determined as 143 cases and 143 controls for 80 percent power. The sample sizes for the two previous studies on cataracts and lead were 642 and 502 (Schaumberg et al., [2004] and Park et al. [unpublished]; respectively). The sample size for this study was 1,416. Therefore, based on sample size and sampling technique, the design of this research study compares well with the designs

of the previous studies on lead and cataracts and the results can be considered to be valid. In addition, when the age group and of the individuals and the low levels of lead are taken into account, the results of this study extend our knowledge of lead and cataracts.

The validity of this study is confirmed by the results of the logistic regression analyses. Many of the significant covariates in this study were significant independent variables in previous analyses: Age (Kanthan et al., 2008), cadmium levels (Mosad et al., 2010), corticosteroid and selective serotonin reuptake inhibitor use (SSRI, 2010), diabetes (Olafsdottir et al., 2012), smoking (McCarty et al., 1999), and being Hispanic or Mexican American (Broman et al., 2005) increase the risk of cataract and/or vision issues. In this study, inverse risks were associated with high income and being born outside the U.S.A. The former is a known inverse risk factor for cataracts and other vision problems and confirms the results obtained by Hunt et al. (2009), Klein and Klein (2013), and Zambelli-Weiner et al. (2012). However, review of the literature did not reveal that being born in the U.S.A. is a risk factor for vision issues. Cooking with biomass fuels is a risk factor for developing cataracts (Mishra et al., 1999) and exposure to UV radiation (Hollows & Moran, 1992) is another independent risk factor for cataracts. Based on these two factors, women were categorized into born in the U.S.A. and born elsewhere. Therefore the finding that being born inside the U.S.A. was an independent risk factor for vision-related issues in this group of women was unexpected.

The phenomenon of being born in the U.S.A. as a significant risk factor for vision issues was further investigated with follow-up Chi-square analysis between the variable born in the U.S.A. and cataract surgeries, general vision issues, and all vision

issues. Cataract surgeries were also tabulated by place of birth. The results are shown in Tables 49 and 50 in chapter four. The Chi-square analyses validate the association observed in the logistic regression. There was no difference in the number of cataract surgeries between the women born in the U.S.A. and women born elsewhere but the categorization in Table 50 in chapter four shows that all the women born elsewhere who had cataract surgeries were either born in Mexico or another Spanish-speaking country. Thus the results of additional analyses validated the work of Broman et al. (2005) but added no new information regarding the reason for the apparent disparity in vision issues between women born in the U.S. and women born elsewhere: A custom-designed study is needed to elicit the cause of the unexpected finding.

Anticipated results of the study included the confirmation that the odds of having cataract surgery are higher for non-Hispanic white individuals as well as Hispanic/Mexican Americans. Based on a previous research which indicated that women who had ever given birth to children had lower blood lead levels during perimenopausal osteopenia than women who had not (Silbergeld et al., 1988) and the hypothesis for this study, I expected an inverse relationship between the breastfeeding variable and vision issues. Breastfeeding was chosen, and not parity, since it can be assumed that a woman who has breastfed a child has also given birth to a child and therefore has been doubly exposed to leaching of lead from the bones prior to the perimenopausal period. As I expected, the coefficient for the breastfeeding variable was negative in every logistic regression analysis. However, the inverse relationships were not significant (p values ranged from .72 to .12). It appeared that, like lead, the significance of having breastfed a

child in this sample of women was masked by the influence of confounders such as smoking, corticosteroids/SSRIs, and age. Therefore additional studies were performed to determine whether women in the sample who had ever breastfed their children had vision issues that were significantly different from the women who had never breastfed their children. The results shown in Table 51 indicate that there was a significant difference between the two groups of women.

Asthma was listed as a predictive factor for cataract surgeries in the results of one study; this finding was not substantiated in this study (Delcourt et al., 2000). However, the, use of corticosteroids which may be used to treat asthma was confirmed as a confounding factor for cataracts. The previous finding by Mishra et al. (1999) that cooking with biomass fuel causes cataracts was not substantiated in this sample of women; more American-born women had cataract surgeries than women who were born outside of the United States. However, overall the validity of the study is confirmed by the number of previous results confirmed by the results of this study.

In Context of Theoretical Concepts

The theoretical framework for this research study was constructed from epidemiological and clinical studies conducted in the past five decades and social cognitive theory (SCT). The premise of the study is that lead sequestered in the body during a woman's lifetime is released into the blood stream as the bones begin to thin in the perimenopausal years. The mobilized lead then reaches the lenses of the eyes and through any of several processes causes the lenses to cloud. Bone lead mobilization in men is a gradual process but in women, the process is more rapid. The release of lead in

the blood stream in the middle years has been reported to cause hypertension, neurological disturbances, and kidney disease (Hu et al., 1996; Nash et al., 2003; Weuve et al., 2009). The hypothesis for this study was that bone lead mobilization is a possible cause for the earlier appearance of cataracts and the higher risk for vision-related issues in women. The reason for performing the study was, based on social cognitive theory. It is expected that individuals will make an effort to undertake the necessary changes once they have appropriate information. They will do so because of moral detachment, observational learning, self-regulation, and the ability to control environmental factors (McAlister et al., 2008).

This is believed to be the first study with results that show any evidence of an association between lead released during the perimenopausal years and cataract surgeries. The association is not as pronounced as the association exhibited by predictive factors such as diabetes and corticosteroids. However, the association is present (as evidenced by the Chi-square analyses) and may be the reason that women worldwide have vision issues for which no distinctive cause has yet been found. One of the strong reasons that points to mobilized lead as being a positive predictive factor for the low occurrence of vision problems, are the results of the follow-up Chi-square analysis between ever having breastfed and vison issues. The results revealed significant differences in vision issues between women who have breastfed their children and women who have not. The coefficient for the breastfeeding variable was negative in the logistic regression analysis and therefore it appears that the leaching of lead in the gestation and lactation periods of

the women's life cycles lowered the women's risk for vision related issues in the perimenopausal years.

The results of this research study indicate that the low-level association between mobilized lead, general vision issues, and cataracts is masked by stronger confounding factors in epidemiological studies. Alternately, the association may have been weak because whole blood lead levels and not plasma lead levels are examined. According to Hu and Hernandez-Avila (2002), plasma lead levels may be a much better indication of lead mobilized from bone than whole blood lead levels because lead bound to red blood cells is not as available. In the data available for this research study, only whole blood lead levels were available.

Bone lead storage, and specifically, storage of lead in the long bones, is generally regarded as an excellent measure of lifetime exposure to lead. However, it is mobilized lead that causes deleterious effects in the body; not lead in stored in the bones (Silbergeld et al, 1988). According Ruegsegger et al. (1984), the period when lead is mobilized in women post menopause may as be short as two years. Based on the work of Armamento-Villareal (1992), bone demineralization and thus, lead mobilization may begin before menopause due to some individuals' declining estrogen levels. Therefore, based on where each woman is in her menopausal transition, unlike men, bone lead content may not be a significant predictor of the deleterious effects of mobilized lead. I believe women should be grouped by biological status and not by chronological years in order to generate data that can illustrate the effect of mobilized lead. In this study, menopausal status was factored into the analysis in order to determine if there was

evidence of mobilization of endogenous lead. Elevated alkaline phosphatase levels with no evidence of elevated total bilirubin and decreased bone mineral density were also included in the analyses in order to make use of the women's biological status.

Lifetime exposure to endogenous lead was considered to be indicative of possible damage to the lens of the eyes in men older than 60 years (Schaumberg et al., 2004). However, the premise of this research study is that the mobilization of lead in women, not inert storage of lead in the bones is a possible cause for the non-specific vision issues and high risk of early cataracts women experience in the postmenopausal and perimenopausal years. The release of lead from the bones is precipitous in women but not as pronounced in men (Hernandez-Avila et al. 2000). Therefore, there is a very narrow window when increased endogenous lead exposure and the beginning of vision issues can be measured. In order to establish proximal damage to the lens and to account for the small window of time when there is rapid exposure to lead, blood lead levels, not so much bone lead levels, are necessary to make a determination regarding exposure to elevated levels of endogenous lead. The use of women's biological status and the decision to focus on the perimenopausal years has resulted in the identification of an association between cataracts and endogenous lead using Chi-square analysis. The results indicate that the hypothesis and the approach to the study were justified.

