Socioecological Factors Associated with Vitamin D Deficiency:
Implications for Adults with Obesity and Chronic Pain

A dissertation presented by
Valeria Anita Ramdin
to
The Bouvé College of Health Sciences
School of Nursing
in partial fulfillment of the requirements for the degree of

Doctor of Philosophy
in the subject of
Nursing

Northeastern University
Boston, Massachusetts
April, 2016
Acknowledgements

When I became a certified registered nurse in 1985, one thing I was sure of, this was the beginning of a journey and certainly one that would result in me obtaining my doctorate. With very little means back then of how to realize my dreams, I started what would be the longest trek of my life: an academic life that would be filled with opportunities and challenges, tears and smiles and a persistent strength that I too could not believe I had. But all of this could not be possible without the support of many persons along the way.

I owe a depth of gratitude first to my doctoral committee chaired by Dr. Elizabeth Howard (fondly called Betsy) who consistently believed in my ability and intellectual capacity. She pushed me to broaden my knowledge from early in the process and redirected me whenever I became too broad or occupied, always tenderly reminding me of my goal. The feedback on my manuscripts and her guidance through the dissertation process was invaluable. Thanks to Dr. Paula Gardiner who met with me for more than a year almost every week to help me understand the population. She also practices integrative medicine and her discussions with me on the findings in the literature was indispensable. Additionally, thanks to her past research assistant, Amanda Fillippelli who helped me navigate under Dr. Gardiner's supervision obtaining my IRB and accessing the records from the hospital. Thanks to Dr. Aziza Jamal-Allial whose expertise as a bio statistician and understanding of the process of starting the research trajectory made the work possible. Finally, thank you to Dr. Mary (Suzie) Tarmina who provided me enough feedback to allow my intellectual ability to be nurtured as a doctoral
student. Overall, I am truly thankful and appreciative to my entire committee for their dedication to my success.

I formally want to thank my family. To my mom Vera Waterman who has been one of my role models, instilling in me the value of education from early. To my children Larry Jr. and Lauren who were always intrigued by my work. Their help, patience and support is remarkable, and their good behavior allowed me the opportunity to concentrate on my studies without distraction. Last but not least, my soul mate and husband Larry Ramdin, who has been by my side through it all, never allowing me to give up. Little did he know that when he brought me the nursing paper application for entry into the profession when I graduated from high school, that there would be many other pieces of paper he would have to read over the past thirty years. I am blessed to have had him by my side through this journey. For his endless love and support it is with deep gratitude that I say, thanks and I LOVE YOU. To my siblings, other family members and mentors whom I did not explicitly mention by name, but like the above persons, have helped me along the journey, thank you.
Dedication

I dedicate this labor of love and work of humanity
to my soul mate, friend and husband Larry Ramdin

and to my adorable children

Larry Jr. and Lauren Ramdin.

Thanks to God for granting me continual inner peace, perseverance, sound mind and

judgment.
Abstract

Blacks and Hispanics are disproportionately affected by vitamin D deficiency (NHANES, 2012). Preventing this deficiency is a national priority as its deficit is linked to chronic diseases, increasing the disease burden within the US population (Annweiler, et al., 2013; Anglin et al., 2013; Anderson et al., 2010; Chung et al, 2009; Holick, 2011; Institute of Medicine, 2002; and CDC, 2012). Focusing on not only race and ethnicity but also socioecological determinants can increase identification of those at risk and promote appropriate treatment and surveillance. Prevention and treatment guidelines provide some direction in screening and treatment (Ramdin, 2015), but do not provide the socioecological aspect among vulnerable populations. A systematic review of the literature on screening for vitamin D deficiency found that there were recommended screening guidelines. Objective testing of the 25 hydroxyvitamin D was to be done in at-risk populations [Blacks and Hispanics and the elderly over 65 years old] but not in the general population. A follow up systematic review on treatment (Ramdin, 2015) found that there were various dosages being used to treat problems, despite what was documented as standard recommended treatment.

Subsequently, a research study was conducted examining vitamin D (VD) concentrations among adults seeking integrative medical care in an urban setting. The aim of the study was to explore the socioecological factors associated with VD concentrations in adults who had chronic illnesses, and to determine if there was an association between vitamin D deficiency and obesity and vitamin D and chronic pain. A secondary data analysis was done examining the medical records of 1268 adults seen at an inner city integrative medicine clinic in the northeast US from 2007-2012. The
resulting study sample was non-institutionalized adults 18 years and older comprised of 80% women, mean age 52±13.9 and 20% men mean age 55±12.4 years-old. The results indicated that seasonality, ethnicity and age were strongly associated with vitamin D deficiency in this population with p values <0.0001. There was evidence to support that adults with high body mass index (BMI) are more likely to have 25-hydroxyVD concentration less than the optimal 50 ng/mL. There was an inverse relation with VD concentration and BMI; the higher the BMI, the lower the vitamin D concentration. Adults with BMI between 25 and 30 had approximately a 30% chance of having low vitamin D levels with P values <0.001, and that percent increases the higher the BMI. There was some association of 25(OH)D and moderate level pain which was found to not be statistically significant when controlled for ethnicity, season and age.

Keywords: Vitamin D deficiency, BMI, pain, Chronic illness
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Chapter One: Introduction

Valeria Ramdin

School of Nursing
The Bouvé College of Health Sciences
Northeastern University
Introduction

Vitamin D deficiency is significantly associated with chronic illness and mortality (Forrest, Stuhldreher, 2011; Autier and Gandini, 2007). It is estimated to affect approximately 28 million Americans (NHANES, 2012). Mounting evidence suggests vitamin D deficiency is linked to cardiovascular disease and cancer (Booth, Cheng, Fox, Hoffman, Jaques, Keyes and Wolf, 2010; Mitchell, Henao, Finklestein and Burnett-Bowie, 2012; Overcash, 2008). The literature indicates that this deficiency is also linked to many other conditions such as multiple sclerosis (Munger, Levin, Hollis, Howard and Ascherio, 2006), chronic kidney disease (Melamed and Thadhani, 2012), anemia, depression, Type 2 diabetes, systemic lupus erythematosus, inflammatory bowel disease, neuromuscular disease and pain (Anglin, Samaan, Walter and McDonald, 2013; Melamed, Michos, Post and Astor, 2008; Vagianos, Bector, McConnell and Bernstein, 2007; Young, Snell-Bergeon, Naik, Hokanson, Tarullo, Gottlieb, Garg and Rewers, 20011; Bjelakovic, Giuud, Nikolova et al., 2011; Ascherio, Munger, and Simon, 2010).

Its link to weakening of the immune system (Holick, 2007; Hewison, 2012) has the potential for far-reaching consequences.

The problem is that unless a patient’s vitamin D using the 25-hydroxyl (D) concentration levels are tested, recognizing when a patient is vitamin D deficient is complex. This complexity results in prevailing under-diagnosis leaving large segments of the population at risk for vitamin D deficiency and problematic health outcomes. Correction of vitamin D deficiency has been shown to reduce mortality in patients with some chronic diseases (Rejmark, Avenell, Masud, Anderson et al., 2012). Based on the available scientific evidence, only persons deemed high risk, predominantly Blacks,
Hispanics, and persons 65 years or older, are recommended for routine 25 hydroxyvitamin 25(OH)D test. (Holick, Binkley, Bischoff-Ferrari, Gordon, Heaney, Murad and Weaver, 2011; U.S. Preventive Services Task Force, 2013). Other adults in the general population require screening to determining risk before objective testing. The latter is difficult when there appears to be many possible variables linked to attaining and sustaining optimal vitamin D levels (Ramdin, 2015). This leaves the clinician with the uncertainty of who and when to test outside those deemed high risk in the literature. With fiscal oversight warranting clinicians to control healthcare cost, it leaves the decisions of recommending vitamin D as a therapy for an existing disease, or use it in health promotion solely by the provider. If we can identify other variables that commonly lead to or are linked with vitamin D deficiency this could help to bridge this gap of uncertainty and potentially improve health outcomes in targeted populations.

Vitamin D deficiency is defined by a serum 25(OH) D level < 50nmol/l or 12ng/mL, while obesity is defined as a body mass index ≥30. In patients who are being managed for their chronic illness in an integrated model of care, there is the traditional [conventional] medical management, supplemented with other treatment modalities including medications that under the Dietary, Supplement, Health and Education Act (DSHEA) 1994 are considered supplemental or alternative. Additionally, there are other mind-body therapies such as acupuncture, massage and yoga. Determining the extent of the problem among at risk populations was called for in a 2007 scientific conference proceeding, asking researchers to nationally address it in the 21st century (Conference Proceedings on Vitamin D and Health in the 21st Century, 2007). Additionally, there has been conflicting evidence on whether vitamin D deficiency is associated with chronic
pain. A few small-scale studies indicate there may be some pain relief in correcting a vitamin D deficiency, but the evidence has not been borne out in large populations to support a practice of adoption for pain management (Knutsen, Brekke, Gjelstad and Lagerlov, 2010; Hicks, Shardell, Miller, Bandinelli, Gurainkik Cherubini, Laurentani and Ferrucci, 2008; Gloth, Lindsay, Zelesnick and Greenough, 1991).

A theoretical framework that captured the complexity of vitamin D adequacy was used in the systematic review for screening, treatment and subsequently in the study examining the socioecological variables associated with vitamin D deficiency. In both systematic reviews, the socioecological model was selected as the guidance framework to organize the information. Selecting this framework reflects the evidence in the literature on factors that affect vitamin D status. This model or similar frameworks has historically been widely used in health promotion and disease prevention (Coreil, 2010).

Through a retrospective design, a secondary data analysis examined the medical records of adult patients seen for various chronic illnesses at an integrative medical clinic in a major urban academic medical center. Data collection reflected visits that covered 6 years, 2007-2012. Statistical analyses were conducted to determine the magnitude of the relationship between variables: Vitamin D deficiency and obesity, and vitamin D and pain in this population. Descriptive statistics, correlation analysis and logistic regression analyses evaluated the statistical significance of the relationship between Vitamin D and BMI, and vitamin D and pain among the sample population.

Research Aims and Manuscript Dissemination Plan

This research achieved three specific aims. The first aim was to determine the status of vitamin D levels among a population of adults seeking care at an inner city
integrative medicine clinic. Secondly, this work examined the significance of the

different socio-demographic and select socioecological factors, controlling for age,
gender and ethnicity, on serum 25(OH) D concentration (ng/mL). The third aim was, to
determine the significance of the difference association of 25(OH) D levels and obesity,
and the association of 25(OH) D levels and pain among this study population. The results
of this research are presented in three separate manuscripts. The manuscript
dissemination plan is presented below.

**Manuscript One:** Screening for Vitamin D deficiency: A clinician’s guide based on a
systematic review of the literature. The purpose of this effort was first, to examine the
variable associated with vitamin D deficiency and secondly, to determine the state of the
science on determining vitamin D risk status. Primary research that focused on examining
vitamin D in adults with relevance to clinical practice was the priority. Medical Literature
On-Line (MEDLINE,) Cumulative Index to Nursing and Allied Health Literature
(CINAHL), and Cochrane Database were the primary sources used for this review.

We found that there were established risks for having low vitamin D levels, not
limited to, but including race and ethnicity, diet and exposure to sunlight. Also implicated
by association were several chronic illnesses including cancer, diabetes type 2, obesity,
cardiovascular disease, rheumatoid arthritis and auto immune conditions. However,
screening was recommended for a select group in the population mostly based on
ethnicity and age. The uncertainty of how, who and when to screen for vitamin D
deficiency was evident. This led to this manuscript [one] which is prepared for
submission to the Journal of the American Association of Nurse Practitioners (JAANP).
Manuscript Two: Subsequent to the determination of risk and gaps in the evidence on screening, the purpose of the second systematic review was to determine if there was adequate treatment for vitamin D deficiency. To address this issue, a synthesis of the literature examining research that focused on the treatment of adults with vitamin D deficiency was done.

We found that despite recommended testing in segments of the population, there was suboptimal treatment. Furthermore, that treatment was essentially being done to treat an existing deficiency and rarely being used for disease prevention. The manuscript presents a tiered approach to treatment as derived from the literature, and highlights gaps based on a socioecological theoretical approach. The manuscript entitled “A Systematic Approach to Treating Vitamin D Deficiency: A clinician’s guide is meant to be a follow up to the manuscript one, and therefore the same journal is targeted for this manuscript submission; Journal of the American Association of Nurse Practitioners (JAANP).

Manuscript Three: The literature searches and the two manuscripts led us to further investigate the phenomena of vitamin D deficiency. The purpose of the third manuscript is to share the results of the research done which examined key sociodemographic factors that are most associated with low vitamin D concentrations. We also examined if obesity was a significant determinant of serum 25(OH)D concentration (ng/mL). Finally, we explore whether serum 25(OH)D concentration is a determinant of chronic pain. We utilized a retrospective chart review of adults with chronic illness who access care at an urban integrative medicine clinic over a six-year period from 2007 to 2012.

We found that seasonality, ethnicity and age were strongly associated with vitamin D deficiency in this population. There was evidence to support that adults with
high body mass index (BMI) are more likely to have 25(OH)D concentration less than the optimal 50 ng/mL. There was an association between 25(OH)D and chronic pain as measured on the pain scale of 1-10. Specifics of these data are supplied in the full manuscript in Chapter Four. The results have implications not only statistically but clinically as well. Given the readership for the Journal of Alternative and Complementary Medicine: Research on Paradigm, Practice, and Policy, this is our targeted journal for the initial dissemination of the results.

**Contribution to Nursing Science**

This study is relevant to nursing practice which is generally concerned with maximizing the health and well-being of a person. Given that low vitamin D may initiate, exacerbate and complicate some diseases, knowing associated factors is crucial (Durup, Jørgensen, Christensen, Schwarz, Heegaard, and Lind 2008; White, 2012; Wortsman, Matsuoka, Chen, Lu, and Holick 2000). If there is a large disease burden because a critical factor that contributes to health is missed (such as low vitamin D concentrations), then the individual’s overall health will be jeopardized. Such would be the case when low levels of vitamin D are not detected through screening or continual surveillance especially in groups known to be at high risk. The clinical implication indicates the need for targeted screening in adults who live in temperate zones especially when they are over ideal body weight.

Knowledge of some of the socioecological factors associated with vitamin D deficiency enables the clinician to optimize each health contact, be it for primary, secondary or tertiary care. It may mean targeted assessment questions and enhanced
treatment for adults with certain categories of chronic disease. This takes into consideration that two of the three basic sources of vitamin D is minimal to non-significant: vitamin D synthesis via sunlight and vitamin D supplied through nutrition. The only other means is by supplementation, but this supplementation needs to be sustained especially in temperature climates. This entails intentional surveillance and supplementation to prevent adults, once treated, from having a prolonged state of deficiency which can ultimately affect the patient’s health. The results of the research are most relevant to clinicians who practice predominantly in urban temperate communities. It extends the body of knowledge by looking retrospectively at a population who is predominantly a minority and of lower socioeconomic status who did not self-select for the study. The dissertation report and research add to existing knowledge by examining the variables associated with vitamin D deficiency. It also contributes to the body of knowledge on vitamin D status in a predominantly urban population living in a temperate zone.
Chapter Two: Screening for Vitamin D deficiency: A clinician’s guide based on a systematic review of the literature.

Valeria Ramdin

School of Nursing
The Bouvé College of Health Sciences
Northeastern University
Manuscript One

Screening for Vitamin D deficiency: A clinician’s guide based on a systematic review of the literature.

Abstract

Vitamin D deficiency is a clinical condition that easily may go undetected. However, with the increasing evidence linking it to a variety of chronic diseases other than bone ailments such as rickets or osteoporosis, screening among at-risk populations is vital. A systematic review was used to analyze 141 studies published between 2005 and 2015 that described screening of vitamin D status in adults. The socioecological model was used as the framework for the extraction of data. The process of assessment was extracted from each article to help answer the question of who should be screened, and when and how screening should be done in different segments of the population.

Screening needs a two-pronged approach: 1) risk assessment based on associated factors including race, gender, age, medications, BMI and 2) serum 25(OH) D test to objectively measure levels in those persons at high risk. This article expands on current recommendations for vitamin D screening of adults in the US by specifying a more concrete guide for practice. Nurse Practitioners and other Primary Care providers can best facilitate treatment of vitamin D deficiency, mitigating its deleterious effect in some chronic diseases. Similarly, clinicians can help the at-risk patients develop a self-management health plan to prevent or reduce morbidity associated with this deficiency.

Keywords: Vitamin D screening, Vitamin D deficiency, Hypovitaminosis D
Introduction

Vitamin D insufficiency and deficiency are among the most common preventable disorders affecting approximately one-third of the US adult population with serum 25(OH)D concentration ≤20 ng/mL (NHANES, 2006). The vitamin, which is naturally available in a limited number of foods, is predominantly otherwise obtained via ultraviolet B light from the sun at wavelengths of 270 to 300 nm (McGreevy and Williams, 2011) or by food fortification. Vitamin D is required for calcium synthesis and bone growth and also for cell growth modulation, immune function and reducing inflammation (IOM, 2010, Holick, 2006). According to the International Osteoporosis Foundation, vitamin D insufficiency is defined as serum 25(OH)D concentration less than 50 ng/mL and deficiency as levels less than 25 ng/mL (Dawson-Hughes et al., 2010), which is consistent with levels reported in a summary from the US Preventive Task Force (USPSTF) (LeFevre, 2015).

