

Screening for Vitamin D Deficiency in Adults with Depression

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Abstract

Purpose & Background: This project evaluates the impact of education on a provider's intent to screen for vitamin D deficiency in adults with depression. An internal Quality Improvement (QI) study at a local mental health primary care clinic revealed that only 1 in 3 patients with depression were routinely screened for vitamin D deficiency. Vitamin D is a crucial component of numerous systemic functions, including mental health, specifically depression.

Methods: This QI project used the Rosswurm and Larrabee Model implementation framework. Institution Review Board (IRB) expedited review approval was received. This project was conducted at 10 Veteran's Affairs (VA) primary care clinics in Arizona. An initial email with a recruitment flyer was sent to providers to launch the project. A second email was sent to participants who volunteered to participate in the project, with instructions and links to the asynchronous pre-survey, recorded education PowerPoint, and post-survey. Responses were analyzed using Intellectus Statistics software.

Results: Provider knowledge of impact and intent to screen for vitamin D deficiency increased after viewing a brief education video (n=30). Frequency distribution analyses revealed a 23% average increase in agreement to screen for vitamin D deficiency at annual visits, "at-risk" individuals, knowledge of the association, and intent to screen regularly in depression.

Conclusion: The education intervention was found to positively impact the provider's intent and demonstrate the importance of screening for vitamin D deficiency in adults with depression.

Keywords: vitamin D, vitamin d deficiency, adults with depression, screening

Screening for Vitamin D Deficiency in Adults with Depression

According to the National Institutes of Health (2021), over 42% of adults in the United States have low vitamin D levels. Adequate vitamin D levels are essential to overall adult health. Vitamin D is a crucial component of calcium absorption for bone strength, decreases insulin resistance, impacts cardiovascular health, promotes healthy immune system function, and impacts mental health, including depression. Cuomo et al. (2019) studied patients with bipolar depression disorder and found that 94% had inadequate vitamin D levels. An internal QI study at a local mental health primary care clinic revealed that only 1 in 3 patients with depression were routinely screened for vitamin D deficiency. Further, an extensive literature review revealed the clinically significant impact of evaluating and addressing vitamin D deficiency in depression (Briggs et al., 2019; Cuomo et al., 2019; Darnton-Hill, 2019; Erensoy, 2019; Gugger et al., 2019; Kaviani et al., 2020). The project aimed to evaluate the impact of education on the provider's intent to screen for vitamin D deficiency in adults with depression.

Problem Statement

In the last decade, tremendous progress has been made in developing evidence-based vitamin D guidelines and policies (Sempos & Binkley, 2020). However, despite this progress, vitamin D screening and management are not consistently utilized in adults with depression.

Purpose and Rationale

Vitamin D is a unique neurosteroid hormone that has a vital role in depression. Vitamin D receptors are present in neurons in the brain, contributing to the pathophysiology of depression (Anglin et al., 2013). Many research studies have shown an association between vitamin D deficiency and increased depression symptoms (Briggs et al., 2019; Cuomo et al., 2019; Darnton-Hill, 2019; Erensoy, 2019; Gugger et al., 2019; Kaviani et al., 2020). The project was

designed to assess the effect of education on the provider's intent to screen for vitamin D deficiency in adults with depression.

Many factors contribute to vitamin D deficiency, especially in individuals with depression. It is difficult to obtain adequate vitamin D from diet alone, as many foods lack enough to maintain appropriate levels. The typical protected indoor environment limits exposure to UV, causing a lack of vitamin D exposure. An individual experiencing symptoms of depression such as lack of appetite and motivation to leave home also contributes to decreased vitamin D levels, typically obtained by exposure to UV sunlight and consuming vitamin D in the diet. As a result, vitamin D supplementation is often the recommended treatment or standard of care (SOC).

Background and Significance

In 1920, Vitamin D's influential discovery led to curing a painful childhood bone disease, known as rickets. Vitamin D is endogenously produced when the skin is exposed to ultraviolet (UV) rays, which triggers vitamin D synthesis, but can require supplementation (Anglin et al., 2013). Vitamin D is converted in the liver and kidneys to its active form, known as calcitriol (National Institutes of Health, n. d.). Vitamin D is a fat-soluble vitamin that is absorbed in the small intestine. Vitamin D deficiency is associated with numerous medical conditions such as osteoporosis, hypertension, cardiovascular disease, diabetes, obesity, and depression.

Vitamin D deficiency is associated with poor outcomes of numerous inflammatory problems. Mediated by elements of the inflammatory cascade, vitamin D deficiency predisposes a patient to certain degrees of pathologic central nervous system (CNS) induced sleepiness, a depression symptom (McCarty, 2010). Depression is associated with inflammation in the body, as evidenced by an elevated C-Reactive Protein (CRP) and there appears to be relationship

between elevated CRP and decreased vitamin D levels (Puglisi, 2014). Many studies indicate that nutritional intake, including lack of vitamin D, is part of the underlying causes of depression symptoms (Alavi et al., 2019, Alghamdi et al., 2020, Anglin et al., 2013, Irandoust and Taheri, 2017, Gugger et al., 2019; Kaviani et al., 2020, Krysiak et al., 2018, Vaziri et al., 2016, Zheng et al., 2019).

Adults with Depression

Depression is a serious mental health condition that can be devastating for people if left untreated. Symptoms of depression can vary in presentation, are evident for over two weeks, and affect daily functioning (National Alliance on Mental Illness (NAMI), 2017). Common symptoms include fatigue, insomnia, lack of appetite, lack of interest in activities, physical aches and pains, hopelessness, or suicidal thoughts (National Alliance on Mental Illness (NAMI), 2017). Over 18 percent of adults over age 18 have regular feelings of depression (Centers for Disease Control and Prevention (CDC), 2021). Numerous studies associate a significant risk of depression symptoms with vitamin D deficiency (Alghamdi et al., 2020, Anglin et al., 2013, Briggs et al., 2019; Cuomo et al., 2019; Darnton-Hill, 2019; Erensoy, 2019; Gugger et al., 2019; Kaviani et al., 2020).

Screening for Vitamin D Deficiency in General Population

Vitamin D levels are typically used to screen for bone disorders. However, vitamin D levels are also checked in people with chronic medical problems such as diabetes, cardiovascular disorders, inflammation, and depression. The Vitamin D Standardization Program (VDSP) established protocols to standardize vitamin D measurement procedures (Sempos & Binkley, 2020). The VDSP, in collaboration with the Institute of Medicine (IOM) and the American Association of Clinical Endocrinology (AACE), determined the appropriate serum vitamin D

levels and the Recommended Daily Allowance (RDA) for adults (Ross et al., 2011). Vitamin D status is measured by serum levels of a total 25-hydroxyvitamin D [25(OH)] concentration (National Institutes of Health, n. d.). A normal level or adequate for healthy adults is 20 nanograms/milliliter (ng/ml) to 50 ng/ml, and a level of less than 20 ng/ml is considered vitamin D deficiency (Bikle, 2014). The SOC, as recommended by VDSP, IOM, and AACE, is to monitor Vitamin D levels at intervals of three months, six months, or annually depending on levels and treatment or deficiency management.

Standard treatment with supplementation for vitamin D deficiency varies depending on the level of deficiency. Supplementation with vitamin D3 or ergocalciferol can range from 1,000 to 2,000 international units (IU) daily to 50,000 IU weekly or even 50,000 IU monthly (Pepper et al., 2009). As vitamin D is fat-soluble, it is recommended that vitamin D supplements be taken with food for optimal absorption.

Screening for Vitamin D Deficiency in Mental Health

Evaluation and management of vitamin D deficiency in adults with mental health diseases are inconsistent. Data is limited regarding the standardization or consistent use of screening and treatment for low vitamin D in patients with depression, and the research field of vitamin D remains controversial. Ethical considerations must be given high priority in study design, given the risk of any severe or irreversible damage caused by insufficiency of vitamin D (Frame et al., 2018). While the science continues to emerge, a relationship between vitamin D deficiency and symptoms of depression are apparent in many observational studies (Anglin et al., 2013; Briggs et al., 2019; Cuomo et al., 2019; Darnton-Hill, 2019; Erensoy, 2019; Gugger et al., 2019; Kaviani et al., 2020). Alghamdi et al. (2020) demonstrated that after three months of vitamin D supplementation, baseline Beck Depression Inventory (BDI) scores decreased

significantly, and vitamin D levels increased. Many other studies had similar results of reduced depression scores and increased vitamin D levels, see Table 1. Studies suggest that adding vitamin D supplementation as a SOC in conjunction with depression treatment should be a gold standard (Alghamdi et al., 2020).

