Improving Vitamin B-12 Screening Rates in Adults with Type 2 Diabetes Mellitus in a Rural Primary Care Setting

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Abstract

Diabetes is a global epidemic affecting approximately 463 million adults aged 20-79 years. The prevalence of diabetes in the United States (US) has risen to more than 34 million with 90-95% of these individuals having type 2 diabetes mellitus (T2DM). Metformin is a common intervention regimen for patients with T2DM. However, several research studies have associated its long-term use with vitamin B-12 deficiency yet monitoring for the deficiency remains low. The purpose of this quality improvement project was to attempt to determine if the use of a vitamin B-12 deficiency screening protocol, following the National Health Service guidelines, will help minimize the number of patients with the deficiency.

The theoretical framework of this project was based on Lewin's Framework for Change Management Theory in order to create and implement the screening protocol as well as an educational intervention for providers. Pre- and post-implementation tests will identify if the providers have learned new and vital information to help better diagnose and treat vitamin B-12 deficiency patients on long-term metformin therapy. Consequently, the post-test scores increased after the educational session with the providers indicating an increase in knowledge on vitamin B-12. In addition, after implementation of the protocol by the providers at the practice site, the compliance and the number of patients screened increased. The outcome suggests that implementation of the intervention was successful in achieving short-term improvements and optimism for sustainable long-term change for screening vitamin B-12 deficiency in T2DM patients at the project site and other community-based primary care facilities.

Keywords: T2DM, Vitamin B-12, Screening, Primary Care, Quality Improvement, Knowledge, Educational Session, Protocol.

Improving Vitamin B-12 Screening Rates in Adults with Type 2 Diabetes Mellitus in a Rural Primary Care Setting

The prevalence of diabetes in the United States (US) has risen to more than 34 million (about 1 in 10) and it is approximated that 90-95% of them have type 2 diabetes mellitus (Centers for Disease Control and Prevention, 2020). Metformin has been the initial preferred pharmaceutical intervention for patients with type 2 diabetes mellitus (T2DM) (Herbert et al., 2019). A well-establish body of literature has linked the use of metformin to vitamin B-12 deficiency, yet monitoring for the deficiency remains low (Longo et al., 2019). Vitamin B-12 deficiency associated with long-term use of metformin in patients with T2DM can increase the risk of developing multiple health conditions such as anemia and peripheral neuropathy (Aroda et al., 2016). Most primary care clinics do not have protocols in place for the routine screening or monitoring of vitamin B12 levels in the T2DM population. In 2017, the Standards of Medical Care in Diabetes from the American Diabetes Association made recommendations to periodically assess vitamin B-12 status in patients that are currently using metformin (Pawlak, 2017). This Doctorate of Nursing Practice (DNP) project will use a collaborative approach to improve patient health outcomes and contribute positively to primary care clinic by translating research into clinical practice. The goal of this DNP project is to implement a protocol to address the lack of screening for T2DM at risk for developing metformin related Vitamin B-12 deficiency. Through leadership, scholarship and research, this DNP project will identify the gaps in knowledge by developing and shaping healthcare protocols within the project site to improve the quality of care and improve patient healthcare outcomes of this underserved population.

Background

The incidence of T2DM is not only a problem in the US, the prevalence is growing worldwide (Centers for Disease Control and Prevention [CDC], 2020; Society for Endocrinology, 2018). Globally, there are approximately 463 million adults ages 20-79 living with all types of diabetes and it is estimated that those numbers will rise to 700 million by 2045. The estimated health expenditures in 2019 were around 760 billion dollars, which is about 10% of total spending in adults (International Diabetes Federation, [IDF] 2019). In the US the staggering healthcare cost of diabetes have increased to approximately 327 billion dollars. In the United States, California has the largest population with T2DM with a cost $39.47 billion in healthcare related expenditures (American Diabetes Association [ADA], 2018). Metformin is the most widely used oral antihyperglycemic agent and it is the first line therapy for all newly diagnosed patients with T2DM as recommended by American Diabetes Association (ADA) (Foretz et al., 2014). The long time use of metformin has been established; since the 1950's, metformin has successfully been used to treat patients with T2DM (Holman, 2007). At present, healthcare providers use metformin monotherapy as their usual first-line treatment, not only because of its efficacy but also because of the low cost associated with its use. The project site serves low income and cash paying agricultural farmworkers in the area. Two recent studies by Herbert et al., (2019) and Longo et al., (2019) quantified evidence that supports the link between the use of metformin and vitamin B12 deficiency. Although the pathophysiology between metformin and vitamin b-12 deficiency is not fully understood, postulated theories do exist (Thaker et al., 2019). One theory by Thaker et al., (2019) postulates the possible modification in the small bowel motility, which can stimulate bacterial overgrowth and subsequently can lead to vitamin B12 deficiency. Another theory set forth by Thaker et al., (2019) involves the competitive inactivation or inhibition of absorption of vitamin B12 in the gastrointestinal (GI) system. An alternative theory suggests that changes in intrinsic factor (IF) levels and the interface with the cubulin endocytic receptor; and the inhibition of the calcium dependent absorption of the vitamin B12-IF complex at the terminal ileum of the GI system (Thaker et al., 2019). Samadanifard et al., (2019) discussed clinical problems associated with vitamin B12 deficiency, they included but are not limited to anemia, gastrointestinal disorders such as diarrhea, constipation, decreased appetite; neurological disorders such as tingle, numbness, muscle weakness; and mental disorders such as memory impairment, depression, behavioral problems. Recently, the Society for Endocrinology (2018) suggested that routine screening of vitamin B12 levels may prevent irreversible nerve damage seen in T2DM taking metformin.

Problem Statement

Longo et al., (2019) has objectively stated that many studies in the past have linked the use of metformin to vitamin B12 deficiency, yet monitoring for the deficiency remains low. If levels go undetected or untreated, vitamin B12 deficiency can lead to major health problems (Samadanifard et al., 2019; Society for Endocrinology, 2018). Timely detection through screening and prompt intervention can minimize vitamin B12 deficiency sequela and inversely can help increase patient health outcomes (Strong et al., 2016). Currently, the project site does not follow vitamin B12 screening recommendations for type 2 diabetics that are on metformin. The DNP project will seek to implement an evidence based protocol to the project site to increase vitamin B12 screenings.

Purpose Statement

The purpose of this DNP project is to create an evidence based protocol that screens for vitamin B12 deficiency in T2DM patients that are actively taking metformin with the aim to increase identification of vitamin B12 deficiency and/or insufficiency for potential intervention and treatment. The DNP project will work closely with project site to educate staff and implement a vitamin B12 screening protocol for T2DM on metformin. The DNP project goal is for early detection and prompt intervention of low levels of vitamin B12 levels to decrease the potential health risks and improve patient healthcare outcomes.

Project Question

Will implementation of a vitamin B12 screening protocol at the project site increase the rate of screening in patients with type 2 diabetes currently being treated with metformin?

Population: Clinic staff, Primary care providers

Intervention: Implementation of a vitamin B12 screening protocol for T2DM patients on metformin

Comparison: Screening rates will be assessed pre and post protocol implementation

Outcome: Increase clinic staff and primary care provider knowledge about vitamin B12 deficiency and increased identification of diabetic patients with vitamin B12 deficiency for potential intervention

Time: By the completion of this project

Project Objectives

The objectives for this DNP project will include:

1) Develop evidence based educational training on vitamin B12 screening protocol
2) Present the developed evidence based educational training to the clinical staff and providers
3) Implement vitamin B12 screening protocol at the project site

4) Evaluate the impact of the implementation of vitamin B12 screening protocol pre and post implementation through chart review

5) Increased vitamin B12 screening rates of T2DM patients on metformin

Significance

A well-established body of literature has linked the use of metformin to vitamin B-12 deficiency, several studies estimated the prevalence range from 5.8% to 52%. (Jajah et al., 2020; Longo et al., 2019). A systematic review and meta-analysis by Chapman et al. (2016) established a relationship between the use of metformin and vitamin B12 deficiency in patients with T2DM. The systematic review comprised of observational 17 studies, of which 10 reported a statistically significant lower levels of vitamin B12 in patients when compared to those treated with metformin. Additionally, the review of four meta-analyses trials demonstrated an overall reducing effect of vitamin B12, which was statistically significant. The systematic review concluded that there was sufficient evidence to demonstrate the association between the use of metformin and lower levels of vitamin B12 and therefore, suggested careful monitoring of vitamin B12 levels in patients deemed at risk.

Jajah et al. (2020) also conducted a cross-sectional observational study of 347 T2DM patients who received metformin antiglycemic therapy for at least 6 months and found Vitamin B12 deficiency in 10.4% of the patients. Borderline levels were found in 20.2% and the remaining 69.5% had normal levels of vitamin B12, however, there was no significant difference between the age groups. Jajal et al. (2020) concluded that a statistically significant relationship exists between metformin use and vitamin B12 deficiency and suggested that vitamin B supplementation should be prescribed for diabetic patients taking metformin to prevent the occurrence of Vitamin B12 deficiency complications. Another cross-sectional study by Ahmed et al. (2016) measured vitamin B12 levels and assessed peripheral neuropathy in T2DM patients using the Neuropathy Total Symptom Score-6 (NTSS-6) questionnaire. The authors found a significant proportion (28.1%) of the participants had Vitamin B12 deficiency, though no difference in the presence of neuropathy between participants with normal vitamin B12 levels and deficient levels. These findings are essential as metformin use has been proven to play a role in vitamin B12 deficiency therefore, careful consideration must be taken before prescribing T2DM patients metformin if no other suitable alternative is available. In this instance, vitamin B12 supplementation must be provided to prevent long-term complications in this group of patients.

Review Coverage and Justification

An extensive review of the most recent peer-reviewed articles was conducted on vitamin B12 deficiency in patients with type 2 diabetics currently treated with metformin. Several databases, such as EBSCO host/CINAHL plus, Cochrane, ProQuest, Medline, Ovid, and Google scholar, were cursory searched for relevant terms and studies. Inclusion criteria for this project were full text, peer-reviewed articles in scholarly journals dated 2012 to the present. Studies considered for review included either documents, case studies or evidence-based diabetes-related articles that involved humans. Studies excluded from this review included blogs, newspapers, or those not published in English.

Implementation of the Boolean search aided in producing a more accurate and relevant review. Search terms included: vitamin B12 deficiency, cobalamin deficiency, non-insulin-dependent diabetes, type 2 diabetes, metformin, hypoglycemic agents and American Diabetes Association. The results from EBSCO host returned 479 articles from 2010-2015, 215 from 2015-2015, 21 Full text, and 19 Peer Reviewed. Adding the keyword “AND type 2 diabetes” narrowed down the search further. A brief cursory search of Google Scholar also using the same keywords "vitamin B12 deficiency and metformin and type 2 diabetes" resulted in 4,510 hits from 2016-2020. A final search attempt was made by adding the keyword to the end of the string "American Diabetes Association" that resulted in only one article.

Additionally, searches on different meaning variations on key terms were also conducted. For example, the searches on "Cobalamin deficiency and metformin and type 2 diabetes", "Vitamin B12 deficiency and metformin and NON-insulin-dependent diabetes" and "Vitamin B12 deficiency and HYPOGLYCEMIC agents and type 2 diabetes" resulted in 12, 11 and 8 peer-reviewed full text articles respectively. Google Scholar as a cursory search tool is very useful if guided by evidence-based scholarly research methods prudently vetting your sources.

Review of Literature

The rate in which T2DM has been diagnosed over the past few decades has increased significantly. Globally, there are approximately 463 million adults aged 20-79 living with all types of diabetes, of which 90% are T2DM cases. It is estimated that those numbers will rise to 700 million by 2045. This means the appropriate medication needs to be accessible to patients resulting is a burden on the healthcare system. Metformin therapy is the first form treated given to patients with T2DM. Though metformin works well in managing the blood sugar levels of these individuals, it is now known that long-tern use may result in vitamin B12 deficiency. The literature review has revealed trended data that the only significant contributing factor was the total number of years of metformin exposure between the metformin and placebo treatment groups in a multivariate model (Aroda et al., 2016).

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One such complication is peripheral neuropathy (PN), which is clinically indistinguishable from diabetic PN (DPN) and could worsen in diabetic patients. If vitamin B12 deficiency leads to peripheral neuropathy and is mistaken for peripheral neuropathy, permanent neurological damage may occur (Yakubu et al., 2019). Diabetic neuropathy affects 44% of older diabetic patients (Jayabalan & Low, 2016). There are several published reports on this subject with conflicting results. A cross-sectional study by Ahmed et al. (2016) measured vitamin B12 levels and assessed peripheral neuropathy in T2DM patients using the Neuropathy Total Symptom Score-6 (NTSS-6) questionnaire. The authors found a significant proportion (28.1%) of the participants had vitamin B12 deficiency, though no difference in the presence of neuropathy between participants with normal vitamin B12 levels and deficient levels. A second publication by Roy et al., (2016) found that 54.28% of the metformin-treated patients had neuropathy compared to 35% and 28.57% in the metformin with other oral hypoglycemic agent treatment and patients not on metformin respectively. These findings are essential as metformin use has been proven to play a role in vitamin B12 deficiency therefore, careful consideration must be taken before prescribing T2DM patients metformin if no other suitable alternative is available. In this instance, vitamin B12 supplementation must be provided to prevent long-term complications in this group of patients.

Although it is well-documented that metformin use is associated with vitamin B12 deficiency, no mandatory screening protocols exist. Develia et al., 2014 reported that no definite advice can be given on the frequency of vitamin B12 level monitoring, but it is recommended that serum cobalamin is checked when deficiency is suspected. Recently, there have been recommendations advocating for screening standardization (Harvard Pilgrim Health Care, 2019; Langan & Goodbred, 2017; Thaker et al., 2019). This is particularly important as it is estimated that the cost of burden of untreated vitamin B12 deficiency over 15 years is $37.8M compared to $9M for the cost of routine testing the same number of patients over the same time period (Thaker et al., 2019). Furthermore, screening will hopefully reduce complications and diabetes-related deaths. Within this DNP project, a proposal will be created from peer-reviewed literature and identified data from best evidence practice for routine vitamin B12 deficiency screening and educating clinical healthcare providers. In addition, there will be issues identified that have not been addressed, issues that are still being investigated, and controversial topics that are being identified for future findings and studies.

Impact of the problem

Despite the overwhelming evidence associating metformin use to low levels of vitamin B12, and the potential clinical complications, assessment of vitamin B12 levels in individuals being treated with metformin has not been integrated into clinical practice procedures. Evidence suggests that such monitoring is rarely performed, and this may be partly to do with the lack of knowledge of the current recommendations among physicians (Pierce et al., 2012).

Alshammari et al., (2019) conducted a cross-sectional study at diabetic clinics in four different hospitals in Saudi Arabia. The goal of the study was to assess the clinic’s vitamin B12 screening data and their physician's knowledge of the current American Diabetes Association (ADA) recommendations on vitamin B12 levels for patients with type 2 diabetes. Their study included 363 patient population and a total of 100 physicians. After analysis, it was found that only 4.4% of the patients had a vitamin B12 serum level available in their medical records. In the physician survey, 44.0% reported knowledge of the current ADA recommendations, 39.0% were unaware of the current ADA recommendation, while 17.0% had no idea about the ADA recommendations revealing that a significant number of physicians were unaware of the current ADA recommendations on vitamin B12 screening. Therefore, raising the awareness for providers to get involved and stay up-to-date with the current literature and recommendations regarding routine monitoring of vitamin B12 levels in diabetic patients taking metformin to optimize diabetic management and minimize complications.

Some older patients may ignore mild symptoms of vitamin B12 deficiency mistaking them to be a part of growing older and others may simply not think the issue is significant enough to address them with their primary physician. Given that the diagnosis is often made opportunistically, it seems likely that there a number of undiagnosed cases who are at risk of developing complications, some of which are potentially irreversible. Furthermore, effective clinician screening and assessments are not common enough and there is no standardized protocol for when to screen patients (Thaker et al. 2019). Assessments and screenings are an important part of disease management. Without a well-defined and structured approach to assessments and screenings, the outcome can be ineffective for patients.

Addressing the Problem with Current Evidence

The Agency for Healthcare Research and Quality along with the Medical Services Commission of British Columbia recommended that providers consider screening patients for vitamin B12 deficiency with a medication history of long-term use of histamine (H2) receptor antagonists, proton pump inhibitors of at least 12 months or on metformin for at least 4 months (Medical Services Commission of British Columbia, 2012; Thaker et al., 2012; Yakubu et al., 2019). Harvard Pilgrim Health Care (HPHC), a subsidiary of Harvard Medical School, has a current medical policy for vitamin B12 screening and testing. HPHC considers testing and screening to be medically necessary in members who are considered to be at high-risk based on certain medical conditions or who are currently clinically symptomatic. However, they consider routine testing of healthy asymptomatic adults unnecessary. According to HPHC's current medical policy, diabetes mellitus patients with neuropathy, amyotrophy, neurologic complication, or prolonged metformin use meet the criteria for vitamin B12 screening and testing (Harvard Pilgrim Health Care, 2019).

Prevention

As a first course of action, patients should endeavor to add foods naturally rich in vitamin

B12 as part of their diet. The Institute of Medicine (IOM), Food Nutrition Board (FNB) recommends that people aged 50 and over should consume a dose of 2.4 μg of synthetic vitamin B12 daily from vitamin supplements or from food fortified with vitamin B12 Kancherla et al., (2016). Strohle et al., (2019) noted that the regular consumption of vitamin B12 rich foods such as dairy products and lean meats, fish, and poultry are generally recommended to ensure sufficient vitamin B12 supply in the body. It is advantageous for patients to get most, if not all, of their dietary requirements from fresh food as it is estimated that about 50% of vitamin B12 levels can be lost during the food processing of cooking or pasteurization.

In diabetic patients where adequate vitamin B12 levels are not being acquired from their diet, Jajah et al. (2020) suggested that vitamin B supplementation should be prescribed for these patients taking metformin to prevent the occurrence of vitamin B12 deficiency complications. While testing for vitamin B12 deficiency in the T2DM patient population is beneficial, the main idea to consider is not simply measuring for deficiency, but measuring the levels of functional vitamin B12 since not all individuals with a biochemical vitamin B12 level will go on to develop clinical signs of deficiency. In a total vitamin B12 test, not all cobalamin is functional, and the functional levels vary between individuals. This means that some people may have low vitamin B12 levels, but high levels of functional vitamin B12 resulting in a reduced likelihood of developing potentially irreversible conditions. On the other hand, some people may have normal vitamin B12 levels, but low functional levels and are more at risk of developing downstream complications (Hannibal et al., 2016). Furthermore, as a secondary prevention, screening for serum methylmalonic acid (MMA) or homocysteine concentrations may be a more sensitive approach in T2DM patients with borderline vitamin B12 levels of 200-400 pg/mL whereby the normal range for MMA and homocysteine are <0.28 mol/L and 5-15 mol/L respectively (Kibirige

& Mwebaze, 2013). When these methods are used effectively, they have a great potential of reducing the number of patients developing vitamin B12 deficiency.

As aforementioned, the older patient population may delay discussing vitamin B12 deficiency symptoms with the healthcare provider. As such, the concomitant use of multivitamins with metformin is likely to prevent patients taking metformin on a long-term basis from developing vitamin B12 deficiency with a significance of $P<0.01$ as reported by Kancherla et al., (2016). Multivitamin use is inexpensive and effective in increasing serum B12 concentrations an should be encouraged in this patient population.

Current management

Currently, the project site has no standardized protocol for vitamin B12 screening in T2DM patients on metformin. Only patients that present symptomatically are routinely checked for vitamin B12 deficiency. If vitamin B12 deficiency is found or is sufficiently suspected, administration of Cyanocobalamin 1000mcg sublingually or intramuscularly once per month is given to patients in the physician's office and serum levels are monitored until corrected. Creation of a standardized clinic protocol that follows current recommendations would help the clinic more efficiently and effectively manage their patients at risk T2DM of vitamin B12 deficiency.