Limitations of the Study

Cataract surgeries can be used as one criterion for assessing vision-related problems in this sample of perimenopausal women; it is not the major criterion. The reasons are multiple: First, gradable cataracts may take years to develop (Brown et al.,

1999); therefore the length of time that it takes cataracts to develop is beyond the scope of this study. Second, the American Optometric Association (2004) advised eye care specialists that cataract surgeries are indicated when the presence of lens opacities interferes with patients' routine activities; the recommendation was not based on the grade of the cataract. Third, the odds that Caucasians will have cataract surgery are 2.8 times higher than the odds for African Americans (West et al., 1998). The odds of having cataract surgery may also be greater in individuals who are Hispanic (Broman et al., 2005). Fourth, underutilization or lack of access to vision care that includes lack of access to surgery may be the reason that individuals may not have cataract surgeries (Sommer et al., 1991). Fifth, individuals with postsubcapsular cataracts are more likely to have surgery to remove the cataract than those individuals who have cortical cataracts or nuclear cataracts without a subcapsular component because subcapsular cataracts can interfere with routine activities at smaller grade levels (Belpoliti et al., 1995; Kanthan et al., 2008; McCarty et al., 2000). Therefore, without standardized grading and the inclusion of gradable cataracts, the results of the analysis for cataract surgeries cannot be extrapolated to all cases of cataracts in this sample of perimenopausal women.

Another limitation was the number of cataract surgeries found in this sample of women: The number of surgeries was insufficient to conduct a valid Chi square analysis. However, it was sufficient to change an insignificant *p* value for general vision issues only to a significant *p* value when the two categories – general vision issues and cataract surgeries – were combined. The coefficient for mobilized lead in the logistic regression analysis was positive. Thus, the association between mobilized and cataract surgeries can

be interpreted as direct and not inverse. Based on all of the foregoing, the finding that women with mobilized lead have an incidence of cataract surgeries that is significantly higher than women who do not have mobilized lead is noteworthy.

The significant finding that mobilized lead is associated with cataracts can only be generalized to women between the ages of 40 and 55 years since only the 40-55 year age group was studied. The age of the study may also contribute to its limitations: No ophthalmologic examination data for cataracts were available in the 2005-2008 surveys and no data from ophthalmologic examinations were available in the years since then. Therefore, years since the survey data were collected and the general trend of blood lead levels in the United States in recent decades should be factored into any interpretation of the data.

No dose response relationship was elucidated in this study. Researchers of the Harvard University School of Public Health and the University of Montreal conducted a study of the National Health and Nutrition Examination Survey data and found that there was a significant association between lead and certain mental health issues (Get the lead out, 2010). The study design was similar in concept to this study but the researchers could not find a linear association between blood lead levels and mental health issues. Get the Lead out (2010) reported that the design was criticized because bone lead levels which are more stable than blood lead levels were not included in the design. However, I believe that since blood is the proximal source of lead to the brain or eyes, the analysis of blood levels should first be addressed before bone lead levels are similarly studied. Once

a proximal relationship is established as was attempted in this study; then the possibility of a linear dose response could be further investigated.

Recommendations for Further Research

The first recommendation for further research is a case control study between perimenopausal women with elevated bone lead levels and signs of bone lead mobilization and perimenopausal women with various bone lead levels and no signs of bone lead mobilization. Signs of bone lead mobilization would include elevated levels of blood lead. The dependent variables in the study would be general vision issues and cataracts identified through ophthalmologic examinations and records of cataract surgery. The aim of a study with cataracts as the dependent variable and bone lead level as the independent variable would be to ensure that the sources of the elevated lead are in the long bones of the survey respondents. The verification of lead levels in the bone would be important for establishing mobilized endogenous lead as the source of the elevated levels of lead in the blood and thereby the source of the proximal damage to the eye lenses. In total, the various steps would provide additional confirmation of the hypothesis for this research study.

The second recommendation for further research is a prospective study for vision issues including cataracts in a cohort of women who are in their perimenopausal years. The study would entail the use of periodic bone lead scans and clinical laboratory analysis for plasma lead levels and bone mobilization markers, as well as periodic ophthalmologic examinations that include the gradation and documentation of types of cataracts. For both the proposed case control study and longitudinal study, the analysis of

stable lead sources in the bones would address the perceived need to demonstrate a linear association between lead levels and vision issues that may include cataracts. In addition, a longitudinal study could establish a sequential timeline effect which is important for establishing a variable as a causative factor. The inclusion of bone lead measurements would ensure there is a stable lead source and would reduce the criticism that Get the Lead Out (2010) reported for other studies on endogenous lead.

The recommendation for ophthalmologic examination is based on the report of the Eye Disease Prevalence Research Group who stated than 17.2 percent of individuals over the age of 40 have cataracts in one or two eyes and the report that 8.6 percent of individuals over the age of 18 have cataracts (Congdon et al., 2004; Ryskulova et al., 2008). Based on the prevalence reports, the number of individuals with cataracts in the sample of 1416 women was underrepresented. Cataract surgeries are based on access to healthcare; the inability to perform routine tasks, and discomfort that may result from the type of cataract that the individual has. Therefore, further research should include standardized ophthalmologic measurement for cataracts; not just the record of surgeries previously performed. Ophthalmologic examinations would also provide details on whether the cataracts that may be associated with mobilized lead are postsubcapsular, nuclear or cortical.

Aside from prevalence studies, additional studies are needed to ascertain what role, if any, mobilized lead plays in the female gender's higher risk for vision issues. The decision to have surgery is not dependent on the grade of cataract; but on the individual's level of discomfort and access to healthcare among other factors. Therefore, although this

research study showed that some variables (namely age and SSRIs and glucocorticoids) were significantly associated with cataracts, the result does not disqualify lead as a possible factor for cataracts. The main reasons lead should not be disqualified are the low-level associations between mobilized lead and cataracts (Chi-square analysis) and low-level association between mobilized lead and general vision issues as evidenced by the results of the logistic regression without the inclusion of strong confounders.

The low level associations that are barely discernible with the current methods used in this study seem to match the generalized, ambiguous deterioration in vision that affects women worldwide. The hypothesis is: Generalized demineralization of bone, leads to generalized release of lead, which leads to generalized problems with vision. In addition, the alpha value generated from the logistic regression of mobilized lead and the 13 cataract surgery cases in this study of 1,416 respondents, was just slightly outside the threshold of significance ($p=0.06$). In contrast, the alpha value for elevated lead levels without any evidence of mobilization for the same analysis was not close to the threshold of significance ($p = .74$). When all of the above factors are considered, the decision to have cataract surgery may have been based on the participants' access to healthcare, type of cataract, racial/ethnic disparities, socio-economic level, or any combination of these factors. Therefore logistic regression analysis in which mobilized lead drops out as predictor of cataracts when stronger predictors are added does not rule out lead as a possible causative factor for women's vision-related issues. Additional research is needed before lead can be ruled out.

The Chi-square analysis of mobilized lead and all vision issues yielded a very significant p value (p=0.003, two-tailed; p=0.001, one-tailed) unmatched by Chi-square analysis of mobilized lead with non-specific symptoms, or nonspecific visual symptoms combined with any of the named vision diseases – glaucoma, retinopathy, or macular degenerative changes. This phenomenon seems to indicate that more work should be conducted to determine which clinical vision symptoms are particularly affected by the presence of lead once lead is ruled in as a possible causative factor. Longitudinal studies and studies that include ophthalmologic examinations may provide definitive information on whether lead or some other agent may be the cause of the earlier and high risk for cataracts seen in women around the world.

An interesting phenomenon discovered during this research study is the finding that being born in the United States constituted a higher risk for vision issues than being foreign-born. Healthcare in the United States is costly and the assumption may be that the more costly the care; the better. However, the results of this research study indicate that costly care may not mean the best care for all U.S. citizens. The source of the disparity in vision between women born in the U.S. and women born elsewhere should be investigated with a study that is specially designed to ascertain the source of the problem.

Implications

Positive Social Change

The results of this study lends credence to the statement of the Centers for Disease Control and Prevention (2013a), "... there is no safe level of lead in blood". The mean blood lead level for the years 2005 – 2008 was 1.5 micrograms per deciliter, lower

than the mean value of 1.64 micrograms per deciliter reported for 2002 (Muntner et al., 2005). However, Chi square analysis revealed that even at such a low average level, there was an association between higher levels of lead and cataract surgeries. Since reports from past decades have already indicated that women are subject to mental issues, hypertension, and other lead related issues after reaching menopause, the findings of this study should provide a catalyst for health officials to make greater efforts to protect women from endogenous lead during the perimenopausal years.