Internal Evidence/Setting Generated Data

Routine vitamin D screening is not being performed in patients with depression in the primary care setting. Upon reviewing 100 charts at a Veteran's Affairs (VA) medical center in the Southwest United States, only one in three patients with depression were screened for vitamin D deficiency. The VA serves approximately 1700 patients in the mental health primary care and homeless primary care clinics, mainly cared for by Nurse Practitioners and Medical Doctors. The VA medical center provider's treatment guidelines are derived from the Veterans Health Administration (VHA) Pharmacy Benefits Management Services (PBM), Medical Advisory Panel (MAP), and Center for Medication Safety (VA MEDSAFE) (National PBM Bulletin, 2009). The VDSP, in collaboration with IOM, determines the national SOC guidelines for evaluating and managing vitamin D deficiency and AACE and aligns with the VA guidelines.

PICOT Question

This inquiry has led to the development of the following PICOT question: In adults with depression, does screening for vitamin D deficiency, compared to not being screened, have an impact on depression symptoms?

Search Strategy

An exhaustive search was performed in the electronic databases PubMed, PsychInfo, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). These databases were selected for components encompassing symptoms of depression, vitamin D deficiency, and

supplemental management and relevance to the PICOT question. All three databases generated pertinent and related articles. The search method for each database has been explained below.

Inclusion Criteria, Exclusion Criteria, and Limitations

The inclusion criteria focused on studies published in English and ranged from 2015 to the present. Articles greater than five years were excluded, except for landmark studies. Criteria for inclusion consisted of adults and primary care, and the terms treatment and management were used synonymously. Studies from several countries were included unless they were not available in English. Most studies examined European and American regions. Opinion articles, studies lacking evidence to support, non-peer-reviewed, and non-primary research studies were excluded, except for landmark meta-analysis or systemic reviews. In all databases, inclusion and exclusion criteria were the same.

Keyword Selection

Keywords were carefully considered based on the PICOT question, and relevant information was generated with each search. The following keywords were utilized in the initial search: *Depression* and *vitamin D*. This search produced numerous articles related to depression and vitamin D; however, not all results met the inclusion criteria. A second search was completed with more specific choice of words: *vitamin D* or *ergocalciferol*, *depression* or *depressive disorder*, *vitamin D insufficiency* or *deficiency*, *screening*, and *supplementation*. This refined search generated a more concise selection of literature to use.

Search Yield

An initial search of CINAHL using *vitamin D*, *depression*, and *fatigue* yielded 39 results; a subsequent search that included *vitamin D*, *depression*, *fatigue*, and *supplementation* produced 6 results. A database search of PsychInfo using key terms *vitamin D*, *depression*, and *supplements* yielded 84 results. A search in PubMed generated 9 results using the terms *vitamin D*, *depression*, *fatigue*, and *supplement*. Critical appraisal was performed on 12 citations, and with careful consideration, 10 have been chosen to use in this review. The chosen studies addressed the PICOT question appropriately and evaluated if screening and treatment with supplementation for vitamin D deficiency impacts adults with depression.

Critical Appraisal and Synthesis of Evidence

Ten studies were saved for this review, including 9 RCTs, one longitudinal study, and one retrospective study. The studies were similar across many components. Detailed measures were taken to ensure blinded methods and randomization were clearly explained. Five out of the ten studies did not compare placebo to the intervention of vitamin D supplementation. However, all ten studies evaluated and described a notable reduction in depression scores and increased serum 25(OH) levels (Appendix A).

The studies reveal various demographic information (Appendix A). The age range was from 18 to over 65 years old. Three out of the ten studies included female participants only; the other seven included both male and female participants. Most studies reported the Beck Depression Inventory (BDI) scale of depression symptoms. The settings designated in the studies were primarily outpatient-based (Appendix A).

Assessment of primary interventions showed that most studies included interventions such as vitamin D supplementation versus placebo. All studies exhibited some degree of regular

monitoring of depression and vitamin D levels throughout and after the study. One study included additional interventions such as physical activity and UV sunlight exposure, and another study evaluated the impact of vitamin D plus calcium supplementation on depression. Most studies assessed vitamin D supplementation from 2,000 international units (IU) daily to 50,000 IU monthly. The length of the studies were mixed, ranging from 2 months to 24 months.

Key outcomes of interest mainly focused on reducing depression scores and increasing serum vitamin D levels (Appendix A). Five of the studies measured and reported BDI scores for depression symptoms and serum vitamin D levels; four of the studies utilized Geriatric Depression Scale (GDS), Hamilton D-17 Depression Score (HAM-D17), or Patient Health Questionnaire (PHQ-9). The remaining study used Edinburgh Postnatal Depression Scale (EPDS). All studies utilized standardized serum 25(OH) assay levels (Appendix A).

Measurement instruments were similar and included self-completion of depression questionnaires, interviews, and blood draws. A variety of reliable instruments were used to measure the effect of vitamin D supplementation on depression, showing an affect on reducing depression symptoms. The BDI was used in several studies. This questionnaire is a commonly used, reliable instrument to quantify levels of depression. The BDI has a reported coefficient alpha rating of 0.92 for outpatients (Sepehrmanesh et al., 2016). The BDI and HAM-D1 positively correlate and have test-retest reliability of $r = 0.93$ and confidence interval (CI) $a = 0.91$ (Sepehrmanesh et al., 2016). Most of the studies used analysis of variance (ANOVA), independent t-test, chi-square, regression analysis, and level of significance (p) to test heterogeneity. The overall significance of the effect consistently indicated a significant degree of certainty that vitamin D supplementation on depression positively affects depression symptoms and vitamin D levels.

Theoretical Framework

While only one study mentioned an applied theoretical framework, this project used Bandura's Self-Efficacy Theory. Bandura suggests that following self-efficacy-based interventions, particularly performance of the behavior of interest, increases outcome probabilities and self-efficacy (Smith & Liehr, 2018). Life as a busy primary care provider is demanding and stressful, which requires higher levels of independence, initiative, and self-regulation. This applies to the project's purpose to evaluate the impact of education on the provider's intent to screen for vitamin D deficiency in adults with depression. Virtual learning, as noted in this project, creates a flexible environment that combines structure, freedom and ease of access to the most recent EBP which enables providers to learn when it works best for them; thus promoting self-efficacy and the ability to leverage the most recent evidence to ensure optimal care for their patients.

Integrating evidence-based information on benefits and harms, can potentially lead to improved screening and decision-making for vitamin D deficiency (Rodrigues et al., 2019). There is an inadequate promotion of vitamin D education, including the benefits of routine screening and supplementation as needed. Many healthcare providers, public health professionals, and the public are deficient in information and awareness about the value of vitamin D, protecting against many chronic diseases, and its potential to reduce health disparities (American Public Health Association (APHA), 2008). Consistent screening may improve health outcomes for patients with vitamin D deficiency and depression, affect patient quality of life, and improve holistic care and treatment of individuals (Rodrigues et al., 2019). Self-efficacy is essential to support virtual learning activities. The Self-Efficacy Theory guided and evaluated factors that affect provider self-efficacy to make the project's education intervention successful.

Implementation Framework

The Rosswurm and Larrabee Model, which focuses on utilizing evidence-based practice, supported this project's development (Rosswurm & Larrabee, 1999). This model consists of 6 stages: Assess the need for change, link the problem and interventions and outcomes, synthesize best evidence, design practice change, implement and evaluate change in practice and integrate and maintain change in practice (see Appendix A). In the first stage: Assessing the need for change, internal and external evidence suggests that vitamin D deficiency in depressed adults is a significant problem. In the second stage, link the problem and interventions and outcomes, the lack of screening for vitamin D deficiency in depressed adults suggests a potential knowledge deficit or lack of adherence to established protocols of primary care providers (PCPs). PCPs are inundated with patient care and often cannot stay updated on the most recent evidence-based guidelines. Providing an efficient, condensed education method for primary care providers may increase screening for vitamin D deficiency in depressed adults, optimizing patient health outcomes. The third stage of synthesizing the best evidence revealed several studies that found that many adults with depression had vitamin D deficiency. Designing a practice change's fourth stage includes providing providers with the best evidence by an educational presentation via an asynchronous PowerPoint video. The fifth stage of implementing and evaluating a practice change includes sending a pre-and post-survey with the asynchronous education video to primary care providers. In this stage, data is collected to determine the effectiveness of the education video on a provider's intent to screen for vitamin D deficiency in depression. The last stage of integrating and maintaining a change practice may include regular promotion of the educational video to primary care providers and assess if screening and treating vitamin D deficiency becomes a standard of care.