Current recommendations

Currently, neither the U.S. Preventive Services Task Force nor any other major U.S. medical organization has published clinical practice guidelines for routine and screening of vitamin B12 deficiency. However, in 2017, the ADA and the American Family of Physicians (AFP) made recommendations for vitamin B deficiency screening and management (Harvard Pilgrim Health Care, 2019; Langan & Goodbred, 2017; Thaker et al., 2019). The Medical Services Commission of British Columbia established a guideline in 2012, Cobalamin (vitamin

B12) deficiency investigation and management (Thaker et al. 2019). Harvard Pilgrim Health Care (HPHC), a subsidiary of Harvard Medical School, has a current medical policy for vitamin B12 screening and testing. HPHC considers testing and screening to be medically necessary in members who are considered to be at high-risk due to certain medical conditions or who are currently clinically symptomatic. However, they consider routine testing of healthy asymptomatic adults unnecessary. According to the HPHC's current medical policy, diabetes mellitus with neuropathy, amyotrophy, neurologic complication, or prolonged metformin use meet criteria for vitamin B12 screening and testing (Harvard Pilgrim Health Care, 2019). The consensus of current recommendations include testing individuals displaying unexplained neurological symptoms, cognitive changes, certain types hematological conditions, people at risk of nutritional deficiencies and other gastrointestinal conditions, as well as people on long-term use of certain drugs such as H2 receptor antagonist, proton pump inhibitors or metformin (Harvard Pilgrim Health Care, 2019; Langan & Goodbred, 2017; Medical Services Commission of British Columbia, 2012; Thaker et al., 2019). Treatment options include administering cyanocobalamin either 1000-2000 mcg daily orally or 1000 mcg given once a month for 3 months (Andres et al., 2020; Langan & Goodbred, 2017; Medical Services Commission of British Columbia, 2012). Other treatment options include cyanocobalamin sublingual administration, intranasal spray and drops (Andres et al., 2020; Bensky et al., 2019; Van Campen et al., 2019).

Another area to consider might be to screen patients prior to commencing metformin therapy as it will help determine patients who have borderline levels or are already deficient. That way the appropriate treatment can be administered promptly (Alvarez et al., 2019). The primary care centre should then follow-up with regular screening sessions to continue monitoring all patients.

Benefits of current recommendations

Rapid replacement of vitamin B12 via intramuscular injection should be considered in patients that present with significant neurological symptoms or patients found to have critically low vitamin B12 levels. This can prevent irreversible adverse effects of vitamin B12 deficiency in these patients (Andres et al., 2020; Medical Services Commission of British Columbia, 2012).

Issues still under investigation

Different types of vitamin B12 administration routes are still under investigation. A retrospective study by Bensky et al., (2019) analyzed the data of 4281 patients treated with vitamin B12, 830 were treated with intramuscular (IM) injections and 3451 with sublingual (SL) tablets. This study showed a significantly higher serum vitamin B12 levels in the sublingual group compared to the vitamin B12 intramuscular group. The authors concluded and suggested that sublingual administration might be superior to the IM route and should be the first line option for replacement therapy in patients with vitamin B12 deficiency.

Issues that have not been addressed

In clinical practice, patient preference and cultural considerations should be taken into account when choosing specific treatment options. Culture can be defined in many ways, in the context of this project, culture could be defined as the overriding set of beliefs, assumptions, values, myths, decision-making, or the learned responses and patterns of behavior that unite a group (Betancourt et al., 2016). The project site is an underserved rural internal medicine practice situated in the central San Joaquin Valley and predominantly delivers care to Mexican farmworkers. The ability to successfully interact and deliver culturally appropriate care to a diverse population is known as cultural competence. Having cultural competence usually requires possessing the knowledge, skills and attitudes necessary to provide culturally appropriate care to a diverse population (Loftin et al., 2013). The Latino Population Provider's Handbook on Culturally Competent Care by Kaiser Permanente's National Diversity Council (2018) reported cultural preference for injections over oral medication. Another culture consideration that needs to be addressed is accessibility of care in this underserved population. It is estimated that about 40%-50% of Latinos are uninsured and about 9% receive government assisted health care (Kaiser Permanent National Diversity Council, 2018). At the project site, an estimate 20-30% of the daily patient population are cash paying due to their illegal undocumented status. No one is ever turned away due to their inability to pay and I have seen patients return to the clinic project site with payment in the form of deliciously homemade food.

Controversies

A retrospective cohort study by Henry Ford Health Systems (2019) concluded that despite metformin's potential to cause deficiency of vitamin B12, they did not have enough evidence to implement a formal vitamin B12 screening recommendation in patients on metformin base on medication use criteria alone (Thaker et al., 2019).

Conclusion

The literature supports that the long-term use of metformin in diabetic patients is associated with vitamin B12 deficiency, which can be prevented and treated if detected early as some symptoms are irreversible. While vitamin B12 supplementation has been encouraged and helps these group of patients (Kancherla et al., (2016), other issues need to be addressed. For example, a significant proportion of healthcare professionals were unaware of the current ADA recommendations, therefore, increasing awareness of these guidelines among healthcare professionals is also needed, which the nursing profession can play a part of. Another issue is regarding patient education and lifestyle. Considering that an inadequate healthy lifestyle was likely to play a significant role in the majority of individuals with T2DM, a protocol could be developed in this area to educate patients on healthy foods, in particular vitamin B12 rich foods (Kancherla et al., 2016; Strohle et al., 2019). In addition, implementation of a vitamin B12 screening protocol at the project site could help with early identification and intervention of T2DM patients at risk of developing this type of deficiency (Kancherla et al., 2016; Strohle et al., 2019) thereby, reducing burden on the healthcare sector. Through the implementation of these specific recommendations, there should be a reduction in the number of patients developing vitamin B12 deficiency.

Review of Study Methods

Critical review of evidence is a vital and methodical process of evaluating scientific research to determine its relevance in supporting a particular study (Melnyk & Overholt-Fineout, 2015). The level of evidence derived from the process can contribute towards a nursing practice change where necessary. The seven levels of the Hierarchy of Evidence defined by Melnyk and Fineout-Overholt were used in this project. Level I evidence comes from systematic reviews or meta-analysis of random controlled trials, making this the best available evidence. Level II includes evidence from well-designed random control trials. Level III incorporates evidence obtained from well-designed controlled trials without randomization. Level IV includes evidence from a well-designed case-control and cohort studies. Level V involves evidence from systematic reviews or descriptive and qualitative studies while Level VI includes evidence from single descriptive or qualitative studies. Finally, Level VII includes evidence from authorities' opinions and/or expert opinions reports. Most of the literature reviewed used either systematic reviews or meta-analyses in their studies, which suggest improvement in the care given to metformin-treated T2DM patients.

Significance of Evidence to the Profession

This project seeks to influence the nursing profession by improving the overall quality of care of T2DM patients. After performing a literature review, it was established that there was an urgent need to accurately screen and monitor the vitamin B12 levels in metformin-treated T2DM patients. At the DNP project site, there is no current protocol for screening vitamin B12 levels in these patients, which is a risk for the overall care of diabetic patients. Evidence-based nursing practice promises the likelihood of producing significant positive patient outcomes. The work through evidence-based research is to raise awareness about strategies for making a positive health impact. Evidence-based knowledge on prompt vitamin B12 deficiency screening as advised in this project, could be used as part of an effective treatment option for T2DM patients on long-term metformin use. These patients need to be able to understand the benefits of keeping their vitamin B12 levels well within safe levels and need to be aware of the resources available to them before their vitamin B12 levels dip below normal and start experiencing signs of deficiency.

Evidence has advocated for the use of vitamin B12 deficiency screening methods in the primary care setting for patients considered to be at high-risk due to certain medical conditions or who are currently clinically symptomatic (Harvard Pilgrim Health Care, 2019). The rural location of this project provided a special type of network that enables the targeting of several ethnic groups, including African Americans and Hispanic immigrants. A delay in screening may lead to vitamin B12 deficiency sequela, therefore, timely screening and intervention can help increase patient health outcomes (Strong et al., 2016). DNPs are in a unique position to combine their extensive clinical expertise and the application of scientific knowledge to bring resolutions to specific problems, such as deficiencies and working out the complexities that will manifest in a screening process. It is crucial that DNPs utilize their expert knowledge on disease prevention to influence other healthcare professionals to carry out vitamin B12 screening and for metformin-treated T2DM patients to follow through for the prevention of potential complications like peripheral neuropathy ultimately improving patient outcomes, burden on the healthcare sector, and overall nursing practice.

Theoretical Framework

This project will use Kurt Lewin's Framework for Change Management Theory as a basis for addressing and implementing vitamin B12 deficiency screening protocols and for educating healthcare providers (Appendix A). This protocol will be used in a way that allows healthcare professionals to determine metformin-treated T2DM patients at high risk of developing vitamin B12 deficiency.

Historical Development of the Theory

Kurt Lewin, a psychologist, is recognized as an inventor in the study of dynamics and organizational development (Batras et al., 2016). After his military service during World War I, he was employed as a researcher at the Psychological Institute of Berlin University (from 1926-1932) where he carried out a series of psychological experiments involving motivation, learning, and needs (Burnes & Bargal, 2017).

Lewin and his family moved to the United States during World War II and secured a research grant at Cornell University where he conducted research at the university's day-care studying children (Cummings et al., 2016; Burnes & Bargal, 2017). He later worked at the University of Iowa where some of the first social psychology experiments were performed including those involving organizational development (Burnes & Bargal, 2017). In 1947, Lewin was conducting experiments with collaborators and former students into areas including group decision making and inter-group relations (Burnes & Bargal, 2017). He recognized that individuals must be convinced a change is necessary and this requires disrupting the status quo (Hussain et al., 2018). Importantly, he also discovered that when others, such as employees, are included in the process of change, it was met with reduced resistance (Hussain et al., 2018). This became the foundation of his change theory. In 1947, Lewin established a three-step model of change in his paper titled ‘Frontiers in Group Dynamics’, which consists of the unfreeze-change-refreeze model (Burnes & Bargal, 2017). Since Lewin’s death, his model has prompted further research into the role of human behaviour (Al-Haddad & Kotnour, 2015).

Nursing is an ever-changing profession due to adaptations to practices and policies, so clinical staff and management are likely to encounter challenges when these situations arise. Such challenges might include systems change implementation, research or team development and training. Therefore, an easy to use model is required to manage the situation. The ease of applicability of Lewin’s Change Management Theory has made it a frequently used model in nursing and has been highlighted in the literature for guiding several practice changes (Reimers et al., 2014; Wojciechowski et al., 2016; Gupta et al., 2017). For example, it was used to successfully implement a protocol for preventing and assessing delirium in ventilated patients (Reimers et al., 2014). Another example includes implementing bedside report for improving client and nursing satisfaction, and client outcomes (Vines et al., 2014). While the literature review carried out by Bakaria et al., 2017 found that Lewin’s Change Management Theory is still relevant managing organizational changes (Bakaria et al., 2017). Therefore, Lewin’s framework is a relevant model for this project as change is a vital component of nursing practice.

Change Management Theory

As aforementioned, the historical development of the Kurt Lewin model dates as far back as 1951 (Burnes & Bargal, 2017). The Change Management Theory was developed to identify and examine the factors and forces that influence a situation (Udod & Wagner, 2018). By understanding these forces, one could determine the forces that need to be reinforced or less emphasized to bring about change (Udod & Wagner, 2018). These forces involve two key models – driving forces and resisting forces, of which behaviour is based. Driving forces occur in the desired direction, therefore, resulting in a particular change (Udod & Wagner, 2018). However, restraining forces counteract the desired change and prevent the particular change from occurring since the push is in the opposite direction (Udod & Wagner, 2018). Change can only occur when the driving forces are greater than the resisting forces (Udod & Wagner, 2018). Ultimately, this force field model underpins the three key steps in the Change Management Theory (Burnes & Bargal, 2017).

Applicability of Theory to Current Practice

Change is a key element in any organizational setting. Understanding organizational dynamics and the processes involved are essential for the initiation and successful launch of health promotion programs. The field that drives certain behaviors in the healthcare system may include an organization's internal and external characteristics (Batras et al., 2016). Examples of internal characteristics are the organization's structure, management, training and collaboration while external characteristics include governmental control, communication tract, market or policy changes (Saleem et al., 2019). Analyses of all the relevant identified forces are paramount to enable healthcare professionals to determine why certain groups adopt certain behaviours and the required forces that need to be amended (Batras et al., 2016). Adjustment in the workflow process is required for the change to be efficient and streamlined.

A study by Reimers and Miller (2014), described an example where the Change Management Theory was implemented in a hospital setting (Reimers & Miller, 2014). The aim of the study was to address the role of the clinical nurse specialist (CNS) in assessing and preventing delirium in ventilated patients (Reimers & Miller, 2014). Fifty-eight percent of the staff nurses surveyed did not believe delirium was underdiagnosed or associated with mortality, which reflected the need for change (unfreezing). The CNS created a practice alert, which was an extensive review of the evidence and acted as a guide for the CNS in preparing an ABCDE Bundle (where ABC stands for awakening and breathing coordination, D for delirium management and E for early exercise and mobility) teaching program for the critical care team (Reimers & Miller, 2014). Clinical staff with extensive experience and those who showed particular interest were then trained on how to use the Bundle during their shift assessment (moving stage). Furthermore, ongoing communication and collaboration were maintained with staff during this period, which resulted in a multi-disciplinary acceptance of the Bundle. The refreezing stage was achieved by using the ABCDE Bundle daily with each patient to prevent delirium. Additionally, it meant that any delirium-positive patient to be treated and weaned off the ventilator earlier, leading to an increased independent functional status (Reimers & Miller, 2014). Reimer’s et al., 2014 demonstrated the CNS’s ability to effectively implement a practice change using Lewin’s Change Management Theory.

The Change Management Theory was found to be somewhat effective in several primary care settings where new guidelines were introduced including the creation of new cholesterol guidelines, the cessation of regular liver function tests for patients on statins and breast cancer screening (Gupta et al., 2017). The study by Gupta et al., 2017, which consisted of fifteen primary care physicians established that change interrupts the status quo and finding a new equilibrium was a struggle. This was partly due to the accessible evidence and the tensions between evidence and context (Gupta et al., 2017). For example, one physician had a patient who was unwavering in their resolve to have a mammogram screen even after the risks were explained. Their reasoning was that they would rather have the screening and be cancer-free than to have cancer and be unaware. In this instance, the physician respected the patient's autonomy even when it was not fully in support of the guidelines. While most physicians welcome and follow evidence-based medicine (driving force), it was discovered that what was considered evidence varied greatly among physicians (restraining force), which affected how much their practice was influenced (Gupta et al., 2017). Adding a change was described to be much easier than a change that required a cessation of current practice (Gupta et al., 2017). Additionally, Gupta et al., 2017 established that as clinical practice is ever-changing, change should be implemented in a multi-directional process rather than unidirectionally (Gupta et al., 2017).

One area of Lewin's research that could be applied to the project's objective is the systematic formulation of action research approach, which analyses the organization's current situation, identifies possible changes, and then implements the most appropriate change (Batras et al., 2016). What makes Lewin's Change Management Theory unique is that successful implementation requires a group effort rather than individual, as reported to being one of the core findings (Burnes & Bargal 2017; Batras et al., 2016; Bakaria et al., 2017). By implementing the change at a group level, the model will be used to assess the effectiveness of the protocol created and evaluate current policy in the rural setting. In the initial stages of change, recognition and active participation of those affected by the process can limit the resisting forces (Batras et al., 2016; Hussain et al., 2018). In this scenario, this would be raising awareness so clinicians recognize the problem and then accept the need for change (Unfreezing). Once change has been implemented, Lewin mentions that a group performance may be short-lived, and the situation reverts back to the previous state [Changing/Moving] (Bakaria et al., 2017). Therefore, it is essential that the group performance becomes permanent for a certain period of time before their efforts can be regarded as successful [Refreezing] (Bakaria et al., 2017).

Change Management Major Tenets

Unfreezing Stage

Unfreezing is the first stage of the Change Management Theory. It involves identifying the need for change and creating dissatisfaction with the status quo by finding a method that allows individuals to let go of a particular habit (Bakaria et al., 2017; Udod & Wagner, 2018). According to Lewin, there are three processes that can contribute towards change; convincing people that the status quo is no longer valuable, working with individuals to find applicable ways to support the anticipated change, or connecting with influential leaders that also support the change (Wojciechowski et al., 2016; Hussain et al., 2018; Udod & Wagner, 2018).

The unfreezing stage is where the common goal is set to reduce resistance within the group, which yields conformity (Udod & Wagner 2018). Additionally, there is the need for the identification of driving forces supporting the change and the resisting forces that work against it. In order for the change to be effective, different approaches may be required depending on the situation (Udod & Wagner, 2018). For example, some situations require the increase of driving forces away from the equilibrium while others require a decrease in the resisting forces, or in some situations, a combination of both methods may be needed (Udod & Wagner, 2018; Hussain et al., 2018).

Changing/Moving Stage

Changing or moving stage is the second stage in the Change Management Theory (Udod & Wagner, 2018). Moving facilitates change on individual and group levels. At this point, effective strategies in planning formulation and change implementation are determined, which are likely to result in an individual's commitment (Hussain et al., 2018). Driving forces in clinical practice can include redesigning roles, knowledge sharing, brainstorming, coaching and mentoring, training, a desire by the organization to provide best practices, influences to provide change in practice from colleagues, or advancement in technology that promotes the best clinical outcomes for patients (Reimers et al., 2014; Batras et al., 2016; Wojciechowski et al., 2016). Sharing knowledge is the organizational learning process and involves the interactive participation of individuals to create a standardized change (Hussain et al., 2018). Furthermore, knowledge may be shared in a way that can be easily transferred in documents, databases or protocols (Reimers et al., 2014; Hussain et al., 2018). As the moving stage is associated with a level of uncertainty, it is often the most challenging (Udod & Wagner, 2018). Thus, it is important to communicate effectively with all relevant parties (Hussain et al., 2018).

Refreezing Stage

Refreezing involves ensuring the change becomes a new habit to avoid individuals reverting to their old pattern (Wojciechowski et al., 2016; Udod & Wagner, 2018). For example, aligning reward systems, new organizational structures or the new practice change (Batras et al., 2016). According to Reimers et al., 2014, the refreezing stage was achieved by requiring the use of the ABCDE Bundle daily with each patient (Reimers et al., 2014). For this project, the aim is to ensure the new vitamin B12 deficiency screening protocol becomes the norm in everyday practice. Weekly or monthly audits may be a beneficial way to continue reinforcing the use of the new practice change. Moreover, refreezing means stability at the new stage of equilibrium that brings change in the organizational culture and procedures (Bakaria et al., 2017).

Theory Application to the DNP Project

The Change Management Theory provides a framework for the use of a proposed protocol to screen T2DM patients on long-term metformin treatment to reduce the potential of vitamin B12 deficiency in a rural primary care clinic. With this framework, the protocol is designed around the three main concepts – unfreezing, changing, and refreezing (Batras et al., 2016). These concepts will aid in ensuring the protocol in this project is concise by identifying, measuring, and creating a simple, yet detailed, plan that clinicians will follow when screening for vitamin B12 deficiency. The proposed change of implementing a screening protocol also requires a strategic plan, leadership/management support, and engaged/committed colleagues for change progression (Reimers et al., 2014; Bakaria et al., 2017; Hussain et al., 2018). In other words, the strategic plan disrupts the status quo, influences healthcare professionals to accept the implementation of a new protocol and then refreezing the practice at the project site whereby the screening protocol becomes the norm (Reimers et al., 2014; Batras et al., 2016).

Unfreezing will commence by identifying the focus of the change (Batras et al., 2016). In this case, the project site has no vitamin B12 deficiency screening protocols. Key components of this step will be communicated to all stakeholders including frontline providers, managers, administration and staff in the clinic (Reimers et al., 2014; Hussain et al., 2018). Though, in 2017, the ADA and the American Family of Physicians (AFP) made recommendations for vitamin B deficiency screening and management, most healthcare professionals are not aware of this; therefore, do not follow this guideline – a barrier that needs to be overcome (Harvard Pilgrim Health Care, 2019; Langan & Goodbred, 2017; Thaker et al., 2019). Discussing this issue with key opinion leaders and stakeholders at the project site and making them aware of the lack of screening related to guidelines in the selected patient population will be established (Reimers et al., 2014). According to Hussain et al., (2018), employee involvement, in this case the stakeholders, is key as their input affects the organization's performance and patients' well-being

(Hussain et al., 2018). Additionally, their input should potentially result in a reduced resistance, thereby, yielding a valuable change (Hussain et al., 2018). Discussions with the group will also be used to determine if there might be potential push backs from patients regarding screening for vitamin B12 deficiency and how to address this.

In the unfreezing stage, supporting steps will include investigating current practices at the project site and comparing them to best practices guidelines (Batras et al., 2016). Findings from the group discussions will be presented at stakeholder meetings in order to increase the pressure for change at a higher level (Hussain et al., 2018). Weekly meetings will also be scheduled with stakeholders providing relevant information to help them understand the importance of the DNP project and how it will beneficially affect patient care in the clinic. It also enhances the trust of the clinical staff in the stakeholders and gives a better sense of control. Moreover, a timeline may also be agreed with the stakeholders so among all, there is a sense of purpose and transparency for the change. By doing this, it is hoped that these steps will allow the provision of the necessary resources by the stakeholders.