Screening for suboptimal levels of vitamin D is a priority supported by a growing body of evidence indicating that there may be a correlation between vitamin D deficiency and many chronic diseases (Mitchell, Henao, Finkelstein and Burnett-Bowie, 2012). For centuries it has been acknowledged that deficient levels of vitamin D are associated with bone disease and its complications continues to be studied (DIPART group, 2010). However, emerging evidence links vitamin D deficiency to many other chronic diseases such as multiple sclerosis (Munger, Levin, Hollis, Howard and Ascherio, 2006), chronic kidney disease (Bhan, Burnett-Bowie, Ye et al., 2010), anemia, chronic heart disease, depression, systemic lupus erythematosus, and musculoskeletal pain (Torrenté de la Jara et al., 2006). It has also been linked to cardiac disease (Booth, Cheng, Fox, Hoffman et
al., 2010), and immune system problems (Holick, 2007; Hewison, 2012). But there are many questions that practitioners still need answered such as: is annual screening recommended? Is it okay to treat patients suspected of having low vitamin D levels without objective testing? Are there specific age groups for which screening should be routinely offered and when should screening be done?

According to the USPSTF 2014 screening guidelines that most practitioners use, the answers to some of these questions are still not clear. Additionally, there are few specific presenting symptoms diagnostic of vitamin D deficiency (Holick et al., 2011). Presenting signs and symptoms that may often lead to the practitioner ruling out vitamin D deficiency by diagnostic test are often associated with other diagnoses, for example, fractures, fatigue and chronic pain. Given that patients are not routinely tested for vitamin D deficiency in a well-person visit (screening is typically limited to osteoporosis screening of post-menopausal women), (USPSTF, 2014 guidelines) screening needs to be diligently done. Patients do not attend a health check or sickness visit stating they have a problem with vitamin D inadequacy. Rather, they present with chief complaints of stress, fatigue, depression, or chronic pain, any of which may not point to vitamin D deficiency but could certainly be a contributing factor, prompting further assessment. A major responsibility is for primary care providers to identify patients at high risk or that test positive for the deficiency and institute a course of management.

Despite a call by the Endocrine Society for standard screening among select populations at risk, such as African Americans, Hispanics and the elderly, this practice has not been adopted as a standard of care (Holick et al., 2011). Additionally, recent reports from the Institute of Medicine (IOM) also call for routine screening among at-risk
groups. The IOM defines four categories of vitamin D status as measured by 25-
Hydroxyvitamin D Analysis or 25(OH)D:

(i) risk of deficiency--Serum 25(OH)D less than 12 ng/mL,
(ii) risk of inadequacy--Serum 25(OH)D 12–19 ng/mL,
(iii) sufficiency--Serum 25(OH)D 20–50 ng/mL and
(iv) above which there may be reason for concern--Serum 25(OH)D greater than
50 ng/mL (Looker, Johnson, Lacher, Pfeiffer, Schleicher, and Sempos, 2011).

Likewise, the US Preventive Task Force (USPSTF) recommends testing for vitamin
deficiency in non-institutionalized, non-pregnant adults, 18 years and older who fall into
the following categories: people who have low nutritional intake, known malabsorption
problems (for example celiac disease), live in climates with a winter season, live in high
altitude terrain, are obese, or dark-skinned persons especially Blacks and Hispanics
(LeFevre, 2015). These categories, however, represent a broad cross section of people
well and ill. Having specific guidelines will help to streamline the screening requirements
for practitioners and is the intent of this report.

The purpose of this systematic review was to determine the evidence and
recommendations for vitamin D screening in the primary care setting for adults 18 years
and over. Informal benchmarking discussion with colleagues at a primary care medicine
conference in Fall of 2013 and again in Fall of 2014 suggest there is much quandary
about screening and treatment, and that there is variability with practices among
healthcare providers. The article addresses who needs to be screened, and how and when
screening should be done, based on a review of the literature. We give a practical
summation with algorithm and codes for billing purposes. It is intended to help guide
nurse practitioners in primary care practice given the growing complexity and controversy of vitamin D screening. It will not advise on treatment recommendations or screening for those already known to be deficient, nor for persons institutionalized. Screening of vitamin D is only just that, and does not negate decisions based on clinical presentation or other assessment findings of the patient.

The socioecological model provides the framework for identifying studies that focus on populations and circumstances contributing to suboptimal levels of the vitamin. A literature review was completed and additional evidence from professional forums and established healthcare organizations were evaluated. The motivation for this systematic review is based on empirically supported recommendation and anecdotal evidence from clinical practice. There was no funding source for this review.
Methods and Approach

Several search strategies were used to obtain information on screening for vitamin D deficiency. A descendency approach uncovered primary research on vitamin D screening, then we searched for citation indexes and sources within publications. Reference databases, research bibliographies, research registers, citation indexes and dissertation indexes were used to find information. The PRISMA system including the 27-item checklist was then used to select research that met the high quality criteria for scientific research. Most citations were from CINAHL (Cumulative Index to Nursing and Allied Health), Dissertation Abstracts, PubMed (MEDLINE), Web of Knowledge, Academic Search Premier (EBSCOHost), and Science Citation Index. Search terms used were vitamin D screening, hypovitaminosis D screening and screening for vitamin D deficiency and adults. When the databases were selected, over 10,000 papers were identified. The search was then limited to publications in English, published since 2004, and focused on the US population with a total of 141 sources used.

Inclusion Studies

Research or reviews that examined vitamin D screening in adults 18 years or older that were non-pregnant and did not possess any of the exclusion factors below were used. Also included were expert opinions from reputable policy groups.

Exclusion Studies

Studies in which the participants were pregnant or included institutionalized adults were eliminated. Those studies that focused on pediatrics as well as persons already diagnosed with vitamin D deficiency or conditions for which vitamin D treatment is recommended were excluded. Also excluded were research reports on screening persons already known
to have a disorder that results in vitamin D deficiency, such as end-stage renal disease and terminal cancer.

**Limitations**

Some studies did not specify the assay used to test the participants. According to Holick and Hollis, two renowned experts in the field in the USA, the most reliable serum test is the 25-hydroxyvitamin D [25(OH)D] (Hollis 2010 and Holick et al., 2011. Therefore, if the assay was not specified, the study was not included in the review.

**Data/Findings**

**Data synthesis**

The social ecological health model was used to help extract the information from the studies. This model, a framework for prevention (Fielding et al., 2010), focuses on determinants of health with origins in psychology and human development (Frieden, 2010). However, today it has a broader perspective of factors that impact a person's well being: health behaviors, health promotion and even policy that can impact population health. The IOM has defined the model as: “a model of health that emphasizes the linkages and relationships among multiple factors (or determinants) affecting health.” (IOM, 2003, p.7). Unlike a medical model that focuses on the biological aspect of health, the social ecological health model takes into perspective a broader view including socioeconomic, biological and environmental factors. These factors range from micro-determinants to macro-determinants. The factors are typically illustrated in a pyramid or concentric ovals with each subset or level having a cascading affect on a person’s health depending on their circumstances and characteristics. This approach for screening for
vitamin D status is essential as there are multiple reasons (Kulie et al. 2009) why a person may have suboptimal levels of vitamin D (Melamed, Michos, Post et al., 2007).

Commonly adapted levels or constructs in this model are:

1. **Intrapersonal/Individual**: These are factors that impact the individual at a personal level, for example: education, attitudes, genetics, food preferences (include lactose intolerance) and demographics.

2. **Interpersonal**: This usually represents social networks and family characteristics or relationships in the immediate community that influence health care behaviors. Medical provider health teaching and commonly prescribed treatment for disease can be included here.

3. **Organizational/Institutional**: These factors include social and cultural norms established by schools, workplaces, and neighborhoods. It explores the health impact based on where people live, work or play. It also takes into consideration societal factors such as culture and religion (for example, people wearing full body covers) as well as the physical environment including climate.

4. **Social/Policy**: This could be public policy and regulation for example, the use of fortification of vitamin D in staple foods such as milk, breads, cereal etc.; even patterns of health care discrimination can be addressed at this level.

These levels were used to help label and extract the relevant data from the published articles.
Who Should Be Screened for Vitamin D Status

Intrapersonal Factors

Vitamin D status may be a determinant of health based on intrapersonal factors. With roughly 33% of the US population at risk of inadequacy and/or deficiency, one must examine the factors that contribute to this condition. The prevalence for suboptimal levels of the vitamin D differed by age, sex, race, ethnicity and genetic makeup, thus placing select groups at higher risk for developing the deficiency (Looker et al., 2011).

The elderly is particularly vulnerable to vitamin D deficiency (Yousseff, 2011). High deficiency levels were reported in a small prospective observational study by Dharmarajan, Adyula and Kuppachi who studied gait imbalance and falls (2005). This pilot study revealed that 54% of the older population screened positive for the deficiency (Dharmarajan et al., 2005). Congruence for placing the older adult in the high risk category was also determined in a 2014 study by Annweiler et al., who found that decrease executive function in older adults was linked to vitamin D deficiency (Annweiler, Cedric et al., 2014). Rianon et al., (2014), also found a disturbing paucity of screening among elderly with bone disease, which from a retrospective electronic chart review revealed that only 22% were screened despite their vulnerability.

Another determining factor is nutrition; second to sunlight exposure, foods provide the next best source of vitamin D. There are, however, few foods that naturally contain sufficient levels of vitamin D; hence, most of this vitamin in the USA comes from fortified foods in accordance with a USDA 1943 government policy (Backstrand, 2002). Studies indicate that food intolerances render fortified food intake ineffective as a way to attain adequate vitamin D levels (Vagianos et al., 2007; Gordon et al., 2008;
Gallagher 2013). Such is the case with African Americans among whom there is a high incidence of lactose intolerance as supported in the study by Calvo and Whiting (2012). This study linked the high incidence of vitamin D deficiency among African American to lactose intolerance and food malabsorption. Similar findings were realized in a small study done on multiple ethnic participants with irritable bowel disease (Vagianos, Bector, McConnell and Bernstein, 2007) in California and (Gordon, Caan, Asgari et al., 2008). A significant source of vitamin D is sunlight; however, in some groups the dark skin color limits this as a source.

The inability to synthesize vitamin D via the skin in dark-skinned persons has been well represented in the literature (Scragg and Calvo (2008); Weishaar and Vergili (2012); Touvier et. al., 2014); Holick 2007). Weishaar and Vergili conducted a large cross-sectional correlational study with data from 12,505 subjects of whom approximately one-quarter (3, 402) were non-Hispanic Blacks and found a strong correlation between skin color and suboptimal vitamin D levels. These scientists determined that socioeconomics played a big role for optimal health in Blacks, and therefore attributed the disparate findings to this. Disease and illness related to vitamin D deficiency was also disproportionate among African American, affecting their mortality. One of the largest studies that examined mortality in relation to vitamin D in the US was completed by Signorello, Han, Cai et al., (2012). In this prospective study on mortality they examined race and vitamin D variables in n=85,000 men and women in Southeastern US states. They found a positive correlation between race and vitamin deficiency. The two main determinants of vitamin D deficiency or insufficiency in this same study were race and the season of the year when the blood was collected. Furthermore, in the same
study there was increased mortality in persons with the suboptimal vitamin D levels. They found African Americans had on average 5.1 ng/mL lower than Caucasians and 5.6 ng/mL lower levels when bloods were drawn in the winter and this resulted in increased mortality due to these factors. Similar results were found across all age groups in the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) research. This was a population-based study done on participants 30-64 years old, dividing them into quintiles, with data collected from 2004 to 2008. This study showed consistently lower levels of vitamin D by 25(OH)D concentrations in Blacks across all age groups (Powe, Evans, Wenger et al., 2013).

Not only does skin color matter, but the amount of time exposed to quality sunrays. Note that headgear and full body clothing whether worn for cultural, habit or health reasons impacts the amount of sun rays that penetrate the skin. The amount of exercise in the sunshine exposing the skin to the UV rays enhances the absorption of vitamin D. Scientists Scragg and Calvo (2008) used the large third NHANES dataset to study n= 15,148 adults >/= 20 years and found there were significant benefits of outdoor sun exposure for obtaining vitamin D. Surprisingly, they found evidence that older adults can attain enough vitamin D level through the skin, contradicting some other studies (Stoker, Buchowski, Bridwell et al., 2013; MacLaughlin and Holick, 1985; Farage, Miller et al., 2013; Wacker and Holick, 2013; Schagen, Zampeli et al., 2012; Gallagher, 2013). The other studies indicate that the wrinkled and aged skin does hinder enough sunlight absorption as a meaningful source for vitamin D. Despite a person’s innate biological status, factors outside them affect a person's vitamin D status.
Interpersonal Factors

Interpersonal factors impact the individual at a personal level. This could be their level of education, socioeconomic status, attitude, beliefs and behaviors. People’s knowledge of, and attitude pertaining to, vitamin D also affects what measures they take to maintain their vitamin D in a healthy range (Thomson, Spedding, Brinkworth et al., 2012). For the clinicians these interpersonal values will impact screening of their patients (Holick et al., 2011; Sherman and Svec, 2009). Sherman and Svec surveyed veterans who were members of the American Academy of Family Practice (AAFP) and American Academy of Pediatrics (AAP) and found that most physicians in the study thought that exposure to sunlight prevented vitamin D deficiency.

Socioeconomics (SES), another interpersonal factor, is more than the ability to buy food; it may also mean the person’s inability to have health insurance that covers preventative healthcare services. Without being financially stable, SES may impact when and how much time a person can take off from work to attend to medical appointments. Seeking healthcare services especially when it conflicts with the time a person works, knowing that every hour of work lost means lost wages, can be problematic in low SES individuals. Although SES status was not supported as an indicator for routine screening in the general population, it was identified as a variable worth evaluating. A study by Lee, Weber and Colon (2013), utilizing a Markov decision model, found that there was much cost effectiveness to population screening in community dwelling adults 85 years and older, rather than blind supplementation in this age group. This is similar to the findings for the adults in the 65 to 80 age group in the same study. In the latter group
screening was more cost effective than just supplementation without known baseline vitamin D status.

**When to Screen for Vitamin D Status**

**Organizational/ Institutional Factors**

Season is important to consider when screening for two reasons. 1) Vitamin D is produced in the skin by sunlight exposure and 2) people tend to wear clothing to protect them from inclement weather, be it extremes of cold or hot. For these reasons, in temperate climate zones, November–March tends to be the time of year when the expectation is for lower vitamin D stores in the body. Conversely, April–October in this same zone would be the time expected for optimal levels to be maintained without intentional supplementation (Looker, Dawson-Hughes et al., 2002; Wacker and Holick, 2013; Weishaar and Vergilli, 2013). Bee, Sheerin Wuest et al., (2013) studied serum levels of vitamin D in a retrospective observational cohort study of patients living in the Northwest United States and found that at a level 2 trauma center, all the patients with orthopedic trauma were vitamin D insufficient. Their criteria for normal range were values between 32 and 80ng/mL which is above the normal for an upper limit of 50ng/mL considered by the IOM as adequate for bone and overall health (IOM, 2010).

Using the Charlson Comorbidity Index, the quality of a person’s health can be measured by the number and type of chronic illnesses they have. There is some new evidence linking vitamin D insufficiency to many commonly prescribed medications that are used to treat chronic ailments. Some of these are medications for treating hypertension, heart disease, cancer, seizures, HIV, high cholesterol, tuberculosis and osteoporosis (Gröber and Kisters, 2012; Young Snell-Berger ad Naik et al., 2011). In the
latter study Young et al. found that vitamin D deficiency was a predictor for developing coronary artery calcification in non-Hispanic whites who had type 1 diabetes mellitus. Similarly, there are other links to suboptimal vitamin D levels in certain chronic conditions such as chronic pain and mental illness, in which screening for vitamin D concentration is also recommended (Youssef, Abbassi, Cutchins et al., 2011). A longitudinal study including participants from the Physician Health Study of $n=14,916$ men, followed for 18 years, found that 1,066 developed prostate cancer. Upon further investigation they found 14\% of those men with European descent were susceptible to this type of cancer in the presence of low 25(OH)D status, and that furthermore, the men who developed cancer generally had suboptimal levels in the winter and spring months when all other variables were taken into consideration (Li et al., 2007). However, sometimes factors targeting the individual are not always the answer; therefore, public policy is necessary.

**Social/Policy Factors:**

Societal factors including public policy help set the agenda for population health. The fortification of foods such as milk, bread, and cereal with vitamin D is now some seventy years old here in the US but we still have much concern over this vitamin deficiency despite established policy. Agenda setting in the society varies, and there was only a single study found that examined policy as a means to keep adequate vitamin D levels in the population. This study was conducted in Australia (Dixon, Warne, Scully et al., 2014) combining policy with attitudes and beliefs. They found that news coverage affects attitudes and beliefs, but no similar study was found here in the USA. However, from a policy perspective, there was a single study examining the nutritional
determinants [fortification] of food, Calvo and Whiting (2012) concluding that fortification with vitamin D is necessary to prevent large-scale hypovitaminosis D and suggesting it be mandatory in the USA. This broad approach to care helps offset some of the health disparities reported to be linked with segments of the population.