Social cognitive theory dictates that we would use this information to make changes that would mitigate the damage from endogenous lead in women. The results of this preliminary analysis indicate that steps should be taken to protect perimenopausal women from the effects of endogenous lead. Even without the results of this study, there is sufficient evidence from previous studies to indicate steps should be taken to protect women's health. However, this preliminary research indicates that protecting perimenopausal women from endogenous lead should be a public health initiative especially since the deleterious effects of mobilized endogenous lead such as hypertension, renal issues, and cardiac diseases are already well-known.

In a country of advanced healthcare, more work needs to be done in the U.S to ensure that the benefits of advanced healthcare are available to more U.S. citizens. Data in the Central Intelligence Agency's (2014) World Factbook showed that the United States is the richest country in the world: The gross domestic product (GDP) of the U.S. was $17.3 billion and ranked at number one in the world in 2013. However, the U.S. is not ranked among the top five countries in the world for the average wealth or average

health of its citizens: Personal GDP was ranked fourteenth and life expectancy was ranked forty-second in the world (Central Intelligence Agency, 2014). The higher risk of U.S. women for vision-related issues may serve as an indicator for the health of successive U.S. generations since, according to Bezrucha (2005), an individual's maternal grandmother's health is the upstream determinant of that individual's health. Whether the American-born woman's greater risk for vision issues is due to less access to healthcare or greater access to cataract-inducing drugs or some other causative factor, disparities in preventive care should be eliminated. If the greater risk for vision problems is caused by use of inhaled corticosteroids (Smeeth et al., 2003), then alternatives should be sought and patients continued to be monitored for significant loss of vision. In any event, efforts should be made to ascertain the source of the problem. However the future studies are performed, the results of this study demonstrate the need to study women in the context of their biology, not as smaller versions of men when women's results in clinical studies do not match those of the male gender.

Theoretical Implications

The theoretical framework for this study was based on social cognitive theory (SCT). SCT encompasses the psychological determinants of behavior, moral detachment, influence of environmental factors, observational learning, and the ability to regulate oneself (McAlister et al., 2008). The significant finding in this study indicates an association between mobilized lead and non-specified vision problems in women. This finding cannot be considered sufficient to evoke a response in individuals to take efforts to curb the effects of endogenous lead, especially when environmental and blood lead

levels are declining. However, women are living longer in contemporary times and women may therefore experience significantly reduced quality of life years and impact the healthcare system in their later years if the deleterious effects of menopause are not addressed in a timely fashion.

Published scientific reports in the past decades have highlighted the ill effects of mobilized lead at menopause, yet there are no known public health efforts to screen women for lead at the critical biological phase. The situation is compounded by the fact that there are well-publicized reports about the ill-effects of smoking; yet people begin or continue to smoke. The results of the logistic regression analysis in this research study highlight the effects of smoking on vision. Informing perimenopausal women about the danger of the poison within" as described by Hu and Hernandez-Avila (2002) may not engender much response especially when individuals realize that environmental and blood lead levels have declined. It therefore behooves health officials to create changes in health policy to effect the necessary changes.

Recommendations for Action

The results of the study indicate there may be disparities in providing eye care to some ethnic groups. For example, being of Hispanic or Mexican American ethnic origin constitutes a higher risk for vision issues and cataracts that interfere with vision. Table 52 highlights the fact that the number of Hispanic and Mexican-Americans women in this subsample who had cataract surgeries was disproportionate to the size of this group of women in the sample. The disproportionate number of cataracts relative to the size of the group may indicate less access to visual health care (Zambelli-Weiner et al., 2012). Table

52 also contains data which illustrate the fact that no African American women had cataract surgery although African American women were 24 percent of the sample. According to Congdon et al. (2004), African American women under the age of 70 have a higher incidence of cataracts than their non-Hispanic White counterparts. The reason for the underrepresentation of African American women in the cases of cataract surgeries may be due to disparities or may be due to cataract type. However, wherever disparities exist, public health initiatives should be undertaken to ensure that all women have access to the primary care they need in order to reduce the risk for vision issues.

The underrepresentation of African American women in this sample of the United States population brings up an important point: Few prevalence studies for cataracts have been performed since the year 2000 (Klein and Klein, 2013). Therefore little information is available to explain the current prevalence of cataracts among the different ethnic groups in the United States. Based on previous studies that indicate that African American women have a high risk for cortical cataracts (Congdon et al., 2004), and a finding that African Americans in Baltimore were found to have unoperated cataracts (Sommer et al., 1991), the lack of reports of cataract surgeries in this ethnic group may indicate large disparities in the American healthcare system. In order to determine the depth of the problem, newer prevalence studies for vision status should be performed.

Conclusion

The “take home” message conveyed by this study is that smoking cigarettes and age continue to be strong predictors for cataracts and other vision-related issues in

women. However, the two predictors were not the only strong confounders in this study: Selective serotonin reuptake inhibitors and/or glucocorticoids were also strongly associated with all types of vision-related issues. Not all women smoke, nor are all women on the selective serotonin or glucocorticoid prescription medications, so the gap for the well-defined, ubiquitous causative factor for the higher risk of vision-related issues in women remains.

The results of the Chi square analysis showed that mobilized lead is significantly associated with cataracts when the strong predictors are not factored in. The results also indicate that that lead should not be ruled out as a possible causative factor for the global phenomenon of vision issues in perimenopausal women that has a vague source: The significant low-level association between lead and general vision issues that disintegrates when known predictors are factored into logistic regression models seems to fit women's ambiguous, generalized risk for vision problems. The low-level association may also explain the reason for the gap in the literature – the reason the cause of women's higher risk for vision issues has eluded investigators for the past few decades. However, more detailed research, tailored for women's biology needs to be performed to definitively identify the cause of the phenomenon.

This study appears to be the first study that addressed lead as a possible causative factor for the early and higher risks for cataracts while women's biology was taken into account. It should not be the last. As Dr. Marianne Legato, an expert in gender-specific medicine is reported to have stated, "Women are not little men" (DeCola, 2012). If an answer to a research question for women is not as readily apparent as it is for men,

then women's life cycle may hold the answer. Recognition of and allowance for this fact in study designs should help to resolve many enigmas that are female gender-specific.

References

Abadin, H., Ashizawa, A., Stevens, Y., Llados, F., Diamond, G., Sage, G., Swarts, S. (2007). *Toxicological profile for lead*. Retrieved from http://www.atsdr.cdc.gov/toxprofiles/tp13.pdf

Agency for Toxic Substances and Disease Registry, Centers for Disease Control and Prevention. (2011). *Lead*. Retrieved from http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=22

Ambrose, T., Al-Lozi, M., & Scott, M. (2000). Bone lead concentrations assessed by in vivo X-ray fluorescence. *Clinical Chemistry, 46*(8 Pt 1), 1171-1178.

American Optometric Association. (2004). *Care of the patient with cataracts (Clinical practice guidelines 8).* Retrieved from http://www.aoa.org/documents/optometrists/CPG-8.pdf

American Optometric Association. (2014). *Cataract*. Retrieved from http://www.aoa.org/patients-and-public/eye-and-vision-problems/glossary-of-eye-and-vision-conditions/cataract?sso=y

Armamento-Villareal, R., Villareal, D.T., Avioli, L.V., & Civitelli, R. (1992). Estrogen status and heredity are major determinants of premenopausal bone mass. *Journal of Clinical Investigation, 90*(6), 2464–2247.

Belpoliti, M., Rosmini, F., Carta, A., Ferrigno, L., & Maraini, G. (1995). Distribution of cataract types in the Italian-American case-control study and at surgery in the Parma area. *Ophthalmology, 102*(11), 1594-1597.

Bezruchka, S. (Producer). (2005). From womb to tomb: The influence of early childhood on adult health [Audio podcast]. Retrieved from http://www.alternativeradio.org/products/bezs002

Bouchard, M.F., Bellinger, D.C., Weuve, J., Matthews-Bellinger, J., Gilman, S.E., Wright, R.O. , Weisskopf, M.G. (2009). Blood lead levels and major depressive disorder, panic disorder, and generalized anxiety disorder in U.S. young adults. *Archives of General Psychiatry*, *66*(12), 1313-9.

