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Optimizing Peripheral Neuropathy Management Through Vitamin B12 Screening in Adults With Type Two Diabetes Mellitus Taking Metformin

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OPTOMIZING PERIPHERAL NEUROPATHY MANAGEMENT THROUGH VITAMIN B12 SCREENING IN ADULTS WITH TYPE TWO DIABETES MELLITUS TAKING METFORMIN

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Abstract

Peripheral neuropathy is a significant co-morbidity for patients with diabetes and as early as 1969, metformin was linked to reductions in vitamin B12, leading to deficiency. Vitamin B12 deficiency causes increased levels of homocysteine and methylmalonyl-CoA which are toxic to the nervous system and therefore can contribute to demyelination. This quality improvement study aimed to optimize the management of peripheral neuropathy symptoms by implementing a process to identify patients with clinical or subclinical vitamin B12 deficiency and initiating replacement therapy. Adult patients presenting for a scheduled office visit with a diagnosis of type two diabetes and are taking metformin or medications containing metformin were included in the study. The Michigan Neuropathy Screening Instrument and the NC-stat DPNcheck was used to evaluate symptoms of neuropathy, and serum vitamin B12 levels were used to evaluate vitamin B12 status. The implementation of this process increased the identification of patients with low vitamin B12, thereby reducing the risk of patients in the sample population from developing peripheral neuropathy, reducing symptoms of peripheral neuropathy, or limiting the progression of peripheral neuropathy symptoms. This, therefore, has the potential to improve the quality of life for patients living with type two diabetes that are taking metformin.

Keywords: type two diabetes mellitus, peripheral neuropathy, metformin, vitamin B12

Optimizing Peripheral Neuropathy Management Through Vitamin B12 Screening in Adults With Type Two Diabetes Mellitus Taking Metformin

Metformin is the first-line treatment for patients diagnosed with type two diabetes. According to the Centers for Disease Control and Prevention ([CDC], 2020) Americans living with a diagnosis of prediabetes or diabetes type two is greater than 100 million. Many studies have demonstrated an association between vitamin B12 deficiency and metformin therapy (Yang et al., 2019). Vitamin B12 is a water-soluble vitamin that plays a key role in DNA synthesis, hematopoiesis, and normal function of the peripheral nervous system (Zalaket et al., 2018). Therefore, vitamin B12 deficiency can lead to peripheral neuropathy like that of diabetic neuropathy, megaloblastic anemia, as well as cognitive and memory impairments (Zalaket et al., 2018). According to Polavarapu and Hasbani (2017) homocysteine and methylmalonyl-CoA accumulate in the body due to vitamin B12 deficiency and are toxic to the nervous system. Polavarapu and Hasbani go on to state that the incorporation of abnormal fatty acids into myelin is the result of dysfunctional adenosylcobalamin-dependant methylmalonyl-CoA mutase and methionine synthase causing demyelination. Demyelination can affect the peripheral nerves, the spinal cord, and the white matter of the brain with large-fiber sensory loss affecting the lower extremities first (Polayarapu & Hasbani, 2017).

The mechanism by which metformin causes vitamin B12 malabsorption is unclear. According to Akinlade et al. (2015) several potential mechanisms may influence vitamin B12 deficiency including alteration in small bowel motility, inactivation or inhibition of vitamin B12 absorption, alteration in interactions with cubilin endocytic receptors, or effects on the absorption of vitamin B12-intrinsic factor complex in the terminal ileum related to calcium channels. Clinic FM serves over 680 patients with a diagnosis of diabetes mellitus type two that are on metformin

therapy or therapies that contain metformin. Clinic FM did not have a system in place to identify and screen these patients for vitamin B12 deficiency.

Problem Statement

Patients receiving metformin therapy are at increased risk of developing vitamin B12 deficiency that can contribute to additional co-morbidities such as peripheral neuropathy. Clinic FM did screen diabetic patients for symptoms of peripheral neuropathy during routine diabetic foot exams with the use of monofilament. However, vitamin B12 screening was not part of the process, and the processes to identify peripheral neuropathy needed to be more robust.