According to the Centers for Disease Control (CDC) “health disparities are preventable differences in the burden of disease, injury, violence, or opportunities to achieve optimal health that are experienced by socially disadvantaged populations (CDC, 2014).” The first study indicating that vitamin D may be a determinant of health disparities was conducted by Peiris, et al., 2011, who studied n=14,148 veterans (retrospectively) across their Integrated Service Network 9 systems, which was the Southeastern US. They found Whites were more likely to be initially tested and have follow-up surveillance for vitamin D status than African Americans. Incidentally, they also found there was greater health care cost associated with the health maintenance of Blacks who were tested and found to be vitamin D deficient than their white counterparts. Since then, Weishaar and Vergili (2012), concluded that vitamin D status is a biological determinant of health disparities. Their findings highlight the growing concern of meeting the needs of clients, regardless of class or socioeconomic status, and are similarly supported in a study by Gordon et al., 2012 who used the 2008 Kaiser Permanente Northern California (KPNC) general health survey to evaluate variations in vitamin D supplementation among n=11,003 adults, age 25-85 years in multi-race/ethnic health plan populations. Whether or not the supplementation resulted from large-scale screening was not identified, but this study represents some of the social and policy factors that affect vitamin D status among US adults.
How to Screen for Vitamin D status

Clinical Assessment

Screening for vitamin D deficiency consists of two parts: completing a risk assessment and performing targeted objective serum test. Because serum 25(OH)D is stable over weeks and serves as a biomarker of the adequacy of vitamin D supplies in the body (Gallagher and Sai, 2010; NIST 2009; Hollis, 2010), this is considered the most appropriate testing for adequacy. Note that tests that measure serum levels of 25-hydroxyvitamin D [25(OH)D] are not standardized (Holick et al., 2011, Binkley et al., 2010) and therefore should be used in conjunction with a thorough clinical assessment. This assessment may include a history and physical examination as well as evaluation of other diagnostic tests that may have been done. Diagnostic test results with low serum or 24-hour urine calcium, elevated parathyroid levels, high alkaline phosphatase or low phosphorus levels (Kennel, Drake and Hurley, 2010) are of concern. Similarly, if X-rays indicate osteopenia, osteoporosis, non-traumatic or pseudo-fractures, a vitamin D level test is suggested (Kennel, Drake and Hurley, 2010).

Discussion

This paper attempted through systematic review to answer the question of who should be screened, and how and when vitamin D screening should be done. The hope was that we would find some randomized control studies with a breakdown by age groups and frequency of testing. However, these were not found. The socioecological framework which was used indicates there were several factors that place an adult at risk for vitamin D deficiency, concluding that maintaining vitamin D within optimal levels is complex.
Looking at the factor of who to screen, there were several intrapersonal and interpersonal factors that places one in a category for which screening is prudent. It appears that race was one of the stronger determinants for being at high risk for vitamin D deficiency. For persons who are Black or Hispanic, the melanin in their skin protects them from harmful UV sun rays but also prevents them from absorbing sufficient quantities of sunlight for conversion to adequate vitamin D levels. The studies referenced throughout also indicated that biological age was a deciding factor of determining risk, especially when this variable was coupled with a population that had a tendency to fall. Therefore, the older adults were considered in the high risk group and needed to be screened for vitamin D deficiency. In most studies this was seen as 65 years and older, especially when they were post-menopausal women or persons with cognitive decline. A more difficult determination would be finding out which persons were resistant to synthesizing vitamin D because of a gene variant, for this also places a patient at moderate risk. Healthy People 2020 calls for effort to mitigate disparities in health, and some studies done as recently as 3 to 4 years ago found race as a determinant of lower screening and surveillance for vitamin D deficiency (Looker et al., 2011; Forrest and Stuhldreher, 2011).

To determine if healthcare organizations as an institutional determinant of health also influence screening, one need only to examine the evidence for monitoring vitamin D sufficiency when certain medications were being routinely prescribed. There was one published study found that concluded that taking certain categories of drugs (Grober and Kisters, 2012) placed persons at risk for vitamin D deficiency. Refer to the illustration in Appendix A. Fig. 1a for a list of these medications. There are some implications that
Blacks are not being screened at the same rate as other races (Forrest et al., 2011). Regardless of who is being screened, one thing was clear and that was how screening was to occur. 

**How** to screen was clearly documented with serum 25(OH)D being the assay recommended as the test of choice for accuracy. However, there is evidence that the range for what is considered normal varies between studies. Most used the lower limit of 25(OH)D concentration of 20ng/mL as the deficiency levels, and greater than 20ng/mL but less than 30ng/mL as insufficiency, consistent with that used by the Endocrine Society. Only routine objective testing in at-risk populations such as the elderly and dark-skinned races was supported by the evidence found. Other testing was to be done in conjunction with some clinical assessment to determine risk category.

Who and how to screen is in agreement with the USPTF (LeBlanc et al., 2015), and IOM advisory group (IOM, 2010), which also indicated there is insufficient scientific evidence to recommend routine screening for vitamin D deficiency in primary care practice. Additionally, the USPTF made recommendations that are consistent with those made by the US Endocrine Society, the Agency for Health Care Research and Quality AHRQ (2010) and the American Colleges of Physicians.

The decision of **when** to screen focused either on the time of the year or life span. Looking at the lifespan, most representation was for testing of persons who were elderly as noted above. Because vitamin D is a fat soluble vitamin and is crucial not only to the development of healthy bones, but may be associated with various other systemic conditions, it is prudent to screen for its status in healthy or ill adults. Knowing vitamin D status and treating appropriately is important even before falls, bone loss or cognitive
decline starts, which is where the focus for when to screen for vitamin D deficiency in the adults centered. There were no published studies found that examined when to start specific vitamin D screening in the young well adult. It would seem according to practice guidelines when assessing for nutrition, BMI and thyroid etcetera, this would yield some data to trigger the need for serum testing. But no studies were found to identify generalized 25(OH)D population testing, a starting age range for screening, nor screening by age groups except in the elderly, and even then, did not specify how often screening should be done.

In summary, an important strength of this paper was the added viewpoint to the literature, for clinicians to examine the socioecological aspects of a person when assessing vitamin D status. Consideration has to be given not only to a person’s demographic and intrapersonal factors, but to ecological, organizational, social and political aspect that impact health. For example, in temperate climates, consideration as to how many actual days of direct sunlight there are and what type of clothing the person wears are important. If a patient is being supplemented and not responding to rising levels consistent with what is expected, perhaps genetic variation may be something else to think about. These are all part of a systematic approach to maintaining a healthy population.

This systematic review has its limitations as the focus was on studies done with adult participants living in the USA. Moreover, there is no statistical analysis of the studies found; therefore, the results and discussion are based on a description only. To minimize any limitation in the process, the emphasis was placed on being methodical
starting with randomized control studies (RCT)s and ensuring that all levels of studies were included.

**Conclusion**

Currently, there are no guidelines or specific study results that support routine testing for vitamin D deficiency among the general adult population living in the community. Most recommended determining risk, and then screening of the at-risk populations. The implication for practice is that testing should not be a cost/benefit approach especially in the older old population (Lee R, Weber T, Colón-Emeric C. (2013), but rather a judicious effort for targeted screening except with African Americans and Hispanics for whom the entire segment of the population is at risk. When testing, the following codes are helpful for reimbursement claims;

ICD-9-CM Diagnostic Codes Index:

- 82306 Vitamin D; 25 hydroxyl, includes fraction(s), or
- 82652 Vitamin D; 1, 25 dihydroxy, includes fraction(s), used in establishing the deficiency.
- ICD-9-CM 268.9 is a billable medical code that can be used for unspecified vitamin D deficiency

*Expect these codes to be adjusted or changed with the ICD-10 –CM Diagnosis Codes Index.*

Primary care practitioners must continue preventive care to help treat disease and promote wellness (IOM 2002 and IOM 2003). They are in unique positions to encourage people at risk for vitamin D deficiency or when objective test indicates same, to take measures to reduce illness because of the risk. In the meantime, providers should remain
vigilant and screen people known to be at risk. Primary care providers should either read
the results of well-designed studies or attend conference sessions focused on vitamin D to
learn of contemporary management of vitamin D in their patients. From an intrapersonal
perspective they can help develop or revise protocols in their practice settings.
Management is a challenge as blind supplementation without monitoring is a risk.
Appendix A Algorithm for Vitamin D Screening will help the provider with a concise
format and quick reference to determine who needs objective test with serum 25(OH)D.
Appendix A

FIG. 1 Algorithm For Vitamin D Screening In The Asymptomatic Adult

Is patient African American or Hispanic?

Yes → 25(OH)D → Manage according to results

No

In patient older adult ≥70 years old

Yes → 25(OH)D → Manage according to results

No → Have any of the following diagnoses:
- Obesity with BMI >30
- Parathyroidism
- Malabsorption syndrome
- Chronic kidney disease
- Terminally cancer
- Osteoporosis/osteopenia
- Severe liver disease or failure

Yes → 25(OH)D → Manage according to results

No

Taking the following medications routinely:
- Antisepic
- HMGC-CoA-Reductase inhibitors/statins
- Antihypertensive drugs
- Antipernicious acidosis
- Cytostatic agents
- Antiretrovirals
- Bisphosphonates
- Glucocorticoids

Or

Routinely did the following:
- Wear full body clothing
- Used SPF on sun-exposed skin
- Spend most sunlight days indoors

No further screening recommended at this time.
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Running Head: VITAMIN D DEFICIENCY IMPLICATIONS FOR ADULTS


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Chapter Three:

A Systematic Review: Treating Vitamin D Deficiency - A Clinician's Guide

Valeria Ramdin

School of Nursing
The Bouvé College of Health Sciences
Northeastern University
Abstract

**Background and Purpose:** Vitamin D deficiency is problematic for the primary care provider as it has been implicated with many chronic illnesses. Having a synopsis of method, duration and amount of vitamin D supplementation can help healthcare providers tailor their practice in treating this deficiency. **Methods:** A systematic review and analysis of the literature was conducted to extract data on vitamin D treatment. Patterns of recommendation were found for supplementing vitamin D according to age range and some chronic illness, but not for other variables such as race/ethnicity, or gene variants. **Findings:** Overall, there is inconclusive evidence for treatment in the general population. Treatment is based on diagnosed deficiency or the presence of a chronic condition in which the bioavailability of vitamin D is severely affected. Although there are numerous factors that impact vitamin D status, this is not represented in the literature for replenishing its deficiency. **Conclusions:** There are three main choices for supplementing vitamin D: sunlight, food sources and medication. **Implications for Practice:** This paper offers a new stepwise approach to treating patients for vitamin D deficiency. It is based on the presence of gastrointestinal problems, the health of the person’s liver and kidneys, and the state of their skin. Determinant factors from the socioecological framework were used to guide the systematic literature review of supplementing vitamin D. However, little was found in the literature supporting treating according to the sociological context.

Keywords: Vitamin D treatment, Vitamin D deficiency, Hypovitaminosis D,
Introduction

Sub-optimal levels of vitamin D are a widespread problem (Autier 2007, NHANES 2006, Bischoff-Ferrari 2009, Forrest and Stuhldreher 2011, Overcash 2008). According to the US Preventive Task Force, a vitamin D insufficiency is a serum 25(OH)D level less than 50 ng/mL and vitamin D deficiency is less than 25 ng/mL (LeFevre, 2015). The problem leads to poor bone health and is also implicated in a number of other chronic diseases. The benefits of vitamin D supplementation in the presence of a vitamin D deficiency for all-cause morbidity in a variety of chronic diseases are well documented (Autier et al., 2007; Chung et al., 2009; Rejnmark et al., 2012). For the purpose of bone health alone, it is a national public health priority with a 2005-2008 National Health and Nutrition Examination Survey (NHANES, 2012) indicating that 9% of the population had osteoporosis, and another 49% had osteopenia (Looker et al., 2012). As a result, over 44 million adults are affected by poor bone health and the projected annual direct cost by 2025 is estimated at $25 billion to treat this largely preventable condition (National Osteoporosis Foundation, 2009).

There is evidence that a vitamin D deficiency is linked to other chronic conditions not specific to bone disease (Mitchell, Henao, Finkelstein and Burnett-Bowie, 2012): multiple sclerosis (Munger, Levin, Hollis, Howard and Ascherio, 2006), chronic kidney disease (Bhan, Burnett-Bowie, Ye et al., 2010), anemia, chronic heart disease, depression, systemic lupus erythematosus, musculoskeletal pain (Torrenté de la Jara et al., 2006), cardiac disease (Booth, Cheng, Fox, Hoffman et al., 2010), and immune system problems (Holick, 2007; Hewison, 2012). Approximately one-third of adults in the US need some treatment for suboptimal levels of vitamin D (NHANES, 2006);
therefore, the primary care clinician is often faced with the task of prescribing some form of vitamin D therapy. Research reports indicate that in most cases, relying on cutaneous vitamin D synthesis and fortified foods is not enough (Gordon et al. 2012). Adult patients at high risk for vitamin D deficiency, including African Americans, Hispanics, the elderly, those on medication that will interfere with vitamin D synthesis and those with genetic predisposition, are especially in need of regular supplementation (Gordon et al. 2012, Holick and Binkley 2011). Clinicians need to take steps to relieve the burden of these illnesses by enhanced preventative care; this action by clinicians align with the initiatives for Healthy People 2020.

To bring a patient to within optimal vitamin D range as measured by 25(OH)D serum blood test, no one treatment option is suggested, thus challenging the primary care clinicians to practice a comprehensive approach. A review of the literature indicates that there are various end points or goals for treating vitamin D deficiency. Furthermore, prophylaxis treatment for recurrent vitamin D deficiency differs from that for treatment of the acute condition. Additionally, there is controversy regarding the recommended amount of vitamin D supplementation (Veugelers et al., 2014 and Heaney et al., 2015). As a result, there is considerable variance in prescribed dosages, and in some cases, the pharmaceutical vitamin D dosages recommended by clinicians differ from labeled use. There are two other sources of the vitamin that need consideration, food intake and ultraviolet rays. Clinicians are often taught to begin with the less invasive treatment first, then advance as needed. Assessing intake amounts from food or ultraviolet rays is challenging when suboptimal levels of vitamin D have been established. Food intake quantities do not always provide the active amount in the body. Similarly, duration of
exposure to sunshine does not unequivocally determine vitamin D quantities available through this synthesizing process. The only objective determination is a repeat of the 25(OH)D concentration.

Population-based health determinants of vitamin D adequacy indicate multiple factors that affect a person's vitamin D status; consequently, treatment for any deficiency will similarly be multifactorial. However, this paper will focus on three common sources of Vitamin D: UVB sun rays, fortified foods, and pharmaceutical drugs. Anecdotal evidence from both practitioners and laypersons indicate that a variety of strategies, dosages and frequency are being prescribed for similar conditions and diagnoses. The practitioner must contemplate whether everyone diagnosed with suboptimal levels of vitamin D needs medication. Also to be considered are the following questions: Is there documented consensus that can streamline the approach to treatment? Do clinicians know how much and with what frequency they should prescribe vitamin D supplements? Does the evidence indicate a stepwise approach beginning with UVB rays, food sources and then medications? What indicator is used to determine the end point for treatment? Is treatment being used to mitigate some ailment or prevent an illness from occurring? Finally, how does vitamin D supplementation dosing differ?

To answer these questions, a literature review was completed and additional evidence from professional forums and established healthcare organizations was evaluated. The impetus for this systematic approach to vitamin D supplementation grew from the vast differences in dosing found in the literature while conducting a systematic review pertaining to screening of patients for vitamin D deficiency. Subsequently, discussions with colleagues revealed a variance in prescribing frequency; ranging from
daily to weekly dose, and in a few cases even a single monthly dose. Paralleling this frequency variability, are dosages that range from low dosing calciferol 200 IU 3 times a day to mega-dosing once annually with 500 000 IU calciferol. It is noteworthy that there are two forms of the pharmaceutical preparation. This article differs from previous articles in that it gives a more comprehensive overview of treating vitamin D deficiency, taking into consideration two of the other socioecological factors, food intake and sunlight exposure that contribute to a person’s vitamin D status.
Methods and Approach

Several search strategies were used to obtain information on treating vitamin D deficiency in adults. Where appropriate, the variable that contributed to the deficiency and guided treatment, for example age or race, was identified. We first looked at the National Clearing House to see what clinical guidelines for treatment were documented. This was followed by a search in the published literature for primary research, meta-analysis and/or systematic review with specific dosages studied and or recommended. The research was further examined to determine the strength of the evidence using the Grading Recommendations, Assessment, Development and Evaluation (GRADE) working group concepts. Guideline validation by external peer review and internal peer review were taken into consideration in determining the quality and strength of the recommendation. It was also considered a quality worth including if the draft guideline was sent out for public comment. Reference databases were used; most citations were from PubMed (MEDLINE), CINAHL (Cumulative Index to Nursing and Allied Health), Dissertation Abstracts, Academic Search Premier (EBSCOHost), Science Citation Index and Google Scholar. The method used to formulate the guidelines for the clinicians is based on the expert consensus found in the literature. Search terms used were vitamin D treatment, hypovitaminosis D treatment, vitamin D deficiency with a focus on adults.