The moving stage involves developing evidence-based training on vitamin B12 deficiency screening protocol, which is then presented to the clinical staff (Reimers et al., 2014; Wojciechowski et al., 2016). Clinical staff will be educated and trained on how to implement the screening protocol at the project site (Batras et al., 2016). Leadership/management team support will be given to healthcare professionals reinforcing the practice change, the use of the ADA recommendations and addressing any concerns that may arise (Bakaria et al., 2017; Hussain et al., 2018). Ongoing communication will be maintained with the clinical staff at the project site, which will be important to reinforce the need for change. This will be done, for example, by organizing brainstorming and knowledge sharing sessions with the group to analyze how well the protocol is being implemented and whether there are any ideas for optimization in the clinic (Batras et al., 2016; Wojciechowski et al., 2016). Senior professionals will influence younger colleagues to provide a change in practice. Additionally, the involvement of the group will be used to educate patients on the importance of the new screening protocol. Regular feedback from both healthcare professionals and management team will be used to revise the protocol, if necessary.

In the final stage of the Change Management Theory, the process of freezing the changed practice occurs (Udod & Wagner, 2018). At this point, the implementation of the vitamin B12 deficiency screening protocol has been integrated into practice. The protocol should be the standard of care when managing maintenance care for metformin-treated T2DM patients (Reimers et al., 2014; Wojciechowski et al., 2016). The impact of the pre- and post-implementation will be evaluated through chart review and surveys, which will be reviewed and discussed with staff (Reimers et al., 2014). Moreover, the new routine of using the screening protocol will be communicated to new providers during orientation (Wojciechowski et al., 2016). Finally, strategies including policy drafting will be aligned to support change continuation.

Setting

The setting will be a rural internal medicine clinic in Bakersfield, California with a population of 384, 145 as of 2019 (US Census Bureau, 2020). The patient population at the clinic is 90% Hispanics, 5%, Caucasian, and 5% other. On average, over 5,000 patients are seen annually for medical care at the practice site (personal communication). Practice Fusion EHRS is currently the electronic medical record (EHR) utilized at the project site. In addition, the practice site accepts Preferred Provider Organization (PPO) insurance plans, Health Maintenance Organization (HMO) plans, Medicare, Medical, and cash pay patients.

Population of Interest

The providers who will implement the protocol at the practice site, will be the direct population of interest. The doctor at the practice is a certified member of the American Board Internal Medicine with forty years' experience. There are two nurse practitioners including the project lead who are certified members of the American Board Family Practice awarded by the American Nurses Credentialing Center. The other nurse practitioner has been practicing for almost two years with nearly a year at the clinic. The two medical assistants both have 10 years' experience, and one is a Certified Medical Assistant awarded by the American Association of Medical Assistants (AAMA) The phlebotomist has a Certified Phlebotomy Technician (CPT I) Certificate issued by the California Department of Public Health with five years' experience. All of the providers work at the practice full-time except for the project lead (a volunteer) and the phlebotomist, who is a contractor. Additionally, all the providers are fluent in Spanish except for one nurse practitioner; and translation is performed by the medical assistant. The inclusion criteria are all healthcare professionals who provide direct patient care at the practice site. Front office staff, medical and nursing students who do not work directly with the patients do not meet the inclusion criteria.

The indirect population of interest will be the patients examined at the practice site. The results of the protocol implementation will be determined through the use of chart reviews. Specific inclusion criteria include patients aged between 18-80 years, and patients on metformin therapy for more than six months. and have been registered at the clinic for more than six months. Patients excluded from the study were those that had not been on metformin therapy longer than six months.

Stakeholders

The main stakeholders involved in this protocol implementation comprise of the clinical staff, project site administration/management, practice site owner, and patients. The participants of this DNP project are considered stakeholders. The clinical staff are vested in the project as the screening protocol and treatment implementation will increase the number of T2DM adults on metformin being screened for vitamin B-12 deficiency and treated as necessary. The medical assistants also play a role in the change process as they are responsible for storing clinical data into the electronic system. An increase in screening will assist providers in detecting patients at risk of vitamin B-12 deficiency. This will allow for early intervention to decrease complications such as peripheral neuropathy, which correlates with improved quality of life for patients. Improvement on quality of life is an interest also shared by the patients themselves since the screening protocol directly impacts how care is given to them.

Moreover, the practice site administration/management, practice site owner, and general manger are responsible for the planning, budgeting and coordination of the site. These stakeholders are vested in the project as it means reducing the number of patients with vitamin B-12 deficiency. Additionally, it means the time and cost needed for treating these patients will be reduced, therefore, decreasing the budget channelled into these patients.

A strong communication line has been established with the stakeholders over the course of the project by speaking with them individually about the aims of the protocol, how it will be implemented and the duration. Any questions asked by the stakeholders whereby the answers were unknown were researched and feedback to them. This ensures any concerns were appropriately addressed. Several meetings were scheduled at the project site for brainstorming ideas and discussing the criteria required for the project protocol to be efficient and achievable. Stakeholder engagement and communication will be continued throughout the project by providing updates of the progress through weekly meetings and ensuring any questions have been adequately addressed (Petkovic et al., 2020). Verbal permission to complete the project was given by the owner of the clinic. A written agreement was obtained authorizing the project to be completed at the project site (see Appendix B) and no affiliation agreement is required.

Intervention/Project Timeline

The project timeline is estimated to take five weeks. This timeframe includes educating participants, the implementation of the project intervention, data collection, and analysis/interpretation. Project implementation will commence at the start of November, 2020. The first week of the implementation phase will include providing education to the clinical staff, conducting pre- and post-knowledge tests, pre-implementation of chart audit, implementation of the vitamin B-12 screening protocol at the practice site, monitoring the implementation process and supporting participants, and collection of data. The conference room at the project site will be used as the setting for the educational session. The second, third, fourth and fifth week involves monitoring the implementation process, supporting participants by answering any questions and being present while ensuring that security and privacy measures are followed. Data collection and analyses will also take place during these four weeks. Week 5 is the final week of implementation with the final data collection and compilation. Finally, in week six, the project lead will interpret, and discuss the findings from the data collected. When completed the project lead will prepare for dissemination. Established rapport will be maintained during the DNP project by checking in with the clinic on a weekly basis and being available via cell at any time (as currently being practiced) should any questions arise. Please refer to Table one for an outline.

Week 1 November 4- November 10	Provide education to the participants (clinical staff) Conduct pre and post tests Pre-implementation of chart audits Implementation of the vitamin B-12 screening protocol at the practice site. Monitor implementation process and support participants

Week 2	Monitor implementation process and support participants Data collection Analyze data using the parametric techniques identified by the SPSS survival manual and SPSS excel for specific statistical analysis Analyze data using the non-parametric techniques identified by the SPSS survival manual and SPSS excel for specific statistical analysis
Week 3	Monitor implementation process and support participants Data collection Analyze data using the parametric techniques identified by the SPSS survival manual and SPSS excel for specific statistical analysis Analyze data using the non-parametric techniques identified by the SPSS survival manual and SPSS excel for specific statistical analysis
Week 4	Monitor implementation process and support participants Data collection Analyze data using the parametric techniques identified by the SPSS survival manual and SPSS excel for specific statistical analysis Analyze data using the non-parametric techniques identified by the SPSS survival manual and SPSS excel for specific statistical analysis
Week 5	Monitor implementation process and support participants Final week of data collection Analyze data using the parametric techniques identified by the SPSS survival manual and SPSS excel for specific statistical analysis Analyze data using the non-parametric techniques identified by the SPSS survival manual and SPSS excel for specific statistical analysis
Week 6	Further data analysis Interpretation of the findings (comparisons, scores, ranks, similarities, and significant factors identified).

Tools

Content Validity Index Tool

The content validity tool developed by the project lead includes the purpose and learning objectives, the population of interest, the length of the test, difficulty and discrimination level of items, and the scoring procedure to be used (Appendix C). Moreover, in the test blueprint, the content contains different levels of cognitive skills according to Bristol and Liner (2015). Further information is outlined in the test item development document. At the end of the test item development document, an expert ratings form and content validity index (CVI) calculation will be detailed as these help to determine relevance of the questions.

Pre- and Post-Test/Score Sheet

The pre- and post-test (Appendix D) was developed by the project lead and will be offered to providers in a paper format to test their clinical knowledge of vitamin B-12 deficiency and screening for patients diagnosed with T2DM and on metformin therapy. After taking the pre-test, the providers will be educated on the different aspects of the deficiency. Then the same test will be given to the clinical staff immediately after the educational training. The pre- and post-test scores will be compared to assess gains in knowledge acquired during the educational session and to collect statistical data that will optimistically show an improvement in vitamin B-12 knowledge. Multiple-choice questions were chosen to assess the providers' breadth of knowledge and application level. Alexander (2016) noted that multiple-choice questions are the preferred test format and explained that there is correlation between a superior clinical performance and a high score on a test made up of multiple-choice questions.

Before sharing this tool with the clinical staff, it will be validated through the aforementioned CVI process. If a low score is achieved on the test, an opportunity for additional training will be provided. A score of at least 80% is required to pass the test and only the project lead will have access to the scores. The participants' scores from the pre- and post-test survey will be entered in a scoresheet (Appendix E).

Educational Tool

An educational tool in the form of a PowerPoint presentation (Appendix F) will be developed by the project lead and presented to the clinical staff at the project site. Before presenting the tool, the content of the document along with the vitamin B-12 deficiency and treatment screening protocol will be validated with the stakeholders and project team. The document will contain facts and information regarding vitamin B-12. Such information includes dietary sources of vitamin B-12, daily requirements, normal ranges of vitamin B-12 in the blood, deficiency screening guidelines, causes of vitamin B-12 deficiency, symptoms, the relationship between cobalamin and vitamin B-12 deficiency, metformin use and vitamin B-12 deficiency, and treatment. Moreover, information in the PowerPoint presentation will aid in answering the questions set in the pre and post-test. The document will cover specific information regarding how the protocol should be implemented such as how to test for vitamin B-12 levels, how to treat a patient who has low vitamin B-12 levels with or without neurological symptoms or if the cause of the deficiency is dietary related. Additionally, a questions and answers session will be offered immediately after the presentation. The portable document format (PDF) version of the NHS protocol will be given as handout for reference as well as the printed version of the PowerPoint document.

Vitamin B-12 Deficiency Screening Protocol

The vitamin B-12 deficiency screening and treatment protocol (Appendix G) that will be used in the DNP project will be based on the recommendation and guidelines of UpToDate, a medical resource site that follows the National Health Service guidelines (the UK's health system) (Devalia et al., 2014). The protocol will be used according to the recommendation and will not be modified. No permission is required to use this clinical information as NHS England believes that providing accessible information will help to improve access to services and help people make informed choices about their care. For staff, accessible information provision aids in communication with service users, supporting personalization and empowerment. Furthermore, it can promote the effective use of resources and reduce inequalities and barriers to good health (NHS England Accessible Information and Communication Policy, 2016).

The screening protocol will be given to providers to use as a guide to initiate screening and treatment if needed. The providers will follow the protocol recommendations to ensure vitamin B-12 serum levels stay within the range of 200-800 ng/L (Devalia et al., 2014). The protocol will provide information needed for identifying vitamin B-12 deficiency and guide the appropriate management of deficiency. After education, the providers will use an outlined protocol to detect vitamin B-12 deficiency, initiate treatment or refer patients to a specialist if required. All individuals with a detected vitamin B-12 deficiency should be treated unless there is a strong reason not to including palliative care or patient refusal. Depending on the levels of vitamin B-12 detected, intrinsic factor antibodies (IFAB) test could be performed. For patients with neurological symptoms, the initial treatment should involve IM hydroxocobalamin 1000 mcg every two days until no more improvement, then the maintenance regimen will be IM hydroxocobalamin 1000 mcg every two months for life (oral cobalamin is not recommended) (Devalia et al., 2014). However, for patients without neurological symptoms, initial treatment involves IM hydroxocobalamin 1000 mcg three times a week for two weeks then the maintenance regimen will be IM hydroxocobalamin 1000 mcg every three months for life (oral cobalamin is not recommended) (Devalia et al., 2014). Vitamin B-12 levels could be rechecked in one to two months. If the cause of vitamin B-12 deficiency is dietary, oral cyanocobalamin tablets 50-150 mcg daily between meals (in adults) or twice-yearly hydroxocobalamin 1000 mcg injection may be better especially in adults who are likely to experience malabsorption. For patients with a negative IFAB test and vitamin B-12 levels >200 ng/L, no further investigation is required, but consider low dose oral cobalamin (outlined in Appendix F) (Devalia et al., 2014).

Chart Audit Tool

The chart audit tool (Appendix H) that will be used in the DNP project will be a simple one developed by the project lead using the Checklist and Audits Tool from the AHRQ as a reference (The Agency for Healthcare Research and Quality, 2015). The tool will be validated with the stakeholders and project team. The purpose of the tool, which is in a table format, is to collect data on the patients' health record from the EHRS and check compliancy. These include variables on the chart audit tool and laboratory information such as blood work and dates, and whether the diabetic patient is on metformin therapy. Manual extraction of data from the EHRS system will be utilized. Furthermore, the tool will be used to collect data before and after implementation of the protocol to collect data required for statistical analysis. The audit chart tool will use numeric system to replace patients' numbers to maintain confidentiality. A six-digit date of birth system (year/date/month) as well as the patient's first and last name initials will be used as the ID. For example, a patient called Joe Smith born on 70/01/10 will have the ID: JS700110. The variables in the chart audit tool will include seven questions to review (see Appendix G) as these will also be used to before and after protocol implementation to collect data for statistical analysis.

Study of Interventions/Data Collection

During the educational training in week one, data will be collected using the scores from the pre- and post-tests, which will be recorded on the score sheet. This aligns with the project's objectives of developing and presenting evidence-based educational training to the providers.

Scores for the post-test will allow the project lead to measure the effectiveness of the teaching and educational materials. The collected score sheets will be kept in a locked filing cabinet at the project site. The total number of patient charts reviewed and the number of patients screened for vitamin B12 deficiency will be collected weekly during weeks one to five (November 4-December 8) of the implementation process. This will be in the form of a chart review to evaluate protocol compliancy. Collection of these sets of data align with the project's objective of implementing the screening protocol. Additionally, the data collected will be stored on an excel spreadsheet, which will then be exported into a Statistical Package for Social Sciences (SPSS) software for comparative analysis of pre- and post-implementation of the vitamin B-12 deficiency screening protocol.

Moreover, the data collected electronically will be protected by an encrypted password that will only be utilized by the project lead. There will be no identifying patient or staff information in order to maintain confidentiality of collected data from the EHRS system. The information extracted from the patient charts will be documented in the chart audit tool and Health Insurance Portability and Accountability Act (HIPAA) compliance will be followed. HIPPA is a sequence of regulatory standards that outline the lawful use and disclosure of protected health information (PHI) (Drolet et al., 2017). According to HIPAA, healthcare providers and facilities must take reasonable precaution to limit the use or disclosure of PHI to achieve the intended purpose (Drolet et al., 2017). To comply with HIPAA, patients' will be identified using a numeric system (for example, a patient called Joe Smith born on 70/01/10 will have the ID: JS700110).

Ethics/Human Subjects Protection

The Institutional Review Board (IRB) determination form was submitted for review by the project team in order to remain compliant with Touro University Nevada's policy, which was subsequently approved. An IRB review of the project site is not required. As the implementation is a quality improvement project and does not involve direct patient care activities or human subjects, the project proposal should be exempt from IRB review. There will be no monetary compensation provided to participants. To ensure further protection of human subjects, the project lead has successfully completed all the required collaborative institutional training initiative (CITI) modules. These modules impart knowledge of human subject's protection in research studies. In an effort to maintain staff and patient confidentiality, no identifying data will be asked or collected from the staff or patient records. To maintain confidentially, patients will be identified using a numeric system as described in the section above. The protocol implementation is a mandated practice change for the project site and although participation is mandated, it is not a condition of employment.The benefit of participation on implementing the vitamin B-12 deficiency screening protocol includes providing evidence-based data and information on vitamin B-12 levels in metformin-treated T2DM patients. There are no potential risks to the providers. All electronic files relating to this project will be password protected so they are inaccessible by unauthorized users and destroyed three years after the project has been completed.

Measures/Plan for Analysis

The providers will implement the vitamin B-12 deficiency screening protocol. Data from the pre- and post-test results and chart audit tool will be analysed using SPSS version 27 to determine compliancy of these screening protocol.

For the pre- and post-test, the scores will be shown by person (de-identified and instead 'provider 1' and so on) and then analyzed using a paired t-test to evaluate significance. The protocol compliance is a dependent variable and for data collection, a chart audit before the intervention will be carried out to determine the number of patients who were on metformin and not screened for vitamin B-12 deficiency. Then a chart audit post intervention will be carried out. For analysis, a 2x2 table will be created with the columns being 'screened' and 'not screened' and the rows 'before' and 'after' then a Fisher's exact test would be used for the statistical analysis to evaluate an increase in screening for patients with vitamin B-12 deficiency. A descriptive analysis will be reported with the percentage screened before with 95% confidence interval. A statistician will be consulted to ensure the relevant statistical analyses are being used.

Analysis of Results

The goal of this quality improvement project was to improve healthcare professionals' knowledge about vitamin B-12 deficiency and to implement a protocol in a primary care setting. As the prevalence of diabetes, predominantly T2DM, has increased over the past few years in the United States so has metformin therapy (Centers for Disease Control and Prevention, 2020; Herbert et al., 2019). However, monitoring of vitamin B-12 deficiency as a result of metformin use on a long-term basis remains poor (Longo et al., 2019; Aroda et al., 2016). This project sought to create an evidence-based protocol that screens for vitamin B-12 deficiency in T2DM patients that are actively taking metformin with the aim to increase identification of vitamin B-12 deficiency and/or insufficiency for potential intervention and treatment. The DNP project goal is for early detection and prompt intervention of low levels of vitamin B-12 to decrease potential health risks and improve patient healthcare outcomes. The data analysed included the providers' knowledge of vitamin B-12 before and after the educational session as well as the compliancy of vitamin B-12 protocol screening pre- and post-implementation. Analysis of the data collected was completed utilizing SPSS version 27 and included parametric (paired t-test), and non-parametric

(Fisher's test).

Pre- and Post-Test Scores

The providers completed a ten-item questionnaire regarding their awareness of vitamin B-12 prior to and after attending a short training session on the dietary sources if vitamin B-12, daily requirements, normal ranges of vitamin B-12 in the blood, deficiency screening guidelines, causes of vitamin B-12 deficiency, symptoms, the relationship between cobalamin and vitamin B-12 deficiency, metformin use and vitamin B-12 deficiency, and treatment.

As shown in Table 1, pre- and post-test scores were collected and compared using a paired t-test. In total, five providers attended the educational training session. Data analysis was performed in the Statistical Package for Social Sciences Student's t-test, analysis of variance, χ^2 test, and Fisher's exact test were applied to check the significant difference between groups. Pearson's correlation analysis was used to examine the relationship between vitamin B-12 and other parameters. A two-tailed p value <0.05 was considered statistically significant.

Table 1

Paired Samples Statistics on the Pre- and Post-Vitamin B-12 Knowledge Test Scores

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Pre	4.80	5	2.490	1.114
	Post	10.00	5	.000	.000

Table 1 shows the mean scores achieved by the providers before and after the educational session on vitamin B-12 knowledge. The table shows the descriptive statistics of pre-test and post-test educational training at 95% confidence interval. This shows the pre-test mean value of 4.80 while the post-test mean value was 10. As the post-test mean value was higher, this means the educational session significantly increased the providers' knowledge.

The paired sample t-test results show that the mean difference between pre-test and post-test is 5.2 which means the knowledge on vitamin B-12 has been improved after the educational session. As shown in Table 2, the value of significance for paired sample is 0.010 which is less than α= 0.05 so we conclude the results are statistically significant at 95% confidence interval and there exists a significant difference in providers' knowledge before and after the educational session.

Table 2

Statistical Significance in the Pre- and Post-Test Scores

		Mean Difference	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		t	df	Sig. (2-tailed)
					Lower	Upper			
Pair 1	Pre-Post	5.200	2.490	1.114	2.108	8.292	4.670	4	.010

Table 2 shows the statistical significance in the mean scores before and after the educational training session.

Chart Audit

A total of sixty-nine adult patient charts were reviewed. Thirty-five of those happened one month before implementation of the screening protocol while thirty-four were a month after implementation of the screening protocol. As shown in Table 3, of the thirty-five patient charts audited in the pre-implementation phase, twenty-nine patients were not screened while 6 were screened for vitamin B-12 deficiency. Post protocol implementation, of the thirty-four audited patient records, seven were not screened while twenty-seven were screened. The raw data indicated an increase in compliancy and upon analysis, the data showed a significant value for the

Fisher's exact test to show that there is a non-random association between compliancy pre- and post-protocol implementation.