Knowledge of a link between metformin therapy and alterations in vitamin B12 absorption was discovered over 50 years ago; however, since then few placebo-controlled studies have been conducted (Aroda et al., 2016). There have been many cross-sectional cohort studies that have recommended routine vitamin B12 screening for patients taking metformin. A systemic review with meta-analysis completed by Chapman et al. (2016) included twenty-five studies in its review and four of those twenty-five were included in the meta-analysis. Chapman et al. stated that metformin decreases vitamin B12 levels at a rate of 57 pmol/L every 6 weeks to 3 months, potentially leading to frank vitamin B12 deficiency. In a post hoc analysis of a randomized control trial (Out et al., 2018) concluded that over time, decreases in vitamin B12 associated with metformin therapy can lead to tissue damage. Furthermore, the researchers stated that metformin was associated with a small increase in a validated neuropathy score, and while not significant, this may have been due to metformin's neuroprotective qualities counteracting the damaging effects of low vitamin B12 (Out et al., 2018). This is an important point as diabetic neuropathy can cause great discomfort and increased comorbid risk to patients. Prevention or early detection of vitamin B12 deficiency could reduce the risk for diabetic patients of developing neuropathy and significantly impact their quality of life.

Assessment

Clinic FM is one of two primary care clinic locations offered by the organization. Clinic FM is located near the intersection of Potranco Road and Dugas Road between State Highways 151 and 1604. At the time of assessment, there were three providers, and organization management was searching for a fourth provider for this location. The clinic hours of operation are Monday through Friday from 8:00 a.m to 5:00 p.m. The staff included a practice administrator and a practice manager that split time between the two clinics, two front office personnel, three medical assistants, and a referral coordinator. A third-party lab phlebotomist was on site to complete specimen collection. Day-to-day clinic operations ran smoothly with limited wait times. Appointment time allocations were as follows: 15 min for follow up or sick visits and 30 min for physicals and new patients.

Clinic FM had a large diabetic population with over 680 patients being identified as having diabetes mellitus type two and currently on metformin therapy or therapies containing metformin in 2019. The organization did not have a process in place to screen this patient population for vitamin B12 deficiency. The organization demonstrated pride in preventive care and improving the patient's quality of life. The owner of this organization was also a provider and had one of the largest patient panels in the practice. The owner was involved in the day to day operation and flow of the clinic as well as the continued satisfaction of other providers and staff. The organization participated in a Merit-based Incentive Payment System with one of the quality improvement programs being Diabetes Care Recognition. One of the quality metrics within Diabetic Care Recognition is the diabetic foot exam which included a sensation component to test neurologic function.

Project Identification

Project Purpose

The purpose of this project was to optimize the management of peripheral neuropathy through the implementation of a screening process targeting vitamin B12 levels and a more robust assessment for peripheral neuropathy in patients with a diagnosis of type two diabetes mellitus receiving metformin therapy or therapies containing metformin.

Project Objectives and Anticipated Outcomes

The first aim was to educate the providers and staff on the new screening process and integrate an identification process into the organization's current electronic health record (EHR) to alert providers and staff of specific patients that meet the criteria for screening. The first objective was to increase the identification and screening of patients in the target population for vitamin B12 deficiency by 75%. The second objective was to initiate treatment in 85% of those patients with clinical or subclinical vitamin B12 deficiency. The third objective was to screen 75% of patients in the target population for peripheral neuropathy using the Michigan Neuropathy Screening Instrument. The overarching goal of this improvement project was to increase the identification of patients in the target population with clinical or subclinical vitamin B12 deficiency and optimize the management of peripheral neuropathy symptoms by prescribing replacement therapy.

Summary and Strength of Evidence

The evidence that supports the monitoring of vitamin B12 levels among patients with type two diabetes consists mainly of cohort and cross-sectional studies with few randomized control trials likely due to ethical concerns as metformin is first-line therapy for type two diabetes mellitus. However, a post hoc analysis of a randomized control trial demonstrated a need for vitamin B12 screening for patients taking metformin.