Inclusion Studies

Primary research, meta-analyses and systematic reviews that examined vitamin D treatment in adults 18 years or older were included. Treatments that were intermittent, high dose or regular dosing were included, regardless of whether the patient was
institutionalized or in the community. Also included were expert opinions from reputable policy groups or organizations.

**Exclusion Studies**

Research in which the treatment focused on participants who were pregnant was excluded. Guidelines provided by special interest groups for which there was no citation or reference to empirical research were not used.

**Limitations**

Only articles published in English that examined treatment in adults were included. Given that there were varied types of studies supplementing vitamin D for different ailments, acceptance was given to both the studies as well as the published guidelines focusing on the questions we sought to answer. The search was methodical starting with listing of the databases and proceeded with a more rigorous extraction of the data in tables.

**Data/findings**

There are two different forms of vitamin D: vitamin D\(_2\) or ergocalciferol, the form found in food sources, and vitamin D\(_3\) also known as the natural form or cholecalciferol, the type converted from exposure to UVB rays. Because both are chemically converted into the hormone calcitriol before they are active, and from there on, follow a similar physiological process for use in the body to aid calcium absorption and mineralization of bones etc., (Porth et al., 2014), both sources were critically appraised. Synthesis of vitamin D into active forms for use in the body requires that a person has healthy liver
and kidneys. Persons with either chronic liver or kidney disease are unable to transform vitamin D to active forms (Porth et al., 2014) and are at recurring risk for vitamin D deficiency. The presence of these diseases impact how clinicians will approach their supplementation and treatment. This paper will use the umbrella term of vitamin D for both vitamin D$_2$ and vitamin D$_3$ and will only use the specific type when warranted.

**Consensus Approach for Vitamin D Treatment**

Based on the evidence we know that persons with diagnoses of obesity (diagnosed as BMI >30), Parathyroidism, malabsorption syndrome, terminal cancer, osteoporosis/osteopenia, and severe liver disease or chronic kidney failure all require vitamin D supplementation (Tangpricha et al., 2012; Signorello et al., 2013; McGreevy et al., 2010; Murad et al., 2011; and Peiris et al., 2012). The IOM put forward a guideline in 2010 for 600 IU per day for [children ≥1-year-old, and adults ≤70 years, and 800 IU per day for older adults ≥70-years-old (Institute of Medicine, 2010). However, this came under scrutiny by a group of scientists at UC San Diego and Creighton University as reported in articles by Veugelers et al., (2014) and Heaney et al., (2015) respectively. They both reported that there were statistical errors resulting in underestimation by about tenfold in the quantities of IU recommended for the adults. Most of the established guidelines are for specific conditions with generalized recommendations of when to treat. For example, there is consensus by the Cystic Fibrosis Foundation (CFF) calling for annual screening of patients with cystic fibrosis at the end of winter. This would be done using serum 25(OH)D test, and CFF recommends treatment if the patients have levels below 30ng/mL to bring them back to optimal level (Tangpricha et al., 2012). The reference to seasonality
is a prominent factor in relation to treatment (Holick et al., 2011; Pfeifer et al., 2009; and Rejnmark et al., 2012).

There is conflicting evidence among clinicians as to how much sunlight without SPF protection is healthy and the length of exposure needed to deliver adequate sources of vitamin D (Scragg et al., 2008; Thomson et al, 2012; Weishaar et al., 2013; Zheng et al, 2015). During the spring and summer it is reported that direct sunlight between 10am and 2pm is the most adequate, providing the skin is healthy and is not covered by clothing. There is not enough in the literature to state how many square inches of the body needs the exposure, but most refer to exposure of the arms. What is clear is that there is seemingly a stepwise approach: UVB rays, food and then medications (Scragg, and Camargo, 2008; Lee et al., 2010; Holick et al, 2010; Kennel et al., 2010; Farage et al., 2013).

When to Treat Patient for Vitamin D Deficiency

Season is important to consider when treating or trying to prevent vitamin D deficiency. Two reasons for this approach are 1) Vitamin D is produced in the skin by sunlight exposure and 2) people tend to wear clothing to protect them from inclement weather, be it extremes of cold or hot. For these reasons, in temperate climate zones November–March tends to be the time of year when the expectation is for lower vitamin D stores in the body. Conversely, April–October in this same zone would be the time expected for optimal levels to be maintained without intentional supplementation (Looker, Dawson-Hughes et al., 2002, Wacker and Holick, 2013, Weishaar and Vergilli, 2013). In 2013, Bee, Sheerin Wuest et al. studied serum levels of vitamin D in a
retrospective observational cohort study of patients living in the Northwest United States. They found that at a level 2 trauma center, all the patients with orthopedic trauma had a vitamin D insufficiency. Their criteria for normal range were values between 32 and 80ng/mL which is above the normal for an upper limit of 50 ng/mL considered by the IOM as adequate for bone and overall health (IOM, 2010).

**Who should be treated for vitamin D deficiency?**

**Sunlight source:** Getting 15 micrograms daily dosing of vitamin D via sunlight can be a challenge depending on the time of day, the cloud cover, the clothing worn and the creams on the skin. The goal would be Ultraviolet (UV) B radiation with a wavelength of 290–320 nanometers to penetrate uncovered skin. This in turn will convert that cutaneous 7-dehydrocholesterol to pre-vitamin D₃, which in turn becomes vitamin D₃. Complete cloud cover reduces UV energy by 50%; shade (including that produced by severe pollution) reduces it by 60% (Webb and Engelson 2006; Wacker and Holick, 2013). UVB radiation does not penetrate glass, so exposure to sunshine indoors through a window or the glass of a vehicle does not produce vitamin D.

It has been suggested by some vitamin D researchers, that approximately 5–30 minutes of sun exposure between 10 AM and 3 PM at least twice a week to the face, arms, legs, or back without sunscreen, usually lead to sufficient vitamin D for synthesis (McLaughlin and Holick, 1985; Holick, 2013). Some researchers also state that the moderate use of commercial tanning beds that emit 2%–6% UVB radiation is also effective (Tangpricha et al., 2012; Holick 2004). The latter recommendation is a source of controversy due to the risk of skin cancers. The amount of time spent exercising in the
sun with little clothing enhances the quantity of vitamin D capable of being absorbed. This is supported by the scientists Scragg and Calvo (2008), who utilized the third NHANES dataset to study \( n=15,148 \) adults, \( \geq 20 \) years old and found that there were significant benefits for outdoor sun exposure in getting sufficient vitamin D. Exercise as a variable was not in itself found in the literature to be associated with vitamin D levels. Scragg et al. (2008), found that older adults can attain enough vitamin D level through the skin, contradicting some other studies (Stoker, Buchowski, Bridwell et al., 2013, MacLaughlin and Holick, 1985, Farage, Miller et al., 2013, Wacker and Holick, 2013, Schagen, Zampeli et al., 2012, Gallagher, 2013), which supported the fact that the wrinkled and aged skin does hinder enough sunlight absorption as a meaningful source for vitamin D.

**Food Sources:** The flesh of fatty fish (such as salmon, tuna, sardines and mackerel) and fish liver oils are among the best Vitamin D food sources. Small amounts of vitamin D are also found in beef liver, 3 oz. cooked 42 IU per serving, cheese, and egg approximately 41 IU per serving. The United States milk supply is voluntarily fortified with 100 IU/cup. The US Department of Agriculture (USDA) is a good source for approximating the amount of vitamin D in foods per serving (http://ndb.nal.usda.gov/). Note that consideration has to be given to patients who are vegetarians; their main source will be fortified foods and natural sunlight. Most recommendations for supplementation assume there is inadequate supply of vitamin D from sunlight or food. Therefore, for patients who may not meet the specification outlined in this section, the need to step up the source of treatment is necessary. Determining the end point or goal of treatment is
based on symptom relief and measured in 25(OH)D serum concentrations. The question of how vitamin D supplement is to be utilized either for treating or preventing a disease is a key question. Therefore, the goal of treatment should be based on comorbidities and should be done in conjunction with the patient based on assessed risk and lifestyle.

**How Does the Dosing Differ?**

Mega dosing was examined in a meta-analysis of high dose intermittent vitamin D supplementation among adults 65 years and older by Zheng et al., who reported in January 2015 that there was inconclusive evidence for recommending high dose treatment to allay mortality. These scientists looked at nine randomized controlled studies published between 2003 and 2012 that met their stringent inclusion for intermittent or high dosing criteria out of a total of 811 studies. Dosing was a single dose larger than 100,000IU and with interval times of greater than one month. They found that in the total population of 22,012 adult participants, there was no statistical significance in support of mega-dosing for preventing hip fractures, non-vertebral fractures or falls. They found a few of the studies reported deleterious effects from the toxic dosing of vitamin D which resulted in falls (Smith et al., 2007) and fractures (Sanders et al., 2010). A strength or limitation depending on one’s view is that this meta-analysis included supplementation by oral dosing or by parenteral injections. A limitation as reported by these researchers was the fall statistics that contained the relevant data were heavily influenced by two studies. Also notable was that the participants in the study were predominantly female.

**What Affects the Dosing?**

The literature reflects that patients taking the following medications: antiseizure, anticholesterol, antihypertensive, antituberculosis, antiretroviral, bisphosphonates,
immunologic or cytotoxic drugs routinely are subject to interference of the bioavailability of vitamin D. Similarly, we have different forms of the vitamin; it comes in sublingual preparations (for example, DLux 3000 IU spray for sublingual or inside the cheek) or 5000 IU sublingual spray, with recommended [RDA] doses differing according to route.

Oral doses based on the new 2010 recommended daily allowance (RDA) is 600 IU for those 1-70 years of age and pregnant or breastfeeding women, and 800 IU for those over 71 years of age (Natural Standards Research Collaboration, 2013). An intramuscular dose of Calcitriol (Calcijex), which is the active form of vitamin D3 (cholecalciferol), is typically administered as a bolus usually three times per week. Although this dosing is not specific to vitamin D deficiency, the labeled dosing is for hypocalcemia and renal dialysis patients. The recommended initial dose of Calcitriol Injection, depending on the severity of the hypocalcemia and/or secondary hyperparathyroidism, is 1 mcg (0.02 mcg/kg) to 2 mcg administered (three times weekly), approximately every other day. Note that when this dosing is being administered to the patient, all other forms of vitamin D should be withheld because of its potency. During this time, essential laboratory test of serum calcium, phosphorus, magnesium and alkaline phosphatase should be done at baseline and then periodically.

**Discussion**

Through a systematic approach, an attempt was made to answer the question of who, how and when to treat a patient for vitamin D deficiency. See Appendix A for a table of recommended guidelines for treatment from established organizations. Three health determinant factors from the socioecological framework were used to guide treatment choices and an established reputable recommendation was used to provide the
synthesis (See Appendix A). A discussion of critical assumptions, contrary findings and alternative interpretations were presented. Also discussed was the logical link between research results, conclusions and implications of treatments.

Race was one of the stronger determinants for being at high risk for vitamin D deficiency due to the inability of the skin to absorb sufficient quantities of sunlight for conversion to adequate vitamin D₃ levels. Some studies done recently found race as a determinant of lower screening and surveillance for this deficiency (Looker et al., 2011; Forrest and Stuhldreher, 2011). The melanin in the skin of Blacks and Hispanics protects them from harmful UV sun rays but also prevents them from absorbing enough vitamin D. Therefore, as Healthy People 2020 calls for efforts to mitigate disparities in treatment, Black, Hispanic and dark skinned people need to be targeted for treatment that stresses sources of vitamin D other than sunlight. However, this was not isolated for a treatment protocol or surveillance different from that of the general population with low vitamin D levels. The studies referenced throughout also indicated that elders (age-based determinant) were at risk for low vitamin D, demineralization of bones and potential high fall incidence, but did not specify a tiered approach to supplementing them with vitamin D. In most studies, the age for automated supplementation was stated as 65 years and older, especially when they were post-menopausal women or persons with cognitive decline. A more difficult determination would be finding out which persons were resistant to synthesizing vitamin D because of a gene variant (physiologic determinant), for this also places a patient at moderate risk and they should be routinely treated.

**Treating vitamin D** deficiency in primary care practice is challenging, but with individualized and patient centered care, much can be done with a stepwise approach to
minimize this deficiency and its associated morbidity in the population. Additionally, the USPTF recommendations are consistent with those made by the US Endocrine Society, the Agency for Healthcare Research and Quality AHRQ (2010) and the American Colleges of Physicians. See Figure 1 below for a primary care approach after thorough assessment and diagnostics are completed. Because of the controversial issue of how much wrinkling may be too much, a stepwise approach from food sources to pharmaceuticals can be used in all ages.

The model will not reflect gene variant as the literature or guidelines examined does not extrapolate to this specifically. What follows in Figure 1 is a stepwise approach to treating vitamin D deficiency based on three major factors, skin color, liver and/or kidney disease and gastrointestinal disturbance (GI). Gastrointestinal disturbance includes patients with lactose intolerance or those with inflammatory disorders. The latter will impair the amount of vitamin D absorbed from the GI tract. Although there were no specific recommendations in the guidelines for treatment of vegans, clinicians will need to consider the fact that this fat soluble vitamin will need to be routinely supplemented as their diets are absent of animal products and subsequently low in fat.
This paper encourages clinicians to examine the socioecological aspects of a person when treating patients for vitamin D deficiency. Consideration has to be given not only to their demographics and intrapersonal factors, but to ecological, organizational, social and political aspects that impact health. For example, in temperate climate, consideration as to how many actual days of direct sunlight there are and what type of clothing the person wears are important to assess. Note that headgear and full body clothing whether worn for cultural, habit or health reasons impacts the amount of sun rays that penetrate the skin. If a patient is being supplemented and not responding to rising levels consistent to that which is expected, genetic variation needs to be considered. These are all part of a systematic approach to maintaining a healthy population.
This systematic review has its limitations as the focus was on studies done with adult participants living in the USA. Plus, there is no statistical analysis of the studies found, and therefore the results and discussion is based on a description only. To minimize any of the limitations in this review, it was started with a detailed review of any professional practice guidelines followed by an examination and synthesis of randomized control studies (RCTs).

**Conclusion**

Currently, there are no definitive guidelines that support a single dosing depending on a measured vitamin D deficiency; most are generalized or based on other factors such as seasonality, symptoms reported by the patient, chronic illness and medications. There is no conclusive evidence that high intermittent dosing is better than recurrent weekly or daily dosing. There is still much uncertainty, and research is needed to determine health outcomes based on specific desired endpoints. Knowing who is high risk with proper screening, followed by treatment with different regimes, are all needed to help provide efficient and effective vitamin D management in patients. In the meantime, the guidelines produced in this article are only meant to help guide the clinician, and you as an individual provider need to critically process the full history and physical of your patient to determine where variations are necessary.
# Table 1. Recommended Dosing Guidelines for Treatment

<table>
<thead>
<tr>
<th>Organization</th>
<th>Clinical Practice Guidelines for Treatment</th>
<th>Comments</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>US Institute of Medicine (IOM)</td>
<td>600 IU per day for children aged 1 year of age and more adults up to 70 years. 800 IU per day for older adults</td>
<td>Recommended Dietary Allowance (RDA): average daily level of intake sufficient to meet the nutrient requirements of nearly all (97% – 98%) healthy people.</td>
<td>Pramyothin, P. and Holick, M. (2012). Vitamin D supplementation: guidelines and evidence for subclinical deficiency. <em>Curr Opin Gastroenterol</em>, 2012 Mar; 28(2):139-50. doi: 10.1097/MOG.0b013e32835004dc.</td>
</tr>
<tr>
<td>US Endocrine Society</td>
<td>600-1000 IU per day for children aged 1 year or more, 1500-2000 IU per day for adults aged 19</td>
<td>The Endocrine Society's Clinical Guidelines Subcommittee recommendation based on a</td>
<td>Holick, M., Binkley, N., Bischoff-Ferrari, H., Gordon, C., Hanley, D., Heaney, R., Murad, M., Weaver, C., Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: An Endocrine Society clinical practice guideline. <em>J Clin</em></td>
</tr>
<tr>
<td>years or more to maintain 25(OH)D above the optimal level of 30ng/ml.</td>
<td>systematic review of the literature</td>
<td>To maximize bone health and musculoskeletal function</td>
<td></td>
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<td>The Task Force also suggests to double or triple the dose for patients that are obese, are on anticonvulsant medications, glucocorticoids, antifungals such as ketoconazole, and medications for acquired immune deficiency syndrome (AIDS). As the latter list of drug</td>
<td></td>
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*Endocrinol Metab.* 2011 Jul;96(7):1911-30
Interfere with synthesis and or storage of vitamin D in the body.

| Food and Nutrition Board (FNB) at the Institute of Medicine of the National Academies (formerly National Academy of Sciences) | Even though sunlight may be a major source of vitamin D for some, the vitamin D RDAs are set on the basis of minimal sun exposure |


| US Preventive Task Force | Either has no recommendation or does not recommend based on the evidence |

This recommendation does not apply to the treatment of persons with osteoporosis or vitamin D deficiency.