Project Method

Institutional Review Board (IRB) expedited review approval was received from Arizona State University (ASU) and the Veterans Affairs Health Care System (VAHCS) prior to the commencement of this project. All efforts were made through secure links to preserve the participant's privacy. The review of the education video and completion of the surveys were considered the participant's consent to participate in the project. The data was reviewed in aggregate only. The collection consisted of evaluating the impact of the educational intervention on the provider's intent to screen for vitamin D deficiency in adults with depression. The collection of email addresses and personally identifiable information (PII) was for recruitment purposes only, and the study did not identify PII in the data collection process. There was no apparent risk to the participants.

Participants and Recruitment

The co-investigator recruited and educated the project participants. A week before the project launch date, a recruitment email was sent to primary care clinics at the VAHCS via global network addresses titled "xx Agave" and "xx CBOC All." Week -1: The recruitment email included an embedded recruitment flyer and consent form. The flyer and consent form described the project to the potential participants in the primary care clinics. The initial project launch email was sent to 5 primary care clinics with approximately 60 providers. However, the initial response only yielded 10 completed responses. The co-investigator collaborated with site stakeholders, and the decision was made to send the invitation email to 5 additional primary care clinics, with approximately 130 providers. In the initial pre-survey, the response was 49 providers. However, only 30 completed responses were used in the final data analysis, a 23% response rate.

Intervention

The participant's total involvement in the project did not exceed 10 minutes. The education video took approximately 7 minutes to view, while each 5-item Likert-type survey took approximately 1 minute to complete. The expected education review and completed survey responses were within one week of email receipt. The total project occurred within an eight-week timeframe. The estimated study completion date, including primary analysis, was approximately March 1, 2022. During week 1, participants across the selected VA clinics received an email that consisted of 3 parts: A link to the pre-survey, the education video, and the post-survey. All three steps needed to be completed in sequential order to complete the project. The pre-survey collected deidentified demographics, including gender, role (i.e., physician, nurse practitioner, physician's assistant,) years of practice, and primary area(s) of practice, such as outpatient primary care and inpatient or internal medicine. The recorded education PowerPoint covered the history of vitamin D, prevalence, the association between vitamin D deficiency and depression, and the benefits of screening and treating vitamin D deficiency. During week 8, the co-investigator sent a final thank you email to providers for participation in the project. Incomplete participant responses were not used in the final data analysis.

Project Results

Data Analysis Procedure

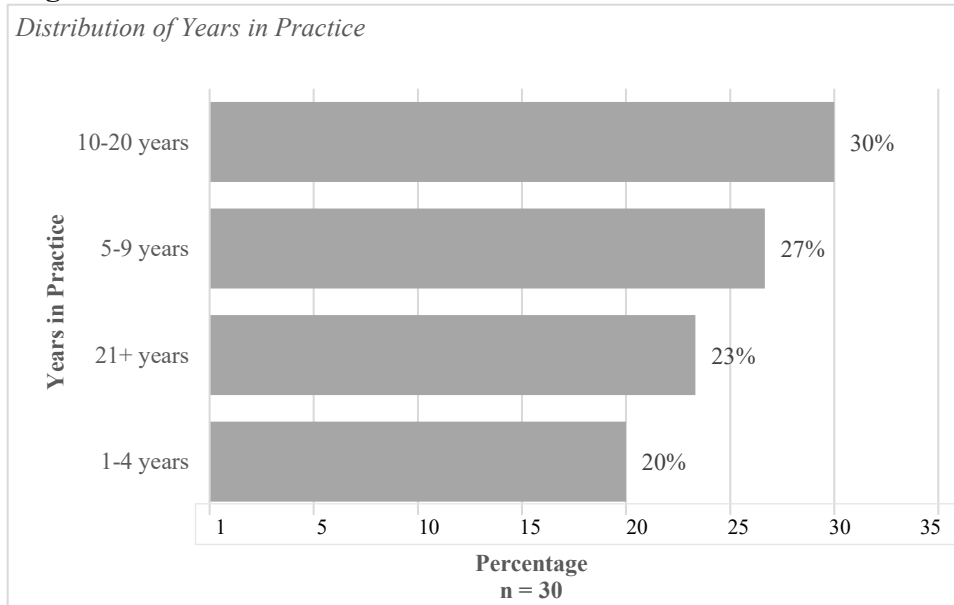
Intellectus Statistics software was used to complete the data analysis, and descriptive statistics and frequency distribution examined the outcome variables. Standard frequency analysis was performed to describe and compare the PCP demographics who completed the surveys. The outcomes measured included knowledge of the impact of vitamin D deficiency on depression and the PCP's intent to screen for vitamin D deficiency in depression.

The data was converted to percentage values from Survey Monkey into Intellectus Statistics.

Long-term data was not collected. No cost was associated with the project, and participants were not responsible for any costs related to participation in the project.

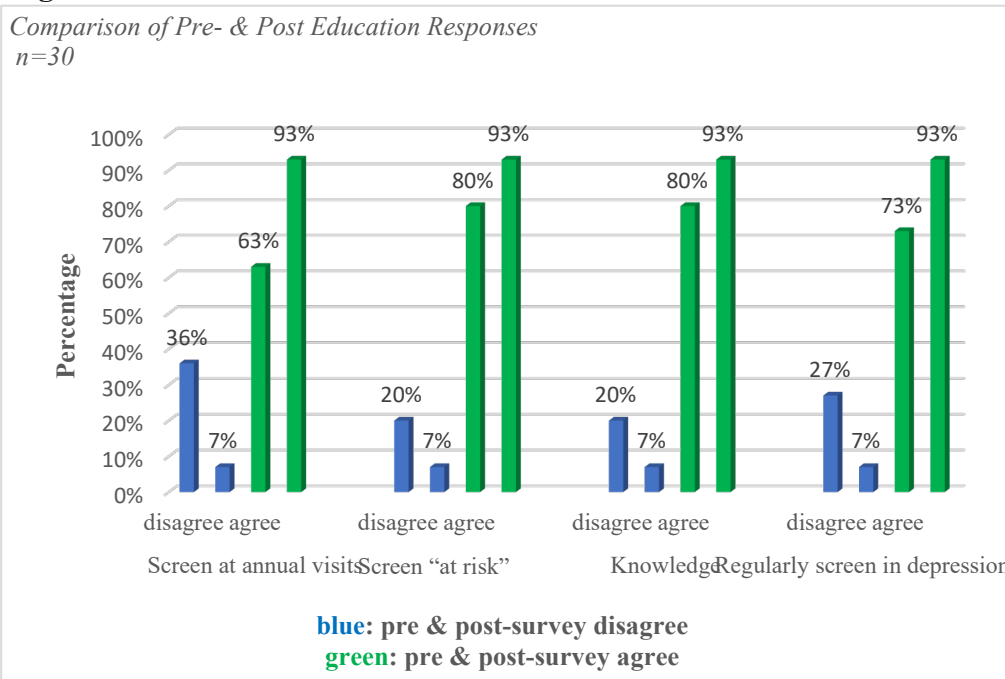
Demographic Data

The first four pre-survey questions were demographic inquiries, followed by five pre-education questions. The recruitment email was sent to approximately 60 providers. Forty-nine providers completed the pre-survey. However, thirty providers (n=30) fully completed both pre- and post-surveys, making them eligible for the project. The 19 incomplete survey responses were removed and were not used in the final data analysis. Of the remaining participants, 2 were male (6.7%), and 28 (93.3%) were female. All 30 (100%) providers were Nurse Practitioners, and worked in Primary Care (43%), Outpatient (23%), Internal Medicine (10%), inpatient providers (3.3%), Neurology/Headache (3.3%), Nurse Leadership (3.3%), Psychiatry (3.3%) and Education (3.3%). Most of the providers were in practice an average of 10-20 years (30%), followed by 5-9 years (27%), 21+ years (23%) , and 1-4 years (20%) in practice.

Figure 1**Outcome Data**

The co-investigators developed the pre-and post-surveys. Each survey contained 5 Likert-type scaled questions, ranging from 1-strongly disagree to 6-strongly agree. The co-investigators were unable to find an applicable instrument or survey of interest, therefore created these short surveys for the sake of this project. The pre-and post-survey demonstrate face validity having been reviewed by various content experts to assess provider knowledge and intent to screen for vitamin D deficiency. The surveys took 2 minutes to administer with clear directions, and they were easy to score. The comparison of all pre-and post-survey responses revealed a 23% average increase in agreement to screen for vitamin D deficiency at annual visits, "at-risk" individuals, knowledge of the association, and intent to screen regularly in depression. The corresponding level of disagreement decreased by an average of 19% comparing the pre-and post-survey responses.