Broman, A.T., Hafiz, G., Muñoz, B., Rodriguez, J. Snyder, R., Klein, R., & West, S.K. (2005). Cataract and barriers to cataract surgery in a US Hispanic population. *Archives of Ophthalmology, 123*, 1231-1236.

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

Brown, L., Rimm, E.B., Seddon, J. H., Giovannucci, E.L., Chasan-Taber, L., Spiegelman, D., … Hankinson, S.E. (1999). A prospective study of carotenoid intake and risk of cataract extraction in U.S. men. *The American Journal of Clinical Nutrition, 70*(4), 517-524.

Brown, M., & Margolis, S. (2012). Lead in drinking water and human blood lead levels in the United States. *Morbidity and Mortality Weekly Report. Surveillance Summaries (Washington, D.C.: 2002), 61*(Suppl 1-9).

Bruening, K., Kemp, F., Simone, N., Holding, Y. , Louria, D., & Bogden, J. (1999). Dietary calcium intakes of urban children at risk of lead poisoning. *Environmental Health Perspectives, 107*(6), 431-435.

Callendar, E., & Van Metre, P.C. (1997). Reservoir sediment cores show US lead declines. *Environmental Science & Technology, 31*(9), 424A-428A. doi:10.1021/es972473k

Center for Food Safety and Applied Nutrition. (2005). *Supporting document for recommended level for lead in candy likely to be consumed frequently by small children. [Docket No. 2005D-0481]*. Retrieved from http://www.fda.gov/ohrms/dockets/dockets/05d0481/05d-0481-ref0001.pdf

Centers for Disease Control and Prevention. (1998). Lead poisoning associated with imported candy and powdered food coloring -- California and Michigan. *MMWR,47*(48),1041-1043. Retrieved from http://www.cdc.gov/mmwr/preview/mmwrhtml/00055939.htm

Centers for Disease Control and Prevention. (2002). Childhood lead poisoning associated with tamarind candy and folk remedies – California, 1999-2000. *MMWR, 51*(31), 684-686. Retrieved from http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5131a3.htm

Centers for Disease Control and Prevention. (2007). Toxic anterior segment syndrome after cataract surgery --- Maine, 2006. *MMWR, 56*(25), 629-630. Retrieved from http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5625a2.htm

Centers for Disease Control and Prevention. (2012). *Lead*. Retrieved from http://www.cdc.gov/nceh/lead/ACCLPP/blood_lead_levels.htm

Centers for Disease Control and Prevention. (2013a). *Lead*. Retrieved from http://www.cdc.gov/nceh/lead/

Centers for Disease Control and Prevention. (2013b). *Lead hazards in some holiday toys*. Retrieved from http://www.cdc.gov/features/leadintoys/

Centers for Disease Control and Prevention. (2013c). *The 1999-2006 dual energy X-ray absorptiometry (DXA) multiple imputation data files and technical documentation*. Retrieved from http://www.cdc.gov/nchs/nhanes/dxx/dxa.htm

Centers for Disease Control and Prevention (CDC). (2013d). *Vision Health Initiative (VHI): Common Eye Disorders.* Retrieved from http://www.cdc.gov/visionhealth/basic_information/eye_disorders.htm

Centers for Disease Control and Prevention (CDC). (2014a). *National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. National Health and Nutrition Examination Survey. (2006-2008).* Retrieved from http://www.cdc.gov/nchs/nhanes.htm

Centers for Disease Control and Prevention. (2014b). *National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Questionnaire (or Examination Protocol, or Laboratory Protocol). Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, [2005-2006 & 2007-2008]*. Retrieved from http://www.cdc.gov/nchs/nhanes/nhanes_questionnaires.htm

Central Intelligence Agency. (2014). *The world factbook*. Retrieved from https://www.cia.gov/library/publications/the-world-factbook/

Cekic, O. (1998). Copper, lead, cadmium, and calcium in cataractous lenses. *Ophthalmic Research*, *30*(1), 49-53.

Champion, V.L., & Sugg Skinner, C. (2008). The Health Belief Model and stages of change. In K. Glanz, B.K. Rimer, & K. Viswanath. (Eds.), *Health Behavior and Health Education*. Wiley Publishing. Kindle Edition.

Chillrud, S.N., Bopp, R.F., Simpson, H.J., Ross, J.M., Shuster, E.L., Chaky, D.A., Yarme, A. (1999). Twentieth century atmospheric metal fluxes into Central Park Lake, New York City. *Environmental Science & Technology*, *33*(5), 657-662.

Chodick, G., Heymann, A., Flash, S., Kokia, E., & Shalev, V. (2010). Persistence with statins and incident cataract: A population-based historical cohort study. *Annals of Epidemiology*, *20*(2), 136-142. doi:10.1016/j.annepidem.2009.10.007.

Christen, W., Glynn, R., Ajani, U., Schaumberg, D., Buring, J., Hennekens, C., & Manson, J. (2000). Smoking cessation and risk of age-related cataract in men. *The Journal of the American Medical Association*, *284*(6), 713-716.

Christen, W., Liu, S., Glynn, R., Gaziano, J., & Buring, J. (2008). Dietary carotenoids, vitamins C and E, and risk of cataract in women: A prospective study. *Archives of Ophthalmology*, *126*(1), 102-109. doi:10.1001/archopht.126.1.102

Ciraj-Bjelac, O., Rehani, M., Sim, K., Liew, H., Vano, E., & Kleiman, N. (2010). Risk for radiation-induced cataract for staff in interventional cardiology: Is there reason for concern? *Catheterization and Cardiovascular Interventions: Official Journal*

of the Society for Cardiac Angiography & Interventions, 76(6), 826-834. doi:10.1002/ccd.22670

Congdon, N., Vingerling, J.R., Klein, B.E., West, S., Friedman, D.S., Kempen J., …Eye Diseases Prevalence Research Group. (2004). Prevalence of cataract and pseudophakia/ aphakia among adults in the United States. *Archives of Ophthalmology, 122*(4), 487- 494.

Cumming, S.R., Kelsy, J.L, Nevitt, M.C., & O'Dowd, K.J. (1985). Epidemiology of osteoporosis and osteoporotic fractures. *Epidemiology, Review, 7,* 178-208.

Cumming, R.G., & Mitchell, P. (1999). Inhaled corticosteroids and cataract: Prevalence, prevention and management. *Drug Safety, 20* (1), 77–84.

D'Agata, E. M. C. (2005). Methodologic issues of case–control studies: A review of established and newly recognized limitations. *Infection Control and Hospital Epidemiology, 26*(4), 338–341. doi:10.1086/502548.

DeCola, P. (2012) Gender effects on Health and Healthcare. In K. Schenck-Gustafsson, P.R. DeCola, D.W. Pfaff, & D.S. Pisetsky (Eds.). *Handbook of Clinical Gender Medicine.* Basel, Switzerland: Karger Medical and Scientific Publishers.

Delcourt, C., Cristol, J., Tessier, F., Léger, C., Michel, F., Papoz, L., & the POLA Study Group. (2000). Risk factors for cortical, nuclear, and posterior subcapsular cataracts: The POLA study. *American Journal of Epidemiology, 151*(5), 497-504.

Do, K., Treloar, S., Pandeya, N., Purdie, D., Green, A., Heath, A., & Martin, N. (1998). Predictive factors of age at menopause in a large Australian twin study. *Human Biology, 70*(6), 1073-1091.

Elder, M.J. (1997). The process of community involvement--a case study: The Bartlesville, Oklahoma, lead project. *Toxicology and Industrial Health*, 13(2-3):395-400.

Environmental Protection Agency. (1995). *Air quality trends – 1994*. Retrieved from http://www.epa.gov/airtrends/pdfs/aqtrnd94.pdf

Environmental Protection Agency. (2001). *Lead-safe yards: Developing and implementing and monitoring, assessment, and outreach program for your community.* Retrieved from http://www.epa.gov/region01/leadsafe/pdf/entire_document.pdf

Environmental Protection Agency. (2013). *Human health and lead.* Retrieved from http://www.epa.gov/superfund/health/contaminants/lead/health.htm

Field, A. (2009). *Discovering statistics using SPSS* (3rd ed.). London: Sage.