For persons with osteoporosis or vitamin D deficiency no specific dose was recommended. A meta-analysis was prepared by the Tufts Evidence-based Practice Center (EPC) for use by the US Preventive Services Task Force (USPSTF).

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Chapter Four:

Socioecological factors associated with vitamin D deficiency: implications for adults with obesity and chronic pain

Valeria Ramdin

School of Nursing
The Bouvé College of Health Sciences
Northeastern University
Abstract

This paper reports on research examining vitamin D concentrations among adults seeking integrative medical care in an urban setting. The aim of the study was to explore the socioecological factors associated with vitamin D concentrations in adults who had chronic illnesses, and to determine if there was an association between vitamin D deficiency and obesity and vitamin D and pain. A secondary data analysis was done examining the medical records of 1268 adults living in the northeast region of the US who were seen at an urban health clinic from 2007 to 2012. The study sample was non-institutionalized adults 18 years and older, 80% women, mean age 52±13.9 and 20% men, mean age 55±12.4 years-old The results indicated that seasonality, ethnicity and age were strongly associated with vitamin D deficiency in this population. There was evidence to support that adults with high body mass index (BMI) are more likely to have 25(OH)D concentration less than the optimal 50 ng/mL. There was an inverse relation with vitamin D concentration and BMI: the higher the BMI, the lower the vitamin D concentration. Adults with BMI between 25 and 30 had approximately a 30% chance of having low vitamin D levels, p values <0.001. There was some association between 25(OH)D and moderate level pain which was found to not be statistically significant when we controlled for ethnicity, seasonality and age.

Keywords: Vitamin D deficiency, obesity, chronic pain, vitamin D, 25(OH)D
Contributors:

Valeria A. Ramdin PhD, Northeastern University
Elizabeth Howard PhD, Northeastern University
Paula Gardiner MD, Boston University School of Medicine and Boston Medical Center
Aziza Jamal-Allial PhD, Northeastern University
Mary S. Tarmina PhD, Northeastern University
Introduction

The role of micronutrients in the body is well established. Like minerals, vitamins are essential to the intricate functioning of the body, including ensuring that the musculoskeletal structure is strong, the immune system is healthy, cellular damage is repaired and there is sufficient energy to conduct its work. Vitamins are referred to as micronutrients, as only small amounts are needed to keep the human organism in homeostasis or health. These essential vitamins include vitamin D, which the body needs but cannot manufacture in sufficient quantities to support its functioning. Even though only small quantities are needed, the required amount of this synergistic fat-soluble vitamin makes a difference between health and disease. For example, insufficient vitamin D will cause imbalance in calcium levels and this results in a ripple effect of loss of bone mass, fragile bone and fractures. Conversely, sufficient quantities in conjunction with vitamin A and vitamin K will enable bone formation and healthy teeth. Previously, low levels of vitamin D have been associated with many chronic illnesses among various populations and this study was designed to better understand some of these relationships.

Presentation of the Problem

Hypovitaminosis D is associated with significant chronic illness, mortality and healthcare costs and is estimated to affect approximately 28 million Americans (NHANES, 2012). Mounting evidence suggests vitamin D deficiency is linked to cardiovascular disease and cancer (Booth, Cheng, Fox, Hoffman, Jaques, Keyes and Wolf, 2010; Mitchell, Henao, Finklestein and Burnett-Bowie, 2012; Overcash, 2008). There is evidence that this deficiency is also linked to many other conditions such as multiple sclerosis (Munger, Levin, Hollis, Howard and Ascherio, 2006), chronic kidney
disease (Melamed and Thadhani, 2012), anemia, depression, Type 2 diabetes, systemic lupus erythematosus, inflammatory bowel disease, neuromuscular disease and pain (Anglin, Samaan, Walter and McDonald, 2013; Melamed, Michos, Post and Astor, 2008; Vagianos, Bector, McConnell and Bernstein, 2007; Young, Snell-Bergeon, Naik, Hokanson, Tarullo, Gottlieb, Garg and Rewers, 20011; Bjelakovic, Giuud, Nikolova et al., 2011; Ascherio, Munger, and Simon, 2010). Its link to weakening of the immune system (Holick, 2007; Hewison, 2012) has the potential for far-reaching consequences. The effect of such large-scale associations is not only important for individual health, but may also reflect the health of a population.

**Significance**

According to the largest population-based survey of National Nutritional Health in the US, vitamin D deficiency has improved (NHANES, 2012). Suboptimal levels of vitamin D were found in approximately 33% of the US population in 2006 (NHANES, 2006) and this percentage has decreased to 9% in 2012. Although the more recent 2012 NHANES survey indicates improvement in some segments of the population, non-Hispanic Blacks and Mexican Americans continue to have some of the highest rates of deficiency at 31% and 12% respectively as compared to Whites at 3% (CDC, 2012). Based on these prevalence rates, it is estimated that millions of Americans may still need some intervention. The problem of inadequate vitamin D, based on its association with many chronic diseases, poses a threat to population health. The social determinants of health indicate there are unique circumstances that the urban population face especially when they are living in temperate zones. These determinants include safety in inner city
neighborhood, or extremes in temperatures both of which can affect outdoor activity, and food security that may contribute to inadequate nutritious food intake (Coreil, 2010).

**Background**

Clinicians’ ability to appropriately manage patients’ vitamin D level is hampered by inadequate screening and treatment of adults. Given the potential for multiple confounding variables, the connection between vitamin D deficiency and chronic disease is complex. This makes it a challenge for clinicians to isolate the variables associated with vitamin D deficiency and a specific illness. Despite the fortification of food with vitamin D, and the recognition that sunlight is the primary source of this vitamin, the continuous finding of vitamin D deficiency among patients with chronic diseases raise reasonable questions of other causative factors for these persistent rates (Mitchell, Henao, Finklestein, and Burnett-Bowie, 2012). Furthermore, one has to ponder the unique conditions that may be causing this phenomenon in certain populations. In essence, how can clinicians expand their knowledge and help to mitigate the inherent risk that accompanies vitamin D deficiency?

According to the US Preventive Task Force, vitamin D insufficiency is a serum 25(OH)D level less than 50 ng/mL and vitamin D deficiency is less than 25 ng/mL (LeFevre, 2015). Insufficiency or deficiency leads to poor bone health and is also implicated in a number of other chronic diseases as mentioned previously. For the purpose of bone health alone, it is a national public health priority. The 2005-2008 NHANES results indicated that 9% of the population had osteoporosis and another 49% had osteopenia (Looker et al., 2012). Consequently, over 44 million adults are affected by poor bone health with a projected annual direct cost by 2025 of $25 billion to treat this
largely preventable condition (National Osteoporosis Foundation, 2009). Although the estimated costs associated with other diseases are not quantifiable in the literature, the benefits of supplementation in the presence of a vitamin D deficiency for all-cause morbidity is well documented (Autier et al., 2007; Chung et al., 2009; Rejnmark et al., 2012).

The urban and temperate zone environments present unique circumstances that make this a targeted area for advancing the scientific knowledge on vitamin D. In the US some foods have vitamin D$_2$ added to help offset the lack of a constant and adequate supply from UV sunlight. However, some people have lactose intolerance or other digestive disorders that limit their intake of this fat-soluble vitamin from food sources. Additionally, it is estimated that in order for the skin to be a conduit for 7-dehydrocholesterol (7-DHC) a precursor of Vitamin D, there needs to be ultraviolet B (UVB) radiation present between rays of 290 and 315 nm (Tangpricha, 2012). If the skin is covered, has too much melanin or is protected by sun blocking creams, then there is not enough absorption to provide a good supply of this vitamin. Relying on cutaneous vitamin D$_3$ synthesis and fortified foods is insufficient (Gordon et al., 2012). The initiatives for Healthy People 2020 call for more attention to preventative care and attention to vitamin D adequacy falls under this umbrella, to bring a patient to within optimal vitamin D range as measured by 25(OH)D serum blood test.

**Problem statement**

Recognizing when a patient is vitamin D deficient is complex. This complexity results in prevailing under-diagnosis leaving large segments of the population at risk for vitamin D deficiency and subsequent negative health outcomes. Correction of vitamin D
deficiency has been shown to reduce mortality in patients with chronic diseases (Rejmark, Avenell, Masud, Anderson et al., 2012). Currently, based on the available scientific evidence, only persons deemed high risk, predominantly Blacks, Hispanics, and those 65 years or older, are recommended for routine assay test (Holick, Binkley, Bischoff-Ferrari, Gordon, Heaney, Murad and Weaver, 2011; U.S. Preventive Services Task Force, 2013). Other adults in the general population require screening to determine risk. The latter is difficult when there appears to be so many possible variables linked to attaining and sustaining optimal vitamin D levels.

This multivariate complexity of vitamin D sufficiency leaves the clinician with the uncertainty of knowing who and when to assess for vitamin D levels, and who and when to treat with supplemental vitamin D therapy. Clinicians may choose one of two approaches, 1) to use vitamin D as a therapy for an existing condition, or 2) to use vitamin D to help prevent disease. Identifying other common variables linked with vitamin D deficiency may help bridge the gap of uncertainty, and potentially improve health outcomes in targeted populations. In this research, we examined the socio-ecological factors associated with vitamin D deficiency in an urban setting of adults seeking integrative medical care. We also focused on analyzing the relationship between vitamin D and obesity and similarly the relationship between vitamin D and pain.

**Statement of the Purpose**

The purpose of this descriptive exploratory study was to examine the socio-ecological factors associated with vitamin D deficiency in an urban population. Furthermore, this research tested the hypothesis that among urban dwelling people, vitamin D deficiency is both clinical and statistically significant in adults with chronic
pain and obesity. Screening for suboptimal levels of vitamin D and knowing the factors most commonly associated with this condition is a priority, supported by evidence indicating that the greatest impact to supporting health is complex and may not be only at the individual level (Freiden, 2010). The prevalence of both mild-moderate and severe deficiency of vitamin D is higher among women and minority populations (Zadshir et al., 2005), but there is little evidence to support isolating factors for screening, treating and surveillance in the urban population living in temperate zones. While systematic reviews on screening (Ramdin, 2015 manuscript #1) and treatment for vitamin D deficiency (Ramdin, 2015 manuscript #2) offer significant insight into some factors associated with vitamin D status in a patient, there is still a gap in knowing the socioecological factors that are associated with this phenomenon especially in urban populations. For people with disease risks that are modifiable, much can be done if these risks are known, except in a few cases that have genome-wide statistically significant variant genes that render the individual prone to low vitamin D levels (Wang et al, 2010).

Literature Review

A two-pronged literature review was completed to examine both theoretical and empirical literature. The key words or phrases used were vitamin D, hypovitaminosis D and low vitamin D. A Boolean search was conducted mostly in the Cumulative Index for Nursing and allied Health Literature (CINHAL), PUBMED or MEDLINE and Google Scholar. We first examined the key variables associated with vitamin D deficiency and secondly, we searched for diagnoses associated with low vitamin D. Our search strategy entailed following leads from within articles, which were then used to determine the state of the science and gaps in the literature, and to help formulate research questions and
hypotheses. The literature review was an iterative process and an ancestral approach was used to track relevant studies.

The body of knowledge that existed on vitamin D deficiency in human dates back to the early 1900s but at that time centered on dental and bone health predominantly in children and pregnant populations. Sporadic research continued with arbitrary treatment to mitigate malformations in bones and teeth and to further investigate the association of this deficiency with other conditions. It was not until 1985 that an objective serum measurement for vitamin D, a radioimmunoassay (RIA) was developed for 25(OH)D which captured the circulating vitamin D with acceptable specificity (100%), thus promoting the advent of more biological research focused on sufficiency of the vitamin (Holick, 2009). In the past few decades, there have been varying levels of evidence ranging from expert opinions to systematic reviews, with some randomized controlled studies in small populations.

The basic question to start the search was to determine how vitamin D impacts health status. A dual search strategy using bibliographic databases interspersed with cited references within study reports was used. The complexity of vitamin D adequacy was soon realized and led to the need to organize this effort around a framework. The socioecological model (in Coreil, 2010), established in the 1970s by Urie Bronfenbrenner with continued revision in the 21st century, was the system prevention framework used to provide the theoretical approach that guided the review. This theory is discussed in more detail in the conceptual framework section.

Primary research that focused on examining vitamin D in adults with relevance to clinical practice was the priority. We found that there were established factors that
suggested risks for having low vitamin D levels. These were not limited to; but included race and ethnicity, diet and exposure to sunlight. Also implicated by association were several chronic illnesses including cancer, diabetes type 2, obesity, cardiovascular disease, rheumatoid arthritis and autoimmune conditions. The uncertainty of how, who and when to screen for vitamin D deficiency was evident. We found over 20 chronic diagnoses that were associated with vitamin D in the literature. The complexity of the associated variables uncovered a gap in the research, which was the use of socioecological constructs to explain vitamin D status. Furthermore, the urban population was not identified as a key population of concern.

**Conceptual Framework**

The Socioecological Model (SEM), a framework for prevention, provided the theoretical framework for this study. This focus shifts the current paradigm of care from a purely medical model to that of a socioecological model of care. There are a few variations of the model, which was first developed as an ecological systems theory by Urie Bronfenbrenner in the 1970s. This was further developed by McElroy in 1988 to capture not only the physiological determinants of a human problem but also the behavioral and public health aspects of a problem or phenomenon under investigation (Coreil, 2010). According to Coreil (2010), these models are some of the most widely used for application to health promotion (Glanz et al, 2008). The Center for Disease (CDC) also has used this model in health promotion and disease prevention efforts.

The SEM model has twenty-one domains which are divided into five hierarchical levels. Level 1 is *Intrapersonal/Individual*. These are factors that impact the individual at a personal level for example; education, attitudes, genetics, food preferences (include
lactose intolerance) and demographics. Level 2 is Interpersonal. This usually represents social networks and family characteristics or relationships in the immediate community that influence health care behaviors. Medical-provider health teaching and commonly prescribed treatment for disease can be included here. Level 3 is Organizational/Institutional. These factors include social and cultural norms established by schools, workplaces, and neighborhoods. It explores the health impact based on where people live, work or play. It also takes into consideration societal factors such as culture and religion (for example, people wearing full body covers) as well as the physical environment including climate. Level 4 is Social/Policy. This could be public policy and regulation, for example, the use of fortification of staple foods such as milk, breads, and cereal etc. with vitamin D. It may also examine the effects from the built environment, socioeconomic, public facilities and ethnicity and culture. Level 5 of the SEM is most distal to the individual and the level at which the individual has the least control over, it deals with the societal environment, such as the health facilities, economics, educational institutions, policies, national ethos and other large scale infrastructure of society (Coreil, 2010).

A model of this type is fitting when studying a condition as complex as vitamin D status. The status can be affected by having a physiologic (i.e., genetic predisposition, malabsorption syndrome, skin condition, adiposity), or social (inability to obtain adequate food sources or religious practice or ethno-cultural coverings) implications. There may also be health literacy concerns in which the subject lacks the knowledge or understanding of the risk or benefits of vitamin D. The environmental changes with the varied seasons, bring different levels of ultraviolet light availability for vitamin D
synthesis, or pollution that may block sun UV rays in the urban built environment. Even standards of care or policies that leave varied levels of uncertainty among practitioners for screening and treating adults for vitamin D deficiency can contribute to the phenomenon. The levels for this framework are illustrated in Figure 1 below.

The IOM has defined the model as “a model of health that emphasizes the linkages and relationships among multiple factors (or determinants) affecting health” (IOM, 2003). Unlike a medical model that focuses on the biological aspect of health, the SEM considers a broader view including socioeconomic, biologic and environmental factors.
ranging from micro-determinants to macro-determinants. These factors are typically illustrated in a pyramid or concentric ovals with each subset or level having a cascading affect on a person’s health depending on their circumstances and characteristics. This approach for screening for vitamin D status is essential as there are multiple reasons (Kulie et al. 2009) why a person may have suboptimal levels of vitamin D (Melamed, Michos, Post et al., 2007).

Research Questions, Aim, Hypotheses

Given the purpose of this study, which is to examine the socioecological factors associated with vitamin D deficiency in an urban population with implication for adults with obesity or chronic pain, we pose the following questions and their associated hypotheses.

Research Question One: What key sociodemographic factors are most associated with low vitamin D in an urban population of adults seeking integrative care?

Specific Aim 1: To determine the significance of the different sociodemographic factors, i.e., age and race, on serum 25(OH)D among adults seeking integrative care.

Hypothesis 1.1: Serum 25(OH)D concentration is not associated with age among adults seeking integrative medicine care.

Hypothesis 1.2: Serum 25(OH)D concentration (ng/L) is not associated with ethnicity among adults seeking integrative medicine care.

Research Question Two: Is obesity a determinant of serum 25(OH)D concentration (nmol/L) among adults seeking integrative medicine care?

Specific Aim 2: To determine the adjusted cross-sectional association between serum 25(OH)D and obesity.
Hypothesis 2.1: Obesity as measured by BMI is not associated with serum 25(OH)D concentration in a cross-sectional analysis among patients seeking integrative medicine care in an urban setting.