Figure 2



The first pre-survey question was, "I screen all my patients for vitamin D deficiency during my annual office visits." The disagree response percentage was 36%, and the agree response percentage was 63%. The post-survey question was, "I *will* screen all my patients for vitamin D deficiency during my annual office visits." The disagree response percentage decreased to 7%, and the agree response percentage increased to 93%. The post-education intervention revealed an increase in providers' intent to screen for vitamin D deficiency during annual office visits.

The second pre-survey question was, "I screen for vitamin D deficiency in "at-risk" individuals such as those with osteoporosis and cardiovascular disease." The disagree response percentage was 20%, and the agree response was 80%. The question on the post-survey was, "I *will* screen for vitamin D deficiency in "at-risk" individuals such as those with osteoporosis and cardiovascular disease. The disagree response percentage decreased to 7%, and the agree

response increased to 93%. The post-education intervention revealed a 13% increase in providers' intent to screen for vitamin D deficiency in "at-risk" individuals such as those with osteoporosis and cardiovascular disease.

The pre-and post-survey questions were "I (will) screen for vitamin D deficiency in adults with depression. The disagree response percentage was 20%, and the agree response was 80%. The percentage of the post-survey disagree response decreased to 7%, and the agree response increased to 93%. This information revealed an increased knowledge of the association vitamin D deficiency and depression.

A question on the pre-and post-survey was, "I am knowledgeable about the impact of vitamin D deficiency in adults with depression. The pre-survey disagree response percentage was 27%, and the agree response was 73%. The percentage of the post-survey disagree response decreased to 7%, and the agreed response increased to 93%. This information reveals a 20% increase in providers' knowledge of the impact of vitamin D deficiency on depression.

The last pre-survey statement was, "I routinely access information about current evidence-based practice guidelines." Nine out of 10 respondents agree with this statement. All 30 respondents agreed to the post-survey question, "The education format was an effective method to convey information about current evidence-based practice guidelines." This data comparison pre-and post-education intervention demonstrates the increased likelihood of providers to seek a concise, practical, and convenient delivery method such as demonstrated by this project

Discussion

The progression through this DNP project has evolved and revealed exciting outcomes. All providers that completed the project were Nurse Practitioners, the majority of whom have

been in practice for 10 to 20 years. Continuing education and staying up to date on the latest evidence-based information is critical to support better patient outcomes.

Studies are sparse or outdated regarding Nurse Practitioners continuing education. However, according to Smith et al. (2021), providing continuing education training via a distance-accessible education model for Nurse Practitioners in rural areas without traveling was beneficial. This example exemplifies the need to provide providers with alternative means, such as asynchronous, virtual, or online formats, to promote continuing education and provide the most recent evidence. Nurse Practitioners are busy, and providing an education format such as this project has great potential. Studies on virtual provider learning or continuing education are emerging and warrants dissemination of this project's outcomes and pursuance of further investigation. Organizations should consider using credible, in-house experts to present the most recent EBP guidelines. Providers may be more inclined to participate in educational forums presented by a credible peer or individual that they recognize and are comfortable with. Another future recommendation is to perform a follow-up chart audit to determine if the intent to screen for vitamin D deficiency in depression was performed.

Strengths and Limitations

There were several notable strengths and limitations of this project. The facilitators of the project implementation were very helpful. Barriers were also faced during and contributed to the project journey, although they were learning experiences. The widespread information technology usage has increased the convenience of accessing information and knowledge sharing for medical providers. Providers are subjected to numerous educational methods, especially virtual learning, and are often inundated with too much information. This project demonstrated that a compressed, asynchronous education delivery method was effective.

Many strengths arose during the progression of the project. The education intervention enhanced the provider's intent to screen for vitamin D deficiency in adults with depression. The intervention was short and practical for PCPs and they were able to participate at their convenience. The site mentor was instrumental in facilitating the project and providing guidance throughout the process.

The project site encouraged the success of the project. Many VA facilities are academically affiliated and encourage research promotion. The site mentors and key stakeholders were well prepared to guide the project. The site mentors were also doctoral-prepared nurses. As a result of this, the facilitation of the project was well executed.

The feasibility of the project is considerable. This strength was revealed by the participants' increased percentage of the agreement responses. The use of evolving information technology potentially increases a busy provider's satisfaction by promoting quality of care through enhanced access to and adherence to the latest evidence-based guidelines. Virtual learning such as this project creates a flexible environment that combines structure and freedom.

A few limitations occurred through the progression of this project. The sample size was small; therefore, the findings are not generalizable. The pre-survey was completed by 49 providers (38%), whereas 30 (23%) providers only completed the entire project protocol. A few providers commented that they had technical difficulties listening to the recorded PowerPoint. The providers' responses were solely from Nurse Practitioners. The respondent roles were not diverse enough to draw substantive conclusions about providers overall. No physicians participated in the project, possibly due to higher workloads than their NP colleagues, or perhaps they were less inclined to receive education from an NP. All providers, including NPs, should be

equally supportive of another's professional development. Interdisciplinary education and perspectives on issues that primary care providers commonly confront are important.

Another limitation is that the project was implemented during the holidays from December 2021 to January 2022. Responses were initially limited, as many providers were out of the office. The project was also performed amidst the COVID-19 pandemic. Although this was considered a barrier, it was also a strength due to the nature of the delivery method. The COVID-19 pandemic spring-boarded numerous virtual delivery methods like this project protocol.

Implications for Practice Change

As this project demonstrated, the evidence regarding the evaluation and management of vitamin D deficiency in adults with depression is underutilized. Internal and external evidence suggests a lack of consistency in evaluating and managing vitamin D deficiency in adults with depression. For potential data collection, research studies recommend the usage of depression questionnaires such as BDI and PHQ-9 and measurement of serum 25(OH) levels to evaluate the association between low vitamin D levels and depression. A clinical decision-making tool or protocol for primary care providers to consistently screen for vitamin D deficiency could be helpful. Appropriate use of professional knowledge and skills is a controlled personal activity of a self-system such as Self-Efficacy (Smith & Liehr, 2018). Life as a primary care provider can be demanding and stressful, which requires higher levels of independence, initiative, and self-regulation.

Another fundamental provider implication is the effectiveness of presenting the most recent evidence in a condensed, efficient manner. The convenience, brevity, and timeliness of the education delivery method increased a provider's knowledge of the impact of vitamin D deficiency in depression. The way in which the content was delivered potentially increases a

provider's intent to implement a practice change. This project demonstrates that providers may be more inclined to seek out short yet effective education offerings.

Sustainability

The impact of the project on the provider and patient was studied. The intent was to raise awareness about vitamin D deficiency and depression and craft an intervention to be mindful of a provider's time and busy schedule. The total project intervention time was less than 10 minutes. The short education intervention notably affected the provider's knowledge and the impact of vitamin D deficiency on depression. It increased the likelihood of the provider to screen for vitamin D deficiency in at-risk individuals. The impact on patients is also insightful. The literature evaluation revealed a noteworthy impact of screening and treatment for vitamin D deficiency in depression. Consideration for evaluation and treatment has shown to decrease depression symptoms. Access to timely evidence-based information and guidelines potentially enhances a patient's overall health; and can increase the provider's confidence in applying the most recent evidence to ensure optimal care for their patient.

Numerous hours went into the project's progression, preparing the relatively simple intervention. This project can easily be resumed, extended, and further developed. The use of VA's information technology, such as Microsoft Outlook and Teams, are easy to use and is conducive to future education presentations.

The project intervention is sustainable for several reasons. The data demonstrates effectiveness in provider education via an asynchronous mechanism. The evaluation and treatment of vitamin D deficiency are also cost-effective. The research on vitamin D deficiency is evolving, and the education delivery method is concise and practical. Vitamin D has numerous health implications brought to light with this project's development. Providers responded that

they are more inclined to regularly screen for vitamin D deficiency not only in depression but also in at-risk individuals. A project goal of developing and delivering the most recent evidence-based information and guidelines was proven successful and demonstrated effectiveness in the delivery. The format is usable and sustainable for further use.

Future Recommendations

The project aimed to evaluate the impact of education on the provider's intent to screen for vitamin D deficiency in adults with depression. Other on-line delivery forums should be examined to promote provider self-efficacy. Additional evaluation is also necessary to determine if this form of education delivery actually changed provider practice, versus "intent" to change practice. Future recommendations include consistent vitamin D screening and treatment; and to further explore the education protocol with a larger and more diverse sample size.