According to the American Diabetes Association (ADA, 2020) providers should consider monitoring vitamin B12 levels for patients who are taking metformin. Also, for patients with diabetic peripheral neuropathy, vitamin B12 deficiency should be considered as a potential cause (ADA, 2020). Most studies available recommend routine screening of vitamin B12 for diabetic patients taking metformin. In a randomized placebo-control trial conducted over 4.3 years, De Jager et al. (2010) concluded that long-term treatment with metformin increases the risk of vitamin B12 deficiency and that regular measurement should be strongly considered because vitamin B12 deficiency is preventable. Furthermore, Aroda et al. (2016) completed a secondary analysis of the Diabetes Prevention Program and the Diabetes Prevention Program and Outcomes Study and concluded that metformin was associated with lower vitamin B12 levels when compared with placebo after 5 years and there was an association between low vitamin B12 and neuropathy. Aroda et al. (2016) went on to recommend routine screening due to an increased risk of vitamin B12 deficiency with long-term use of metformin.

Neuropathy is an early symptom of vitamin B12 deficiency that presents before megaloblastic anemia, and while the anemia is reversible with supplementation, the neuropathy may not be reversible in all patients (Zalaket et al., 2018). However, the evidence is not consistent in saying that metformin and vitamin B12 deficiency are associated with peripheral neuropathy. Osama et al. (2015) concluded that there was a significant correlation between peripheral neuropathy and vitamin B12 and that supplementation could prevent the condition. Out et al. (2018) reported that it may be difficult to determine if low vitamin B12 is the culprit of peripheral neuropathy because metformin is also known to have neuroprotective properties by lowering HgbA1c that may be counteracting the damaging effects of low vitamin B12. Similarly, Alharbi et al. (2018) concluded that metformin was associated with vitamin B12 deficiency but found no association with peripheral neuropathy. Conversely, Aroda et al. (2016) reported that

the secondary analysis of the Diabetes Prevention Program study data revealed a higher prevalence of peripheral neuropathy in the metformin-treated patients. Gupta et al. (2018) concluded that there was an association between metformin and peripheral neuropathy and recommended that patients receiving metformin treatment should be screened annually for peripheral neuropathy.

Treatment specifically for vitamin B12 deficiency related to metformin has not been widely studied. Due to the hypothesized mechanism by which metformin affects the absorption of vitamin B12, it would seem logical that the parental route of supplementation would be preferred. However, according to Kancherla et al. (2016) patients who took a daily multivitamin while on metformin had significantly higher vitamin B12 levels when compared to those who did not take a daily multivitamin. This would suggest that the enteral route may be acceptable, although this is only one study. Traditionally vitamin B12 replacement is accomplished by the parental route, usually 1,000 µg IM injection daily or weekly to start and then monthly for maintenance (Pawlak, 2017). Recently however, the oral route has begun to gain favor due to the less-invasive nature; it is thought that oral supplements remain in the plasma for longer periods, and there is a significant cost reduction when compared to the parental route (Pawlak, 2017). Furthermore, according to Bauman et al. (2000) calcium supplementation can be used to reverse the malabsorption of vitamin B12 caused by metformin.

Methods

Setting and Population

This quality improvement project was conducted in a suburban primary care clinic in the city of San Antonio, Texas. The target population included adult patients with a diagnosis of diabetes type two that were currently taking metformin or medication that contains metformin as part of their treatment regimen.

Intervention

The intervention began when a patient that was included in the target population entered the clinic. When checking the patient in, the front office staff provided the patient with the patient portion of the Michigan Neuropathy Screening Instrument (MNSI) and asked them to complete the questionnaire. The questionnaire was given to patients at this time as to not cause a delay in the normal workflow. The questionnaire was later collected and scored by the medical assistant (MA) that brought the patient to the exam room; see Appendix A for copy of MNSI. The MA then proceeded to complete the assessment portion of the neuropathy exam to include the appearance of the feet, noting any deformities, fissures, dry skin or calluses, or signs of infection. The MA also completed monofilament testing by applying the monofilament to 10 different locations on each foot with enough pressure to slightly bend the monofilament. The patient having their eyes closed during this test was asked to respond yes when they felt the monofilament touching their foot. The medical assistants at FM were previously trained to execute a diabetic foot exam which included this portion of the neuropathy exam. The MAs were also educated on the vibration sense exam using a 128 Hz tuning fork and how to test ankle reflexes with a reflex hammer. Using the teach-back method the MAs were able to demonstrate competence with these tests. The MAs then scored the responses to the monofilament test and indicated normal sensation as at least eight out of ten correct responses, one to seven correct responses meaning reduced sensation, and zero correct responses as absent sensation (University of Michigan, 2000). MAs also tested vibration perception through the application of a 128 Hz tuning fork to the distal interphalangeal joint of the right and left great toe. Vibration perception was documented as normal if the vibration was sensed by the person administering the test for less than 10 s after the patient no longer sensed the vibration, reduced if the person administering the test sensed vibration for greater than or equal to 10 s after the patient no longer sensed the