Research Question Three: Is pain a determinant of serum 25(OH)D concentration among adults seeking integrative medicine care?

Specific Aims 3.1: To determine if the level of pain is a determinant of serum 25(OH)D among adults with a diagnosis of chronic pain who are seeking integrative medicine care.

Hypothesis 3: Self report of the current level of pain using the pain scale of 1-10 is not associated with Serum 25(OH) D concentrations.

Methods

Setting

The study site was selected for its robust practice of integrative medicine and comprehensive care to populations including the vulnerable patients. Many of the patients seeking care at the integrative medicine clinic are there because they have not attained satisfactory health using allopathic treatments. This clinic provides data for multiple research projects, so detailed, health assessments are typically completed. The integrative medicine clinic is located in the family medicine clinic in a large safety-net [academic] institution that has nearly one million patient visits per year. They offer a comprehensive range of clinical and diagnostic services in more than 70 specialties and subspecialties of medicine and surgery. Based on US rankings on data collected by the Centers for Medicare & Medicaid Services (CMS) and the Hospital Quality Alliance
(HQA), this academic institution has some of the highest ranking of patient outcomes for chronic disease management.

The integrative health care providers at the clinic promote health through counseling: on dietary needs, vitamin supplementation, exercise, yoga, meditation and pain management. Nutrition counseling is one aspect of the care as many of these adults may have either digestive problems that affect nutrient absorption or have food insecurities due to lack of access to nutritious food. Consequently, weight and height are routinely collected and the measurement for vitamin D is done at the initial visit if risk is determined. The study population was a diverse group of patients with primary languages of English, Spanish, Vietnamese, Arabic, Chinese, Bengali, Portuguese and Haitian Creole.

**Subjects**

A retrospective chart review of all patients presenting to the integrative medicine clinic from January 2007 to December 2012 was done to select adults who had a blood test of serum 25(OH)D concentration drawn. This effort resulted in a sample of 1268 adults. The members of the sample population were 18 through 90 years old.

A descriptive retrospective chart review design allowed for a secondary analysis of vitamin D deficiency in a population considered at risk, while minimizing selection bias. It also allowed for access to a larger representative number of subjects over a short timeframe, which may not be feasible in a prospective study in this urban setting. The integrative medicine model at the clinic could have a profound impact on those who seek health care management there. It could positively affect many things including vitamin D
and obesity status as well as pain management due to the integration of non-pharmacological and pharmacological interventions. The six-year sample provides data from approximately 6000 consultative visits representing 4 office-based physicians and other collaborating medical provider care.

Information from the medical records was then delivered de-identified for patients seen at the integrative medical clinic over a 6-year period. Relevant data was extracted making this approach a secondary data analysis.

**Inclusion Criteria**

Adult patients seen at the clinic within the time period specified (January 2007 to December 2012) who had 25(OH)D levels drawn were included in the sample. The primary or secondary diagnoses of this sample included: vitamin D deficiency, depression, osteoporosis, hip fracture, chronic renal failure, diabetes, anemia, unspecified nutritional deficiency or digestive disorders, systemic lupus erythematosus, arthritis, fibromyalgia, heart disease, cardiomyopathy, conductive disorders, heart failure, nutritional and metabolic disorders, cardiomyopathy, chronic pain syndrome, back pain, insomnia, shingles, cancers of the breast, ovary, and colon. In addition, all patients had to be community dwelling or living in other non-institutionalized settings. They were seen independently and not as part of a planned hospitalization.

**Exclusion Criteria**

Children under the age of 18 were excluded as there is an emerging body of evidence indicating that the thymus gland, which is not active in adults, may act as a reserve for vitamin D in children. This presents a unique extraneous variable, and thus the data from the eight children found in the sample were excluded. In addition, patients with
end-stage renal disease were excluded as hemodialysis will interfere with vitamin D levels although none were found in the sample.

Design

Data Collection Procedures

The primary study was done by hand reviewing charts. From these we collected demographical, social, past and present medical history, perceived pain status, and nutritional status. Data mined for medication intake contained; prescribed and nonprescription medication including supplements, herbs and vitamins. Physician and other healthcare provider notes are also included to capture other socioecological determinants of health.

To obtain a representative sample we first identified those chronic clinical disease or problems of interest based on the literature on vitamin D. What followed was the request for charts that specifically had the following conditions listed as a primary or secondary diagnosis: Vitamin D deficiency, depression, osteoporosis, hip fracture, chronic renal failure, diabetes, anemia, unspecified nutritional deficiency, systemic lupus erythematosus, arthritis, fibromyalgia, heart disease, cardiomyopathy, conductive disorders, heart failure, nutritional and metabolic cardiomyopathy, chronic pain syndrome, back pain, insomnia, shingles, cancers of the breast, ovary, and colon. We then developed a medical record request list with all possible corresponding ICD-9 (9th Revision, International Classification of Diseases) and DSMIV (Fourth Edition, Diagnostic and Statistical Manual of Mental Disorders), codes for the chronic illnesses noted above. We had to be assured that we had access to the medical and physiologic measurement in the charts. The list was sent to the medical records manager for a
preliminary pull of charts to see if there would be sufficient records for patients who also had Vitamin D labs reported. IRB approvals were obtained. The next few paragraphs describes how measures were done and the rationale for these.

The laboratory data obtained were only from tests done at the institution’s Clinical Laboratory Improvement Amendment (CLIA) federally certified lab. This lab conforms to the standards recommended from the Joint efforts of National Institute of Standards and Technology (NIST), the Centers for Disease Control and Prevention (CDC), the Office of Dietary Supplements (ODS) of the National Institute of Health (NIH) and with national surveys worldwide (NIST; 2009). In addition to the diagnoses classified according to ICD-9 and DSMIV codes, we documented the date of visit in relation to time of year. We also validated that each subject had a chronic disease consistent with our targeted study population, and that physician procedure codes were classified by CPT-4 (Current Procedural Terminology, Version 4). Merging of the data was then done to combine several visits by a single subject into one to avoid duplication of the data. Final data extraction included the following sociodemographic, main outcome and health related variables as listed and operationally defined below:

**Sociodemographic variables Demographic variables:** Age was recoded as 18-30, 31-50, 51-70 and then over 70 years of age. This grouping was to reflect the young adult, young middle age, older middle age, older adult and then the elderly. Categorizing like this enables a better pattern to be seen based on physiological status as many chronic diseases occur in middle and older adults. The older adult was already in the literature as most associated with poor vitamin D concentration status. Race was classified as Black,
White, Asian, Hispanic, and Other if the race/ethnicity was not documented, or if this variable was missing. Gender was simply coded as male or female as documented in the chart.

**Main Outcome Measures:**

**Vitamin D measures:** Serum 25-hydroxyvitamin D concentration was used as this is the accepted objective measure of vitamin D status. It was used as a continuous level measurement to capture any subtle changes that could affect the analysis and then grouped according to deficient, insufficient and sufficient categories for reporting.

Vitamin D deficiency/Hypovitaminosis D/Low vitamin D may be used interchangeably and is referenced in this study as 25(OH)D or 25 hydroxyl vitamin D < 20 ng/mL.

At risk of vitamin D inadequacy: Serum 25(OH)D 21-29 ng/mL

Sufficient in vitamin D: Serum 25(OH)D 30–50 ng/mL

High vitamin D: Serum 25OHD greater than 50 ng/mL. Endocrine Society guidelines as referenced by Holick et al., (Holick, 2011)

**Body Mass Index (BMI)** is a measure of an adult’s weight in relation to his or her height, specifically the adult’s weight in kilograms divided by the square of his or her height in meters (kg/m²) and can be used to categorize body weight. Obesity was determined according to BMI which was operationally defined by the World Health Organization (WHO) obesity class III and calculated as weight (kg) divided by height ((kg/m²). A BMI <25 was considered normal weight, BMI 25-29.9 was overweight, and BMI >30 was obese). BMI is widely used and consistent with the objective determination for obesity.
Seasonality measure: Seasonality was categorized by meteorological seasons. This reflected the months of the year in which the typical season falls in the temperate zone in the Northeast USA where the study was conducted. The northeast is affected by extremes in temperature that affects the quantity and quality of sunlight therefore it was important for this division to be made which can affect the level of vitamin D from sunlight. This demarcation was reflected as below:

Spring - from April to June
Summer - from July to September
Fall - from October to December
Winter - from January to March

Pain measures: If the presence of pain was recorded in the medical record as a response to a yes and no question, then we looked for the self-reported pain scale level. We used the pain scale of 0-10, a continuous level measurement to better analyze and correlate with vitamin D which was also at the continuous level. While pain is a subjective experience, its management necessitates an objective way of monitoring the intensity. On the pain scale low intensity pain was classified as 1-3, moderate intensity pain, 4-6 and >6 was equated with high intensity pain.

Health-related variables: Smoking status was classified as never, former and current. Classifying it like this is common in biomedical studies especially as smoking can interfere with some biomarkers, in this case 25(OH)D levels.

Physical activity was dichotomized as yes or no, with yes representing the intentional physical exercise for at least one half hour for four or more days per week. Intentional
exercise for health maintenance is correlated with other healthy behaviors and can make the difference between attaining optimal vitamin D and vitamin D deficiency. Taking prescribed vitamin D supplements was captured as yes or no. It does not capture those who may have been prescribed vitamin D at the visit as they would not yet be taking it yet.

In a 2013 study of US adults dietary supplement use and smoking were found to be important correlates of biomarkers for water-soluble vitamin status after adjusting for sociodemographic and lifestyle variables. (Pfeiffer et al., 2013). It therefore was prudent to see how the prevalence of these variables fell in this study on vitamin D which is a fat-soluble vitamin [vitamin D].

**Data Entry and Quality Control**

Since the study is a secondary analysis, there was one collection time for the chart review of adults who had chronic illness and sought care at the clinic. All provided data were de-identified and each case was given a unique identification number (UID) in an encrypted and password protected Excel spreadsheet. The primary study collected a signed consent form allowing the use of the de-identified data in future secondary analysis studies that are designed for health promotion and disease prevention. The proposed study did not require further recruitment, a consent form, nor additional data collection.

**Analytical Plan**

Data analysis was performed using SAS® 9.3 (SAS Institute Inc., Cary, NC). Hypothesis testing was non-directional, with alpha equal to 0.05. For each specific aim,
linear regression model assumptions were assessed to insure model accuracy. Results were summarized using regression estimates and 95% confidence intervals (CI). A \( P \) value < 0.05 was considered statistically significant. Skewed variables were natural log-transformed to normalize their distributions before the analyses were done and all models were adjusted for the different covariates.

To address the aim of exploring the association between the demographic factors and serum 25(OH)D concentrations, Student's t-tests were used for continuous variables, and chi square tests were used for categorical variables. Characteristics were compared across gender using two-tailed t-tests. Linear regression analysis (PROC GLM) was used to examine relationships between serum 25(OH)D concentration and main predictors, adjusting for age, ethnicity and seasonality. Dunnett -Hsu or Tukey adjustments were used for multiple comparison.

Final Sample:

The original sample consisted of over 6,000 subjects drawn from the database received from the Urban Health Clinic. Consolidation was done to avoid duplication and 2,247 subjects were identified for potential inclusion. There were 1,268 subjects who had a 25(OH)D level done following the initial visit. For obesity, only those who met the criteria of having either BMI documented or both height and weight from which the BMI could be calculated were used in the analysis, therefore this subsample for obesity was \( n = 763 \). For the pain analysis, only those who had pain captured on the pain scale of 0 to 10 were used to test the hypothesis for the association of pain and vitamin D (\( n = 138 \)).
Results

The mean ages of women and men were 52.0±13.9 years-old and 55.1±12.4 years old, respectively. Age groups showed significant difference in the means for VD concentration controlling for ethnicity and seasonality. The regression model of age predicting VD concentrations controlling for ethnicity and seasonality was associated with VD concentration $B = 27.9$ and $P < 0.0001$. As the age increased the VD concentrations decreased except among the subjects who were in the 31-50 age group. The age category with the lowest mean VD concentration [19.2 ng/mL] were the 18-30-year-old, with a 95% CI [16.6 -21.8]. Conversely, those subjects with the highest mean VD concentration [27.5] were the young to middle age adults who were 31 to 50 years old with a 95% CI [17.7 – 36.7]. On average VD concentrations was $7.4 \pm 1.3$ ng/mL less between subjects in the lowest VD concentration age category [18-30-year-old] and those subjects in the highest VD concentration age category [31-50-year-old] with $P < 0.0001$. The most statistically significant differences were seen between the 18-30 year olds and >70 year olds, $p < 0.001$ and 51-70 age group and those subjects >70 years old with $p < 0.0001$.

Although various ethnicities were found in the sample, the majority of the subjects were Black (approximately 41%) who represented just under half of the sample population. This distribution was followed by Whites (27.6%), Hispanics (22.0%) and Asians (9.1%). (Table 1). When ethnicity was crossed with VD concentration, Chi Square analysis indicated there was a significant association between ethnicity and VD concentration. 29% of the Blacks were severely deficient with 25(OH)D concentrations < 12ng/mL and another 10.6 % had insufficient VD concentration, compared to Whites.
for whom 17% of them were severely deficient and another 8% had insufficient VD concentration totaling 39% and 25% respectively. The highest percent of VD concentration among any ethnic group was seen among the Whites followed by the Hispanics in this sample. Using Chi-Square analysis, when 25(OH)D by category [deficient, insufficient and normal] was crossed with ethnicity, almost twice the amount of Black subjects had vitamin D deficiency compared to Whites or Hispanics in this sample (Figure 2 below). Similar patterns were seen for those subjects who had insufficient levels which is represented by a 25(OH)D level of >/= 12ng/mL but less than 20ng/mL. Less than 1% of any of the ethnic groups had optimal vitamin D levels and therefore is not reflected in Figure 2 below.

![Figure 2. Vitamin D crossed with Ethnicity](image)

Ethnicity on the X axis and 25(OH)D on the Y axis measured in ng/mL.

Categories of 25(OH)D concentrations representing deficiency, insufficiency and sufficiency.

Of the total N= 1268 in the study sample, the majority were females n=1012 (80%) and males account for the next n=256 (20%). Although both groups had mean VD
concentration lower than the normal, the mean serum 25(OH)D for women was 26.2 ± 12.1 ng/mL, significantly higher (P=0.01) when compared to men 23.6 ± 11.3 ng/L. Males on average had 25(OH)D mean concentrations measuring 3.2 ng/mL less than that for females, P <0.0001. No significant differences were seen between the females and males for vitamin D correlated with pain. Among our population, the lowest vitamin D serum level for any gender was 4.9 ng/ml, and the highest vitamin D serum level was 88 ng/ml. Chi Square analysis indicated that the majority of our sample (68.6%) were deficient with 25(OH)D concentration <12ng/mL and another 26% had insufficient levels (≥12 ng/mL but < 50 ng/mL) of circulating vitamin D irrespective of gender. This resulted in a total of 94.6% of our subjects with VD concentrations less than optimal P< 0.0001. As will be addressed in the respective sections below VD concentration was inversely correlated with BMI. Additionally, VD concentration also showed some correlation with pain but VD Use was not a significant correlated finding in the analysis.

BMI analysis were reported on n= 763, 51.5 % of these subject were obese and another 30.7 % were overweight making more than three quarters [82.2%] of our subjects over ideal body weight. The mean BMI was 31.7±8.99 and was significantly greater for females with means of 32.1 ± 9.4 versus 30.4 ± 7.1 for males. BMI categories showed significant difference in the means for VD concentration controlling for age, ethnicity and seasonality. Predicting vitamin D using BMI, controlling for age, ethnicity and seasonality, an inverse relationship was observed B 13.6 and P <0.0001. (See Figure below). As the BMI incrementally increased the VD concentrations incrementally decreased. The BMI category with the lowest mean VD concentration [23.2ng/mL] were those subjects with BMI >30, 95% CI [21.7 -24.7]. Those subjects with the highest

mean VD concentration [27.5 ng/mL] were the subjects with the best or optimal ideal body weight [in this study with BMI <25, 95% CI [25.3-29.5]. On average VD concentrations were 3 ng/ml different among the BMI categories with P <0.0001. The most statistically significant differences for VD concentration were seen between the subjects with ideal body weight and the subjects who were obese with p< 0.0001. Figure 3 below depicts the VD concentration trends for BMI categories.

Figure 3. Displays the BMI means trend crossed with VD concentration

Y axis is the 25(OH)D concentrations and on the X axis are the BMI categories.

Ideal BMI <25; Overweight BMI 25-29.9, *Obese BMI 30 and greater
The vitamin D serum was drawn during all seasons on the full sample N=1268. Most of the VD concentration test were done in Spring (30.6%) and Winter (25.9%), followed by Fall (23.1%) and the rest done in the summer. During the Winter subjects were more likely to have VD concentration 5.2ng/mL less than if tested during the Spring. Although the mean Vitamin D level in the sample was 25.7 ng/mL, 20% of the population were deficient with <20ng/mL 25(OH)D concentrations combined for Winter and Spring. A general linear model indicated that the lowest vitamin D concentration was seen in the winter when compared with that seen in the Summer, was the most significant change for 25(OH)D with p<0.08.