Food and Drug Administration. (2014). *Drugs.* Retrieved from http://www.fda.gov/Drugs/default.htm

Frommer, D. (1964). Changing age of the menopause. *British Medical Journal, 2*(5405), 349-351.

Get the lead out. (2010, March). *Harvard health publications. The Harvard mental health letter.* Retrieved from http://search.proquest.com/docview/1370197418?accountid=14872.

Gragoudas, E.S., Egan, K.M., Walsh, S.M., Regan, S., Munzenrider, J.E., & Taratuta, V. (1995). Lens changes after proton beam irradiation for uveal melanoma. *American Journal of Ophthalmology, 119*(2), 157-164.

Gulson, B., Mahaffey, K., Mizon, K., Korsch, M., Cameron, M., & Vimpani, G. (1995). Contribution of tissue lead to blood lead in adult female subjects based on stable lead isotope methods. *Journal of Laboratory & Clinical Medicine, 125*(6), 703-712.

Hammond, C., Snieder, H., Spector, T., & Gilbert, C. (2000). Genetic and environmental factors in age-related nuclear cataracts in monozygotic and dizygotic twins. *The New England Journal of Medicine*, *342*(24), 1786-1790.

Harmon, S. M., & Talbert, G. B. (1985). Reproductive aging. In C.E. Finch & E.L. Schneider (Eds.), *Handbook of the biology of aging* (2nd ed., pp. 457-510). New York: Van Nostrand Reinhold.

Hellekson, K. (2002). NIH releases statement on osteoporosis prevention, diagnosis, and therapy. *American Family Physician*, *66*(1), 161-162.

Hennis, A., Wu, S., Li, X., Nemesure, B., & Leske, M. (2001). Lens opacities and mortality: The Barbados Eye Studies. *Ophthalmology*, *108*(3), 498-504.

Henriksen, K., Leeming, D., Christiansen, C., & Karsdal, M. (2011). Use of bone turnover markers in clinical osteoporosis assessment in women: Current issues and future options. *Women's Health (London, England), 7*(6), 689-698. doi:10.2217/whe.11.74

Hernandez-Avila, M., Villalpando, C., Palazuelos, E., Hu, H., Villalpando, M., & Martinez, D. (2000). Determinants of blood lead levels across the menopausal transition. *Archives of Environmental Health, 55*(5), 355-360.

Hollows, F., & Moran, D. (1981). Cataract – the ultraviolet risk factor. *Lancet*, *2*(8258), 1249-1250.

Hu, H., Aro, A., Payton, M., Korrick, S., Sparrow, D., Weiss, S., & Rotnitzky, A. (1996). The relationship of bone and blood lead to hypertension. The Normative Aging Study. *The Journal of the American Medical Association*, *275*(15), 1171-1176.

Hu, H., & Hernandez-Avila, M. (2002). Invited commentary: Lead, bones, women, and pregnancy--the poison within?. *American Journal of Epidemiology*, *156*(12), 1088-1091.

Hunt, W., Watson, R., Oaks, J., Parish, C., Burnham, K., Tucker, R., … Hart, G. (2009). Lead bullet fragments in venison from rifle-killed deer: Potential for human dietary exposure. *Plos One*, *4*(4), e5330. doi:10.1371/journal.pone.0005330.

Jackson, L. W., Cromer, B. A., & Panneerselvamm, A. (2010). Association between bone turnover, micronutrient intake, and blood lead levels in pre- and postmenopausal women, NHANES 1999-2002. *Environmental Health Perspectives*, *118*(11), 1590-1596. doi:10.1289/ehp.1002158.

Jain, N., Potula, V., Schwartz, J., Vokonas, P., Sparrow, D., Wright, R., & Hu, H. (2007). Lead levels and ischemic heart disease in a prospective study of middle-aged and elderly men: The VA normative aging study. *Environmental Health Perspectives*, *115*(6), 871-875.

Jehle, S., Hulter, H., & Krapf, R. (2013). Effect of potassium citrate on bone density, microarchitecture, and fracture risk in healthy older adults without osteoporosis:

A randomized controlled trial. *Journal of Clinical Endocrinology & Metabolism, 98*(1), 207-217. doi:10.1210/jc.2012-3099.

Johnson, C.L., Paulose-Ram, R., Ogden, C.L., Carroll, M.D. Kruszon-Moran, D., Dohrmann, S.M., …Curtin, L.R. (2013). National Health and Nutrition Examination Survey: Analytic guidelines, 1999–2010. *National Center for Health Statistics. Vital Health Statistics*, *2*(161).

Jonasson, F., & Thordarson, K. (1987). Prevalence of ocular disease and blindness in a rural area in the eastern region of Iceland during 1980 through 1984. *Acta Ophthalmologica, Supplement, 18, 24*0-43.

Jones, R., Homa, D., Meyer, P., Brody, D., Caldwell, K., Pirkle, J., & Brown, M. (2009). Trends in blood lead levels and blood lead testing among US children aged 1 to 5 years, 1988-2004. *Pediatrics*, *123*(3), e376-85. doi:10.1542/peds.2007-3608

Kanthan, G.L., Wang J.J., Rochtchina, E., Tan, A.G., Lee, A., Chia, E.M., & Mitchell, P. (2008). Ten-year incidence of age-related cataract and cataract surgery in an older Australian population. The Blue Mountains Eye Study. *Ophthalmology, 115*(5),808-814.

Kanthan, G., Wang, J., Burlutsky, G., Rochtchina, E., Cumming, R., & Mitchell, P. (2010). Exogenous oestrogen exposure, female reproductive factors and the long-term incidence of cataract: The Blue Mountains Eye Study. *Acta Ophthalmologica, 88*(7), 773-778. doi:10.1111/j.1755-3768.2009.01565.x

Khalil, N., Cauley, J. A., Wilson, J.W., Talbott, E.O., Morrow, L., Hochberg, M.C., Muldoon, S.B. (2008). Relationship of blood lead levels to incident nonspine

fractures and falls in older women: The study of osteoporotic fractures. *Journal of Bone and Mineral Research, 23*(9), 1417-1425.

Klein, B., Klein, R., Lee, K., & Meuer, S. (2003). Socioeconomic and lifestyle factors and the 10-year incidence of age-related cataracts. *American Journal of Ophthalmology, 136*(3), 506-512.

Klein, R. & Klein, B.E.K. (2013). The prevalence of age-related eye diseases and visual impairment in aging: Current estimates. *Investigative Ophthalmology and Visual Science, 54*(14). ORSF5-ORSF13.

Korrick, S., Hunter, D., Rotnitzky, A., Howard, H., & Speizer, F. (1999). Lead and hypertension in a sample of middle-aged women. *American Journal of Public Health, 89*(3), 330-335. doi:10.2105/AJPH.89.3.330

Knudtson, M., Klein, B., & Klein, R. (2006). Age-related eye disease, visual impairment, and survival: The Beaver Dam Eye Study. *Archives of Ophthalmology, 124*(24)243-249.

Lai, K., Cui, J., Ni, S., Zhang, Y., He, J., & Yao, K. (2013). The effects of postmenopausal hormone use on cataract: A meta-analysis. *Plos One, 8*(10), e78647. doi:10.1371/journal.pone.0078647

Langkamp, D. L., Lehman, A., & Lemeshow, S. (2010). Techniques for handling missing data in secondary analyses of large surveys. *Academic Pediatrics*, *10*(3), 205–210.

Laskar, A. (2011). Women's health: Beyond reproductive years. *Indian Journal of Public Health, 55*(4), 247-251. doi:10.4103/0019-557X.92399.

Lee, M. G., Chun, O.K., & Song, W.O. (2005). Determinants of the blood lead level of US women of reproductive age. *Journal of the American College of Nutrition, 24*(1), 1-9.

Leske, M., Wu, S., Nemesure, B., Li, X., Hennis, A., & Connell, A. (2000). Incidence and progression of lens opacities in the Barbados Eye Studies. *Ophthalmology, 107*(7), 1267-1273.

Leske, M.C., Suh-Yuh, W., Nemesure, B., & Hennis, A. (2010). Causes of visual loss and their risk factors: An incidence summary from the Barbados Eye Studies. *Rev Panam Salud Publica, 27*(4), 259-267.

