The effects of whole body vibrations on type 2 diabetes adults with painful peripheral neuropathies: a randomised controlled trial

Final project

Maelle Bernard

Mentor: Monique Sartor, PhD

Degree: physiotherapy EUSES

Barcelona, 10th of December 2022

Table of content

I. Acknowledgements

I would like to express my gratitude to my mentor, Monique Sartor, for guiding me throughout this project. I also wish to extend a special thanks to Gerard Munoz who has helped me finalise my project.

II. Abstract

BACKGROUND: Neuropathies can have a large detrimental effect in diabetic populations. Non pharmacological and pharmacological treatments to ease neuropathic symptoms are on the rise, however optimal interventions to improve pain and quality of life in these individuals have not yet been found as there is still a lack of convincing results and research. The aim of this trial is to deepen our knowledge on potential modalities to help these patients. It will attempt to determine the effect of whole body vibrations in comparison to sham whole body vibrations (WBV) on painful neuropathies in type 2 diabetes mellitus (T2DM) subjects.

METHODS: This study is a multi centre, randomized, double-blinded (patients and assessors), controlled trial with a 1:1 ratio. Participants will be sedentary adults over 50 diagnosed with T2DM and associated painful peripheral neuropathy. They will be randomly allocated to one of two groups; the WBV intervention group and the sham WBV group. The intervention will last 6 weeks, there will be 3 sessions of 3x4mins of synchronous WBV or sham WBV per week.
The primary outcome will be pain, which will be measured with the visual analogue scale (VAS) before and after every WBV/sham WBV session.
Secondary outcomes will include quality of life, glycemic profile, plantar sensitivity, aerobic capacity, lower limb strength and balance. These will be measured with the NeuroQoL, a fasting blood glucose test and HbA1c test, nylon Semmes-weinstein monofilament test, O2peak test, sit to stand test as well as Berg balance scale respectively. These assessments will be made at baseline, 3 weeks and 6 weeks. A follow up assessment will take place 6 weeks after the end of the intervention. Data analysis to compare in between group results will be made using a student-t test.

DISCUSSION: Synchronous WBV training is a feasible and cheap intervention that could potentially improve pain as well as QoL, glycemic profile, plantar sensitivity, aerobic capacity, lower limb strength and balance in T2DM patients with painful peripheral neuropathies.

Key words: diabetes, neuropathy, whole body vibrations, neuropathic pain, VAS

III. Introduction

Diabetes mellitus (DM) is a common metabolic disease that is becoming a major global health issue. Indeed, its mortality rate has quickly been rising over the years and today (1), it is estimated that this condition affects around 537 millions adults worldwide. This number is predicted to grow to 643 millions by 2030 (2).
DM is caused by a dysfunction in the glucose storage system, resulting in hyperglycaemia. The exact cause of this problem depends on the type of diabetes.

T2DM accounts for around 90% of all diabetes (3). It is characterised by an improper reaction of the body to insulin, the hormone that allows glucose to get stored in the liver, muscles or fat. It results into a resistance to insulin. With time, this causes further dysregulation in the glucose storing system. The pancreas's Beta cells which create insulin become less efficient eventually causing a decrease of this hormone in the body.
These 2 processes contribute to the abnormally high blood glucose level found in this condition (4).

T2MD is driven by a combination of risk factors which can be both genetical and environmental. Some of the most common ones are a sedentary lifestyle, obesity and lack of physical activity (2).
The main axis of treatment is therefore focused on glycemic control. This is achieved via lifestyle changes like increasing physical activity and healthier eating. It can be combined with pharmacological management such as blood glucose level decreasing agents (4).

If left untreated, this condition can lead to serious macro-vascular complications such as stroke and coronary artery disease as well as microvascular ones like retinopathy or neuropathy (5). Unfortunately, it is estimated that 24,1 to 75,1% of diabetics are not diagnosed (6), this does not allow proper care plan to be put in place. Furthermore, even when diagnosed, many diabetes are not correctly controlled. These 2 factors put individuals at much higher risk of complications.

Diabetic neuropathy (DN) is the most prevalent chronic complication (7). Different types of neuropathies exist, but the most common, peripheral neuropathy, is believed to be found in up to 50% of diabetics, more often affecting individuals with T2DM rather than type 1 (8).
In this condition, the high blood glucose causes damage to the neural structures in the body's extremities. Usually the feet are the most affected (8). Although, diabetic peripheral neuropathy (DPN) may be asymptomatic (8,9), it can also results in sensory or motor nerve damage that translates into strong symptoms which can greatly affect the individual's quality of life.

This damage initially happens on the most distal C fiber neurons. They carry nociceptive information such as heat and pain this therefore translates into burning sensation and pain in the feet. As the disease progresses, larger neuronal fiber loss occurs. This can result in numbness and total loss of proprioception going from the feet and up (10).
Some other common symptoms include stabbing, shooting or lancinating pain, tingling sensations and loss of lower limb strength and reflexes. (9,10) These can vary from one DPN individual to another.
These symptoms can lead to decrease in balance, increasing the risk of fall, as well as the formation of foot ulcers or even amputations.
DN has also been associated with anxiety, depressive symptoms and lower quality sleep, which further contribute to a drop in quality of life (11).