Conclusions

The evidence suggests that evaluation and management for vitamin D deficiency conducted primarily in the outpatient or primary care setting can reduce depression symptoms and increase vitamin D levels. The evidence also suggests that screening for vitamin D deficiency in adults with depression is inconsistent. This project's education intervention positively impacts a provider's intent to screen for vitamin D deficiency in adults with depression and consistently during annual visits and "at-risk" individuals such as those with osteoporosis, diabetes, cardiovascular disease, autoimmune disorders, and numerous other health issues. This project demonstrates that providers may be more motivated to pursue brief, efficient education offerings. Therefore providing similar educational formats and delivering the most recent evidence-based guidelines potentially optimizes patient health outcomes and primary care provider satisfaction.

Appendix A
Evaluation Tables

Table 1

Evaluation Table for Quantitative Studies

Citation	Theory/ Conceptual Framework	Design/ Method	Sample/ Setting	Major Variables & Definitions	Measurement/ Instrumentation	Data Analysis (stats used)	Findings/ Results	Level/ Quality of Evidence; Decision for practice/Applica tion to Practice
<p>(Alhamdi et al., 2020) Vit D supplement ameliorates severity of MDD.</p> <p>Country: Saudi Arabia.</p> <p>Funding: Deanship of scientific research (DSR), King Abdulaziz University, Saudi Arabia under Grant.</p> <p>Bias: None stated or noted.</p>	<p>Self-Efficacy Theory</p>	<p>Design: RCT 2 randomized treatment groups.</p> <p>Purpose: Evaluate adding vit D supplement to existing MDD treatment such as SSRI's.</p>	<p>N=1 n=62</p> <p>Demographics: Adults 18-65 yo</p> <p>Inclusion criteria: Dx w/ MDD.</p> <p>Exclusion criteria: Abn PTH levels, renal and hepatic impairment.</p>	<p>IV : Vit D suppl 50,000IU/wk x 3 mo.</p> <p>DV1 : BDI1 depression symptoms.</p> <p>DV2: 25 (OH) & serotonin levels.</p>	<p>DV1: BDI.</p> <p>DV2: serum 25(OH).</p>	<p>T-test, One-way ANOVA, Tukey's multiple comparison test.</p>	<p>DV1: -Females severe depression, improved from 36 ± 0.9 to 27 ± 3.6 ($p < 0.05$) -Males: decrease in their BDI scores after vitamin D supplementation ($p < 0.05$).</p> <p>DV2: levels rose significantly at 3 months in male and female subjects in comparison to the baseline levels</p>	<p>LOE: 1</p> <p>Strengths: RTC.</p> <p>Limitations: Lacks placebo tx. Sample size may be too small. Some pts had disclosed adjunct tx with SSRI's for depression; some already on Vit D supplementation</p> <p>Feasibility: Adds additional</p>

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								support to prior data suggesting a relationship between mood regulation, depressive symptoms, and vitamin D level.
<p>(Alavi et al., 2019) Effect of vit D suppl on depression in elderly pts.</p> <p>Country: Iran</p> <p>Funding: Grant (no. 93160) from Kashan University of Medical Sciences.</p> <p>Bias: None stated or noted.</p>	Self-Efficacy Theory	<p>Design: RCT</p> <p>Purpose: Eval effect of Vit D supplement and placebo of depression in psych clinics.</p>	<p>N=1 n=78</p> <p>Demographics: Adults over 60 yo w/ mod to severe depression.</p> <p>Inclusion criteria: Iranian citizenship, speak Farsi, no hx mental illness except depression, no physical disability and GDS score >5.</p> <p>Exclusion criteria: Uncooperative and refused to cont tx and those with severe stress such as hospitalization or death of relatives.</p>	<p>IV: Vit D suppl 50,000U vit D3 pearl/wk vs placebo x 8 wks vs placebo.</p> <p>DV1: Depression symptoms.</p> <p>DV2: 25(OH) level.</p>	<p>DV1: GDS-15.</p> <p>DV2: Serum 25(OH).</p>	<p>GDS-15 questionnaire, 25(OH) serum levels, Mann-Whitney U Test, Wilcoxon signed rank test, chi-square and multiple regression analysis.</p>	<p>DV1: Scores decreased from 9.25 to 7.48 in vitamin D group (p = 0.0001)</p> <p>DV2: Vit D increased from baseline (22.57 ± 6.2 ng/ml in vitamin D group).</p>	<p>LOE: 1</p> <p>Strengths: RCT, placebo tx included.</p> <p>Weekly Rx of supplements increased compliance.</p> <p>Only 1 pt declined in each group to participate in study, 78 completed trial, 100% adherence in both groups.</p> <p>Vit D and placebo groups has mostly equal sex, age, and severity in depression.</p> <p>No adverse</p>

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								<p>effects reported during trial.</p> <p>Limitations: Some uncontrolled variables such as severity of depression, depression tx, sun exposure, hx of depression, possible cross contamination between groups.</p> <p>Feasibility (relevance): Vit D supplementation can safely improve depression score in adults >60 yo.</p>
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<p>(Briggs et al., 2019)</p> <p>Country: Ireland</p> <p>Funding: None</p> <p>Bias: Self report to define CV and chronic dx cases, may be subject to report bias.</p>	<p>Self-Efficacy Theory</p>	<p>Design: Longitudinal study</p>	<p>N=1 n=400</p> <p>Demographics: ≥ 50 years old</p> <p>Inclusion criteria: Community-dwelling people with depression dx</p> <p>Exclusion criteria: ≤ 50 yo noncommunity dwelling people.</p>	<p>IV : vit D levels</p> <p>DV1 : depression symptoms</p> <p>DV2: vit D levels</p>	<p>DV1: CES-D scale</p>	<p>Logistic regression, t-test with adjusted Wald test.</p>	<p>DV: 95% confidence interval (CI) 15.1–24.7] vs [12.4 (95% CI 11.1–14.0); Z = 3.93; P < .001]</p> <p>Logistic regression models demonstrated that participants with vitamin D deficiency had a significantly higher likelihood of incident depression (odds ratio 1.75, 95% CI 1.24–2.46; t = 3.21; P = .001)</p>	<p>LOE: 1</p> <p>Strengths: Statistical significance of increased risk for vit D deficiency in depressed adults.</p> <p>Limitations: CES-D is valid for older population, but clinical interview is gold standard for depression dx.</p> <p>Feasibility: Supplementation has low risk of toxicity or side effects for older adults, depression has significant adverse effect on functional status later in life.</p>
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<p>(Cuomo et al., 2019) Prevalence, correlation of Vit D deficiency in pts with mental illness</p> <p>Country: Italy</p> <p>Funding: None</p> <p>Bias: None</p>	<p>Self-Efficacy Theory</p>	<p>Design: Retrospective study</p>	<p>N=1 n=290</p> <p>Demographics : Inpatient psychiatric unit adults</p> <p>Inclusion criteria : diagnosis of depression</p> <p>Exclusion criteria : Malnutrition syndromes, malabsorption, metabolic bone diseases, hyperprolactinemia, CRF, dialysis</p>	<p>IV: vit D levels</p> <p>DV: also vit D levels</p>	<p>DV: serum vit D level</p>	<p>Descriptive statistics, logistic regression model</p>	<p>DV: 94% (n = 272) of the 290 study subjects showed vit D levels below the normal range (vit D \geq30 ng/ml). Specifically, 31% met criteria for vit D deficiency (vit D levels <10 ng/ml), and 63% had vit D insufficiency (vit D levels = 10–30 ng/ml)</p>	<p>LOE: 1</p> <p>Strengths: Significant statistical significance</p> <p>Limitations: retrospective design of the study, the evaluation of vit D levels via blood samples collected in different seasons of the year</p> <p>Feasibility: Findings highlight a higher degree of concern for vit D def in mental illness, need for routine screening of vit D, supplement may improve outcomes of depression.</p>
<p>(Gugger et al., 2019)</p> <p>Country: Switzerland</p>	<p>Self-Efficacy Theory</p>	<p>Design: Double blind randomized</p>	<p>N=1 n=200</p> <p>Demographics: adults \geq 70 yrs</p>	<p>IV : D3 suppl/mo</p> <p>DV : depression symptoms</p>	<p>DV: Depression score</p>	<p>GDS, MCS mixed model linear regression</p>	<p>DV: participants achieving the highest 25(OH)D quartile (Q) at 12 months (44.7-98.9</p>	<p>LOE: 1</p> <p>Strengths: Statistically significant. No difference in scores with</p>