Li, L., Duker, J., Yoshida, Y., Niki, E., Rasmussen, H., Russell, R., & Yeum, K. (2009). Oxidative stress and antioxidant status in older adults with early cataract. *Eye (London, England), 23*(6), 1464-1468. doi:10.1038/eye.2008.281

Lindblad, B.E., Håkansson, N., Philipson, B., & Wolk, A. (2008). Metabolic syndrome components in relation to risk of cataract extraction: A prospective cohort study of women. *Ophthalmology*, *115*(10),1687-92.

Machida, M., Suna, S-J, Ogumaa, E., & Kayamaa, F. (2009). High bone matrix turnover predicts blood levels of lead among perimenopausal women. *Environmental Research*, *109*, 880–886.

Mares, J.A., Voland, R., Adler, R., Tinker, L., Millen, A.E., Moeller, S.M., & CAREDS Group. (2010). Healthy diets and the subsequent prevalence of nuclear cataract in women. *Archives of Ophthalmology*, *128*(6),738.

Mayo Clinic. (2014). *Alkaline phosphatase, total and isoenzymes, serum.* Retrieved from http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/89503

McAlister, A.L., Perry, C.L., & Parcel, G.S. (2008) In K. Glanz, B. K. Rimer & K. Viswanath, (Eds.), *Health behavior and health education.* Wiley Publishing. Kindle Edition.

McCarty, C.A., Mukesh, B.N., Fu, C.L., & Taylor, H.R. (1999). The epidemiology of cataract in Australia. *American Journal of Ophthalmology*, *128*(4), 446–465.

McCarty, C.A., Nanjan, M.B., & Taylor, H.R. (2000). Attributable risk estimates for cataract to prioritize medical and public health action. *Investigative Ophthalmology & Visual Science*, *41*(12), 3720-3725.

Mendola, P., Brett, K., DiBari, J.N., Pollack, A.Z., Tandon, R., & Shenassa, E.D. (2012). Menopause and lead body burden among US women aged 45-55, NHANES 1999-2010. *Environmental Research*, *121*, 110-113.

Merriam-Webster. (2014). *Dictionary.* Retrieved from http://www.merriam-webster.com/dictionary/

Mitchell, M., & Jolley, J. (2013). *Research design explained* (8th ed.). Belmont, CA: Wadsworth Cengage Learning.

Miglior, S., Marighi, P., Musicco, M., Balestreri, C., Nicolosi, A., & Orzalesi, N. (1994). Risk factors for cortical, nuclear, posterior subcapsular and mixed cataract: A case-control study. *Ophthalmic Epidemiology*, *1*(2), 93-105.

Mishra, V.K., Retherford, R.D., & Smith, K.R. (1999). Biomass cooking fuels and prevalence of blindness in India. *Journal of Environmental Medicine, 1*, 189-199.

Montaño, D.E., & Kasprzyk, D. (2008). Theory of Reasoned Action, Theory of Planned Behavior, and the Integrated Behavioral Model. In K. Glanz, B.K. Rimer, & K. Viswanath. (Eds.), *Health Behavior and Health Education*. Wiley Publishing. Kindle Edition.

Mosad, S. M., Ghanem, A. A., El-Fallal, H. M., El-Kannishy, A. M., El Baiomy, A. A., Al–Diasty, A. M., & Arafa, L. F. (2010). Lens cadmium, lead, and serum vitamins C, E, and beta carotene in cataractous smoking patients. *Current Eye Research*, *35*(1), 23-30.

Mukesh, B., Le, A., Dimitrov, P., Ahmed, S., Taylor, H., & McCarty, C. (2006). Development of cataract and associated risk factors: The Visual Impairment Project. *Archives of Ophthalmology*, *124(*1), 79-85.

Muntner, P., Menke, A., DeSalvo, K.B., Rabito, F.A., & Batuman, V. (2005). Continued decline in blood lead levels among adults in the United States: The National Health and Nutrition Examination Surveys. *Archives of Internal Medicine, 165*(18), 2155-2161.

Nash, D., Magder, L., Lustberg, M., Sherwin, R.W., Rubin, R.J., Kaufman, R..B., & Silbergeld, E.K. (2003). Blood lead, blood pressure, and hypertension in perimenopausal and postmenopausal women. *Journal of the American Medical Association*, *289*(12), 1523-1532.

Nash, D., Magder, L., Sherwin, R., Rubin, R., & Silbergeld, E. (2004). Bone density-related predictors of blood lead level among peri- and postmenopausal women in the United States: The Third National Health and Nutrition Examination Survey, 1988-1994. *American Journal of Epidemiology*, *160*(9), 901-911.

National Eye Institute & Prevent Blindness America. (2002).*Vision problems in the U.S.: Prevalence of adult vision impairment and age-related eye disease in America.* Retrieved from http://www.preventblindness.net/site/DocServer/VPUS_report_web.pdf

National Institutes of Health. (2000). Osteoporosis prevention, diagnosis, and therapy. *National Institutes of Health Consensus Statement, 17*(1). Retrieved from http://consensus.nih.gov/2000/2000Osteoporosis111PDF.pdf

National Institutes of Health. (2014). *Drugs, supplements, and herbal information.* Retrieved from http://www.nlm.nih.gov/medlineplus/druginformation.html

National Osteoporosis Foundation. (2013). *2013 Clinician's guide to prevention and treatment of osteoporosis.* Retrieved from http://nof.org/files/nof/public/content/resource/913/files/580.pdf

Neal, R., Aykin-Burns, N., Ercal, N., & Zigler, J.S. (2005). Pb2+ exposure alters the lens alpha A-crystallin protein profile in vivo and induces cataract formation in lens organ culture. *Toxicology*, *212(1*), 1-9.

Needleman, H. (2000). The removal of lead from gasoline: Historical and personal reflections. *Environmental Research*, *84*(1), 20-35.

Nemet, A.Y., Hanhart, J., Kaiserman, I., & Vinker, S. (2013). Are cataracts associated with osteoporosis?. *Clinical Ophthalmology*, *7*, 2079-2084.

Occupational Safety and Health Administration. (n.d.). *Lead.* Retrieved from https://www.osha.gov/SLTC/lead/index.html

Olafsdottir, E., Andersson, D., & Stefánsson, E. (2012). The prevalence of cataract in a population with and without type 2 diabetes mellitus. *Acta Ophthalmologica, 90*(4), 334-340. doi:10.1111/j.1755-3768.2011.02326.x

Ozcura, F., Dündar, S., Cetin, E., Beder, N., & Dündar, M. (2010). Effect of estrogen replacement therapy on lens epithelial cell apoptosis in an experimental rat model. *International Ophthalmology*, *30*(3), 279-284. doi:10.1007/s10792-009-9327-6.

Panteghini, M., & Bais, R. (2014) In Burtis, C.A., Ashwood, E.R. & Bruns, D.E. (Eds.). (2014). *Tietz textbook of Clinical Chemistry and Molecular Diagnostics.* Retrieved from http://www.barnesandnoble.com/read/9781455759422?referring_ean=9781455759422

Park, S.K., Schaumberg, D., Weisskopf, M.G., Hu, H., & Korrick, S.A. (unpublished). Conference Paper: Cumulative lead exposure and age-related cataract in middle-aged and elderly women. *Environment and Health*. Abstract Number: 5335 | ID: P-2-18-03. Retrieved from http://ehp.niehs.nih.gov/ehbasel13/p-2-18-03/

Pirkle J.L., Brody, D.J., Gunter, E.W., Kramer, R.A., Paschal, D.C., Flegal, K.M., & Matte, T.D. (1994). The decline of blood lead levels in the United States: The

National Health and Nutrition Examination Surveys (NHANES). *Journal of the American Medical Association*, *272*(4), 284-291.

Prochaska, J.O., Redding, C.A., & Kerry, K.E. (2008). The Transtheoretical Model and stages of change. In K. Glanz, B.K. Rimer, & K. Viswanath. (Eds.), *Health Behavior and Health Education*. Wiley Publishing. Kindle Edition.

Rabinowitz, M., Wetherill, G.W., & Kopple, J.D. (1976). Kinetic analysis of lead metabolism in healthy humans. *The Journal of Clinical Investigation*, *58*, 260-270.

Resnikoff, S., Pascolini, D., Etya'aale, D., Kocur, I., Pararajasegaram, R., Pokharel, G., & Mariotti, S. (2004). Global data on visual impairment in the year 2002. *Bulletin of the World Health Organization*, *82*(11), 844-851.