Table 3

*Pre- and Post-Implementation Comparisons of Vitamin B-12 Deficiency Screening: Fisher's Exact Test. Date Treatment of Vitamin B-12 * Screening Crosstabulation*

Count

		Date of Serum		
		Screened	Not Screened	Total
Level of Audit	Before	6	29	35
	After	27	7	34
Total		33	36	69

Table 3 shows the cross-tabulation results and this indicates that there were thirty-five patient charts that were audited before implementing the screening protocol and thirty-four patient charts after implementation. So, there were sixty-nine patient charts in total. Before applying the vitamin B-12 screening protocol, only six patient charts were screened. However, after implementing the screening protocol, twenty-seven patient charts were screened while seven charts were not.

Table 4

Statistical Significance in the Screening Protocol Compliancy Pre- and Post-Implementation: Fisher's Exact Test

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	6.205[a]	1	.013	.025	.015	
Continuity Correction[b]	4.257	1	.039			
Likelihood Ratio	8.517	1	.004	.025	.015	
Fisher's Exact Test				.025	.015	
Linear-by-Linear Association	6.113[c]	1	.013	.025	.015	.015

N of Valid Cases	69

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 2.91.
b. Computed only for a 2x2 table
c. The standardized statistic is 2.473.

Table 4 shows the statistics of Fisher's exact test. The p-value exact sig. (2-sided) is 0.025 which is less than $\alpha=0.05$ therefore, the two variables for compliancy pre- and post-screening implementation are associated with each other.

Number of Patients Screened for Vitamin B-12 Deficiency Pre-audit.

Table 5 below shows the number of patient charts screened for serum vitamin B-12 deficiency before protocol implementation. The analysis shows that most of the patients N=29 (82.9%) were not screened for serum vitamin B-12 levels while six (17.1%) were screened. The result has been represented by a bar graph in Figure 1. Table 6 shows that the number of patients screened had been increased significantly after protocol implementation from seven (20.6%) to twenty-seven (79.4%). From Figure 2, it is clear that the number of patients screened for serum vitamin B-12 deficiency after protocol implementation has increased.

Table 5

Number of Patient Charts Screened for Vitamin B-12 Deficiency Pre-audit: Descriptive Analysis

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	N/D or Not Screened	29	82.9	82.9	82.9
	Screened	6	17.1	17.1	100.0
	Total	35	100.0	100.0	

Table 5 shows the number and percentage of patient charts screened pre-implementation of the protocol.

Figure 1

Number of Patient Charts Screened for Vitamin B-12 Deficiency Pre-audit: Descriptive Analysis

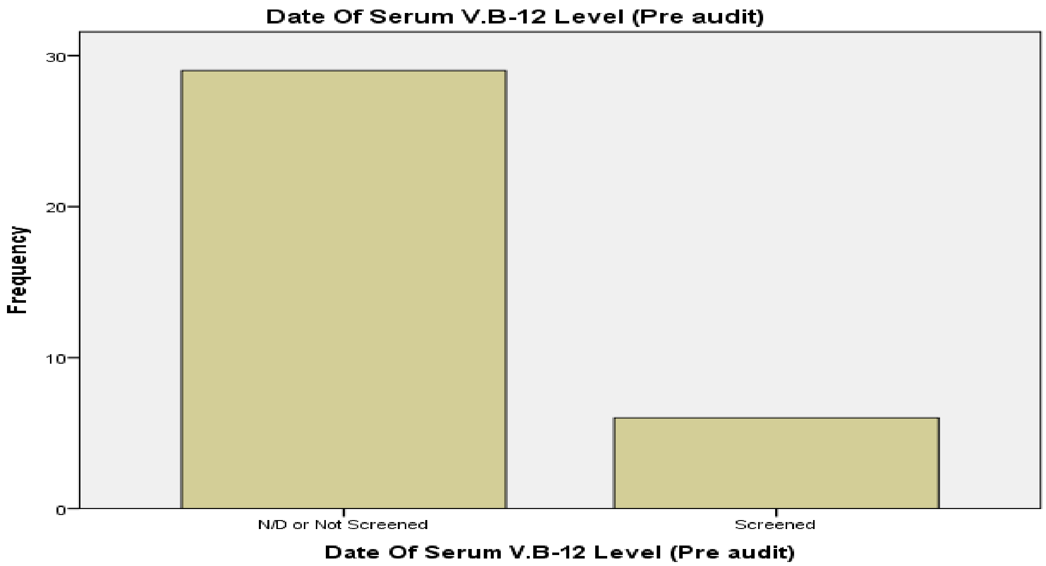


Figure 1 shows the number of patient charts screened for vitamin B-12 deficiency pre-audit.

Table 6

Number of Patient Charts Screened for Vitamin B-12 Deficiency Post-audit: Descriptive Analysis

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	N/D or Not Screened	7	20.6	20.6	20.6
	Screened	27	79.4	79.4	100.0
	Total	34	100.0	100.0	

Table 6 shows the number and percentage of patient charts screened post-implementation of the protocol.

Figure 2

Number of Patient Charts Screened for Vitamin B-12 Deficiency Post-audit: Descriptive

Analysis

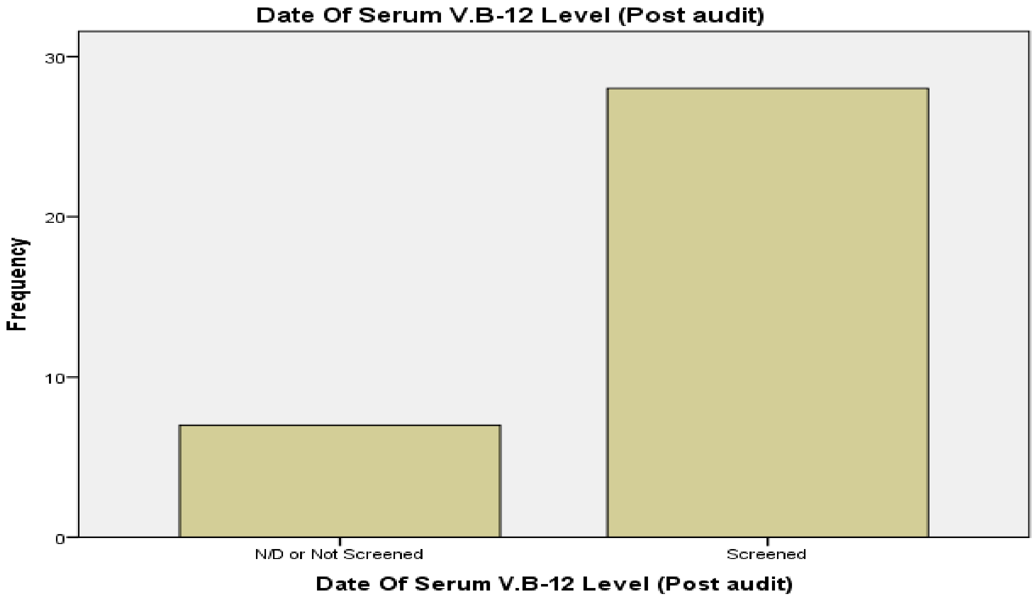


Figure 2 shows the number of patient Charts screened for vitamin B-12 deficiency post-audit.

Discussion of Findings

The implementation of the project was found to be successful in meeting all of its objectives, which included developing evidence-based educational training on vitamin B12 screening protocol, enhancing staff knowledge of vitamin B12 deficiency, implementing a screening protocol and increasing the compliancy of the serum vitamin B12 level screening at the project site. Despite the overwhelming evidence associating long-term metformin use to low levels of vitamin B12, evidence suggests that such monitoring is rarely performed, and may be partly due to the lack of knowledge of the current recommendations among physicians (Pierce et al., 2012). As stated by Alshammari et al., (2019) in a cross-sectional study, only 4.4% of the patients reviewed had a vitamin B12 serum level available in their medical records while 56% of the physicians were unaware of the current ADA recommendation or had any idea about it. Therefore, education was an area of focus in this DNP project.

For the first and second objectives, the evidence-based educational training was developed and presented to the clinical providers according to Reimers et al., (2014); Wojciechowski et al., (2016); Batras et al., (2016). In order to determine whether the educational training was successful, the results of the pre- and post-test scores were analysed using a paired sample t-test. Knowledge scores increased from an average of 4.80 before participation in the educational training session to an average score of 10.00 after participation, resulting in a mean difference of 5.20. The increase in vitamin B12 knowledge scores reflected statistical significance for all participants ($t=4.670$, $p=.010$).

The ADA and the American Family of Physicians (AFP) made recommendations, in 2017, for vitamin B deficiency screening and management, though most healthcare professionals were not aware of this – a barrier that needed to be overcome (Harvard Pilgrim Health Care, 2019; Langan & Goodbred, 2017; Thaker et al., 2019). Hence, the third objective required evaluating the compliancy of the providers with using the protocol after implementation. According to Hussain et al., (2018), employee involvement is key as their input affects the organization's performance and patients' well-being (Hussain et al., 2018). The Fisher's test was used for the chart audit. It was noted that the compliancy of the screening protocol utilization increased among the providers. Prior to protocol implementation, only six patients out of thirty-five were screened. However, after protocol implementation, this increased to twenty-seven out of thirty-four. The raw data indicated an increase in compliancy and upon analysis, the data showed a statistically significant increase for the Fisher's exact test of $p=.025$. This means that there was a difference between the compliancy pre- and post-chart audits further corroborating the finding that the providers had learned from the education and the implementation of the screening protocol.

The fourth objective involved evaluating the screening of serum vitamin B12 levels in patients. Before the protocol implementation, 17.1% of patients were screened, which increased to 79.4% afterwards. Therefore, there was a 62.3% increase in the number of patients screened for serum vitamin B12 deficiency. This is a great result as detecting vitamin B12 deficiency promptly is crucial for early treatment and avoiding complications as diabetic neuropathy affects 44% of older diabetic patients (Jayabalan & Low, 2016; Strong et al., 2016).

This quality improvement project proposed to answer the following clinical questions: Can implementation of a vitamin B12 deficiency screening protocol in a primary care setting improve overall knowledge of B12 deficiency and increase B12 screenings in a five-week period? Based on the findings of the project, it was demonstrated that there was a significant increase in the knowledge and compliance with the vitamin B12 deficiency screening protocol

Significance/Implications for Nursing

The project's results are significant to nursing since primary care settings are the initial point of care for many patients with chronic diseases such as T2DM. The results were discussed with the project manager, project site director, and the providers. The providers understand the need to improve adherence to the screening protocol practices while working on efforts to bridge the gaps associated with barriers to utilizing the protocol. According to the International Diabetes Federation, the estimated health expenditures in 2019 were approximately 760 billion dollars, which is 10% of the total spending in adults (International Diabetes Federation, [IDF] 2019). In the US, the staggering healthcare cost of diabetes has increased to approximately 327 billion dollars with $39.47 billion of that spent in California, where the largest population of T2DM patients are residing (American Diabetes Association, 2018). An increase in cost could have a direct impact on nursing by creating a need to increase staffing to meet the demands of patients diagnosed with T2DM.

Continuing monitoring of patients' laboratory and clinical data could decrease the incidence of complications in several organ systems. Also, the costs resulting from chronic diseases have been estimated as 17% of healthcare expenditures, and individuals with such diseases have a poorer quality of life. Therefore, healthcare organizations are endeavouring to monitor costs while ensuring that providers' productivity and time are spent on other areas (White et al., 2018). Another area to consider might be to screen patients prior to commencing metformin therapy as it will help determine patients who have borderline levels or are already deficient. That way the appropriate treatment can be administered promptly (Alvarez et al., 2019). The primary care clinic should then follow-up with regular screening sessions to continue monitoring all patients. Using the data from the evidence-based project, the DNP-prepared nurse is able to evaluate information and apply transformational change to the organizational systems thereby, increasing productivity, job satisfaction and better patient outcomes (Chism, 2017; Porter-O'Grady & Malloch, 2018). The DNP-prepared advanced practice nurse in a leadership role is well-versed and prepared to shape behavioural health policies that bring about transformational change at the macro-organizational level (Chism, 2017).

The aim is that the screening protocol implementation increases compliance among providers and improves early detection of vitamin B12 deficiency, thereby decreasing costs related to nursing and medical services. For example, a reduction in the time spent looking after patients that have developed complications can be channelled elsewhere, which reduces the time patients spend in hospitals. Overall, this will result in an improvement to the patient's quality of life and a decreased nursing and medical costs. It is important that clinical providers screen for potential vitamin B12 deficiency in patients on long-term metformin to ensure an appropriate diagnosis and treatment. Thus, improving screening, patient care, and the quality of life of T2DM patients receiving metformin therapy (Kancherla et al., 2016; Strohle et al., 2019).

Limitations

Project design

While the project was designed for quality improvement at a single primary care setting, perhaps it would benefit from further analysis in multiple settings using a larger group of providers. This will ensure the data collected is more robust and accurate. Increasing the number of participants in a study and settings were mentioned as part of the further analysis required in the study done by VanderKooi and colleagues (VanderKooi et al., 2018).

Data Recruitment

One of the data recruitment limitation was the small sample size of the providers (N=5) that attended the educational training session and completed the pre-and post-tests. Of the five providers, only two were primary care providers. The small sample size was because of the project site being a small, rural primary care clinic with few staff associates. The result of small sample size may cause a reduction in the statistical power to identify changes.

Another limitation was the small sample size of the providers (N=5) that attended the educational training session and completed the pre-and post-tests. Of the five providers, only two were primary care providers. The small sample size was because of the project site being a small, rural primary care clinic with few staff associates. The result of small sample size may cause a reduction in the statistical power to identify changes.

Collection Methods

Another limitation worth mentioning was the time available to measure changes by the project lead with more time being associated with an increased potential for sustainability (VanderKooi et al., 2018). There was a four-week period for implementation and data collection, resulting in an increased ability of the providers to retain and recall information from the educational session thereby inflating the post-test scores. The educational components would benefit from an extended evaluation period between educational session and the administration of the post-test. Also, the short timeframe meant only a small number of charts could be audited. The four-week period also meant the providers' compliance to the screening protocol was measured on a short-term basis (approximately 30 days) (VanderKooi et al., 2018).

Data Analysis

A study based on a small sample can risk an inflated standard deviation and cause erroneous results within the population the sample represents (Smith & Nobel, 2014). As there was only a limited number of participants at the project site, it is vital to mention the limitation that may arise due to providers' strong feeling of wanting to change/improve the status quo, therefore heightening their participation (Smith & Nobel, 2014). This may lead to a bias of the pre- and post-test scores due to an increased interest already developed during the project's early discussion/brainstorming phase.

Dissemination

The target population for dissemination is both Touro University's faculty and the stakeholders at the project site. Dissemination of project findings and outcomes will be delivered to the university's faculty, including the DNP project chair, DNP project members, and School of Nursing professors, in the form of an oral and PowerPoint presentation. After which, the findings will be presented to the healthcare providers and stakeholders at the project site and an oral and

PowerPoint presentation. The presentation will include results from the educational training session, the screening protocol compliance results, and the effect of compliance on the number of patients screened. For the project to have significance in the wider nursing setting, the project lead plans to disseminate the findings to other facilities where T2DM patients are being treated. For example, the practice site is currently planning to expand and open new clinics in the near future, planning to implement the screening protocol. The results of the evidence-based project must be shared on the DNP project repository. Though this archive will not be classified as a publication due to the lack of peer-reviews, other DNP graduates can share the results of their work in the nursing community for enhanced learning.

Project Sustainability

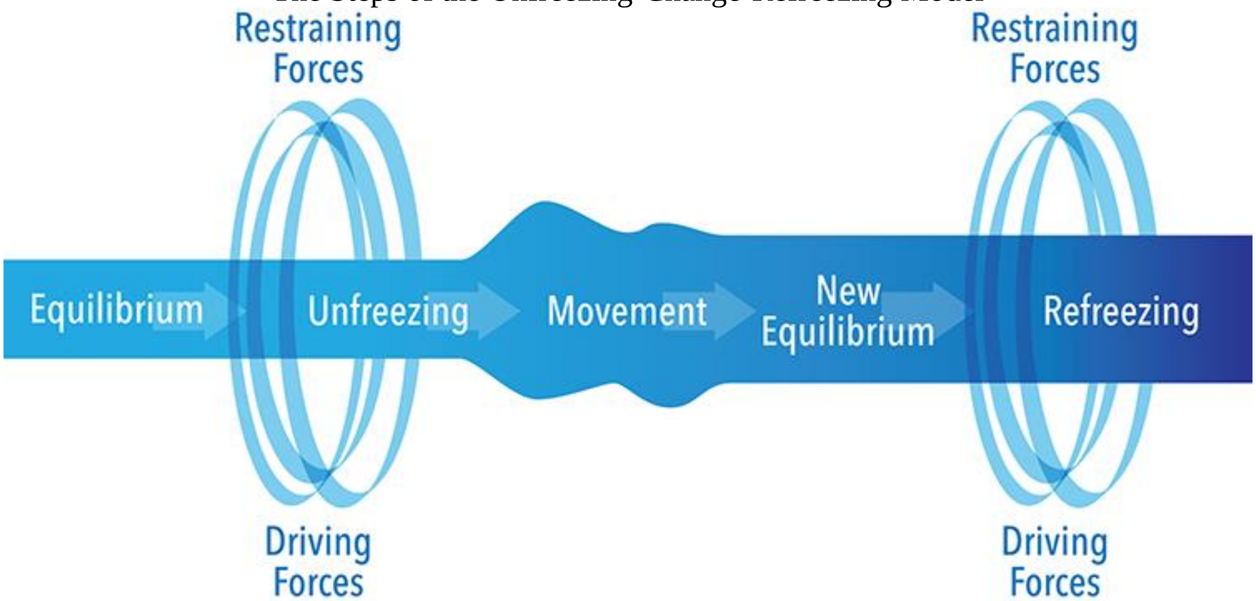
As a result of the DNP project, the providers had accepted the implementation of a vitamin B12 deficiency screening protocol at the practice site, although this was monitored over a short period. Therefore, in order for the practice change to be sustainable, it needs to be made permanent and monitored over a long period (Bakaria et al., 2017). Sustainability can be achieved through new organizational structures for the practice change (Batras et al., 2016). Specifically, ensuring ongoing monthly audits to continue reinforcing the use of the recent practice change. This has been requested and will be achieved as the project lead continues to work at the practice site and has maintained a good working relationship with the practice site owner. It may also be beneficial to create awareness of vitamin B12 deficiency, screening tools and communicate any changes in screening attempts to new staff members. The practice site owner has discussed it with the primary stakeholders to make the new screening protocol as part of the new employment packet to be in place before the opening of the new clinics. Additionally, the project lead will maintain the screening protocol and serve as a consultant at the practice site.

Conclusion

The implementation of a vitamin B-12 deficiency screening protocol in the primary care setting created a change in the status quo and workflow of the facility, validating the need for an outlined protocol to improve vitamin B-12 deficiency screening. This project was completed by incorporating the opinions, questions, and support of all stakeholders. Timely screening, diagnosis, and treatment of vitamin B-12 deficiency improves the quality of life of the affected patients and reduces complications (Kancherla et al., 2016; Strohle et al., 2019). The project findings are consistent with evidence-based studies that reported change in a primary care setting requires a multi-dimensional approach (Batras et al., 2016). Providers with improved awareness of vitamin B-12 deficiency, who support their leadership team, are more likely to utilize the screening protocol and provide the appropriate treatment consistently. Thus, increasing the screening of vitamin B-12 deficiency in a primary care clinic led to an overall improvement in patient care and the quality of life of T2DM patients on metformin therapy.

Appendix

Appendix A
The Steps of the Unfreezing-Change-Refreezing Model



Appendix A shows the tenets in Lewin's Framework for Change Management Theory. Image from Udod, S., & Wagner, J. (2018).

Appendix B

Letter outlining the authorization for the project to be completed at the project site

CARLOS A. ALVAREZ, M.D., INC.

ALVAREZ HEALTHCARE

5400 Aldrin Court
Bakersfield, CA 93313
Tel: (661) 489-5999
Fax: (661) 489-5991

Josephine Hernandez Letter of Approval

09/01/2020

I grant DNP student Josephine Hernandez permission to conduct a quality improvement project titled:

"Improving Vitamin B-12 Screening Rates in Adults with Type 2 Diabetes Mellitus in a Rural Primary Care Setting" at Alvarez Health Care Clinic, in Bakersfield, California.

Sincerely,

Jeannette Camacho

General Manager/Business Administrator for Alvarez Healthcare Inc.

Appendix C

CONTENT VALIDITY INDEX TOOL

Content Validity Index Table

Item	Expert 1 (Dr. Peckham)	Expert 2 (Dr. Zabriskie)	Expert 3 (Dr. C. Grant)	Mean
1	4	4	4	4.0
2	4	4	4	4.0
3	4	4	4	4.0
4	4	4	4	4.0
5	4	4	4	4.0
6	4	4	4	4.0
7	4	4	4	4.0
8	4	4	4	4.0
9	4	4	4	4.0
10	4	4	4	4.0

The procedure consists of having experts rate items on a four-point scale of relevance. Then, for each item, the item (CVI) (I-CVI) is computed as the number of experts giving a rating of 3 or 4 divided by the number of experts.