vibration, or absent if the patient reported no sensation of vibration during this test (University of Michigan, 2000). Next, the MAs tested ankle reflexes and documented as present, present with reinforcement if the Jendrassic maneuver was employed, or absent (University of Michigan, 2000); see Appendix B for instruction of MNSI use. The final component of the exam included the application of the NC-stat DPNCheck device to the medial malleolus of the right or left ankle and testing the velocity and amplitude of the electrical signals transmitted through the sural nerve (NEUROMetrix, 2019). Normal results for the NC-stat DPNCheck were amplitude greater than 4 μV and velocity greater than 40 m/s, mild neuropathy results were amplitude greater than 4 μV and velocity less than 40 m/s, moderate neuropathy results were amplitude less than 4 μV and velocity greater than or less than 40 m/s, and severe neuropathy results were amplitude less than 4 μV and velocity less than 40 m/s (NEUROMetrix, 2019).

The providers then ordered lab tests and patients had blood samples collected by a phlebotomist to evaluate their serum vitamin B12 levels. Patients with documented vitamin B12 deficiency or subclinical deficiency were prescribed treatment with oral vitamin B12 supplementation of 1,000 mcg and calcium 1,000 mg per day (Bauman et al., 2000; Schijns et al., 2018).

Participants completed the patient version of the MNSI, and medical assistance completed the physical exam portion during a regularly scheduled office visit. The total score and individual questions for the patient version were quantified and the physical assessment scores were quantified. A score greater than two on the physical assessment portion was considered abnormal (Moghtaderia et al., 2006). Serum vitamin B12 levels were collected by venipuncture with deficiency being defined as vitamin B12 less than 200 pg/ml and subclinical deficiency being defined as vitamin B12 of 200-400 pg/ml.

The MNSI was validated by Moghtaderia et al. (2006) who concluded that the MNSI is an accurate and useful tool for diabetic neuropathy. The manufacture of NC-stat DPNcheck has over 30 examples of validation that includes published studies, abstracts and posters, and a conference presentation (NEUROMetrix, 2019).

Facilitators and Barriers

Clinic FM was well equipped with knowledgeable staff and motivations to provide high-quality healthcare that improved the quality of life for patients. The clinic had a phlebotomist on site which would increase the likelihood of compliance with blood collection for this study. The equipment that was used for the intervention was readily available at clinic FM. The EHR operating system used by the clinic for documentation was used to provide electronic prescriptions directly to pharmacies. A request was made to the EHRs customer support to add a quality measure that included vitamin B12 screening for patients in the target population to aid in the identification and tracking. This request was denied and presented a barrier that was overcome by manually flagging patients that met the criteria for inclusion in this new process.

Ethical Considerations

Patients who participated in the study were not recruited; participants included in the target population that presented to the clinic for a previously scheduled office visit made up the sample. During the office visit participants were subjected to venipuncture, however venipuncture is minimally invasive and is part of the routine care for this population. Participant's privacy was protected by limiting patient identifiers. Regarding treatment, providers employed shared decision making and education to allow for patient autonomy.

Results

This quality improvement initiative included $N = 47$ patients that had a diagnosis of diabetes mellitus type two and were taking the drug metformin or medication with metformin in

it. The implementation took place during the Spring of 2020 over 10 weeks. Table 1 summarizes the demographics of the 47 participants that were seen in the clinic during the implementation period.