Reynolds, R., & Obermeyer, C. (2005). Age at natural menopause in Spain and the United States: Results from the DAMES project. *American Journal of Human Biology: The Official Journal of the Human Biology Council*, *17*(3), 331-340.

Riggs, B.L., & Melton, L.J. (1984). Involutional osteoporosis. *New England Journal of Medicine*, *314*, 1676-1686.

Riggs, B.L., Khosia, S., & Melton, L.J. (2002). Sex steroids and the construction and conservation of the adult skeleton. *Endocrine Reviews*, *23*(3), 279-302.

Rothenberg, S., Kondrashov, V., Manalo, M., Jiang, J., Cuellar, R., Garcia, M., Todd, A. (2002). Increases in hypertension and blood pressure during pregnancy with increased bone lead levels. *American Journal of Epidemiology*, *156*(12), 1079-1087.

Roy, N., & Rossman, T. (1992). Mutagenesis and comutagenesis by lead compounds. *Mutation Research*, *298*(2), 97-103.

Ruegsegger, D., Ruegsegger, R., Fishcer, J.A., & Anliker, M. (1984). Bone loss in premenopausal and postmenopausal women. *The Journal of Bone and Joint Surgery, 66A,* 1015-1023.

Ryskulova, A., Turczyn, K., Makuc, D.M., Cotch, M.F., Klein, R.J., & Janiszewski, R. Self-reported age-related eye diseases and visual impairment in the United States: Results of the 2002 National Health Interview Survey. *American Journal of Public Health, 98*(3), 454-461.

Salamone, L., Gregg, E., Wolf, R., Epstein, R., Black, D., Palermo, L., ... Cauley, J. (1998). Are menopausal symptoms associated with bone mineral density and changes in bone mineral density in premenopausal women?. *Maturitas*, *29*(2), 179-187.

Schaumberg, D.A., Mendes, F., Balaram, M., Reza Dana, M., Sparrow, D., & Hu, H. (2004). Accumulated lead exposure and risk of age-related cataract in men. *Journal of the American Medical Association*, *292*(22), 2750-2754.

Shukla, N., Moitra, J.K., & Trivedi, R.C. (1996). Determination of lead, zinc, potassium, calcium, copper, and sodium in human cataract lenses. *Science of the Total Environment*, *181*(2), 161–165.

Silbergeld, E., Schwartz, J., & Mahaffey, K. (1988). Lead and osteoporosis: Mobilization of lead from bone in postmenopausal women. *Environmental Research*, *47*(1), 79-94.

Smeeth, L. Boulis, M., Hubbard, R., & Fletcher, A.E. (2003). A population based case-control study of cataract and inhaled corticosteroids. *British Journal of Ophthalmology*, *87*:1247–1251.

Sommer A., Tielsch, J.M., Katz, J., Quigley, H.A., Gottsch, J.D., Javitt, J.C., … Ezrine, S. (1991). Racial differences in the cause-specific prevalence of blindness in east Baltimore. *New England Journal of Medicine*, *325*(20):1412–1417.

SSRIs and cataract risk. (2010). *Brown University Psychopharmacology Update*, *21*(9), 4.

Stanford University. (2003). *Glucocorticoids.* Retrieved from http://www.stanford.edu/group/hopes/cgi-bin/wordpress/2010/06/glucocorticoids/

Stohs, S., & Bagchi, D. (1995). Oxidative mechanisms in the toxicity of metal ions. *Free Radical Biology & Medicine*, *18*(2), 321-336.

Sullivan, L. M. (2011). *Essentials of biostatistics in public health* (2nd ed.). Jones & Bartlett Publishers.

Symanski, E., & Hertz-Picciotto, I. (1995). Blood lead levels in relation to menopause, smoking, and pregnancy history. *American Journal of Epidemiology*, *141*(11), 1047-1058.

Taylor, H. (2002). Fred Hollows lecture. Eye care for the community. *Clinical & Experimental Ophthalmology*, *30*(3), 151-154.

Tepper, L., & Levin, L. (1975). A survey of air and population lead levels in selected American communities. *Environmental Quality And Safety, Supplement*, 2152-196.

Tokar, E.J., Boyd, W.A., Freedman, J.H., & Waalkes, M.P. (2013). Toxic effects of metals. In C. Klaassen (Ed.), *Casarett & Doull's toxicology: The basic science of poisons* [Kindle 8th Ed.]. NY. McGraw-Hill Professional.

United Nations Environment Programme. (2006). *The environment in the news*. Retrieved from http://www.unep.org/cpi/briefs/2006May12.doc

United States Census Bureau. (2013). *Census 2010*. Retrieved from www.census.gov/

United States Census Bureau. (2014). *American factfinder*. Retrieved from www.census.gov

Wagner, H., Fink, B., & Zadnik, K. (2008). Sex- and gender-based differences in healthy and diseased eyes. *Optometry (St. Louis, Mo.), 79*(11), 636-652. doi:10.1016/j.optm.2008.01.024

Walden University. (2013). *Mission and vision*. Retrieved from http://www.waldenu.edu/about/social-change/mission-and-vision

Walden University. (n.d.). *What is social change?* Retrieved from www.waldenu.edu

Weitzmann, M.N. & Pacifici, R. (2006). Estrogen deficiency and bone loss: An inflammatory tale. *Journal of Clinical Investigation, 116* (5), 1186-1194. doi:10.1172/JCI28550.

West, S., Muñoz, B., Schein, O., Duncan, D., & Rubin, G. (1998). Racial differences in lens opacities: The Salisbury Eye Evaluation (SEE) project. *American Journal of Epidemiology*, *148*(11), 1033-1039.

West, S. (2000). Looking forward to 20/20: A focus on the epidemiology of eye diseases. *Epidemiologic Reviews*, *22*(1), 64-70.

West, S.K., Muñoz, B., Istre, J., Rubin, G.S., Friedman, S.M., Fried, L.P., Bandeen-Roche, K., & Schein, O.D. (2000). Mixed lens opacities and subsequent mortality. *Archives of Ophthalmology*, *118*(3), 393-397.

Weuve, J., Korrick, S., Weisskopf, M., Ryan, L., Schwartz, J., Nie, H., ... Hu, H. (2009). Cumulative exposure to lead in relation to cognitive function in older women. *Environmental Health Perspectives*, *117*(4), 574-580. doi:10.1289/ehp.11846

Weyermann, M., & Brenner, H. (1998). Factors affecting bone demineralization and blood lead levels of postmenopausal women--a population-based study from Germany. *Environmental Research*, *76*(1), 19-25.

Wolverton, M. L. (2009). Research design, hypothesis testing, and sampling. *The Appraisal Journal*, *77*(4), 370–382.

World Health Organization. (2006). *Fifty-Ninth World Health Assembly. Report by the Secretariat on prevention of avoidable blindness and visual impairment*. Retrieved from http://apps.who.int/gb/archive/pdf_files/WHA59/A59_12-en.pdf

World Health Organization. (2013). *Women's health*. Retrieved from http://www.who.int/mediacentre/factsheets/fs334/en/

World Health Organization Collaborating Centre for Metabolic Bone Diseases, University of Sheffield, UK. (n.d.). *FRAX ® WHO fracture risk assessment tool*. Retrieved from http://www.shef.ac.uk/FRAX/tool.aspx?country=9

Wright, J., Dietrich, K., Ris, M., Hornung, R., Wessel, S., Lanphear, B., Ho, M., & Rae, M. (2008). Association of prenatal and childhood blood lead concentrations with

criminal arrests in early adulthood. *Plos Medicine*, *5*(5), e101. doi:10.1371/journal.pmed.0050101.

Yuki, K., Dogru, M., Imamura, Y., Kimura, I., Ohtake, Y., & Tsubota, K. (2009). Lead accumulation as a possible risk factor for primary open angle glaucoma. *Biological Trace Element Research*, *132*, 1-8.

Zambelli-Weiner, A., Crews, J., & Friedman, D. (2012). Disparities in adult vision health in the United States. *American Journal of Ophthalmology*, *154*(6 Suppl), S23-30.e1. doi:10.1016/j.ajo.2012.03.018.

Appendix A – Approval to Use Table 1

Action Needed: Permission to use table in article

Alina Foo <afoo@aacc.org> To: Imogene Drakes <imogene.drakes@waldenu.edu> Cc: permissions <permissions@aacc.org>

Dear Imogene,

Thank you for requesting permission.