There were n= 138 subject analyzed for pain. Pain scores ranged from a score of 0 (no pain) to 10. The mean pain score was 2.9 ±3.4 on the pain scale with 10 being the most intense pain reported and ‘0’ meaning no pain. Males reported on average 2.7 ±3.4 scale points less pain than females 2.9±3.5. There was no statistically significant difference between females and males for the pain reported using the pain scale. Pain was correlated with VD concentration at the moderate pain level P=0.04, 95% CI, [21.6-28.6], with the average mean VD concentration level for this group being 25ng/mL. The regression model of pain predicting VD concentrations controlling for age, ethnicity and seasonality showed no statistically significant findings.

See Table 1 below for a descriptive summary of key variables used in the study. Smoking, physical activity and vitamin use as seen in Table 1. below, were not analyzed, but is referenced to show the prevalence of these variables among the study subjects.
Table 1: Descriptive Summary of Demographic and key Variables Frequency

<table>
<thead>
<tr>
<th>Demographic Characteristic</th>
<th>Category</th>
<th>Count N=1268 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Categories</td>
<td>18-30 Years</td>
<td>90 (7.1%)</td>
</tr>
<tr>
<td></td>
<td>31-50 Years</td>
<td>6 (0.4%)</td>
</tr>
<tr>
<td></td>
<td>51-70 Years</td>
<td>452 (35.7%)</td>
</tr>
<tr>
<td></td>
<td>Greater than 70 Years</td>
<td>720 (56.8%)</td>
</tr>
<tr>
<td>Race</td>
<td>Black</td>
<td>520 (41.1%)</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>350 (27.6%)</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>116 (9.1%)</td>
</tr>
<tr>
<td></td>
<td>Hispanic</td>
<td>279 (22%)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>3 (0.2%)</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>1012 (80%)</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>256 (20%)</td>
</tr>
<tr>
<td>Vitamin D Categories</td>
<td>Deficient (&lt;12 ng/ml)</td>
<td>870 (69%)</td>
</tr>
<tr>
<td></td>
<td>Insufficient (&gt;= 12 &amp; &lt; 20 ng/ml)</td>
<td>331 (26%)</td>
</tr>
<tr>
<td></td>
<td>Sufficient (=&gt; 20 &amp; &lt; 50 ng/ml)</td>
<td>51 (4%)</td>
</tr>
<tr>
<td></td>
<td>Above Sufficient (50 ng/ml &amp; more)</td>
<td>16 (1%)</td>
</tr>
<tr>
<td>BMI: Categories</td>
<td>Missing</td>
<td>505 (39 %)</td>
</tr>
<tr>
<td></td>
<td>Ideal (&lt;25)</td>
<td>135 (11%)</td>
</tr>
<tr>
<td></td>
<td>Overweight (25-30)</td>
<td>235 (19%)</td>
</tr>
<tr>
<td></td>
<td>Obese (&gt;30)</td>
<td>393 (31%)</td>
</tr>
<tr>
<td>Season of blood drawing for testing 25(OH)D</td>
<td>Winter</td>
<td>325 (25.7%)</td>
</tr>
<tr>
<td></td>
<td>Spring</td>
<td>387 (30.5%)</td>
</tr>
<tr>
<td></td>
<td>Summer</td>
<td>263 (20.7%)</td>
</tr>
<tr>
<td></td>
<td>Fall</td>
<td>293 (23.1%)</td>
</tr>
<tr>
<td>Pain Scale Categories</td>
<td>Missing</td>
<td>1130 (89 %)</td>
</tr>
<tr>
<td></td>
<td>No Pain</td>
<td>72 (6 %)</td>
</tr>
<tr>
<td></td>
<td>Mild Pain</td>
<td>9 (1 %)</td>
</tr>
<tr>
<td></td>
<td>Moderate Pain</td>
<td>28 (2 %)</td>
</tr>
</tbody>
</table>
### Demographic Characteristic Categories and Counts

<table>
<thead>
<tr>
<th>Demographic Characteristic</th>
<th>Category</th>
<th>Count N=1268 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High intensity Pain</td>
<td></td>
<td>29 (2%)</td>
</tr>
<tr>
<td>Pain Scale Categories 0/1</td>
<td>Missing</td>
<td>1130 (89%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>72 (6%)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>66 (5%)</td>
</tr>
<tr>
<td>Smoking status</td>
<td>Missing</td>
<td>92 (7%)</td>
</tr>
<tr>
<td></td>
<td>Never</td>
<td>761 (60%)</td>
</tr>
<tr>
<td></td>
<td>Current</td>
<td>213 (17%)</td>
</tr>
<tr>
<td></td>
<td>Former</td>
<td>202 (16%)</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>No</td>
<td>148 (12%)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>1120 (88%)</td>
</tr>
<tr>
<td>Taking Prescribed Vitamin D Supplements</td>
<td>Missing</td>
<td>988 (78%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>222 (17%)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>58 (5%)</td>
</tr>
<tr>
<td>Vitamin D Supplements as Collected by Clinician</td>
<td>No</td>
<td>1136 (90%)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>132 (10%)</td>
</tr>
</tbody>
</table>

Most of the sample population (88%) reported that they were involved in some kind of physical activity or exercise. The majority of the subjects (60%) never smoked. Of the remaining 40%, 17% of these subjects were current smokers, with the remaining 16% being former smokers. The majority of the sample (90%) were not taking vitamin D supplements at the time of their visit.
The top six diagnoses that brought the subjects to the integrative care clinic are listed in Table 2 below. The majority of subjects were there for pain syndrome (20%), or for depression management (15%).

Table 2. Top ICD 9 Codes Among Subjects.

<table>
<thead>
<tr>
<th>CODE</th>
<th>DESCRIPTION</th>
<th>FREQUENCY</th>
<th>% of Total subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICD-724.5</td>
<td>Pain syndrome</td>
<td>448</td>
<td>19.95</td>
</tr>
<tr>
<td>ICD-311</td>
<td>Depressive disorder</td>
<td>333</td>
<td>14.83</td>
</tr>
<tr>
<td>ICD-729.1</td>
<td>Myalgia</td>
<td>212</td>
<td>9.44</td>
</tr>
<tr>
<td>ICD-250.00</td>
<td>Diabetes</td>
<td>150</td>
<td>6.68</td>
</tr>
<tr>
<td>ICD-307.42</td>
<td>Insomnia</td>
<td>144</td>
<td>6.41</td>
</tr>
<tr>
<td>ICD-268.9</td>
<td>VD deficiency</td>
<td>105</td>
<td>4.67</td>
</tr>
</tbody>
</table>

Research Question One:

What are the key socio-demographic factors that are most associated with low vitamin D in an urban population of patients seeking integrative care?

**Hypothesis 1.1** Serum 25(OH)D concentration (ng/mL) was associated with age among adults seeking integrative medicine. Therefore, we rejected the null hypothesis in favor of the alternative which is that there is a significant relationship between 25(OH)D and age.

**Hypothesis 1.2:**

Serum 25(OH)D concentration (ng/mL) was associated with the different ethnicities among adults seeking integrative medicine care. Therefore, we rejected the null hypothesis as there is a significant relationship between 25(OH)D and ethnicity. With
Blacks being approximately 1.5 times more likely to have VD deficiency compared to their White counterparts.

First we sought to determine what socio-ecological factors were associated with vitamin D deficiency using ttest with the categorical data. Vitamin D deficiency was prevalent across age groups, seasons and race in the subjects. The analysis results provide evidence to conclude that the key socio-demographic factors that are most associated with low vitamin D in an urban population of patients seeking integrative care were age and ethnicity.

Obesity Determined by BMI

As shown in Table 3. below, approximately 82% (n=763) were either overweight or obese and the mean BMI of the sample was 31.7 ± 8.99.

Table 3. Distribution of Sample by BMI

<table>
<thead>
<tr>
<th>BMI Value</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>1268</td>
<td>100</td>
</tr>
<tr>
<td>Missing data</td>
<td>505</td>
<td></td>
</tr>
<tr>
<td>Valid n (People with BMI data)</td>
<td>763</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese &gt; 30</td>
<td>393</td>
<td>51.5</td>
</tr>
<tr>
<td>Overweight 25-30</td>
<td>235</td>
<td>30.7</td>
</tr>
<tr>
<td>Normal &lt; 25</td>
<td>135</td>
<td>17.8</td>
</tr>
</tbody>
</table>
The result of this analysis indicated that vitamin D is associated with BMI adjusting for seasonality and ethnicity with \( P < 0.0001 \). Overweight subjects are significantly different from normal weight subjects with 25(OH)D, \( P = 0.0018 \) and \( P = 0.0001 \) respectively. Similarly, obese subjects were significantly different from normal weight subjects with \( P < 0.0001 \) when compared to the reference group of the normal weight subjects.

The results indicated that seasonality is associated with vitamin D adjusting for age and ethnicity. There was high deficiency [25(OH)D concentration < 12ng/mL seen across all seasons. Although the mean Vitamin D level in the sample was 25.7 ng/mL, one fifth of the population were deficient with \(<20\text{ng/mL}\) 25(OH)D concentrations combined for Winter and Spring. A general linear model indicated that the lowest vitamin D concentration was seen in the Winter when compared with the summer was the most significant change for 25(OH)D with \( p<0.08 \).

**Research Question Two:** Is obesity a significant determinant of serum 25(OH)D concentration (ng/mL) among adults seeking integrative medicine care?

**Hypothesis 2:** Obesity as measured by BMI is significantly associated with serum 25(OH)D concentration in a cross-section of patients seeking integrative medicine care in an urban setting. In a general linear model predicting the effect of obesity on vitamin D level adjusting for age, sex and seasonality which we found to be significant covariates, the results indicated a significant association between serum 25(OH)D concentrations and obesity levels, \( P<0.0001 \).
**Results:** The data analysis results provided evidence that BMI is significantly associated with serum 25(OH)D concentration. Furthermore, we concluded that the association has an inverse relationship with some trending. The higher the level of BMI the lower the level of 25(OH)D concentration. See Table 4 below for details of the LS means and significance of this association. There was a significant difference between obese and very obese subject for vitamin D concentrations. But there was no significant difference between overweight and the normal weight categories.

Table 4. BMI crossed with vitamin D concentration

<table>
<thead>
<tr>
<th>BMI</th>
<th>VITD</th>
<th>SE</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 &lt;25</td>
<td>27.48</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>2-25-30</td>
<td>26.18</td>
<td>0.79</td>
<td>0.5347</td>
</tr>
<tr>
<td>3-31-35</td>
<td>24.46</td>
<td>0.88</td>
<td>0.0456</td>
</tr>
<tr>
<td>4- &gt;35</td>
<td>22.60</td>
<td>0.84</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

The GLM Procedure. Least Squares Means.
Adjustment for Multiple Comparisons: Dunnett-Hsu

The mean of serum 25(OH)D among the different BMI categories ranged from 22.6 to 27.4 ng/mL with larger deficiencies among the higher BMI categories. The most significant for rejecting the null hypothesis was the morbid obesity association category, as reflected in BMI >35 with mean vitamin D of 22.6 ng/mL.
Pain

**Research Question Three:** Is self-reported pain level among adults with chronic illness a determinant of serum 25(OH)D concentration among adults seeking integrative medicine care? The only pain used in the analysis was the present pain intensity as reported to the nurse using the numeric pain scale. Of the 1268 subjects identified for inclusion in the study, 138 had numeric pain scale measurement for their pain. See Table 5 below for the pain intensity by categories.

Table 5. Frequency and description of pain categorized by intensity

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total n (in study)</td>
<td>1268</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Subjects without Chronic Pain Scale data</td>
<td>1123</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Pain Scale Data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valid n (Subjects with Chronic Pain data)</td>
<td>138</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Chronic Pain (n=138)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High Intensity</td>
<td>29</td>
<td>21.0</td>
<td></td>
</tr>
<tr>
<td>Moderate Intensity</td>
<td>37</td>
<td>26.8</td>
<td></td>
</tr>
<tr>
<td>Low Intensity</td>
<td>72</td>
<td>52.2&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

**Hypothesis 3:** Present pain using a pain scale of 1-10 with level 10 being the highest intensity or discomfort is associated with 25(OH) D concentration,

Analysis of an association between self-reported pain and 25(OH)D using LS means with Dunnett-Hsu adjustments, we found that moderate pain reached significance;
p value 0.04. (As shown in Table 6, below). Moderate pain was significantly different from low intensity pain, but high intensity pain showed no statistical significant difference from low intensity pain. When we controlled for gender, seasonality and age moderate pain predicting VD concentration we lose the statistical significance.

Results 3: The data analysis results fail to reject the null hypothesis. There is insufficient evidence that pain as measured on the pain scale of 1-10 is associated with 25(OH) D concentration.

Table 6. Self-Reported pain crossed with Vitamin D

<table>
<thead>
<tr>
<th>PAIN Category</th>
<th>n</th>
<th>VD Mean</th>
<th>SE</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-Low Intensity Pain</td>
<td>72</td>
<td>20.45</td>
<td>1.31</td>
<td></td>
</tr>
<tr>
<td>B-Moderate Intensity Pain</td>
<td>37</td>
<td>25.09</td>
<td>1.77</td>
<td>0.0429</td>
</tr>
<tr>
<td>C-High Intensity Pain</td>
<td>29</td>
<td>21.33</td>
<td>2.00</td>
<td>0.9041</td>
</tr>
</tbody>
</table>

The GLM Procedure. Least Squares Means. Adjustment for Multiple Comparisons using Dunnett-Hsu

Discussion of Major Findings

From the results of this study, vitamin D deficiency was common among urban dwelling adults seeking integrative care, and significantly so among subjects who were young, Black and obese. Refer to Appendix A for main variables used in the analyses.

In this study the younger adults were those found to have the highest deficiency levels. This could be due to the fact that this age group tend to be healthier and unless
they have a determined illness with risk that warrants testing with 25(OH)D assay test, they may never know that they were deficient. The over 70 age group has according to the literature the highest risk for deficiency, though not the highest deficiency group in our study, the high prevalence of deficiency among this group is consistent with previous studies (Annweiler et al., 2013; Forrest et al., 2013; Holick et al, 2011; LeBlanc et al., Rianon et al.; and Ramdin, 2015).

Findings for ethnicity were consistent with prior work (Looker et al., 2001, Gordon et al., 2012, Peiris et al., 2011; and Forest et al., 2011 Signorello et al, 2013; Leung et al, 2015 and Weishaar et al. 2013), in that the most deficient were among the Blacks. Chi-Square analysis indicates that 29% of Blacks compared to 17% of Whites had vitamin D deficiency. Surprisingly, fewer than 6% (n=76) of the total population (N=1268) had vitamin D levels that were adequate. In established studies this is usually about 1/3 of the population who are deficient (LeBlanc et al., 2015 and Peiris et al, 2011).

Based on prior studies including a study by Jamal-Allial and colleagues, they found that among Puerto Rican adults living in the Greater Boston area, adiposity was inversely related to vitamin D concentration adjusting for age, gender, vitamin D intake, and SES among other factors. (Thomson et al., 2012; Touvier et al., 2015; Jamal-Allial et al. 2014). This may mean that adults who are overweight should also be included in the at-risk category for VD deficiency.

Although there was a difference in the VD concentration means between females and males, this was not statistically significant and corroborates what has been found in the literature (Weishaar et al., 2013; Sherman et al, 2013). Refer to Appendix B for a table of the age, BMI, VD and pain crossed by gender. Vitamin D concentration, the key
variable was found across regression analysis to be statistically significant in this vulnerable population to be linked with BMI and moderate pain. It is clear that the inverse relationship between VD and BMI warrants intervention as this finding is consistent with prior research on this correlation (Tangpricha et al., 2012 and Holick et al., 2011; Touvier et al. 2015).

The preliminary review of the charts indicated that the majority had a zip code from the major metropolitan area, which is in a temperate climate zone. It is evident that seasonality affected the VD outcome for subjects in this study. Seasonality impacts the amount of days that a person may have enough UV sunlight exposure to facilitate the synthesis of vitamin D through their skin. In this predominantly at risk population the variable seasonality, was found to be relevant and consistent with prior works (Wacker et al, 2013; Touvier et al., 2015), therefore it was used as a control in the analysis. Most of the 25(OH)D test was done in the Winter and Spring and this is consistent with the standards of practice documented in the literature (Holick 2009 and Holick et al., 2011). In this study, less than 10% of adults had optimal levels of vitamin D in any of the seasons, this finding is consistent with other researchers such as Holick et al., (2011). While this deficit is expected in the Winter and Spring coming off cloud covered days when multiple layers of clothing are worn to keep the body warm, it was not expected in the Fall when vitamin D stores from Summer should be sufficient to last a few weeks.