Table 1

Summary Characteristics

Demographics	*n*	%
Ethnicity		
Hispanic	26	55.3
Non-Hispanic	6	12.8
Patient Declined	5	31.9
Gender		
Male	15	31.9
Female	32	68.1
Payer Mix		
PPO/HMO	18	38.3
Medicare/Medicaid	11	23.4
Commercial	4	8.5
Other	14	29.8

Note. Total sample size ($N = 47$) with a mean age of 54.74 years old ranging from 34-76 years old ($SD = 10.8$).

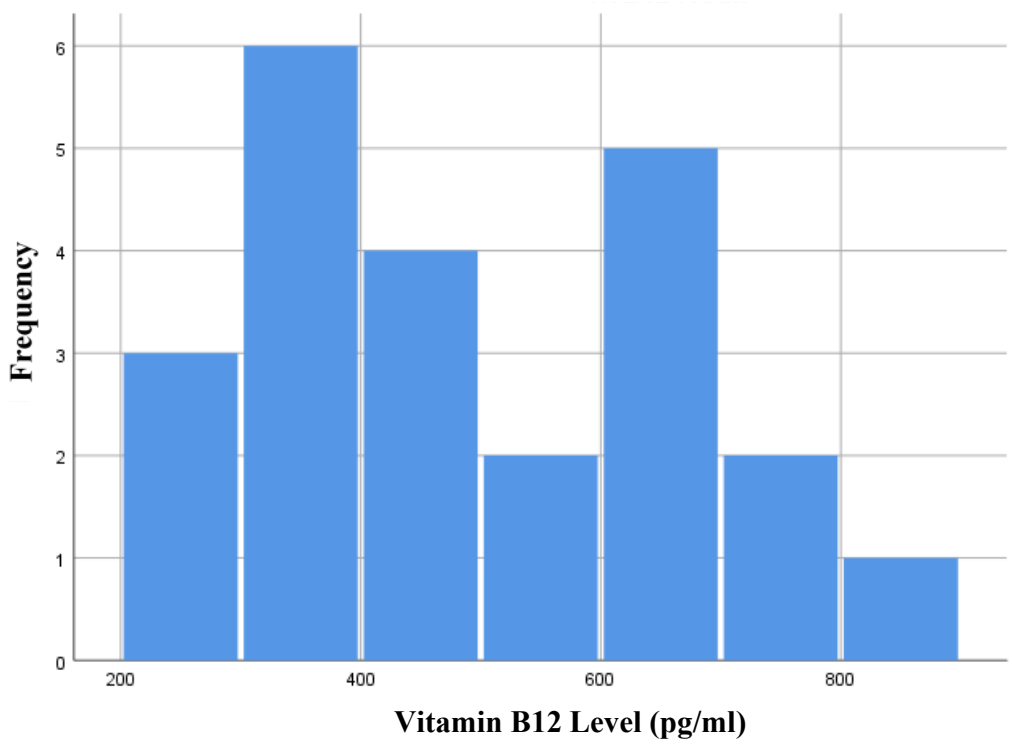
Patient questionnaires and the FMH flow chart were collected for review each week by the Doctor of Nursing Practice (DNP) student. Also, Vitamin B12 results were collected from the EHR weekly by the DNP student. Each intervention was completed at different rates with the patient questionnaires being completed by 40 participants, Vitamin B12 results for 23 participants, and 16 participants were assessed using the NC-stat DPNCheck. Using a Pearson *r*, negative relationships were demonstrated between vitamin B12 levels and the other assessment

interventions. However no significant correlations were demonstrated between any of the interventions. The most significant relationships were seen between vitamin B12 results and the objective assessment (p = .061) as well as that between vitamin B12 and the patient questionnaire (p = .09).