The content validity index is calculated using the following formula:

CVR = [(E-(N/2)) / (N/2)] with E representing the number of experts who rated the item as Moderately Relevant or Highly Relevant and N being the total number of experts.

The mean total of all of the means was 4.0 indicating that all of the questions were moderately/highly relevant.

The calculation is as follows:

CVR = [(3-(3/2)) / (3/2)]

CVR = (3-3/2) / (3/2)

CVR = (6/3-3/2) / (3/2)

CVR = 3/2*2/3 = 6/6 = 1

Appendix D

PRE-TEST

1. What is the normal range of vitamin B-12 in the body?

A. 150-180 ng/L
B. 200-300 ng/L
C. 200-800 ng/L
D. <150-200 ng/L

2. What are the symptoms of vitamin B-12 deficiency?

A. Fatigue
B. Constipation
C. Neurological changes
D. All of the above

3. What are some of the causes of vitamin B-12 deficiency?

A. Diet and medications
B. Exercise
C. Dietary supplements
D. None of the above

4. Complications of vitamin B-12 deficiency:

A. Peripheral neuropathy
B. Oral Sores
C. Memory loss
D. All of the above

5. Vitamin B12 is naturally found in which of the following?

A. Fish, meat
B. Poultry, eggs,
C. Milk, and milk products.
D. All of the above

6. You suspect your patient has low or borderline levels of vitamin B-12, which of the following methods should be used for diagnosis? <u>Select all that apply</u>.

A. Methylmalonic acid
B. Holo transcobalamin
C. Serum vitamin B-12 levels
D. Intrinsic factor antibodies

7. Treatment for vitamin B-12 deficiency. Select all that apply.
A. IM injections of hydroxocobalamin 1000 mcg every 2nd day until no further improvement
B. IM injections of hydroxocobalamin 1000 mcg every 2 months for life
C. Oral cobalamin 3 times a week for 2 weeks
D. Twice yearly hydroxocobalamin 1000 mcg injections

8. Maintenance of vitamin B-12 levels in patients with neurological symptoms.
A. IM injections of hydroxocobalamin 1000 mcg every 4 months for life
B. IM injections of hydroxocobalamin 1000 mcg every 2 months for life
C. Oral cobalamin 3 times a week for 2 weeks
D. Quarterly hydroxocobalamin 1000 mcg injections

9. What is the recommended daily dietary intake of vitamin B-12 for 14-year-olds and above?
A. Male 2.4 mcg; female 2.4 mcg; during pregnancy 2.6 mcg; lactation 2.8 mcg
B. Male 2.6 mcg; female 2.6 mcg; during pregnancy 2.8 mcg; lactation 3.0 mcg
C. Male 2.2 mcg; female 2.2 mcg; during pregnancy 2.4 mcg; lactation 2.6 mcg
D. Male 2.8 mcg; female 2.8 mcg; during pregnancy 3.0 mcg; lactation 3.2 mcg

10. How is vitamin B-12 used in the body? Select all that apply.
A. Vitamin B12 is involved in the formation of red blood cells and helps to create and regulate DNA synthesis
B. Vitamin B-12 enables the release of energy by helping the human body absorb folic acid
C. The metabolism of every cell in the body depends on vitamin B- 12, as it plays a part in the synthesis of fatty acids and energy production
D. Vitamin B-12 is required for amino acid metabolism

POST-TEST

1. What is the normal range of vitamin B-12 in the body?
A. 150-180 ng/L
B. 200-300 ng/L
C. 200-800 ng/L
D. <150-200 ng/L

2. What are the symptoms of vitamin B-12 deficiency?
A. Fatigue
B. Constipation
C. Neurological changes
D. All of the above

3. What are some of the causes of vitamin B-12 deficiency?
A. Diet and medications
B. Exercise
C. Dietary supplements
D. None of the above

4. Complications of vitamin B-12 deficiency:
A. Peripheral neuropathy
B. Oral Sores
C. Memory loss
D. All of the above

5. Vitamin B12 is naturally found in which of the following?
A. Fish, meat
B. Poultry, eggs,
C. Milk, and milk products.
D. All of the above

6. You suspect your patient has low or borderline levels of vitamin B-12, which of the following methods should be used for diagnosis? <u>Select all that apply</u>.
A. Methylmalonic acid
B. Holo transcobalamin
C. Serum vitamin B-12 levels
D. Intrinsic factor antibodies

7. Treatment for vitamin B-12 deficiency. <u>Select all that apply</u>.

A. IM injections of hydroxocobalamin 1000 mcg every 2nd day until no further improvement
B. IM injections of hydroxocobalamin 1000 mcg every 2 months for life
C. Oral cobalamin 3 times a week for 2 weeks
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B. IM injections of hydroxocobalamin 1000 mcg every 2 months for life
C. Oral cobalamin 3 times a week for 2 weeks
D. Quarterly hydroxocobalamin 1000 mcg injections

9. What is the recommended daily dietary intake of vitamin B-12 for 14-year-olds and above?
A. Male 2.4 mcg; female 2.4 mcg; during pregnancy 2.6 mcg; lactation 2.8 mcg
B. Male 2.6 mcg; female 2.6 mcg; during pregnancy 2.8 mcg; lactation 3.0 mcg
C. Male 2.2 mcg; female 2.2 mcg; during pregnancy 2.4 mcg; lactation 2.6 mcg
D. Male 2.8 mcg; female 2.8 mcg; during pregnancy 3.0 mcg; lactation 3.2 mcg

10. How is vitamin B-12 used in the body? Select all that apply.
A. Vitamin B12 is involved in the formation of red blood cells and helps to create and regulate DNA synthesis
B. Vitamin B-12 enables the release of energy by helping the human body absorb folic acid
C. The metabolism of every cell in the body depends on vitamin B- 12, as it plays a part in the synthesis of fatty acids and energy production
D. Vitamin B-12 is required for amino acid metabolism