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<p>Funding: None</p> <p>Bias: None</p>			<p>Inclusion criteria: Community dwelling adults, MMSE \geq27, hx of falls.</p> <p>Exclusion criteria: Vit D supplementation, insufficient mobility to go to study center.</p>				<p>ng/mL) had the greatest improvements in MCS (Q4 = 0.79 vs Q1 = -2.9; $p = .03$) and MH scales (Q4 = 2.54 vs Q1 = -3.07; $p = .03$)</p>	<p>varied supplement dose, but there was an improvement in depression scores with supplementation</p> <p>Limitations: Lack of true placebo group.</p> <p>Feasibility: Supplementation has low risk of toxicity or side effects for older adults, depression has significant adverse effect on functional status later in life.</p>
<p>(Irandoust & Taheri, 2017) Effect of vit D supplement & indoor vs outdoor physical activity on depression of obese depressed women.</p> <p>Country: Iran</p>	<p>Self-Efficacy Theory</p>	<p>Design: Prospective cohort study using purposeful sampling method.</p> <p>Purpose: 1. Whether vit D can improve depression. 2. Whether</p>	<p>N=1 n=75</p> <p>Demographics: Women, ages 35-50yrs</p> <p>Inclusion criteria: Severely depressed and vit D deficiency,</p>	<p>IV1: 25(OH) suppl. 2000 IU vit D daily x12 wks.</p> <p>IV2: Indoor vs outdoor PA.</p> <p>DV1: 25(OH) level.</p> <p>DV2: depression symptoms.</p>	<p>DV1: Serum 25(OH).</p> <p>DV2: BDI.</p>	<p>BDI score, 25(OH) serum total assay, coefficient alpha rating, One-way ANOVA, Tukey post hoc analysis, independent t-test.</p>	<p>DV1: OPA + VD and IPA + VD groups were no more deficient (respectively, 38.99 and 31.47 ng/mL; $P < 0.05$)</p> <p>DV2: Decreased rate of depression in</p>	<p>LOE: I</p> <p>Strengths: Purposeful sampling method used. NNT adequate.</p> <p>Limitations: Only studied women. Lacks placebo</p>

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<p>Funding: Imam Khomeini International University grant.</p> <p>Bias: None stated or noted.</p>		<p>outdoor PA elicits greater effective benefits that indoor PA.</p>	<p>BMI >40%, scored >30 BDI</p> <p>Exclusion criteria: Physical limitation to exercise, no prior vit D suppl, estrogens, calcium, steroids or other that would inhibit vit D metabolism, significant MSK disease, atherosclerosis, renal and liver function impairment, current psychotherapy or anti-depressant use, participated in exercise during past 6mo.</p>				<p>OPA+VD, IPA+VD, OPA, and IPA groups than the control groups [P = 0.001].</p>	<p>tx.</p> <p>Results might be d/t wt loss or other confounding factors.</p> <p>Smaller sample size, lack of a more controlled environment.</p> <p>Feasibility: Incorporating OPA + vit D suppl is instrumental in any aspect of MH.</p>
<p>(Kaviani et al., 2020)</p> <p>Effects of vit D supplementation on depression & some involved neurotransmitters.</p> <p>Country: Iran</p>	<p>Self-Efficacy Theory</p>	<p>Design: Double blind randomized clinical trial.</p> <p>Purpose: To evaluate the effects of vit D supplementation on depression severity</p>	<p>N=1 n=56 Demographics: 18-60 yo</p> <p>Inclusion criteria: age 18-60 yo, mild to moderate depression.</p>	<p>IV-Vitamin D suppl 50,000IU/2 wks, vs placebo.</p> <p>DV1-BDI depression symptoms.</p> <p>DV2- 25(OH) levels.</p>	<p>DV1: BDI.</p> <p>DV2: serum 25(OH).</p>	<p>Shapiro-Wilks test, Chi-square, paired-sample t-test or Wilcoxon test, independent sample t-test or Mann-Whitney test</p>	<p>DV1: Decreased (-11.75±6.40 vs. -3.61±10.40, P = 0.003).</p> <p>DV2: 25(OH)D concentrations increased (+40.83±28.57 vs. +5.14±23.44 nm</p>	<p>LOE: 1</p> <p>Strengths: RCT.</p> <p>Limitations: Study duration may not reflect long term effects of vit D supplement on depression.</p>

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<p>Funding: National Nutrition and Food Technology Research Institute (NNFTRI).</p> <p>Bias: None stated or noted.</p>			<p>Exclusion criteria: other psychiatric disease., h/o MI, angina, CVA, kidney stones, HTN, liver disease, hyperparathyroidism, pregnancy or lactation, reproductive-aged women not receiving contraception, consumption of supplements with vit D prior to intervention, lack of willingness to continue study and failure to follow</p>				<p>ol/L, $P < 0.001$)</p>	<p>At the beginning of the study, most subjects had optimal levels of serum 25 (OH), potentially hindering true effects of vit D supplementation .</p> <p>Difference in dosing and types of vitamin D supplement, duration, method, age of target group and additional simultaneous interventions.</p> <p>Feasibility: Great need for further clinical trials with longer durations on depressive patients with vit D deficiency to determine exact effects and follow up</p>
<p>(Krysiak et al., 2018) Effect of vit D supplementation on sexual functioning &</p>	<p>Self-Efficacy Theory</p>	<p>Design: RCT</p> <p>Purpose: Assess if vit D suppl affects sexual</p>	<p>N=1 n=47</p> <p>Demographics: Women 20-40yo</p>	<p>IV: vit D suppl</p> <p>Deficiency: 4000IU daily x6 mo.</p>	<p>DV1: FSFI.</p> <p>DV2: BDI.</p>	<p>FSFI score, BDI score, Kolmogorov-Smirnov test, analysis of covariance,</p>	<p>DV1: Decreased to 14% in vit D treated pts.</p> <p>DV2: Down to 9.1 from 13.4 in</p>	<p>LOE: 2</p> <p>Strengths: RCT. Different doses for insufficiency vs</p>