Please accept this email as your authorization to use Table 1 as described in your correspondence below, and be sure to include a complete citation to the original source:

Theresa M. Ambrose, Muhammad Al-Lozi, and Mitchell G. Scott. Bone Lead Concentrations Assessed by in Vivo X-Ray Fluorescence Clinical Chemistry 2000; v. 46, p.1171-1178. (Reproduced with permission from the American Association for Clinical Chemistry).

Kind regards,

Alina

AlinaFoo

Editorial Specialist, *Clinical Chemistry*

AACC

1850 K Street, NW // Suite 625 // Washington, DC 20006 2215 // United States

PHONE: +1 202.420.7611// FAX: +1 202.833.7012

Appendix B – Approvals to use Cataract Images and Information

Gmail by Google

Imogene Drakes <imogene.drakes@waldenu.edu>

images of cataracts

2 messages

Hiatt, Rebecca M. <RHiatt@aoa.org> Mon, Nov 3, 2014 at 12:52 PM
To: "imogene.drakes@waldenu.edu" <imogene.drakes@waldenu.edu>

Hi Imogene,

Thank you for your email about using the cataract images in your dissertation. You may use the photos and information. Please cite the American Optometric Association for the information and please give photo credit to the American Optometric Association.

Thank you and good luck with your dissertation!

Sincerely,

Rebecca Hiatt
Public Relations and Graphic Support Specialist
American Optometric Association
314-983-4119

RHiatt@aoa.org

Jeffrey Day <jday@eyemaginations.com> Mon, Nov 3, 2014 at 11:49 AM
To: Imogene Drakes <imogene.drakes@waldenu.edu>

Hello Imogene,

You have our authorization to use these images in your dissertation.

Please let us know if you need anything else!

Jeffrey "Marty" Day | **Technical Support Manager** | **Eyemaginations, Inc.**
t 410.321.5481 | **d** 410.616.8686| **f** 410.616.8657 | jday@eyemaginations.com
1820 Lancaster Street, Suite 110, Baltimore, MD 21231
Contact us today for a free demo of Echo, the new Cloud-Based Patient Education Solution from Eyemaginations!
Facebook | Twitter | LinkedIn | Google+ | YouTube
[Quoted text hidden]

Curriculum Vitae

Imogene Drakes, M.S., M.B.A., B.Sc.

Spring Valley, New York 10977
(845) 425-4561
E-mail: imogene.drakes@waldenu.edu

ACADEMIC EXPERIENCE

2011 - Present	Candidate for Doctor of Philosophy – Public Health **Walden University,** Minneapolis, Minnesota
2002 - 2007	Graduate Research – Environmental Health Science, Public Health **Columbia University,** New York, New York
1998 - 2000	Master of Business Administration – Management **Pace University,** New York, New York
1992 - 1994	Master of Science – Forensic Science **John Jay College of Criminal Justice,** New York, New York
1980 - 1984	Bachelor of Science – Biology, **University of Guyana,** Turkeyen, Guyana

RELEVANT PROFESSIONAL EXPERIENCE

2009 - Present **Chemistry and Hematology Laboratory Supervisor (full-time)**
Champlain Valley Physicians Hospital, Plattsburgh, NY

Manage laboratory operations for Clinical Chemistry, Hematology and Special Chemistry, 15 Direct FTE Reports and 15 Dotted Line FTE Reports. Annual operational budget is $3 million dollars.
Highlights: Streamlining of operations to reduce 1.5 FTEs as staff attrit. Processes included implementation of autofiling of main chemistry analyzers to Laboratory Information System and implementation of special chemistry and hematology analyzers to increase efficiencies. Stewardship also included significant reduction in survey deficiencies.

2010 - 2011 **Assistant Professor, Adjunct**
State University of New York, Plattsburgh, Plattsburgh, NY

Lecturer, Mathematics and Chemistry, Bachelor of Science Program.

2009 Sabbatical - Nyack Hospital Laboratory, Nyack, New York

Updated skillset for testing in hematology and chemistry in a large hospital laboratory.

2006 - 2008 **Laboratory Administrator (full-time)**
Refuah Health Center Laboratory, Spring Valley, New York.

Upgraded Physicians' Office type Laboratory to a fully certified New York State Clinical Laboratory. Highlights included implementation of standardized ordering forms for physicians and mentoring staff through licensure to achieve compliance. Trained staff in customer service for predominantly Hasidic patient population.

2004 - 2010 **Assistant Professor, Adjunct, MPH Program**
State University of New York, Brooklyn, Brooklyn, NY

Lecturer - Issues in Environmental Health for MD/MPH program. Students included chiefs of medical departments.

1999 - 2006 New York City Health and Hospitals Corporation, New York, NY

2003 - 2006 **Assistant Director, Quality Management Department**
Bellevue Hospital, New York, NY

Highlights: Coordinated hospital's preparation for first JCAHO patient tracer survey, prepared reports for HHC Quality Management Board meetings, Review of Core Measures and resolution of related issues. Coordinated QA for Medicine and Surgical Service lines. Coordinated responses to regulatory agencies including IPRO, New York State Department of Health and JCAHO.

1999 - 2003 **QA/Operations Manager, Pathology Department**
Bellevue Hospital, New York, NY

Laboratory operations for large referral laboratory for New York City hospitals and diagnostic treatment centers including Coler-Goldwater, Harlem, Metropolitan, Lincoln, Gouverneur, Belvis and Morrisania. Clinical tests were approximately 6,000,000 per year and staff numbered 420+). Quality Assurance for 14 Anatomic and Clinical Pathology laboratories. Assisted Administrative Pathology Director in administrative duties. Trained Operations and Customer Service Managers. Blood donor recruitment. Promoted to Assistant Director, Quality Management.

1995 - 1999 Quality Control Coordinator, Pathology Department
Lincoln Hospital, Bronx, New York

Point-of-Care Coordinator for hospital and Quality Control Coordinator for Chemistry Division. Highlights: Implemented computerized, real-time Quality Control system in Chemistry Division and computerized Point-of-Care Testing program. Interdisciplinary collaboration with medical and nursing directors to improve laboratory service. All programs managed were JCAHO and NYSDOH compliant.

1990 - 1995 Clinical Laboratory Supervisor/Technologist
New York Blood Center – New York, NY 1990–1995

Supervised 30 pre-transfusion viral testing and ancillary personnel. In-serviced fellows on aspects of quality control. Performed testing per cGMP and FDA requirements. Highlights: Member, New York Blood Center Quality Management Board; Head, Employee Motivation Committee, Laboratory Quality Management Board. Promoted to Supervisor.

1984 - 1989 Analytical Scientific Officer
Ministry of Health, Georgetown, Guyana

Managed STAT Laboratory for Main Public Hospital of the country of Guyana. Supervised Clinical and Forensic Toxicology Division of the Government Analyst Department. Highlights: Reviewed laboratory operations and submitted acceptable proposal to the Minister of Health; Lecturer, Police Officer Academy, Expert witness for forensic analyses. Two fellowship nominations.

ASSOCIATED PROFESSIONAL EXPERIENCE

1983 - 1984 **Practicum Student**
Central Medical Laboratory, Guyana

Duties and learning experience included identification of microbial pathogens, basic hematology and clinical chemistry.

COMMUNITY SERVICE AND CONSULTING EXPERIENCE

2012 - 2014 American College of Healthcare Executives, Book Award Committee Member, Chicago, Illinois

2010 - Present State University of New York, Plattsburgh State Gospel Choir Community Member, Plattsburgh New York.

LICENSURE AND CERTIFICATIONS
Licensed Clinical Laboratory Technologist, State of New York, 2007 to present.

PROFESSIONAL ORGANIZATIONS

American College of Healthcare Executives, Fellow
American Public Health Association, Member
Clinical Laboratory Management Association, Member
American Association for Clinical Chemistry, Member

HONORS, AWARDS, ADDITIONAL SKILLSETS

Open Entrance Book Award, University of Guyana, Turkeyen, Guyana
Three subjects, Advanced Levels General Certificate of Education, London
Temporary Grade 1, Class 1 Teacher, Ministry of Education, Guyana
Fellowship, United States, Drug Enforcement Administration
Fellowship, United States Bureau of Alcohol, Tobacco, Firearms and Explosives

CLINICAL/RESEARCH INTERESTS

The possible role of endogenous lead in the phenomenon of early appearance of cataracts in women worldwide.