Appendix E

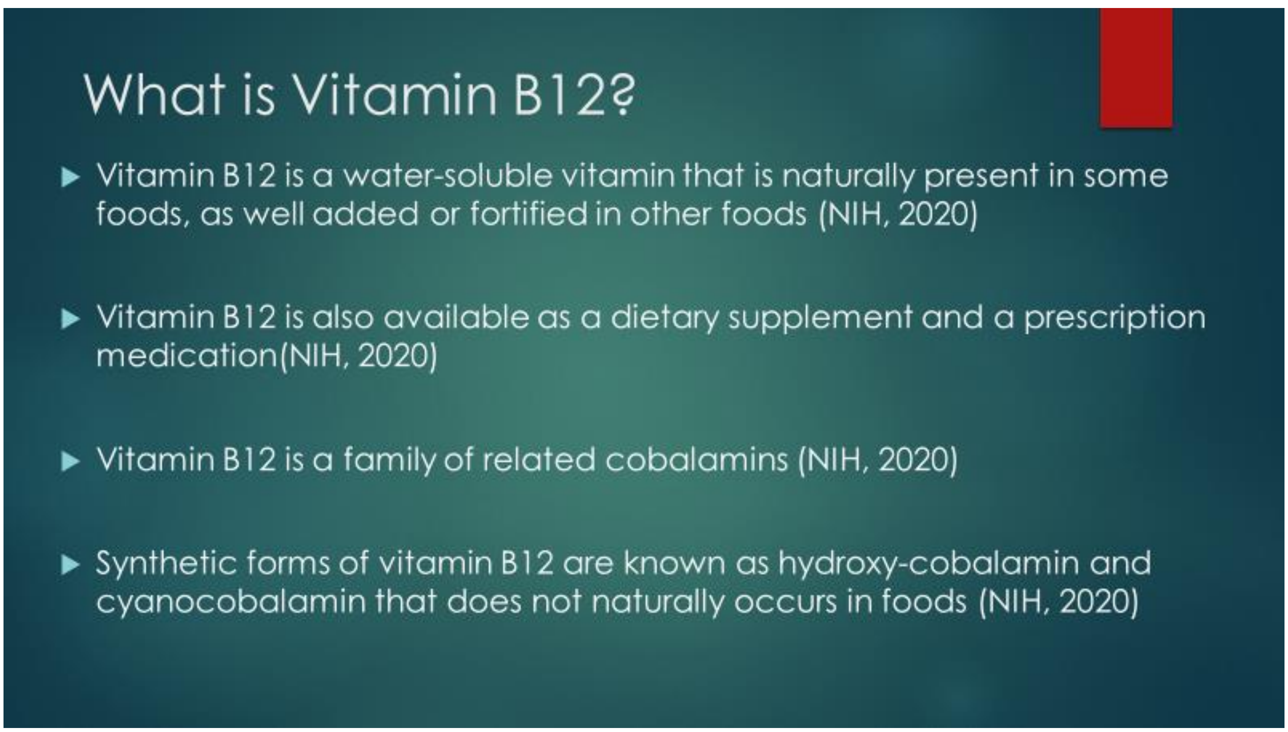
PRE AND POST TEST SCORE SHEET

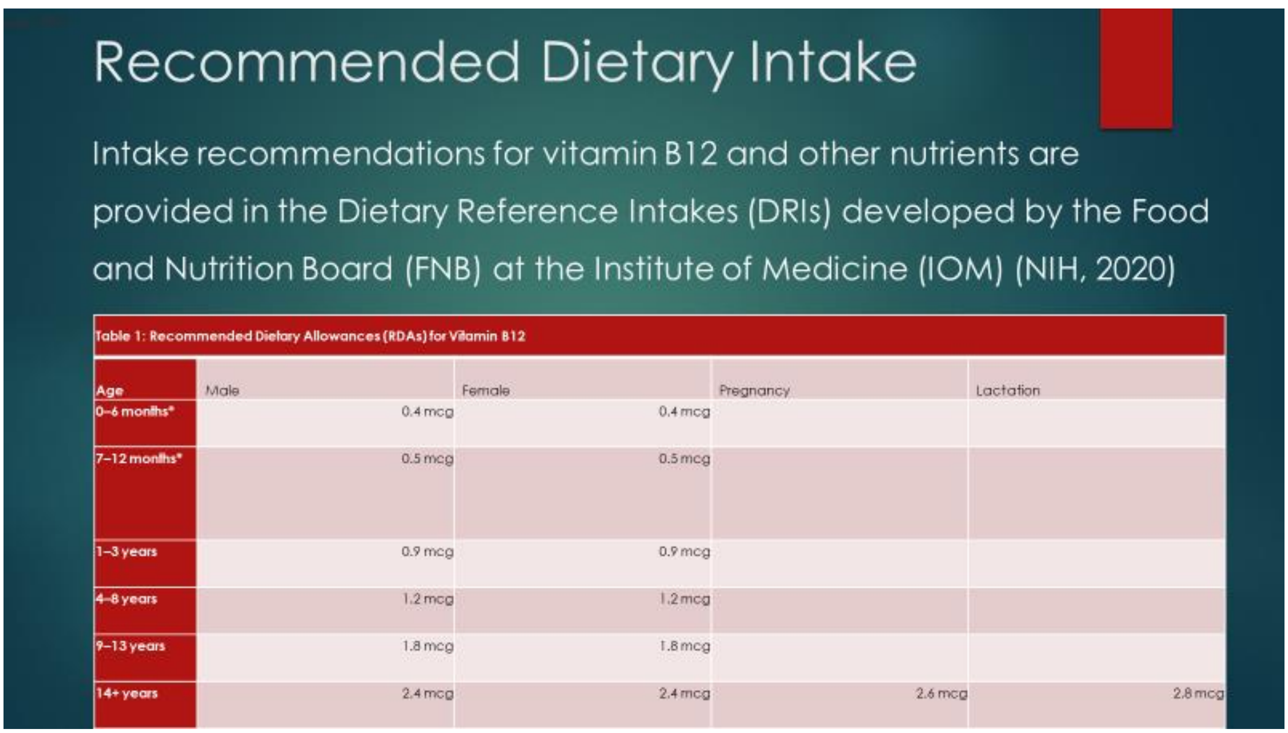
VITAMIN B-12 DEFICIENCY PRE AND POST TEST SCORE SHEET

Participant #	PRE TEST SCORE	POST TEST SCORE	Remediation needed Yes/No

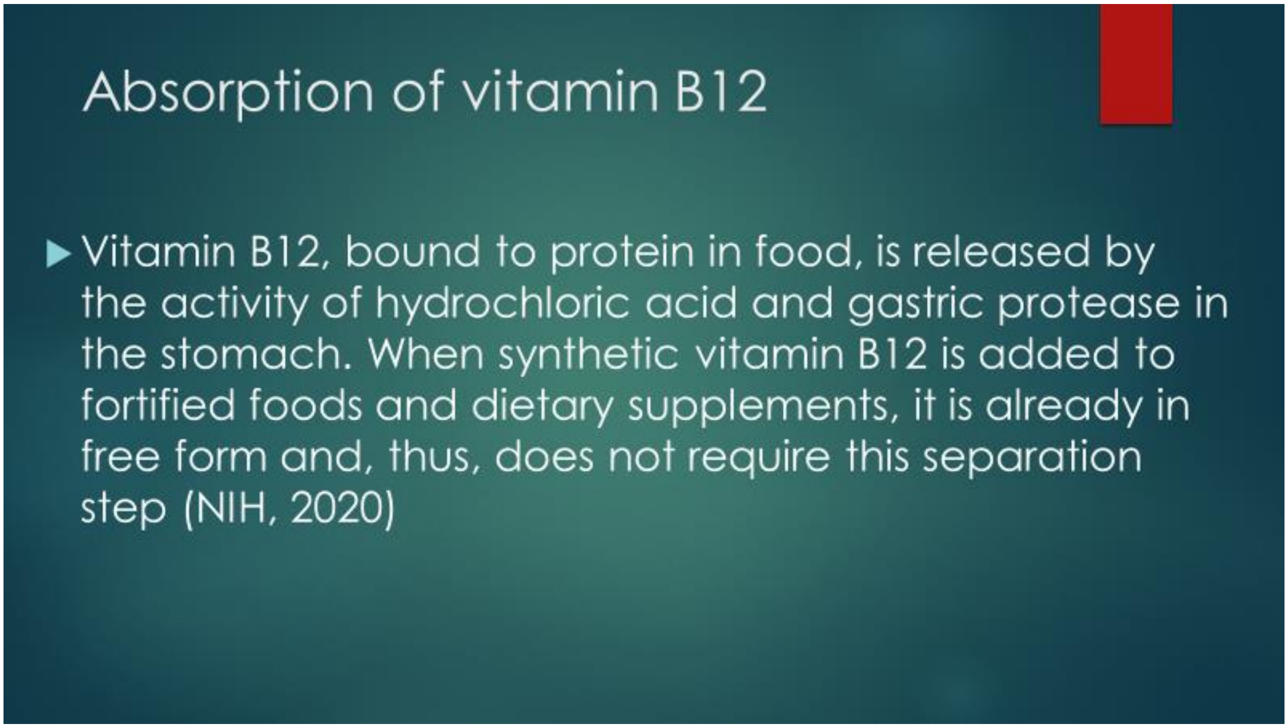
Appendix F

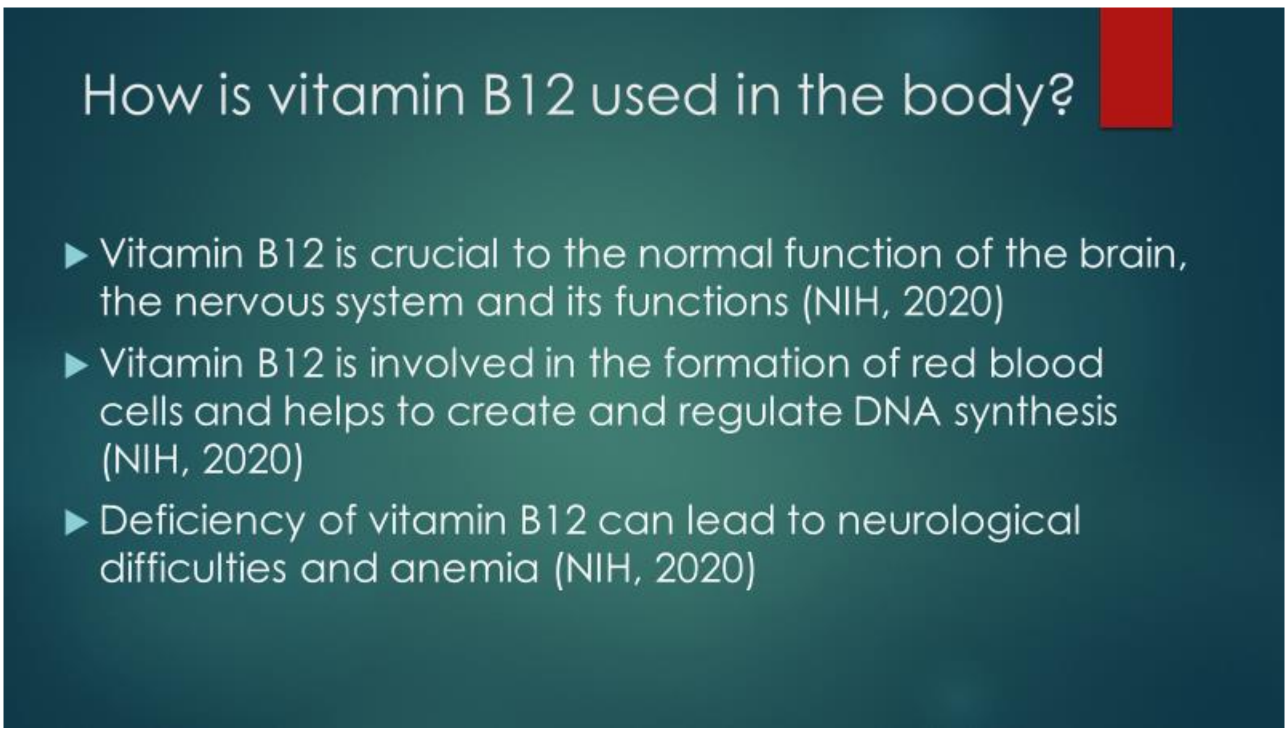
EDUCATIONAL PRESENTATION

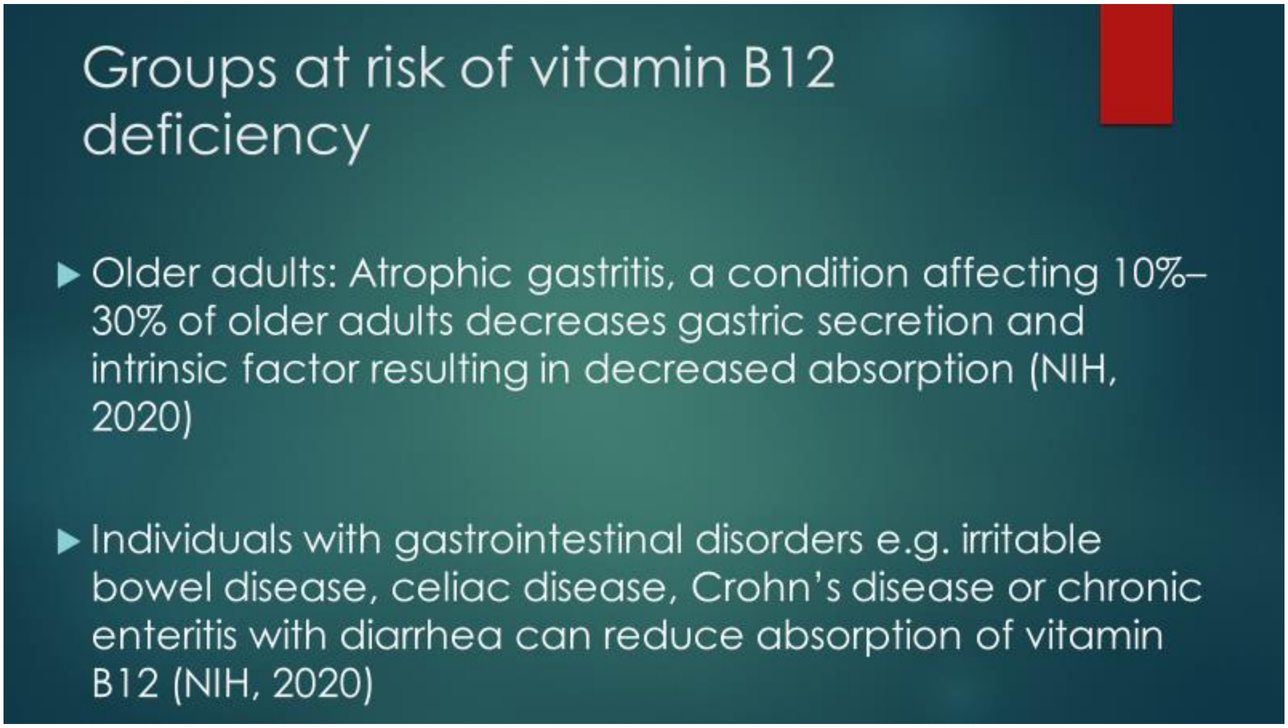


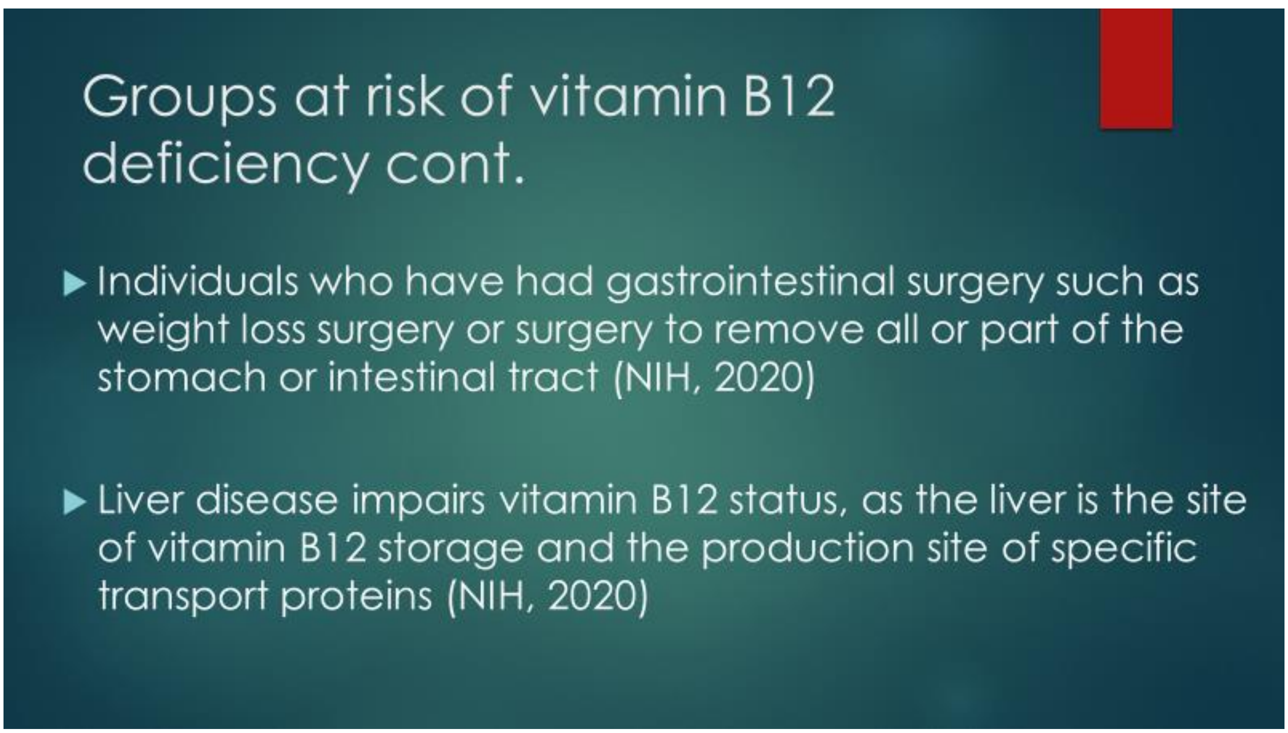


Age	Male	Female	Pregnancy	Lactation
0–6 months*	0.4 mcg	0.4 mcg		
7–12 months*	0.5 mcg	0.5 mcg		
1–3 years	0.9 mcg	0.9 mcg		
4–8 years	1.2 mcg	1.2 mcg		
9–13 years	1.8 mcg	1.8 mcg		
14+ years	2.4 mcg	2.4 mcg	2.6 mcg	2.8 mcg

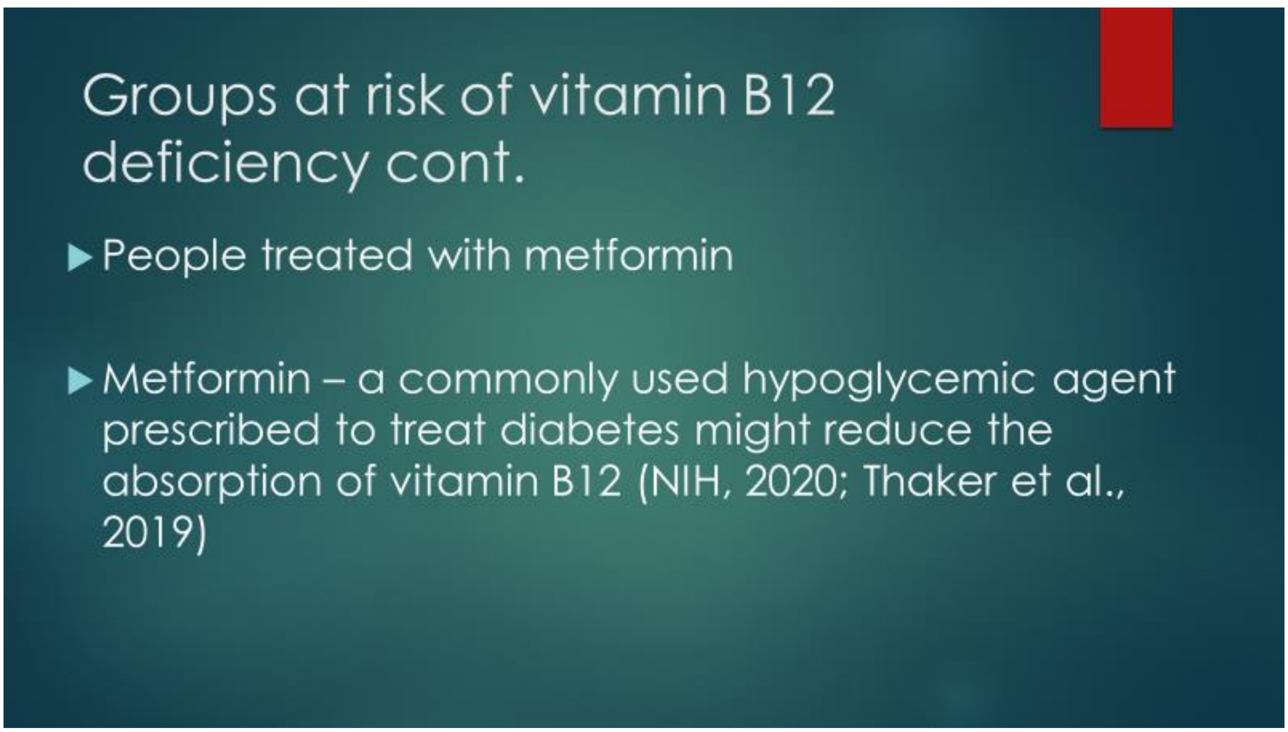

Absorption of vitamin B12
Vitamin B12, bound to protein in food, is released by the activity of hydrochloric acid and gastric protease in the stomach. When synthetic vitamin B12 is added to fortified foods and dietary supplements, it is already in free form and, thus, does not require this separation step (NIH, 2020)

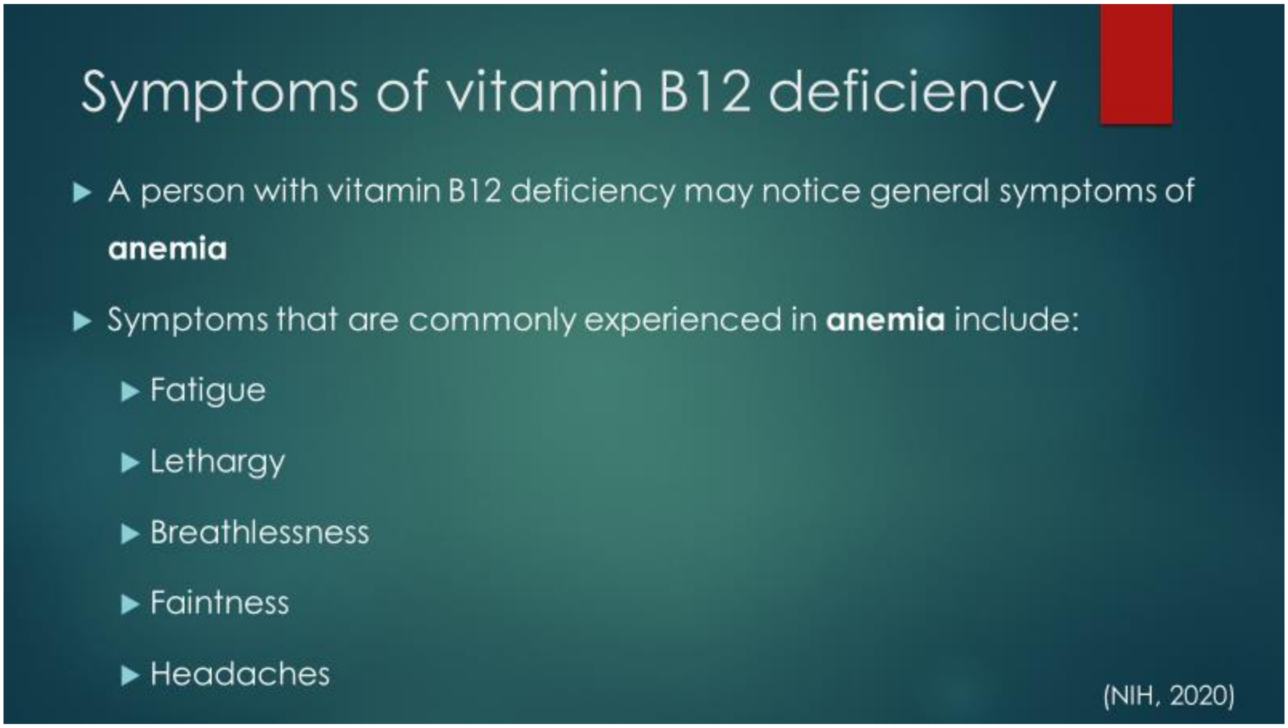

How is vitamin B12 used in the body?
Vitamin B12 is crucial to the normal function of the brain, the nervous system and its functions (NIH, 2020)
Vitamin B12 is involved in the formation of red blood cells and helps to create and regulate DNA synthesis (NIH, 2020)
Deficiency of vitamin B12 can lead to neurological difficulties and anemia (NIH, 2020)

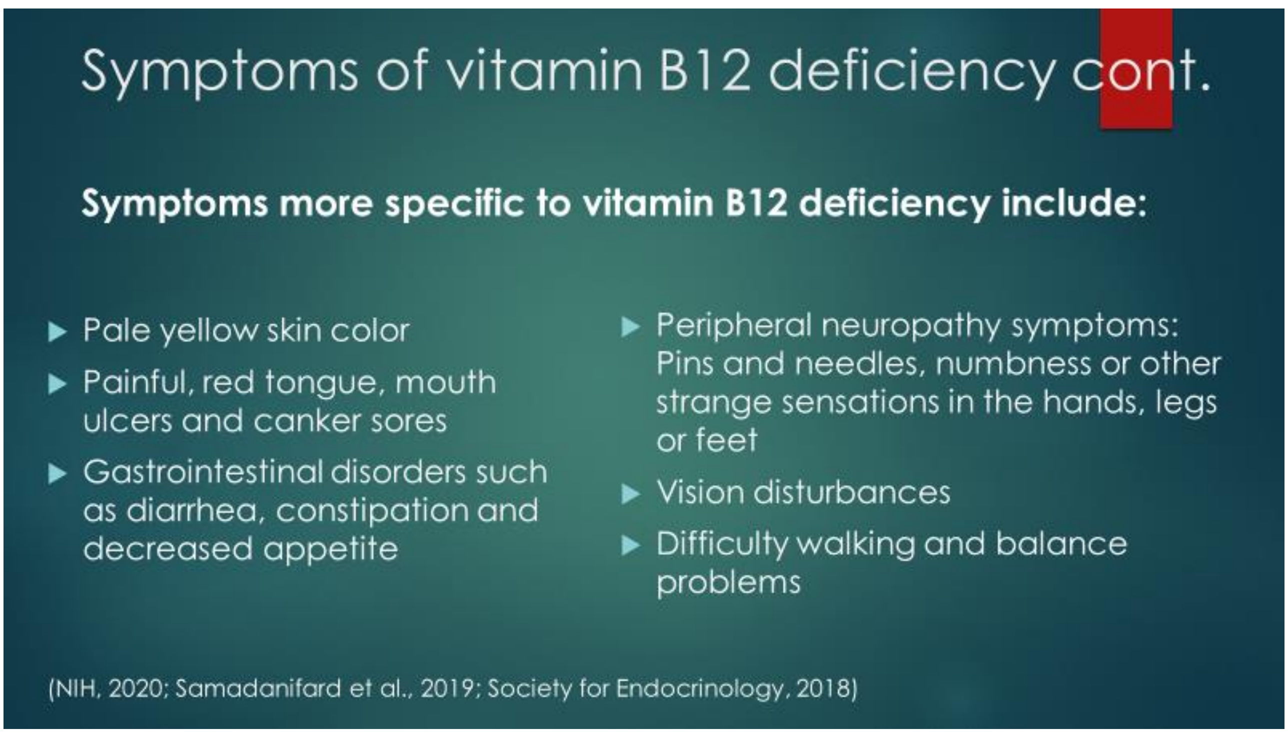

Groups at risk of vitamin B12 deficiency
Older adults: Atrophic gastritis, a condition affecting 10%–30% of older adults decreases gastric secretion and intrinsic factor resulting in decreased absorption (NIH, 2020)
Individuals with gastrointestinal disorders e.g. irritable bowel disease, celiac disease, Crohn's disease or chronic enteritis with diarrhea can reduce absorption of vitamin B12 (NIH, 2020)

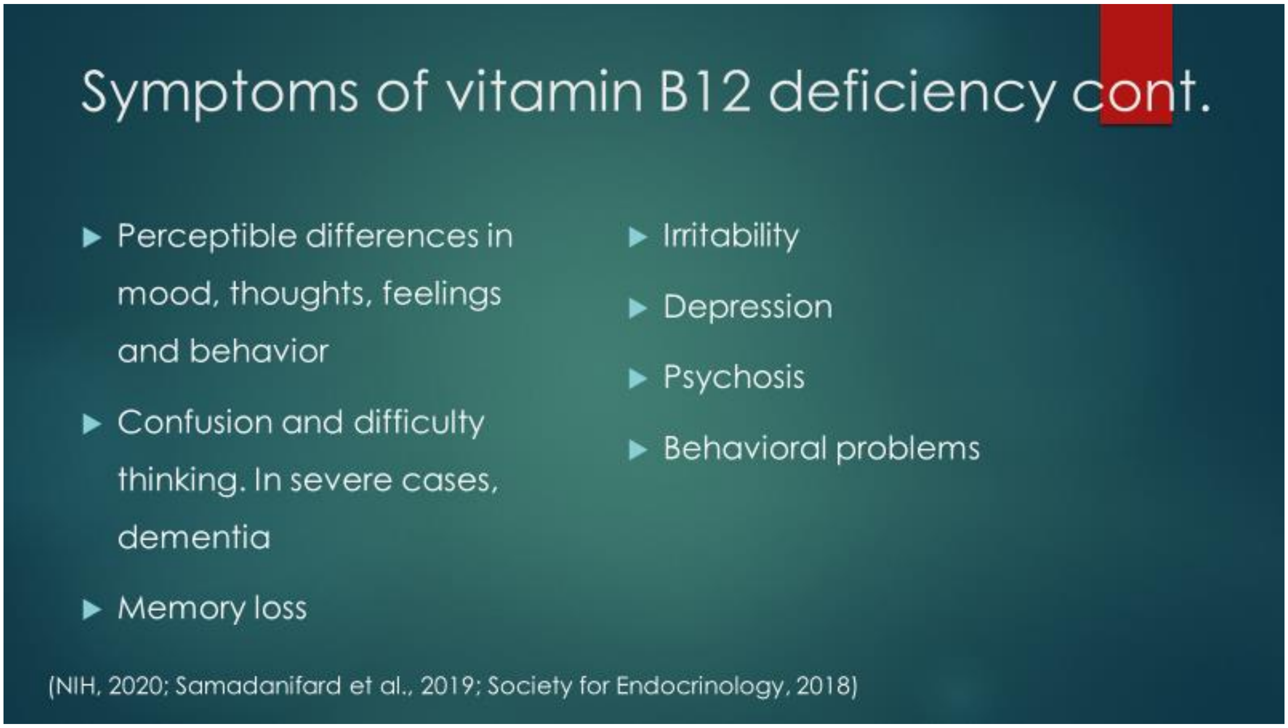

Groups at risk of vitamin B12 deficiency cont.
Individuals who have had gastrointestinal surgery such as weight loss surgery or surgery to remove all or part of the stomach or intestinal tract (NIH, 2020)
Liver disease impairs vitamin B12 status, as the liver is the site of vitamin B12 storage and the production site of specific transport proteins (NIH, 2020)

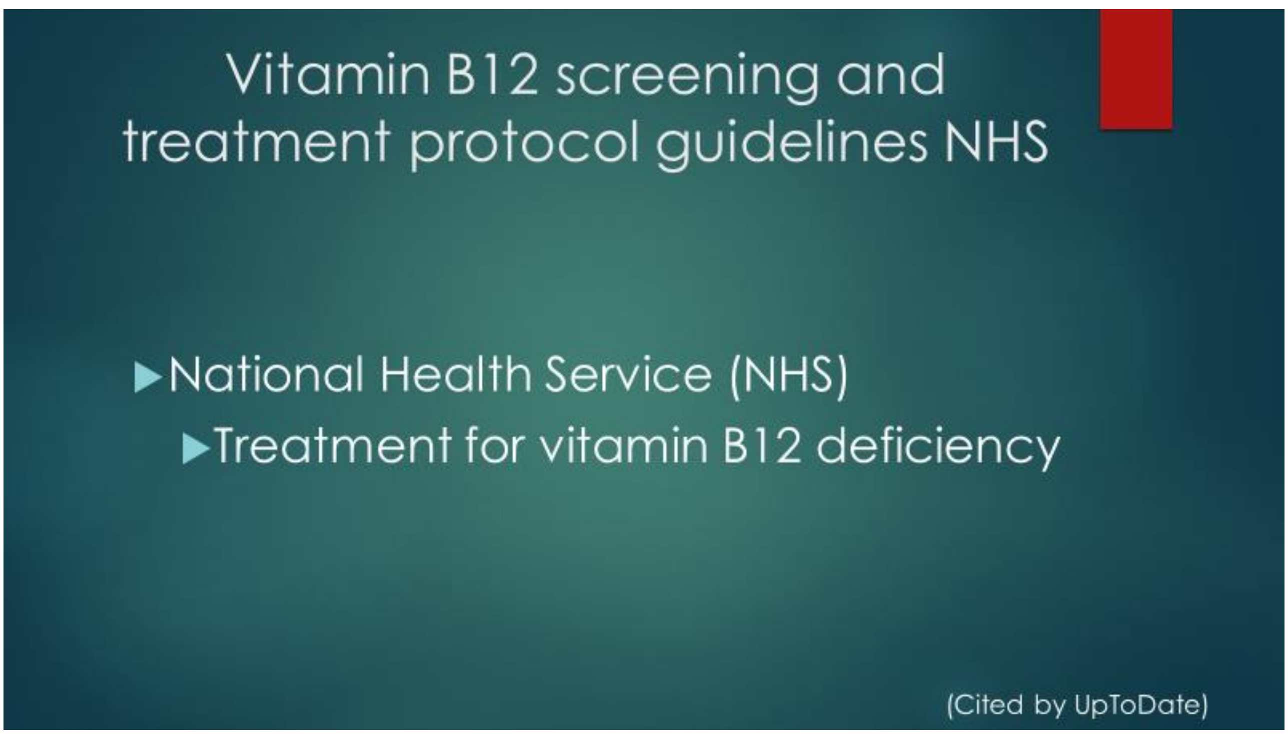

Groups at risk of vitamin B12 deficiency cont.
Vegetarians and vegans: Strict vegetarian and vegan diets (devoid of animal products) are at high risk because natural food sources of vitamin B12 are limited to animal foods (NIH, 2020)
Individuals on certain medications such as proton pump inhibitors or H2 receptor antagonists (NIH, 2020)