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<p>depressive sx in young women with low vit D status.</p> <p>Country: Poland.</p> <p>Funding: None</p> <p>Bias: None stated or noted.</p>		<p>functioning and depressive sx.</p>	<p>Inclusion criteria: vit D insufficiency or deficiency.</p> <p>Insufficiency: 25(OH) <20ng/ml</p> <p>Deficiency: 25(OH) 20-30ng/ml</p> <p>Exclusion criteria: Any acute/chronic do, sexual inactivity, pregnant or lactating, hx of urogynaecologic al operation that might affect sexual function, any pharmacotherapy, poor patient compliance.</p>	<p>Insufficiency: 2000IU daily x6mo.</p> <p>DV1: 25(OH) levels</p> <p>DV2: Female sexual function (FSFI) symptoms.</p> <p>DV3: BDI depressive symptoms.</p>		<p>Bonferroni post-hoc tests, paired t-test, Pearson’s correlation coefficient.</p>	<p>vit D tx w/ deficiency. P<0.05. - Down to 8.1 from 10.2 in vit D tx with insufficiency. P<0.05.</p>	<p>deficiency. Length of trial (6mo).</p> <p>Limitations: Lack of placebo group. Small # participants. Self-report inventories like FSFI and BDI scales. Seasonal variations can affect 25(OH) concentrations. Effect of vit D suppl may be different in women suffering from other disorders or taking other Rx.</p> <p>Feasibility: Effect on vit D suppl is positive on women with sexual dysfunction and low vit D levels, however, not enough info based on this study thus far.</p>
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<p>(Vaziri et al., 2016) Vit D supplementation on perinatal depression in Iranian pregnant mothers.</p> <p>Country: Iran</p> <p>Funding: Research Vice-chancellor of Shiraz University of Medical Sciences. Bias: Note stated or noted.</p>	<p>Self-Efficacy Theory</p>	<p>Design: RCT, single blind study.</p> <p>Purpose: Study relationship between low vit D and perinatal depression.</p>	<p>N=1 n=169</p> <p>Demographics: >18 yo women, mean age 26, max age 39.</p> <p>Inclusion criteria: No hx of mental illness & internal dx, have a single live fetus, no pregnancy complications, gestational age 26-28 wks, depression score 0-13.</p> <p>Exclusion criteria: EPDS baseline >13, not providing blood sample at start of study, <8wks vit D suppl.</p>	<p>IV: Vit D suppl. 2000IU D3 daily.</p> <p>DV1: 25(OH) levels.</p> <p>DV2: depression symptoms.</p>	<p>DV1: Serum 25(OH).</p> <p>DV2: EPDS.</p>	<p>EPDS, Chemiluminescence immunoassay (CLIA) to eval vit D level, stratified random sampling, block randomization strategy, Pearson's correlation coefficient; Fisher's exact test, Kolmogorov-Smirnov test, t-test and paired t-test parametric tests, Mann-Whitney U test.</p>	<p>DV1: -Nulliparous 18.40 at delivery [13.13 at baseline] $p=0.01$. -Multiparous 16.58 [12.49 at baseline] $p=0.02$.</p> <p>DV2: Lower in the vitamin D group than the control one at 38-40 weeks of gestation ($p=0.01$) also, at 4 and 8 weeks after birth ($p>0.001$).</p>	<p>LOE: 1</p> <p>Strengths: RCT, 1st study to eval vit D suppl consumption during antenatal and postnatal depressive dx.</p> <p>Limitations: Participant's honesty. Selected from 1 prenatal clinic. Population may be too small. Statistical authority to ID differences in depressive sx vs dx MDD.</p> <p>Feasibility: Vit D deficiency & depression higher prevalence in pregnant women. Vit D suppl is imperative in tx more than just depression in this population, esp in decreasing risk</p>
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Key: **Abn**-abnormal; **add'l**-additional; **ANOVA**-analysis of variance; **BDI**-Beck Depression Inventory; **BPAD**-Bipolar affective disorder; **Ca**-calcium; **CBC**-complete blood count; **CES-D**-Center for Epidemiologic Studies Depression; **Cont**-continue; CRF-chronic renal failure; CRP-C-reactive protein; **DSM-IV**- Diagnostic and Statistical Manual of Mental Disorders; **d/t**-due to; **DV**-dependent variable; **Dx**-diagnosis; **EPDS**-Edinburgh Postnatal Depression Scale; **Eval**-evaluate; **FSFL**-female sexual function levels; **GDS**-Geriatric Depression Scale; **HAM-D17**-Hamilton D-17 depression score; **Hx**-history; **ID**-identify; **IPA**-indoor physical activity; **IV**-independent variable; **LFT**-liver function test; **LOE**-level of evidence; **MCS**-Mental Component Summary; **MDD**-major depressive disorder; **MH**-mental health; **MMSE**-Mini-Mental State Exam; **mo**-month; **MSK**-musculoskeletal; **N**-number of studies; **n**-number of participants; **NNT**-number needed to treat; **OA**-osteoarthritis; **OPA**-outdoor physical activity; **PHQ-9**-Patient Health Questionnaire; **PTH**-parathyroid hormone; **Pts**-patients; **Psych**-Psychiatric; **P**-value probability; **RCT**-randomized control trial; **Rx**-prescription; **S/E**-side effects; **SOC**-standard of care; **SSRI**-Selective serotonin reuptake inhibitor; **suppl**-supplement; **sx**-symptoms; **TB**-Tuberculosis; **TSH**-thyroid stimulating hormone; **Tx**-therapy; **IU**-international units; **Vit D**-Vitamin D; **Wk**-week; **wt**-weight; **25(OH)**-Vitamin D; **YO**-year old; **yr**-year.

								of rickets in the fetus.
<p>(Zheng et al., 2019) Effects of vit D supplementation on depressive sx in pts w/ knee oa.</p> <p>Country: Australia</p> <p>Funding: Australian National Health and Medical Research Council Grant.</p> <p>Bias: Potential selection bias, baseline PHQ-9 was higher in group maintaining vit D sufficiency.</p>	<p>Multilevel mixed-effect model</p>	<p>Design: RCT double blind study.</p> <p>Purpose: Determine effect of vit D suppl and maintaining sufficient vit D levels on depressive sx in pts w/ OA and vit D deficiency.</p>	<p>N=1 n=340</p> <p>Demographics: Mean age 63 yo</p> <p>Inclusion criteria: PHQ-9 score >5</p> <p>Exclusion criteria: Taking vit D suppl, exclusionary comorbidities, surgery scheduled, withdrew consent, severe radiographic OA, ineligible pain, declined participation, physically unwell, contraindication to MRI, ineligible age.</p>	<p>IV : vit D suppl 50,000IU/mo x24 mo</p> <p>DV1 : 25(OH) concentration.</p> <p>DV2 : depression symptoms.</p>	<p>DV1: Serum 25(OH).</p> <p>DV2: PHQ-9.</p>	<p>25(OH) concentration, PHQ-9 scores, independent t-test, chi-square</p>	<p>DV1: Increased from 43.7 ± 11.8 nmo l/L to 84.5 ± 17.3 nmo l/L in the vitamin D group.</p> <p>DV2: Improved more in the vitamin D supplementation group compared to the placebo group [β: -0.66, 95% confidence interval (CI): -1.22 to -0.11].</p>	<p>LOE: 1</p> <p>Strengths: Double blind RCT, length of trial 24 mo, large sample size.</p> <p>Limitations: This was a secondary analysis of an RCT. Adjustments needed for confounders including use of anti-depressants.</p> <p>Feasibility: In adults w/ OA, maintaining vit D sufficiency with suppl may be beneficial.</p>

Key: **Abn**-abnormal; **add'l**-additional; **ANOVA**-analysis of variance; **BDI**-Beck Depression Inventory; **BPAD**-Bipolar affective disorder; **Ca**-calcium; **CBC**-complete blood count; **CES-D**-Center for Epidemiologic Studies Depression; **Cont**-continue; CRF-chronic renal failure; CRP-C-reactive protein; **DSM-IV**- Diagnostic and Statistical Manual of Mental Disorders; **d/t**-due to; **DV**-dependent variable; **Dx**-diagnosis; **EPDS**-Edinburgh Postnatal Depression Scale; **Eval**-evaluate; **FSFL**-female sexual function levels; **GDS**-Geriatric Depression Scale; **HAM-D17**-Hamilton D-17 depression score; **Hx**-history; **ID**-identify; **IPA**-indoor physical activity; **IV**-independent variable; **LFT**-liver function test; **LOE**-level of evidence; **MCS**-Mental Component Summary; **MDD**-major depressive disorder; **MH**-mental health; **MMSE**-Mini-Mental State Exam; **mo**-month; **MSK**-musculoskeletal; **N**-number of studies; **n**-number of participants; **NNT**-number needed to treat; **OA**-osteoarthritis; **OPA**-outdoor physical activity; **PHQ-9**-Patient Health Questionnaire; **PTH**-parathyroid hormone; **Pts**-patients; **Psych**-Psychiatric; **P**-value probability; **RCT**-randomized control trial; **Rx**-prescription; **S/E**-side effects; **SOC**-standard of care; **SSRI**-Selective serotonin reuptake inhibitor; **suppl**-supplement; **sx**-symptoms; **TB**-Tuberculosis; **TSH**-thyroid stimulating hormone; **Tx**-therapy; **IU**-international units; **Vit D**-Vitamin D; **Wk**-week; **wt**-weight; **25(OH)**-Vitamin D; **YO**-year old; **yr**-year.