When analyzing vitamin B12 results (n = 23) the lowest result was 208 and the highest was 876 with a mean of 489.13. Vitamin B12 results that were missing (n = 24) included ordered testing that was not carried out by five participants and testing that was not ordered for 19 participants. Of the results, 39.1% were determined to be in the subclinical range and all

Figure 1

Vitamin B12 Results



Note. Clinical vitamin B12 deficiency was defined as <200 pg/ml while subclinical deficiency was defined as 200-400 pg/ml.

participants with subclinical vitamin B12 deficiency exhibited signs and symptoms of neuropathy based on their responses on the patient questionnaire and the findings of the objective assessment. Participants with vitamin B12 results in the clinical or subclinical range received treatment at a rate of 100%. See Figure 1 for a visual representation of the vitamin B12 results collected during the 10-week implementation period. Analysis of the responses from the Michigan Neuropathy Screening Instrument (Appendix A) (n = 40) demonstrated that 48.9% of participants screened had signs and/or symptoms of neuropathy based on their responses to the patient questionnaire and the findings of the objective assessment.

Discussion

The purpose of this initiative was to implement a new process to identify patients in the target population that would benefit from the optimization of vitamin B12 levels. Optimization of vitamin B12 levels would therefore reduce the risk of progression or the development of symptoms. For the nine patients identified with subclinical vitamin B12 deficiency, this initiative was a success. For the participants that received treatment for low vitamin B12 levels, the risk of developing further symptoms of neuropathy related to vitamin B12 has been reduced. Neuropathy is a well know comorbidity for patients with type two diabetes mellitus. The Diabetes Guideline supports the monitoring of vitamin B12 for patients being treated with metformin and more importantly for those with signs and symptoms of neuropathy. Previously cited literature used to support this initiative reported that rates of vitamin B12 deficiency in the target population as high as 30% (Aroda et al., 2016; Zalaket et al., 2018). While the results of this project were not significant, it is worth noting that for the sample size, it did have a similar rate of low vitamin B12 levels as previous studies.

Limitations

Several limitations considerably affected the results of this quality initiative and its effectiveness. Chief among them was the events surrounding the development of a nationwide pandemic that greatly limited the ability for the process to continue in its entirety. At the onset of the pandemic, clinic visits were transitioned to telemedicine only. This meant that the objective assessment would no longer be possible. Furthermore, lab services were halted at the clinic and lab testing was only ordered if necessary. This placed greater risk and responsibility on patients that now were required to have labs collected at a separate location or not at all. The pandemic also reduced the number of patients in the target population that scheduled a telemedicine appointment reducing the sample size.

While the pandemic presented a great obstacle, the inability of the EHR to automatically flag patients offered an opportunity for human error to reduce the number of patients that were recognized as being in the target population. While the buy-in of the staff and the providers was good, follow through with all interventions was limited. Also, the Michigan Neuropathy Screening Instrument scoring was overly confusing with several inverse questions that frustrated staff and discouraged its use.

Recommendations

For future applications of this process, there are four recommendations to improve and support the maintenance of the interventions. First, having several automated or manual alerts would assist in the consistency of patient identification. Furthermore, this would improve the follow through with the various interventions included in the process.

Second, having the screening questionnaire integrated into the EHR with automated scoring would reduce errors and confusion when scoring the Michigan Neuropathy Screening

Instrument. This would also improve compliance among clinic staff and allow for more efficient data collection.

Third, reducing the number of facilitators involved in the process would limit the possibilities of miscommunication and improve its efficiency. Moreover, limiting the facilitators would minimize errors and improve the effectiveness of the interventions.

Fourth, patient education was not included as an intervention and could have enhanced the experience of the participants. While it was expected that providers would use shared decision making with patients that qualified for treatment, written patient education would have enhanced participants' knowledge about the problem and what they can do to improve their health. This would also provide an avenue to increase patient-provider relationships and improve compliance with recommendations.

Implications for Practice

Many clinics participate in pay-for-performance programs that offer incentives for providing high-quality care. Clinic FM is no exception, with one of their pay-for-performance metrics being diabetic care recognition. A metric within diabetic care recognition is diabetic foot care and more specifically the loss of peripheral sensation. The interventions outlined above provide a process to better identify and assess patients for peripheral neuropathy and identify a potential contributing factor that can easily be treated. As rates of diabetes continue to increase, so too will the prescribing of the medication metformin. This project has demonstrated that patients treated with metformin can experience low vitamin B12 levels that may be contributing to signs and symptoms of peripheral neuropathy.