Not all subjects who had pain, reported their pain intensity on the self-reported pain scale. Since the majority of subjects were either self-referred or referred by their clinician to the integrative medical clinic came for pain management, (refer to Appendix C for a reflection of the ICD codes and diagnoses that reflected some chronic pain
component among the subjects) even with this limitation, it was worthwhile to conduct this analysis. It gave insight into the relationship between vitamin D deficiency and present pain which we found to be statistically associated at the moderate pain level. However, when other variables known to affect vitamin D were added to the model, (age, ethnicity and seasonality) the changed outcome to non-statistical significance, led us to believe there was some other confounding variable responsible for the initial finding related to pain. These results are not surprising given the conflicting evidence from prior studies of the association of pain and vitamin D deficiency (Gloth 111 et al. 1991; Holick 2007; Straube 2009). Given that the sample with self-reported pain captured on the pain scale was small \(N=168\) among those with a diagnosis of chronic illness, further investigation is warranted using a larger sample with isolated pain types, for example musculoskeletal pain versus neuropathic pain associated with diabetes etc.

Using this socio-ecological model for health promotion and disease prevention, one has to consider what other variables may confound the findings. We do know that chronological age is as significant a factor as is the state of the skin (Sherman et al., 2013). We also know that not all vitamin D supplements sold over the counter may have the efficacy desired, as not all have United States Pharmacopeia (USP) seal, which is a signature for quality standards (Gall et al., 2013). Does this mean that those who are supplementing may be inadequately dosing themselves? At least one quarter of the sample were supplementing but a smaller percentage were showing optimum concentration for VD.
Study Limitations

A retrospective study with the outcome variable of 25(OH) D status will result in limitations as the presumed factors have already occurred. The electronic medical record assessment tool used to capture the original data consisted of a comprehensive array of generalized and specific questions. Since these questions were not designed specifically for this study, we had to use the responses as given, excluding some data that were not reported at the research level desired for this study. Example pain categorical data instead of ratio or a continuous level. Some qualitative information in the record such as lifestyle and nutrition did not have information on the availability of food or food insecurities to capture this as a variable to analyze, which would add relevance to nutritional supply as a source of vitamin D in this population. They are varied vitamin D supplement, some are the higher doses of 1000 IU/pill or capsule and others are the 200/300 IU/pill, the specific dose was not always captured and therefore dosing was not used in the descriptive analysis. The pharmaceutical form of vitamin D available in the USA is vitamin D2 (ergocalciferol), but may vary, resulting in different active amounts of the drug (Laurentani et al, 2010). To counteract any change effects due to this, we used the objective serum levels as drawn, and information on vitamin D supplementation was used as categorical data in the discussion. Some of the critical barriers in the field has been the assay drift for the test 25(OH)D and the fact that there may be a slight variation from lab to lab. To minimize this limitation in the study, only results from the serum drawn at the CLIA certified academic institution were used in the study. Similarly, factors such as exercise and chronic illness were treated as categorical data.
Ethnicity for Blacks was captured as a single group. Race and ethnicity may be measured differently depending on who is filling in this information, the provider or the patient. For example, ethnicity in some studies including this one, when referring to Blacks do not differentiate among Blacks from different geographic regions. Black American, Americans from Sub-Saharan African and Afro Caribbean Americans, although they may share similar skin colors, their health values and health practices may differ significantly. This can affect also their use of sun to provide a source of vitamin D. Although we did not stratify the ethnicity, the finding was consistent with that found in many studies including the NHANES studies over the years. (NHANES, 2006, NHANES 2012).

Perhaps one of the more significant limitations was that the variable present pain was not classified as controlled or uncontrolled pain. Additionally, it only tells how the patient was doing on the day they were evaluated. Although using the pain scale was the most objective method to analyze pain on a continuous variable in this study, this prevented the full use of the data set of subjects who may have pain. For example, those patients whose pain was under control from analgesic may have scored lower on the pain scale or may not have reported pain at all. Despite the fact that this study failed to support the association of pain and vitamin D deficiency when known confounding variables were controlled, this warrant further investigation with a larger sample size. Previous studies do show some link especially when isolating pain of a specific diagnosis. For example, the discomfort of painful diabetic neuropathy has been linked to low vitamin D (Tucker, 2015).
Implications for Nursing

Nurses at all levels can play a major role in the health promotion or disease prevention in relation to vitamin D. In some cases, they can take an active role in screening for vitamin D using the socio-ecological model. Nurses are known for providing comprehensive care and using this model will help to identify persons at risk to refer or educate them to be actively involved in the self-management of their vitamin D. Nurse practitioners may use the results from this study for a step wise approach to the management of vitamin D in their patients. Since there are many confounding variables and no standardized recommendation for surveillance, recognizing that in the temperate zone these vitamin D concentrations may vary by seasons the annual health visit is not the only time to have this discussion, but should also be done in the context of specified chronic illness. When a patient reports pain, it should be captured as objectively as possible, and using the pain scale is an acceptable measure for doing so. Consistent use will help when cross coverage is needed to evaluate a specific subject and in this study would have made the N significantly larger and perhaps supported a more robust analysis.

This prevalence of low vitamin D in adults who have chronic illness supported by this study indicates the need for some standard health literacy appropriate education for the adult about supplementing with vitamin D. Efficacy trials /effectiveness trials with randomized controlled studies (RCT) in specified populations are still needed. Dissemination and implementation science still need to be established in specific segments of the population. But nurses can educate the patients about what is already evidenced in the literature and that is the implications of obesity and low vitamin D
levels. In examining the variables using the socio-ecological framework for health, the built environment, socioeconomic factors and culture could be the focus.

**Implications and Future Research**

The result of this research is to be taken in the context in which it was done and by no means generalized to all populations. However, it does add to the knowledge of what is known about a population at risk for hypovitaminosis D. This population of adults with chronic illness offers the researchers the ability to explore some of the variables associated with vitamin D from the literature and determine ones which are both statistically and clinically significant. The socio-ecological model offers a valuable framework for systematically evaluating the strength and weakness in an individual or in a population for health promotion or disease prevention.

Researchers needs to examine these variables in conjunction with at risk population to help determine other relevant factors. The findings suggest that future research may be needed to predict vitamin D status using a prospective longitudinal design. This approach would enable the examination of variables that support the maintenance of optimal vitamin D level and corresponding health status among adults with chronic illness. Nurses, physicians and other health providers should form inter-professional teams to address the problem as the complexity of hypovitaminosis D is obvious. High risk adults may want to self-treat but in doing so may not be aware that they are undertreating unless objectively monitored.

On the basis of our results, there seemed to be a clear indication that some level of pain may be associated with suboptimal levels of vitamin D. Understanding that chronic pain is complex and there are many confounding variables, given the small statistical
The significance of 25(OH)D and pain initially found (moderate pain association of $p < 0.04$), and this group had the highest means for vitamin D, further investigation is recommended. Perhaps using a targeted longitudinal intervention study to examine this variable’s association over time using supplements as the intervention. It has the potential to be clinically significant even if it is for improving the quality of life for these adults. Because the research only showed an initial statistical association of vitamin D and moderate level pain, and not a similar association with low intensity or high intensity pain, this is clinically significant and warrants further investigation. This investigation should examine serum vitamin D concentration in all levels of pain taking into consideration the analgesia being used in a larger population of subjects with chronic pain. The findings also suggest that future research may be needed to predict vitamin D status using a prospective longitudinal design in these patients taking into account the implications of obesity. Given that obesity was so strongly associated with vitamin D deficiency, could this be a biological effect or a genetic effect, the latter should be further investigated as it is already established that some vitamin D is trapped in adipose tissue (Thomson et al., 2012, Touvier et al., 2015).

**Conclusion**

Nurses, physicians and other health providers should form inter-professional teams to address the problem as the complexity of hypovitaminosis D is obvious when using a socioecological theory. Approaching vitamin D deficiency in this way shifts the current paradigm of care from a purely medical model to that of a socioecological model of care. The results of this research is to be taken into the context in which it was done and its limitations and by no means should be generalized to all populations. However, it
does add to the knowledge of what is known about a population at risk for hypovitaminosis D. This population of adults with chronic illness offers the researchers the ability to explore some of the variables associated with vitamin D from the literature, and to determine the significance of those examined. The socio-ecological health model offers a valuable framework for systematically evaluating the strength and weakness in an individual or in a population for health promotion or disease prevention related to vitamin D status.
References


Preferred reporting items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *Ann Intern Med*, 151(4);


Sherman, S., Hollis, B., and Tobin, J. (2013). Vitamin D Status and Related Parameters in a Healthy Population: The Effects of Age, Sex, and Season. Published online 2013 DOI: http://dx.doi.org/10.1210/jcem-71-2-405


Appendix A

Main Variables Used in the Analysis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Measurement</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>25(OH)D (nM)</td>
<td>Serum 25(OH)D</td>
<td>Continuous</td>
</tr>
<tr>
<td></td>
<td>concentrations (ng/mL)</td>
<td></td>
</tr>
<tr>
<td>Anthropometrics</td>
<td>BMI</td>
<td>Continuous and categorical</td>
</tr>
<tr>
<td>Demographics</td>
<td>Age; Gender;</td>
<td>Categorical/continuous</td>
</tr>
<tr>
<td>Chronic Pain</td>
<td>Pain scale 0-10</td>
<td>Continuous</td>
</tr>
<tr>
<td>Physical activity level</td>
<td>Active exercise</td>
<td>Categorical</td>
</tr>
<tr>
<td>Medications</td>
<td>Vitamin D supplements (pure or in multivitamin)</td>
<td>Categorical</td>
</tr>
<tr>
<td>Seasonality</td>
<td>Time of year</td>
<td>Categorical</td>
</tr>
</tbody>
</table>
### Appendix B

Age, BMI, Vitamin D concentration and Pain cross with gender

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total N</th>
<th>Men Mean (Std. Dev)</th>
<th>Women Mean (Std. Dev)</th>
<th>P-value (2 sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at the Visit</td>
<td>1268</td>
<td>55.19 (12.40)</td>
<td>52.05 (13.90)</td>
<td>0.0005</td>
</tr>
<tr>
<td>BMI</td>
<td>763</td>
<td>30.39 (7.09)</td>
<td>32.05 (9.39)</td>
<td>0.0166</td>
</tr>
<tr>
<td>Serum 25(OH)D (ng/ml)</td>
<td>1268</td>
<td>23.66 (11.33)</td>
<td>26.25 (12.12)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Pain Scale</td>
<td>138</td>
<td>2.70 (3.42)</td>
<td>2.92 (3.49)</td>
<td>0.7562</td>
</tr>
</tbody>
</table>

* ttest analysis
Appendix C

Diagnoses and ICD-9 codes from charts that reflect some degree of chronic pain.

<table>
<thead>
<tr>
<th>ICD Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICD-724.5</td>
<td>BACK PAIN</td>
</tr>
<tr>
<td>ICD-053.19</td>
<td>POSTHERPETIC NEURALGIA</td>
</tr>
<tr>
<td>ICD-729.1</td>
<td>FIBROMYALGIA</td>
</tr>
<tr>
<td>ICD-338.4</td>
<td>CHRONIC PAIN SYNDROME</td>
</tr>
<tr>
<td>ICD-733.6</td>
<td>COSTOCHONDritis</td>
</tr>
<tr>
<td>ICD-710.2</td>
<td>SJOGREN'S SYNDROME</td>
</tr>
<tr>
<td>ICD-733.90</td>
<td>BONE PAIN</td>
</tr>
<tr>
<td>ICD-714.0</td>
<td>ARTHRITIS, RHEUMATOID</td>
</tr>
<tr>
<td>ICD-250.40</td>
<td>NEPHROPATHY, DIABETIC</td>
</tr>
<tr>
<td>ICD-250.60</td>
<td>DM W/NEUROPATHY</td>
</tr>
</tbody>
</table>
Chapter Five: Summary and Conclusion

Valeria Ramdin

Northeastern University
School of Nursing
The Bouvé College of Health Sciences
Summary and Conclusion

Treating vitamin D deficiency is a national population health concern (NHANES, 2010). The Social Ecology of Health Model used as the conceptual framework for this study highlights some of the determinants of health as it relates to vitamin D adequacy. The definition of body mass index used was consistent with that of the World Health Organization and proved to be telling when the adult BMI rises to above ideal body weight. This may mean all adults who are overweight should be included in the at-risk category and not only those who are obese with BMI >30 which is the current recommended high risk category.

Using the socioecological model for health promotion and disease prevention, one has to consider what other variables may confound the findings. We do know that chronological age is not as significant a factor when compared to the state of the skin (Sherman et al., 2013). We also know that not all vitamin D supplements sold on the market may have the efficacy desired as not all have United States Pharmacopeia (USP) a signature for quality standards (Gall et al., 2013). Does this mean that those who are supplementing may be inadequately dosing themselves? At least one quarter of the sample were supplementing but less than that were showing optimum levels.

On the basis of our data, there seemed to be an initial indication that some level of pain may be associated with suboptimal levels of vitamin D (with $p = 0.04$) but we lost that significance with control for the known confounding variables; ethnicity and seasonality. Understanding that pain is complex and there are many confounding variables, given the small statistical significance initially, further investigation is recommended using a targeted longitudinal intervention study to examine this variable’s
association over time. Maintaining optimal vitamin D status in the presence of chronic pain has the potential to be clinically significant even if it is only for improving the quality of life for these adults.

This outcome points to the need for some standard health literacy education for the adult with chronic pain and obesity about supplementing with vitamin D. Dissemination and implementation science still need to be established in specific segments of the population. In examining the variables using the socioecological framework for health, the built environment, socioeconomic forces and culture should be investigated.

**Implications and Future Research**

The results of this research is to be taken in the context in which it was done and by no means generalized to all populations. However, it does add to the knowledge of what is known about a population at risk for hypovitaminosis D. This population of adults with chronic illness offered us the ability to explore some of the variables associated with vitamin D and to determine both statistical and clinical significant variables. The socioecological model offers a valuable framework for systematically evaluating the strength and weakness in an individual or in a population for health promotion or disease prevention.

Research should examine more of these variables in conjunction with the at risk population to help determine other relevant factors. The findings suggest that future research may be needed to predict vitamin D status using a prospective longitudinal design. This approach would enable the examination of variables that support the
maintenance of optimal vitamin D level and corresponding health status among adults with chronic illness. Efficacy trials /effectiveness trials with Randomized Control Trials (RCT) in specified populations are still needed. Nurses, physicians and other health providers should form inter-professional teams to address the problem as the complexity of hypovitaminosis D is obvious. High-risk adults may want to self-treat but in doing so may not be aware that they are under treating self unless objectively [25(OH)D] monitored.
References


November 21, 2013DOI: 10.1056/NEJMo1306357


Sherman, S., Hollis, B., and Tobin, J. (2013). Vitamin D Status and Related Parameters in a Healthy Population: The Effects of Age, Sex, and Season. Published online 2013 DOI: http://dx.doi.org/10.1210/jcem-71-2-405


NOTIFICATION OF IRB ACTION

Date: November 30, 2015
IRB #: 15-11-22

Principal Investigator: Elizabeth Howard
Valeria A. Randin

Department: School of Nursing
Bouvé College of Health Sciences

Address: 103 Robinson Hall
Northeastern University

Title of Project: Socioecological Factors associated with Vitamin D Deficiency: Implications for the Adult with Obesity and/or Chronic Pain

Participating Sites: Boston University Medical Center - IRB Exempt approval received (Protocol Number: H-32111)

Approval Status: Approved

DHHS Review Category: EXEMPT, CATEGORY #4

C. Randall Colvin, Ph.D., Chair
Northeastern University Institutional Review Board

Nan C. Regina, Director
Human Subject Research Protection

This approval applies to the protection of human subjects only. It does not apply to any other university approvals that may be necessary.

No further action or IRB oversight is required, as long as the project remains the same. However, you must inform this office of any changes in procedures involving human subjects. Changes to the current research protocol could result in a reclassification of the study and further review by the IRB.

Northeastern University FWA #4630
Appendix B
Boston University Medical Center IRB Outcomes Letter

Title of Study: Vitamin Use and Chronic Illnesses among patients in the Integrative Medicine clinic

Review Type: Exempt Action: Categorical Exemption
Date of Action: October 16, 2012
Funding Source: unfunded

Protocol Version #: 1.3
Dear Paula Gardiner, a qualified member of the BUMC Institutional Review Board (IRB) staff has reviewed the above referenced protocol and has determined that it does not require further review by the BUMC IRB because this study was determined to be EXEMPT in accordance with 45 CFR 46.101. This study qualifies as Exempt under the following categories: (4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Protocol Specific Determinations: -Approved HIPAA Waiver of Authorization Requirements: -Investigators will not have access to master code at any point while conducting this study. -If any investigator related to this study is receiving funding from a T32 or other training grant to fund their activities on this protocol an amendment must be submitted to update the protocol accordingly. This approval corresponds with the version of the protocol indicated above.

All determinations regarding this project have been made based on the information submitted by the investigator. Any modifications to the research plan (including any changes in funding) must be submitted to the IRB for review and approval prior to
initiation, and may change the IRB’s determination. The IRB office does not require continuing review for studies that have been designated as EXEMPT under the categorical exemptions. It is the responsibility of the PI to ensure that any HIPAA requirements have been met prior to initiating this study. Validated HIPAA forms may be found within INSPIR II under Study Documents. It is also the responsibility of the PI to ensure that all required institutional approvals have been obtained prior to initiating any protocol related activities.

Sincerely yours,
Signature applied by Rita Cosgrove on 10/16/2012 10:08:52 AM EDT IRB Board Member

A copy of the original is available on file with the Northeastern University Institutional Review Board.