Appendix B
Synthesis Table

Table 2
Synthesis Table for Quantitative Studies

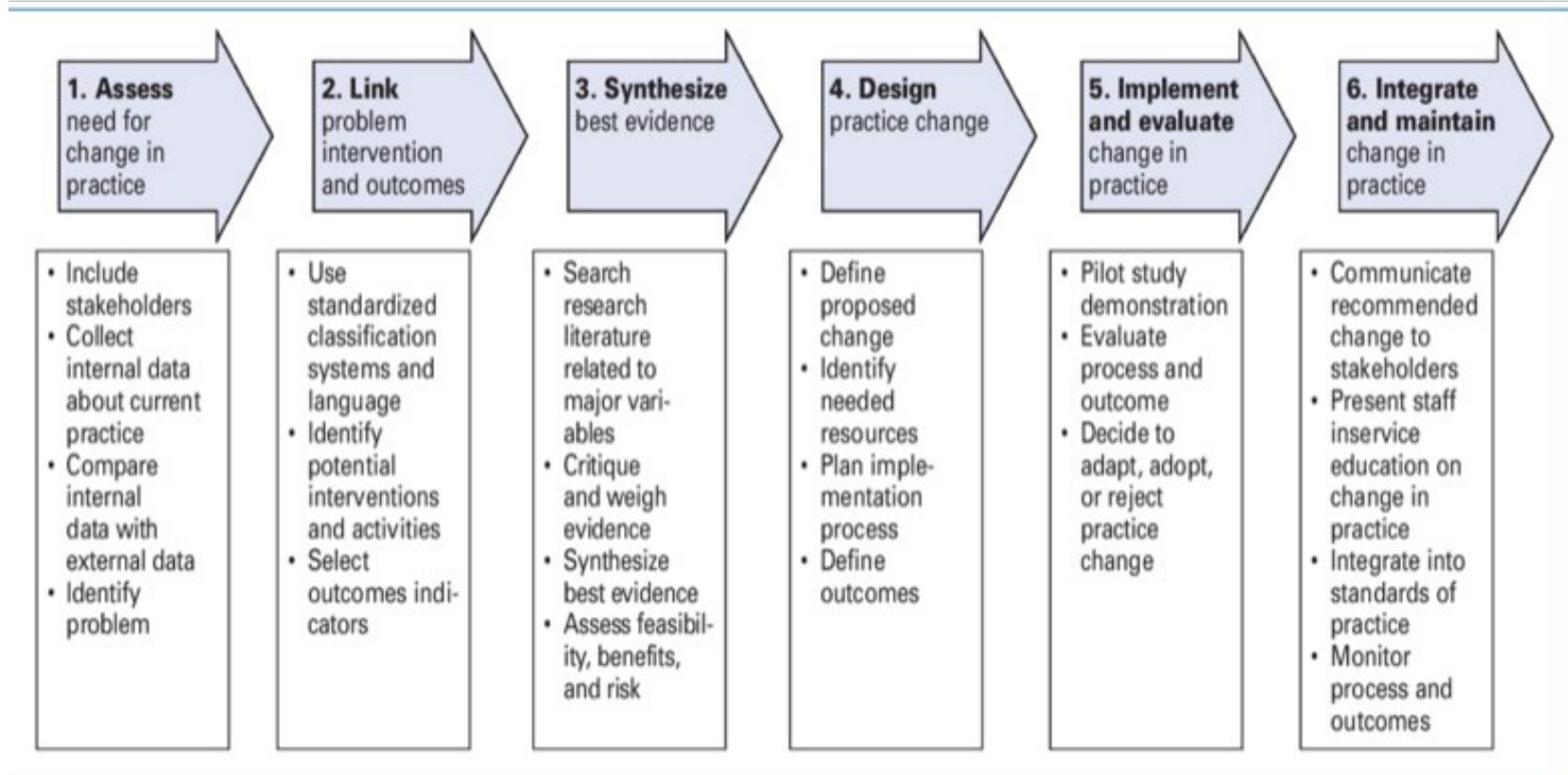
Author	Alghamdi	Alavi	Briggs	Cuomo	Gugger	Irاندوست	Kaviani	Krysiak	Vaziri	Zheng
Year	2020	2019	2019	2019	2019	2017	2020	2018	2016	2019
Design	RCT	RCT	Longitudinal study	Retrospective study	RCT	Cohort	RCT	RCT	RCT	RCT
Country	Saudi Arabia	Iran	Ireland	Italy	Switzerland	Iran	Iran	Poland	Iran	Australia
Number of subjects	62	78	400	290	200	75	56	47	169	340
Demographics	Adults 18-65 yo	Adults over 60 yo	Adults ≥ 50yo	Inpt psych adults	adults ≥ 70 yrs	Women 35-50 yo	Adults 18-60 yo	Women 20-40 yo	Women 18-39 yo	Adults mean age 63 yo
Length of study	3 mo.	2 mo	12 mo	3 yrs	12 mo	3 mo.	2 mo.	6 mo.	3 mo.	24 mo.
Independent variables										
Vit D supplementation	50,000IU/wk	50,000IU/wk	No	No	Yes	2000IU/day	50,000IU/2 wks	2000IU-4000IU/day	2000IU/day	50,000IU/mo
Placebo	No	Yes	No	No	Yes	No	Yes	No	Yes	Yes
Dependent variables										
Depression scale	BDI	GDS-15	CES-D	NA, dx of depression	GDS, MCS	BDI	BDI	BDI, FSFI	EPDS	PHQ-9
25(OH) serum level	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Results										
Reduced depression scores	Yes	Yes	No, high scores	No, dx of depression	Yes	Yes	Yes	Yes	Yes	Yes
Increased 25(OH) levels	Yes	Yes	No, low vit D levels.	No, low vit D levels.	Yes	No	Yes	NA	Yes	Yes

Key: **BDI**-Beck Depression Inventory; **Ca**-calcium; **EPDS**-Edinburgh Postnatal Depression Scale; **FSFI**-Female Sexual Function Index; **GDS**-Geriatric Depression Scale; **HAM-D17**-Hamilton D-17 depression score; **IU**-international units; **mo**-month; **NA**-not available; **PHQ-9**-Patient Health Questionnaire; **RCT**-randomized control trial; **vit D**-vitamin D; **wk**-week; **yo**-year old.

Appendix C

Implementation Framework Diagram

Rosswurm & Larrabee Model

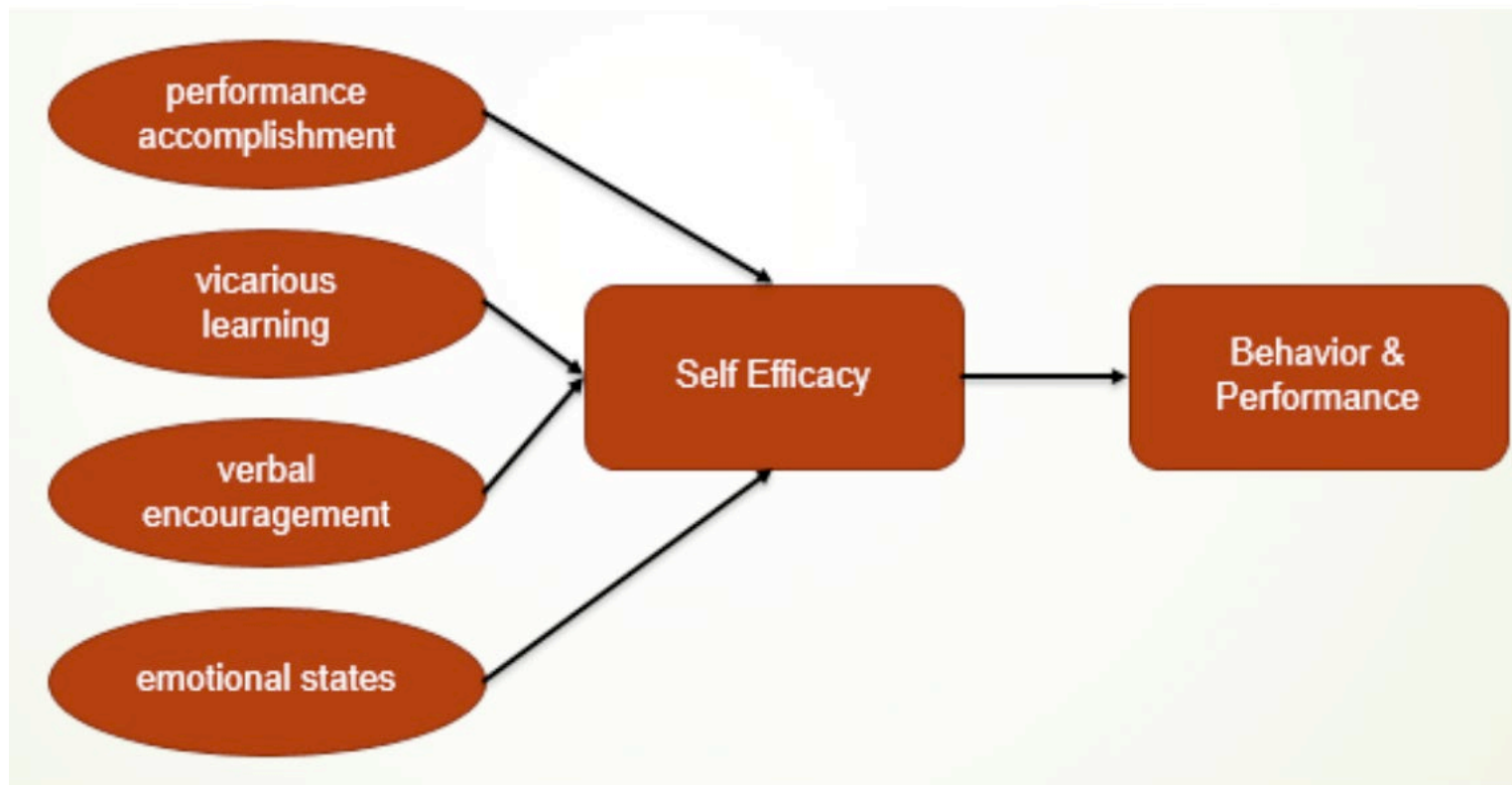


(Rosswurm & Larrabee, 1999)

Appendix D

Theoretical Framework Diagram

Bandura's Self-Efficacy Theoretical Model



(Smith & Liehr, 2018)

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