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Appendix A

Michigan Neuropathy Screening Insstrument

MRN:

Patient Version

MICHIGAN NEUROPATHY SCREENING INSTRUMENT

Please take a few minutes to answer the following questions about the feeling in your legs and feet. Check yes or no based on how you usually feel. Thank you.

1.	Are you currently taking metformin?	☐ Yes	☐ No
2.	Have you had your vitamin B12 level checked in the last year	☐ Yes	☐ No
3.	Are your legs and/or feet numb?	☐ Yes	☐ No
4.	Do you ever have any burning pain in your legs and/or feet?	☐ Yes	☐ No
5.	Are your feet too sensitive to touch?	☐ Yes	☐ No
6.	Do you get muscle cramps in your legs and/or feet?	☐ Yes	☐ No
7.	Do you ever have any prickling feelings in your legs or feet?	☐ Yes	☐ No
8.	Does it hurt when the bed covers touch your skin?	☐ Yes	☐ No
9.	When you get into the tub or shower, are you able to tell the hot water from the cold water?	☐ Yes	☐ No
10.	Have you ever had an open sore on your foot?	☐ Yes	☐ No
11.	Has your doctor ever told you that you have diabetic neuropathy?	☐ Yes	☐ No
12.	Do you feel weak all over most of the time?	☐ Yes	☐ No
13.	Are your symptoms worse at night?	☐ Yes	☐ No
14.	Do your legs hurt when you walk?	☐ Yes	☐ No
15.	Are you able to sense your feet when you walk?	☐ Yes	☐ No
16.	Is the skin on your feet so dry that it cracks open?	☐ Yes	☐ No
17.	Have you ever had an amputation?	☐ Yes	☐ No

Total: _____

A ~~"~~no" response on items 9 and 15 counts as 1 point. Item #6 is a measure of impaired circulation and item #12 is a measure of general asthenia and are not included in scoring.

MRN:

MICHIGAN NEUROPATHY SCREENING INSTRUMENT

B. Physical Assessment (To be completed by health professional)

1. Appearance of Feet

	Right	**Left**
a. Normal	☐ 0 Yes ☐ 1 No	Normal ☐ 0 Yes ☐ 1 No
b. If no, check all that apply:		If no, check all that apply:
Deformities	☐	Deformities ☐
Dry skin, callus	☐	Dry skin, callus ☐
Infection	☐	Infection ☐
Fissure	☐	Fissure ☐
Other	☐	Other ☐
specify:	_____	specify: _____

	Right		**Left**	
	Absent	Present	Absent	Present
2. Ulceration	☐ 0	☐ 1	☐ 0	☐ 1

	Right			**Left**		
	Present	Present/ Reinforcement	Absent	Present	Present/ Reinforcement	Absent
3. Ankle Reflexes	☐ 0	☐ 0.5	☐ 1	☐ 0	☐ 0.5	☐ 1
	Present	Decreased	Absent	Present	Decreased	Absent
4. Vibration perception at great toe	☐ 0	☐ 0.5	☐ 1	☐ 0	☐ 0.5	☐ 1
	Normal	Reduced	Absent	Normal	Reduced	Absent
5. Monofilament	☐ 0	☐ 0.5	☐ 1	☐ 0	☐ 0.5	☐ 1

Signature:_____ Total Score _____ /10 Points

Appendix B

Instructions for Michigan Neuropathy Screening Instrument

How to Use the Michigan Neuropathy Screening Instrument

History

The history questionnaire is self-administered by the patient. Responses are added to obtain the total score. Responses of "yes" to items 1-3, 5-6, 8-9, 11-12, 14-15 are each counted as one point. A "no" response on items 7 and 13 counts as 1 point. Item #4 is a measure of impaired circulation and item #10 is a measure of general asthenia and is not included in the scoring. To decrease the potential for bias, all scoring information has been eliminated from the patient version.

Physical Assessment

For all assessments, the foot should be warm (>30°C).

Foot Inspection: The feet are inspected for evidence of excessively dry skin, callus formation, fissures, frank ulceration, or deformities. Deformities include flat feet, hammertoes, overlapping toes, hallux valgus, joint subluxation, prominent metatarsal heads, medial convexity (Charcot foot), and amputation.