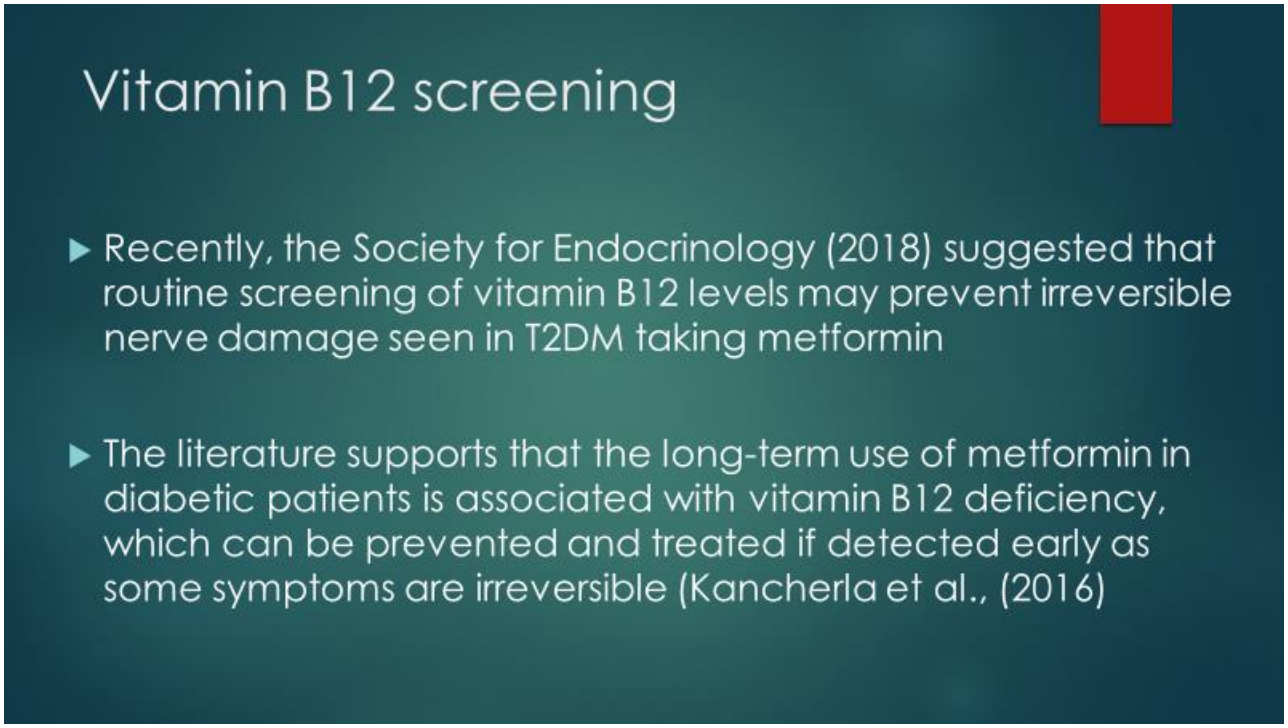

Groups at risk of vitamin B12 deficiency cont.
People treated with metformin
Metformin – a commonly used hypoglycemic agent prescribed to treat diabetes might reduce the absorption of vitamin B12 (NIH, 2020; Thaker et al., 2019)

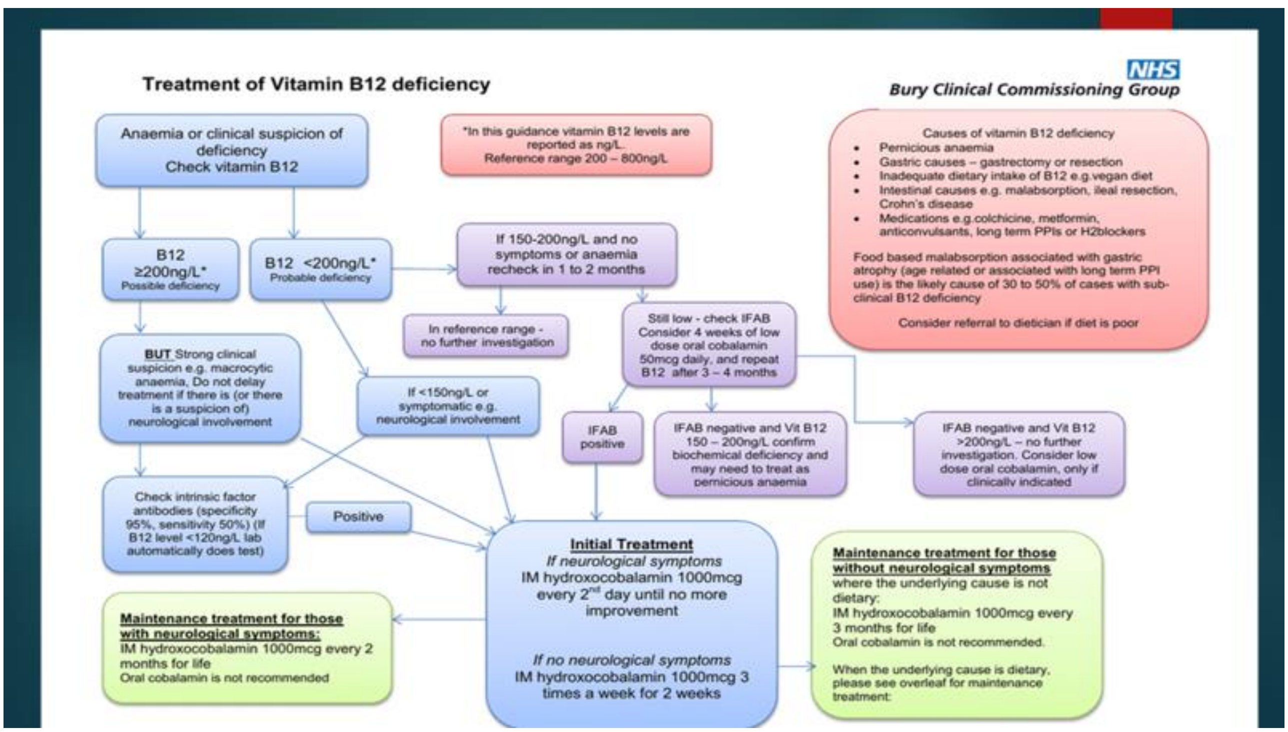

Symptoms of vitamin B12 deficiency
A person with vitamin B12 deficiency may notice general symptoms of **anemia**
Symptoms that are commonly experienced in **anemia** include:
Fatigue
Lethargy
Breathlessness
Faintness
Headaches
(NIH, 2020)

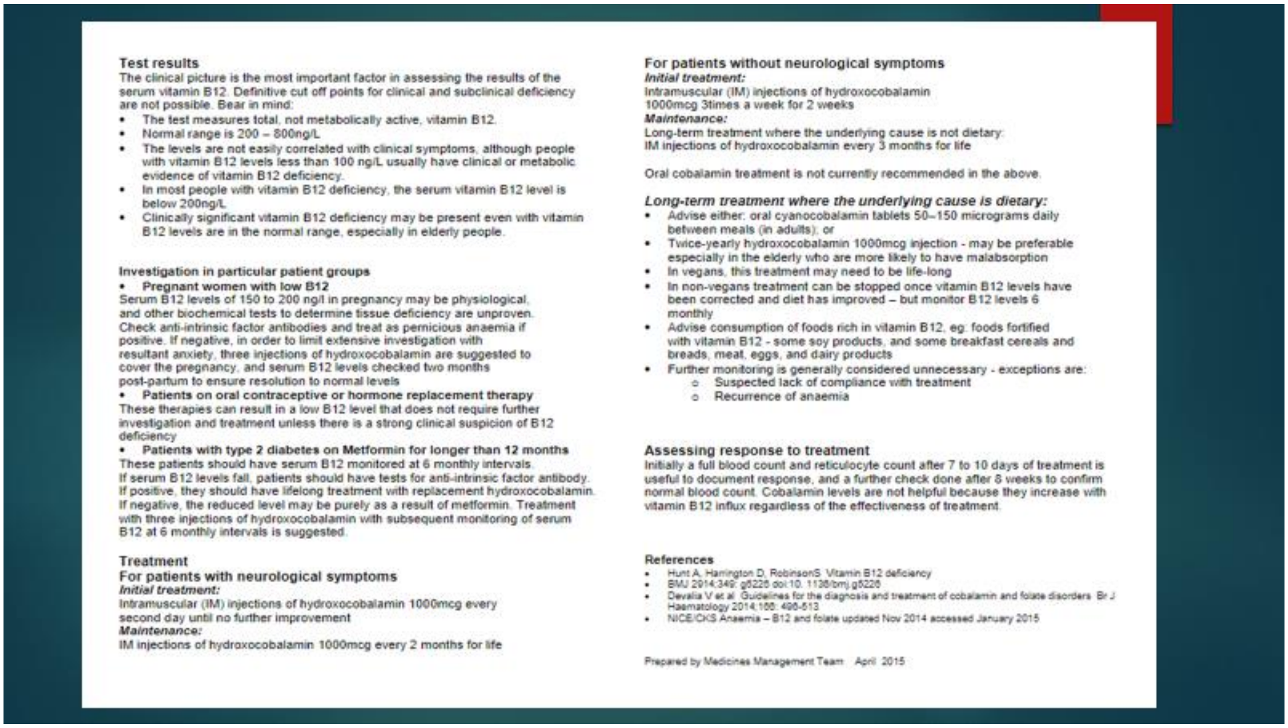

Symptoms of vitamin B12 deficiency cont.
Symptoms more specific to vitamin B12 deficiency include:
Pale yellow skin color
Painful, red tongue, mouth ulcers and canker sores
Gastrointestinal disorders such as diarrhea, constipation and decreased appetite
Peripheral neuropathy symptoms: Pins and needles, numbness or other strange sensations in the hands, legs or feet
Vision disturbances
Difficulty walking and balance problems
(NIH, 2020; Samadanifard et al., 2019; Society for Endocrinology, 2018)


Symptoms of vitamin B12 deficiency cont.
Perceptible differences in mood, thoughts, feelings and behavior
Confusion and difficulty thinking. In severe cases, dementia
Memory loss
Irritability
Depression
Psychosis
Behavioral problems
(NIH, 2020; Samadanifard et al., 2019; Society for Endocrinology, 2018)


Vitamin B12 screening and treatment protocol guidelines NHS
National Health Service (NHS)
Treatment for vitamin B12 deficiency
(Cited by UpToDate)


Vitamin B12 screening
Recently, the Society for Endocrinology (2018) suggested that routine screening of vitamin B12 levels may prevent irreversible nerve damage seen in T2DM taking metformin
The literature supports that the long-term use of metformin in diabetic patients is associated with vitamin B12 deficiency, which can be prevented and treated if detected early as some symptoms are irreversible (Kancherla et al., (2016)


Treatment of Vitamin B12 deficiency
NHS
Bury Clinical Commissioning Group
Anaemia or clinical suspicion of deficiency Check vitamin B12
*In this guidance vitamin B12 levels are reported as ng/L. Reference range 200 – 800ng/L
Causes of vitamin B12 deficiency
Pernicious anaemia
Gastric causes – gastrectomy or resection
Inadequate dietary intake of B12 e.g.vegan diet
Intestinal causes e.g. malabsorption, ileal resection, Crohn's disease
Medications e.g.colchicine, metformin, anticonvulsants, long term PPIs or H2blockers
Food based malabsorption associated with gastric atrophy (age related or associated with long term PPI use) is the likely cause of 30 to 50% of cases with sub-clinical B12 deficiency
Consider referral to dietician if diet is poor
B12 ≥200ng/L* Possible deficiency
B12 <200ng/L* Probable deficiency
If 150-200ng/L and no symptoms or anaemia recheck in 1 to 2 months
In reference range - no further investigation
Still low - check IFAB Consider 4 weeks of low dose oral cobalamin 50mcg daily, and repeat B12 after 3 – 4 months
BUT Strong clinical suspicion e.g. macrocytic anaemia, Do not delay treatment if there is (or there is a suspicion of) neurological involvement
If <150ng/L or symptomatic e.g. neurological involvement
IFAB positive
IFAB negative and Vit B12 150 – 200ng/L confirm biochemical deficiency and may need to treat as pernicious anaemia
IFAB negative and Vit B12 >200ng/L – no further investigation. Consider low dose oral cobalamin, only if clinically indicated
Check intrinsic factor antibodies (specificity 95%, sensitivity 50%) (If B12 level <120ng/L lab automatically does test)
Positive
Initial Treatment
If neurological symptoms
IM hydroxocobalamin 1000mcg every 2nd day until no more improvement
If no neurological symptoms
IM hydroxocobalamin 1000mcg 3 times a week for 2 weeks
Maintenance treatment for those with neurological symptoms:
IM hydroxocobalamin 1000mcg every 2 months for life
Oral cobalamin is not recommended
Maintenance treatment for those without neurological symptoms
where the underlying cause is not dietary:
IM hydroxocobalamin 1000mcg every 3 months for life
Oral cobalamin is not recommended.
When the underlying cause is dietary, please see overleaf for maintenance treatment



Test results

The clinical picture is the most important factor in assessing the results of the serum vitamin B12. Definitive cut off points for clinical and subclinical deficiency are not possible. Bear in mind:

- The test measures total, not metabolically active, vitamin B12.
- Normal range is 200 – 800ng/L
- The levels are not easily correlated with clinical symptoms, although people with vitamin B12 levels less than 100 ng/L usually have clinical or metabolic evidence of vitamin B12 deficiency.
- In most people with vitamin B12 deficiency, the serum vitamin B12 level is below 200ng/L
- Clinically significant vitamin B12 deficiency may be present even with vitamin B12 levels are in the normal range, especially in elderly people.

Investigation in particular patient groups

- **Pregnant women with low B12**

Serum B12 levels of 150 to 200 ng/l in pregnancy may be physiological, and other biochemical tests to determine tissue deficiency are unproven. Check anti-intrinsic factor antibodies and treat as pernicious anaemia if positive. If negative, in order to limit extensive investigation with resultant anxiety, three injections of hydroxocobalamin are suggested to cover the pregnancy, and serum B12 levels checked two months post-partum to ensure resolution to normal levels

- **Patients on oral contraceptive or hormone replacement therapy**

These therapies can result in a low B12 level that does not require further investigation and treatment unless there is a strong clinical suspicion of B12 deficiency

- **Patients with type 2 diabetes on Metformin for longer than 12 months**

These patients should have serum B12 monitored at 6 monthly intervals. If serum B12 levels fall, patients should have tests for anti-intrinsic factor antibody. If positive, they should have lifelong treatment with replacement hydroxocobalamin. If negative, the reduced level may be purely as a result of metformin. Treatment with three injections of hydroxocobalamin with subsequent monitoring of serum B12 at 6 monthly intervals is suggested.

Treatment

For patients with neurological symptoms

Initial treatment:

Intramuscular (IM) injections of hydroxocobalamin 1000mcg every second day until no further improvement

Maintenance:

IM injections of hydroxocobalamin 1000mcg every 2 months for life

For patients without neurological symptoms

Initial treatment:

Intramuscular (IM) injections of hydroxocobalamin 1000mcg 3times a week for 2 weeks

Maintenance:

Long-term treatment where the underlying cause is not dietary:
IM injections of hydroxocobalamin every 3 months for life

Oral cobalamin treatment is not currently recommended in the above.

Long-term treatment where the underlying cause is dietary:

- Advise either: oral cyanocobalamin tablets 50–150 micrograms daily between meals (in adults); or
- Twice-yearly hydroxocobalamin 1000mcg injection - may be preferable especially in the elderly who are more likely to have malabsorption
- In vegans, this treatment may need to be life-long
- In non-vegans treatment can be stopped once vitamin B12 levels have been corrected and diet has improved – but monitor B12 levels 6 monthly
- Advise consumption of foods rich in vitamin B12, eg: foods fortified with vitamin B12 - some soy products, and some breakfast cereals and breads, meat, eggs, and dairy products
- Further monitoring is generally considered unnecessary - exceptions are:
  - Suspected lack of compliance with treatment
  - Recurrence of anaemia

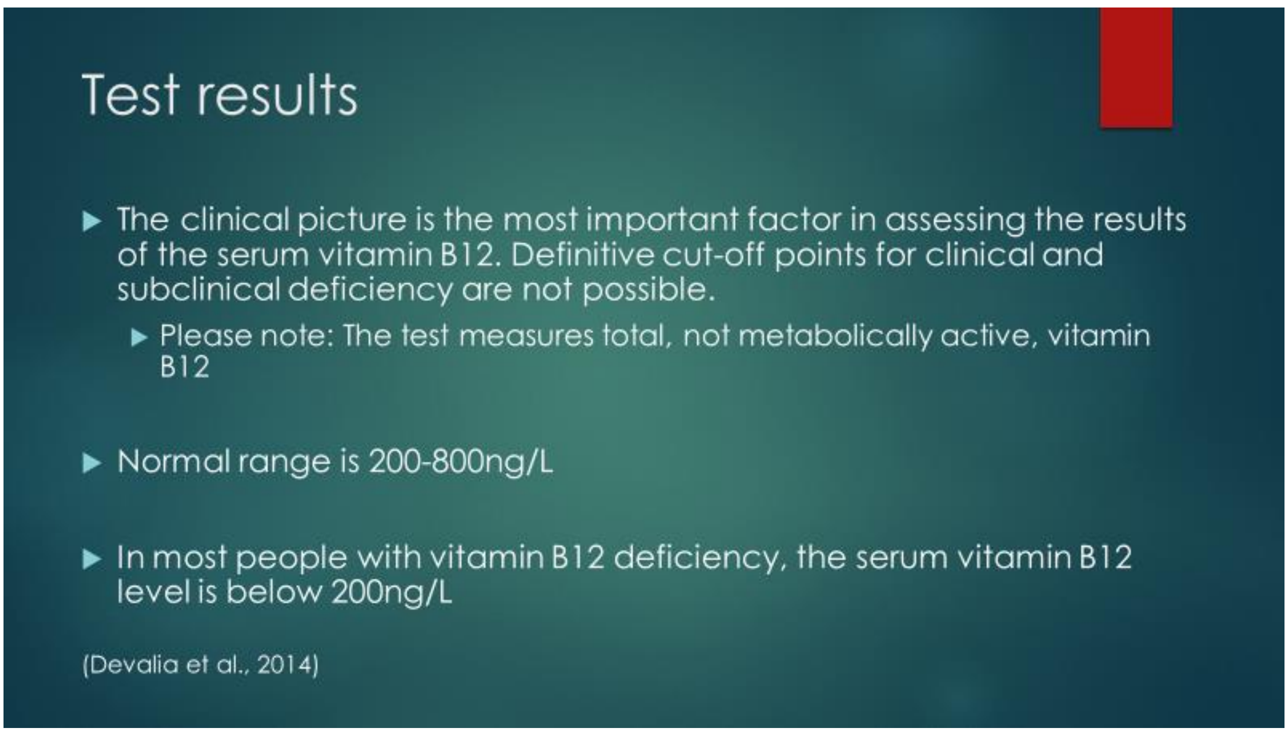
Assessing response to treatment

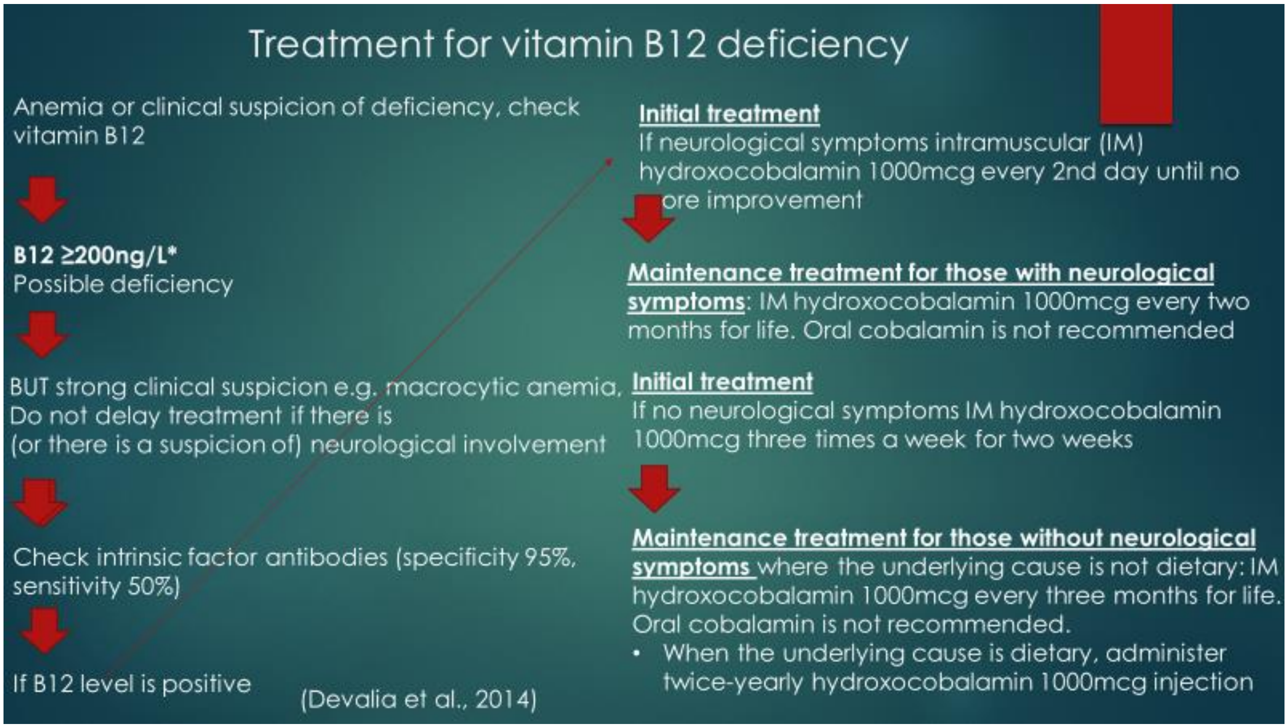
Initially a full blood count and reticulocyte count after 7 to 10 days of treatment is useful to document response, and a further check done after 8 weeks to confirm normal blood count. Cobalamin levels are not helpful because they increase with vitamin B12 influx regardless of the effectiveness of treatment.