Vibration Sensation: Vibration sensation should be performed with the great toe unsupported. Vibration sensation will be tested bilaterally using a 128 Hz tuning fork placed over the dorsum of the great toe on the boney prominence of the DIP joint. Patients, whose eyes are closed, will be asked to indicate when they can no longer sense the vibration from the vibrating tuning fork.

In general, the examiner should be able to feel the vibration from the hand-held tuning fork for 5 seconds longer on his distal forefinger than a normal subject can at the great toe (e.g. examiner's DIP joint of the first finger versus patient's toe). If the examiner feels vibration for 10 or more seconds on his or her finger, then vibration is considered decreased. A trial should be given when the tuning fork is not vibrating to be certain that the patient is responding to vibration and not pressure or some other clue. Vibration is scored as 1) present if the examiner senses the vibration on his or her finger for < 10 seconds, 2) reduced if sensed for ≥ 10 or 3) absent (no vibration detection.)

Muscle Stretch Reflexes: The ankle reflexes will be examined using an appropriate reflex hammer (e.g. Trommer or Queen square). The ankle reflexes should be elicited in the sitting position with the foot dependent and the patient relaxed. For the reflex, the foot should be passively positioned and the foot dorsiflexed slightly to obtain optimal stretch of the muscle. The Achilles tendon

should be percussed directly. If the reflex is obtained, it is graded as present. If the reflex is absent, the patient is asked to perform the Jendrassic maneuver (i.e., hooking the fingers together and pulling). Reflexes elicited with the Jendrassic maneuver alone are designated "present with reinforcement." If the reflex is absent, even in the face of the Jendrassic maneuver, the reflex is considered absent.

Monofilament Testing: For this examination, it is important that the patient's foot is supported (i.e., allow the sole of the foot to rest on a flat, warm surface). The filament should initially be prestressed (4-6 perpendicular applications to the dorsum of the examiner's first finger). The filament is then applied to the dorsum of the great toe midway between the nail fold and the DIP joint. Do not hold the toe directly. The filament is applied perpendicularly and briefly, (<1 second) with even pressure. When the filament bends, the force of 10 grams has been applied. The patient, whose eyes are closed, is asked to respond yes if he/she feels the filament. Eight correct responses out of 10 applications are considered normal: one to seven correct responses indicates reduced sensation and no correct answers indicate absent sensation.

Appendix C

Clinic Flow Chart

Vitamin B12 Screening

Inclusion criteria: Adult patient with Dx of Diabetes Mellitus type 2 and is taking metformin.

Front desk - Patient to complete neuropathy questionnaire at check in

- Questionnaire to be collected and scored by a medical assistant.
- Total score:_____

Medical Assistant - complete diabetic foot exam to include:

- Appearance of feet
- Ulceration
- Monofilament
  - With patient's eyes closed, ask patient to respond yes if he/she feels the filament.
  - Eight correct responses out of 10 is "normal": one to seven responses indicate "reduced" sensation: no correct responses indicates "absent" sensation.
- Ankle reflexes
  - If reflex is absent examiner can ask the patient to perform the Jendrassic maneuver.
  - If reflex is elicited with maneuver document "present with reinforcement", if not document reflex as "absent".
- Vibration perception at great toe with 128 Hz tuning fork
  - Present if examiner feels vibration for < 10 seconds longer than the patient.
  - Decreased if examiner feels vibration for ≥ 10 seconds longer than the patient.
  - Absent if no vibration is sensed by the patient.
  - Total score:_____
- Sural nerve conduction test using DPNCheck
  - DPNC result: Amp-_____ Vel-_____

Provider – Review and sign Michigan Neuropathy Screening Instrument scoring.

Provider - order serum vitamin B12 true

Provider - interpret lab results and prescribe treatment if indicated

- Vitamin B12 result: _____

- If vitamin B12 deficiency (< 200 pg/ml) or subclinical deficiency (200-400 pg/ml) is identified treat with vitamin B12 supplementation of 1,000 mcg and calcium supplementation of 1,000 mg per day.