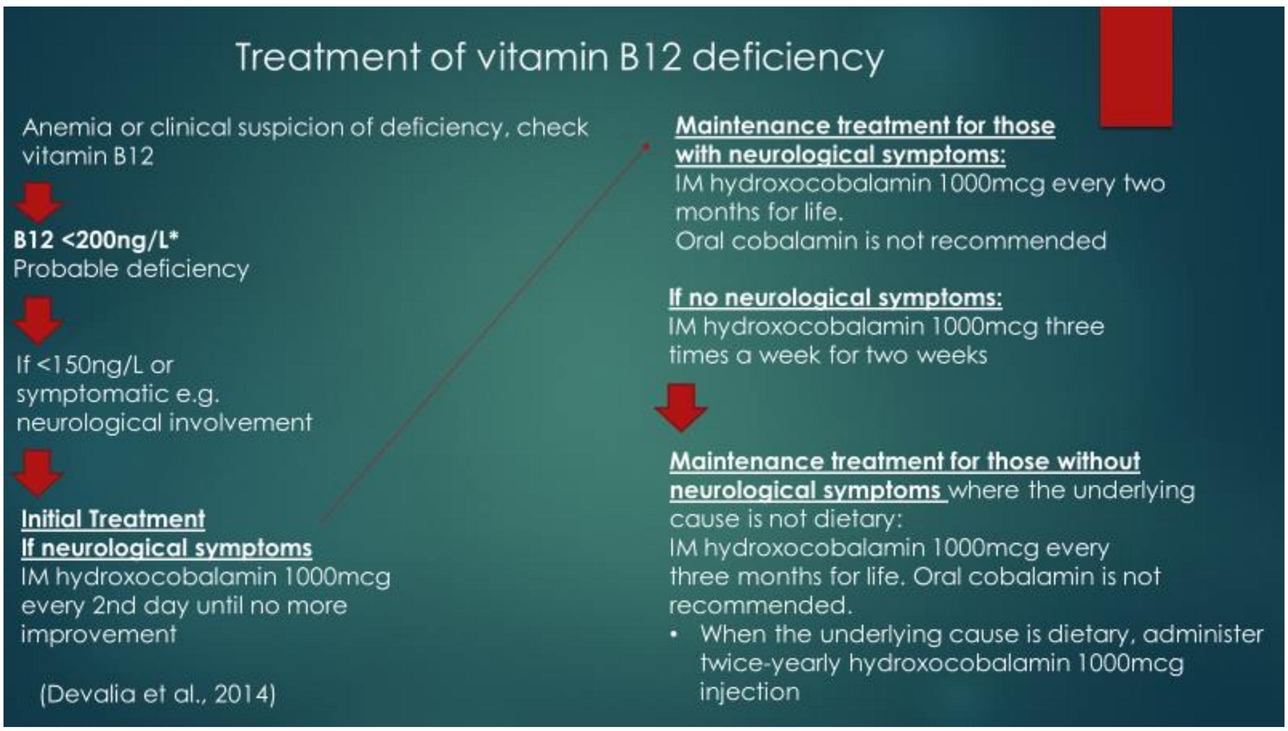
References

- Hunt A, Harrington D, RobinsonS. Vitamin B12 deficiency
- BMJ 2014;349: g5226 doi:10. 1136/bmj.g5226
- Devalia V et al. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. Br J Haematology 2014;166: 496-513
- NICE/CKS Anaemia – B12 and folate updated Nov 2014 accessed January 2015

Prepared by Medicines Management Team April 2015




Treatment for vitamin B12 deficiency
Anemia or clinical suspicion of deficiency, check vitamin B12
B12 ≥200ng/L*
Possible deficiency
BUT strong clinical suspicion e.g. macrocytic anemia, Do not delay treatment if there is (or there is a suspicion of) neurological involvement
Check intrinsic factor antibodies (specificity 95%, sensitivity 50%)
If B12 level is positive
(Devalia et al., 2014)
Initial treatment
If neurological symptoms intramuscular (IM) hydroxocobalamin 1000mcg every 2nd day until no ore improvement
Maintenance treatment for those with neurological symptoms: IM hydroxocobalamin 1000mcg every two months for life. Oral cobalamin is not recommended
Initial treatment
If no neurological symptoms IM hydroxocobalamin 1000mcg three times a week for two weeks
Maintenance treatment for those without neurological symptoms where the underlying cause is not dietary: IM hydroxocobalamin 1000mcg every three months for life. Oral cobalamin is not recommended.
• When the underlying cause is dietary, administer twice-yearly hydroxocobalamin 1000mcg injection


Treatment of vitamin B12 deficiency
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B12 <200ng/L*
Probable deficiency
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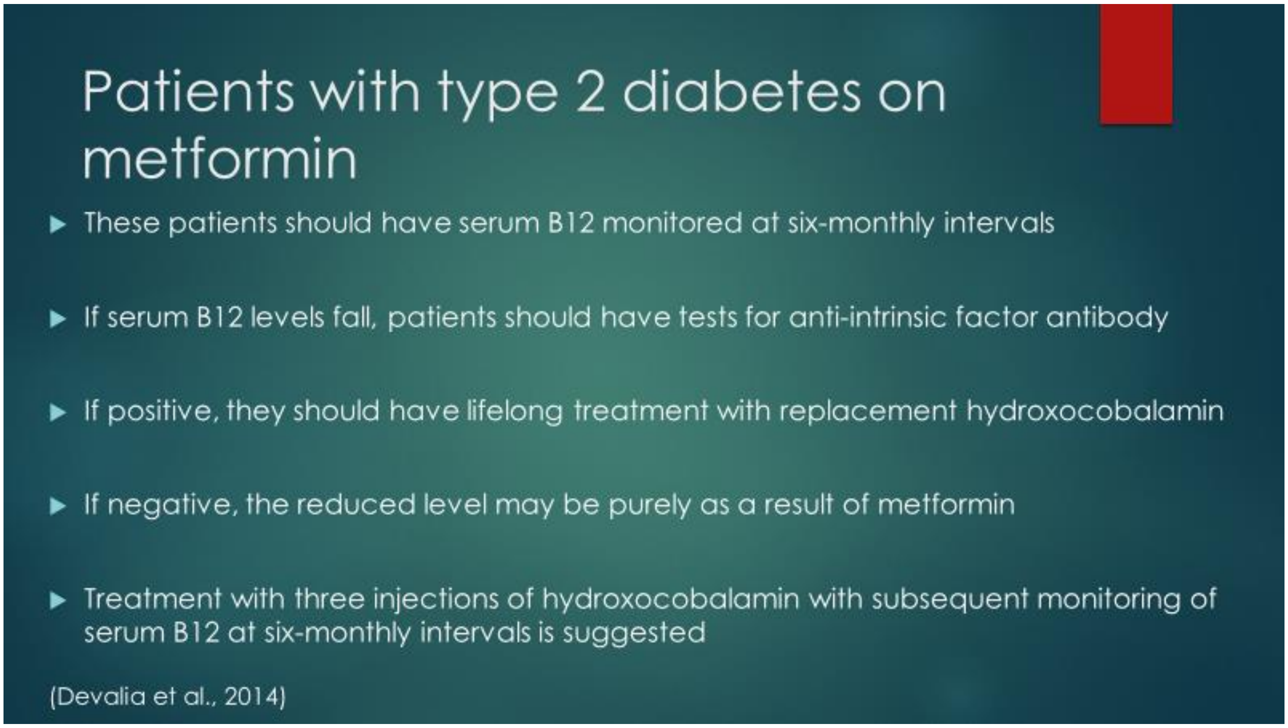
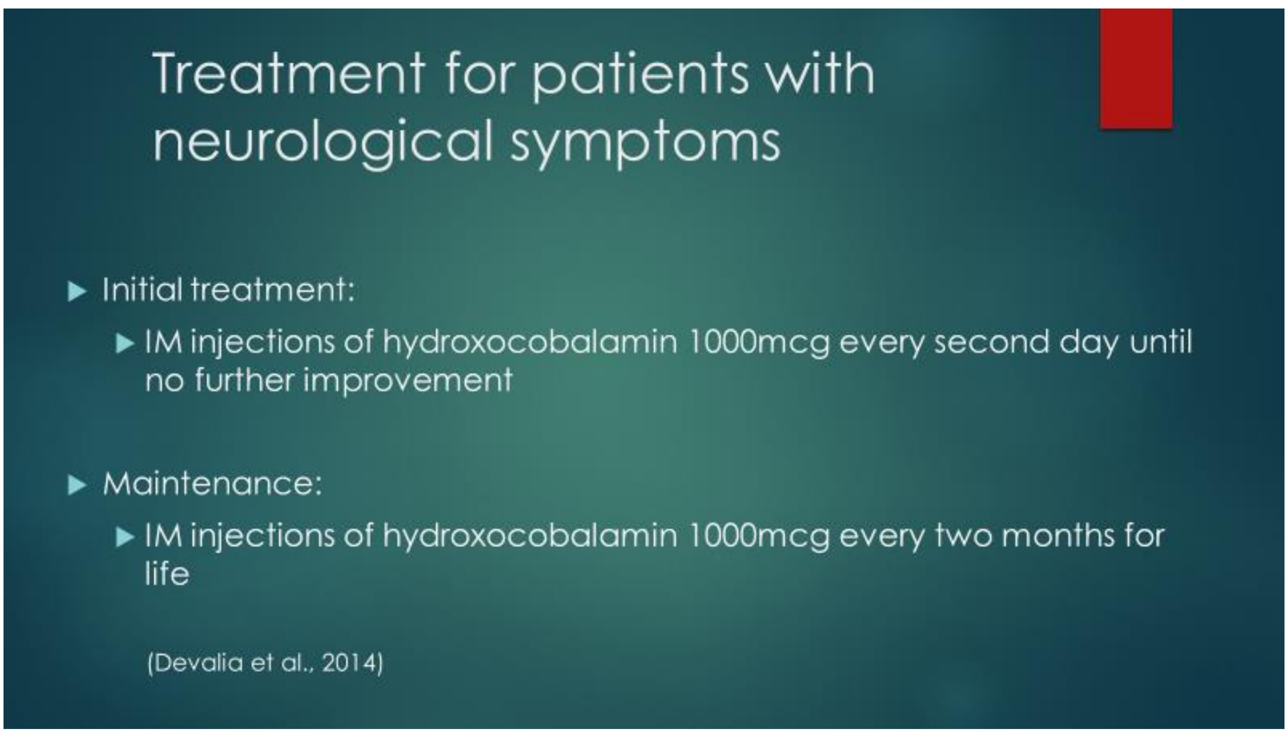
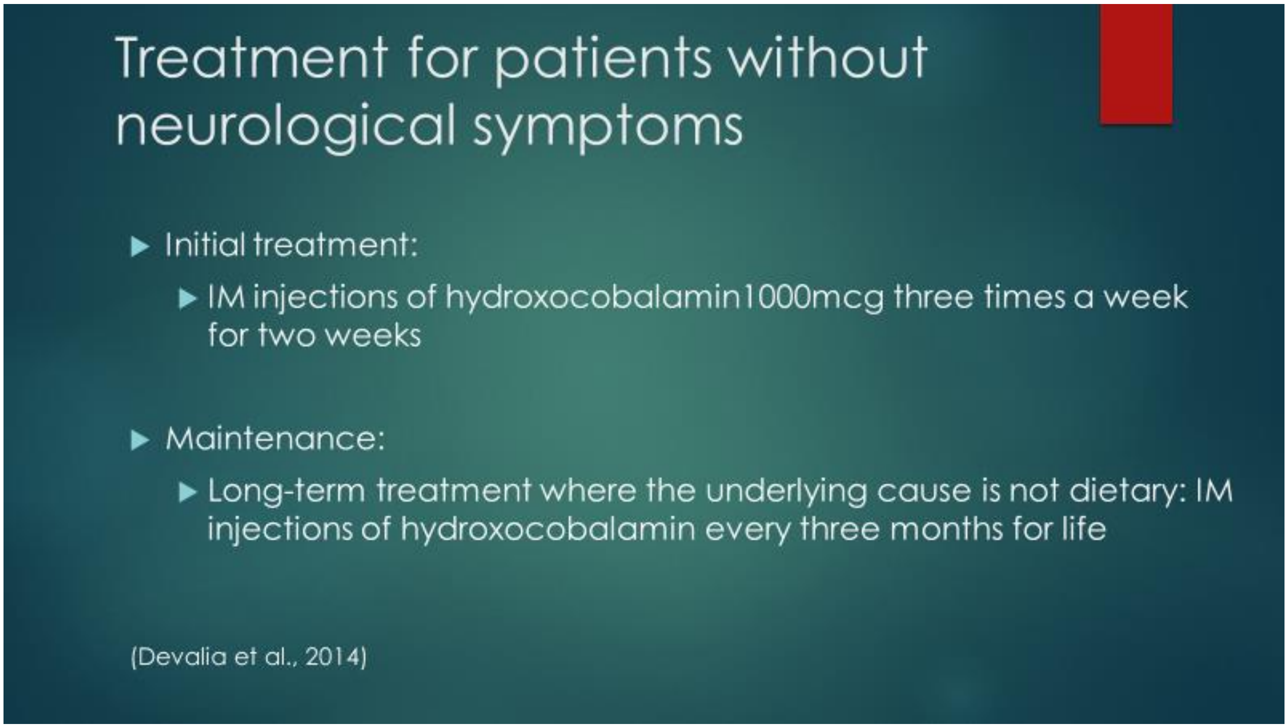

Patients with type 2 diabetes on metformin
These patients should have serum B12 monitored at six-monthly intervals
If serum B12 levels fall, patients should have tests for anti-intrinsic factor antibody
If positive, they should have lifelong treatment with replacement hydroxocobalamin
If negative, the reduced level may be purely as a result of metformin
Treatment with three injections of hydroxocobalamin with subsequent monitoring of serum B12 at six-monthly intervals is suggested
(Devalia et al., 2014)


Treatment for patients with neurological symptoms
Initial treatment:
IM injections of hydroxocobalamin 1000mcg every second day until no further improvement
Maintenance:
IM injections of hydroxocobalamin 1000mcg every two months for life
(Devalia et al., 2014)


Treatment for patients without neurological symptoms
Initial treatment:
IM injections of hydroxocobalamin1000mcg three times a week for two weeks
Maintenance:
Long-term treatment where the underlying cause is not dietary: IM injections of hydroxocobalamin every three months for life
(Devalia et al., 2014)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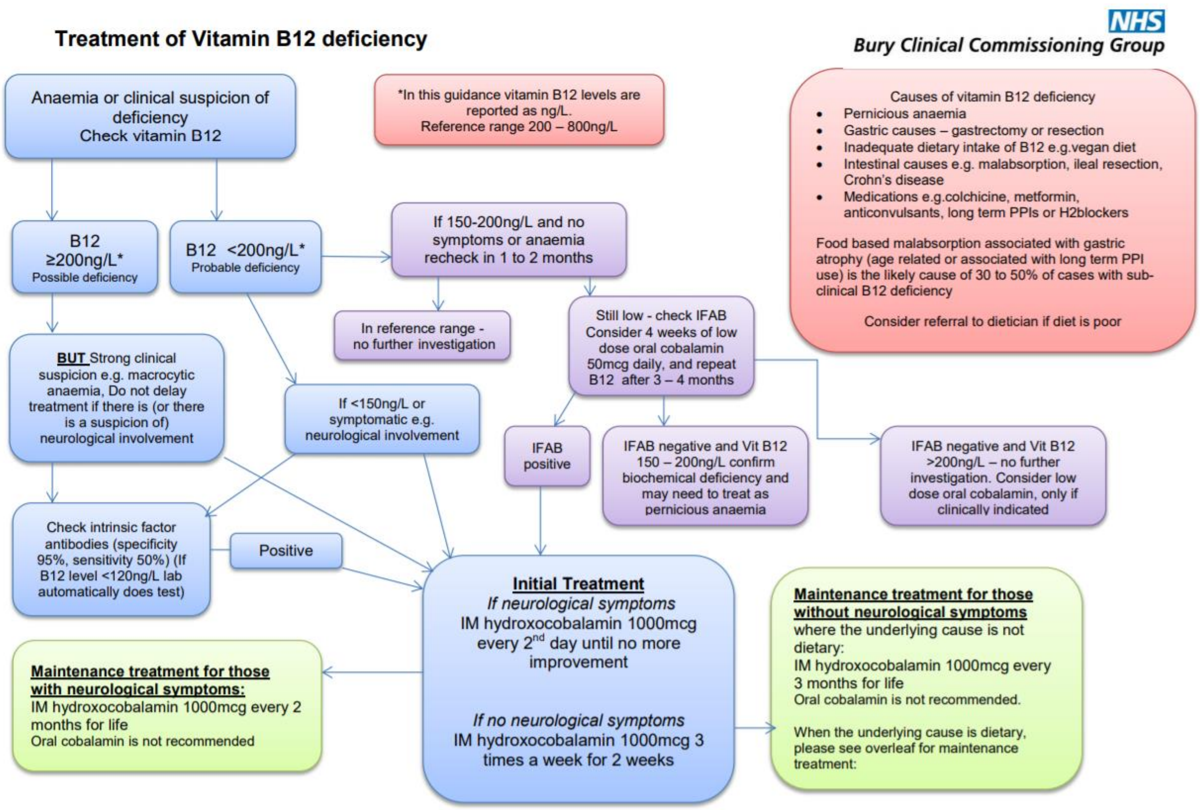
Appendix G

VITAMIN B-12 DEFICIENCY SCREENING AND TREATMENT PROTOCOL



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Treatment

For patients with neurological symptoms
Initial treatment:
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Maintenance:
IM injections of hydroxocobalamin 1000mcg every 2 months for life

For patients without neurological symptoms
Initial treatment:
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Maintenance:
Long-term treatment where the underlying cause is not dietary:
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Oral cobalamin treatment is not currently recommended in the above.

Long-term treatment where the underlying cause is dietary:

- Advise either: oral cyanocobalamin tablets 50–150 micrograms daily between meals (in adults); or
- Twice-yearly hydroxocobalamin 1000mcg injection - may be preferable especially in the elderly who are more likely to have malabsorption
- In vegans, this treatment may need to be life-long
- In non-vegans treatment can be stopped once vitamin B12 levels have been corrected and diet has improved – but monitor B12 levels 6 monthly
- Advise consumption of foods rich in vitamin B12, eg: foods fortified with vitamin B12 - some soy products, and some breakfast cereals and breads, meat, eggs, and dairy products
- Further monitoring is generally considered unnecessary - exceptions are:
  - Suspected lack of compliance with treatment
  - Recurrence of anaemia

Assessing response to treatment
Initially a full blood count and reticulocyte count after 7 to 10 days of treatment is useful to document response, and a further check done after 8 weeks to confirm normal blood count. Cobalamin levels are not helpful because they increase with vitamin B12 influx regardless of the effectiveness of treatment.

References

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Prepared by Medicines Management Team April 2015

Appendix H

CHART AUDIT TOOL FOR VITAMIN B-12 DEFICIENT IN TYPE II DM PATIENTS ON METFORMIN

CHART AUDIT TOOL FOR VITAMIN B-12 DEFICIENCY IN TYPE II DM PATIENTS ON METFORMIN

ID	GENDER M/F	AGE	IS THE DIABETIC PATIENT ON METFORMIN? Y/N	HAS BEEN ON METFORMIN MORE THAN 6 MONTHS? Y/N	DATE OF SERUM VITAMIN B-12 LEVEL	ADDERESSED Y/N	DATE TREATMENT OF VITAMIN B-12

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