Most of the time DPN is not reversible, but the progress can be slowed and the symptoms controlled (8). Pharmacological treatments have been shown to reduce pain and improve function in DPN (12, 13, 14). However, DPN individuals are not always satisfied with the effect of their medications (15). Furthermore, they can come with a fair share of side effects (nausea, dizziness, lethargy, higher glucose value…) and might not be financially accessible to all. Finding cost friendly alternatives with less side effects would be needed.

Regarding non pharmacological interventions further research is needed, but, lifestyle management and exercise seem to have some positive effect on painful DPN (9, 16, 17, 18, 19). There is evidence showing that aerobic training improves quality of life, function, aerobic capacity, as well as reduces pain intensity and interference in T2DM with DPN (19, 20, 21, 22, 23). Some research has also been conducted regarding resistance training, mobility training, balance training and other alternative treatments such as tai-chi or yoga. Although a few articles demonstrated no significant changes in outcomes, most of them showed that these interventions could be beneficial for diabetics with PN as they could improve pain level, balance, strength and sensorimotor function which all contributed to a better quality of life.
When looking at glycemic profile and control, evidence shows aerobic exercise and resistance training can improve blood fasting glucose and HbA1C levels in T2DM, however there is no research evaluating this outcome in DPN. (19).

A problematic often found in diabetic individuals is the difficultly to participate in physical activity. Indeed, the pain or the already low physical fitness they have can make adherence to exercise programs difficult (24, 25, 26). A study conducted in 2018 in Brazil showed that middle to elderly T2DM patients have good compliance to medications but do not necessarily follow recommendations in regards to diet and physical activity. The adherence to exercise programs was particularly lower in participants with PN. This was hypothesised to be due to the general worsening of health in this condition, particularly presence of pain and limited function. Psychosocial factors also seem to play a large role (27, 28).

For this reason, it is important to look into other interventions that differ from the types of exercises previously studied and could potentially increase adherence in real life populations of painful DPN.

WBV is a therapy method that has been getting more and more attention in the last decade. This intervention consist of standing, sitting, lying down or exercising on a vibrating platform. The vibrations transmitted to the body are set to specific parameters (frequency, magnitude and acceleration) and can act in different directions. They are believed, through the excitation of muscle spindles, to trigger a reflex which causes a neuromuscular response equivalent to muscle contraction. Past studies have been numerous to state that WBV have an effect on the tonic muscle reflex in general population, however, results are not yet clear and the implication of this specific reflex is still unsure (29, 30, 31, 32, 33). Other mechanisms including increased hormone secretion and stimulation of proprioceptive pathways have also been discussed to explain WBV effects on the body (32).

In any case, WBV has been showing potential positive effect as a complementary or even an alternative treatment to exercise in sedentary and older adults (19, 32, 34).
It has been proven to help reduce pain, both on its own and in addition to other interventions, in certain chronic musculoskeletal conditions (35, 36, 37), spinal cord injury (38) and metabolic syndrome (39) in adults. WBV also demonstrate its effectiveness on balance and gait in patients affected by stroke, T2DM, fibromyalgia and parkinson's (35, 40, 41, 42).
Some research has shown general health improvements, especially in muscle activity and strength in frail elderlies (43, 44, 45). Another effect that has been studied is the increase of microvascular blood flow in T2DM as well as in healthy adults (31, 32, 46, 47). Finally, WBV is believed to potentially be an effective modality to improve glycemic profile and aerobic capacity in T2DM populations (47).

This treatment modality is particularly interesting as it is affordable and accessible to many types of population. Indeed, it can be used for short bouts of time with repetitions, causes low rates of perceived exertion, has low cardiorespiratory demand and few contraindications. These factors make it an attractive modality for individuals who cannot handle vigorous exercising (32, 48) .

At the moment there are only a few studies which research the effect of WBV on painful DPN. However, results seem to be promising;

A systematic review conducted in 2018 showed that WBV could indeed have a positive effect on pain, balance and glycemic control in DPN (49). However, the included studies showed a high risk

of bias and therefore the evidence on WBV was considered low quality, giving more reasons to further explore this modality.
In the following years, new articles showed that, either on its own or in addition to dietary advice and lifestyle modifications, WBV could allow a significant decrease in DPN associated pain (50, 51, 52). Furthermore, this pain modulation lasted for a few weeks after the end of the intervention, showing WBV could have a chronic effect on pain. They also demonstrated that WBV could increase balance and QOL in DPN.
This 2021 study combined balance training to WBV, improvements in balance and lower limb strength were found to be greater than with only balance training (53).

In addition to its small quantity, the existing evidence on WBV in this population and in general shows a large lack of standardisation. Indeed, exact parameters such as frequency, magnitude, type of vibration, machine brand, treatment time, patient position, footwear for the WBV aren't always stated although guidelines have been put in place (54,55). Furthermore, some important outcomes in PDN such as plantar sensitivity (a predictor of foot ulceration and amputation) are missing.

There is a need for larger, methodologically stronger studies to further understand the mechanisms, limitations and potential benefits of using WBV in DPN, which is what is aimed to be done in this protocol.

IV. Hypothesis

Null hypothesis H0:

There will be no difference in pain between the whole body vibrations intervention and the sham whole body vibrations intervention.

Alternative hypothesis H1:

there will be a decrease in pain in the whole body vibrations intervention compared to the sham whole body vibrations intervention.

V. Objectives

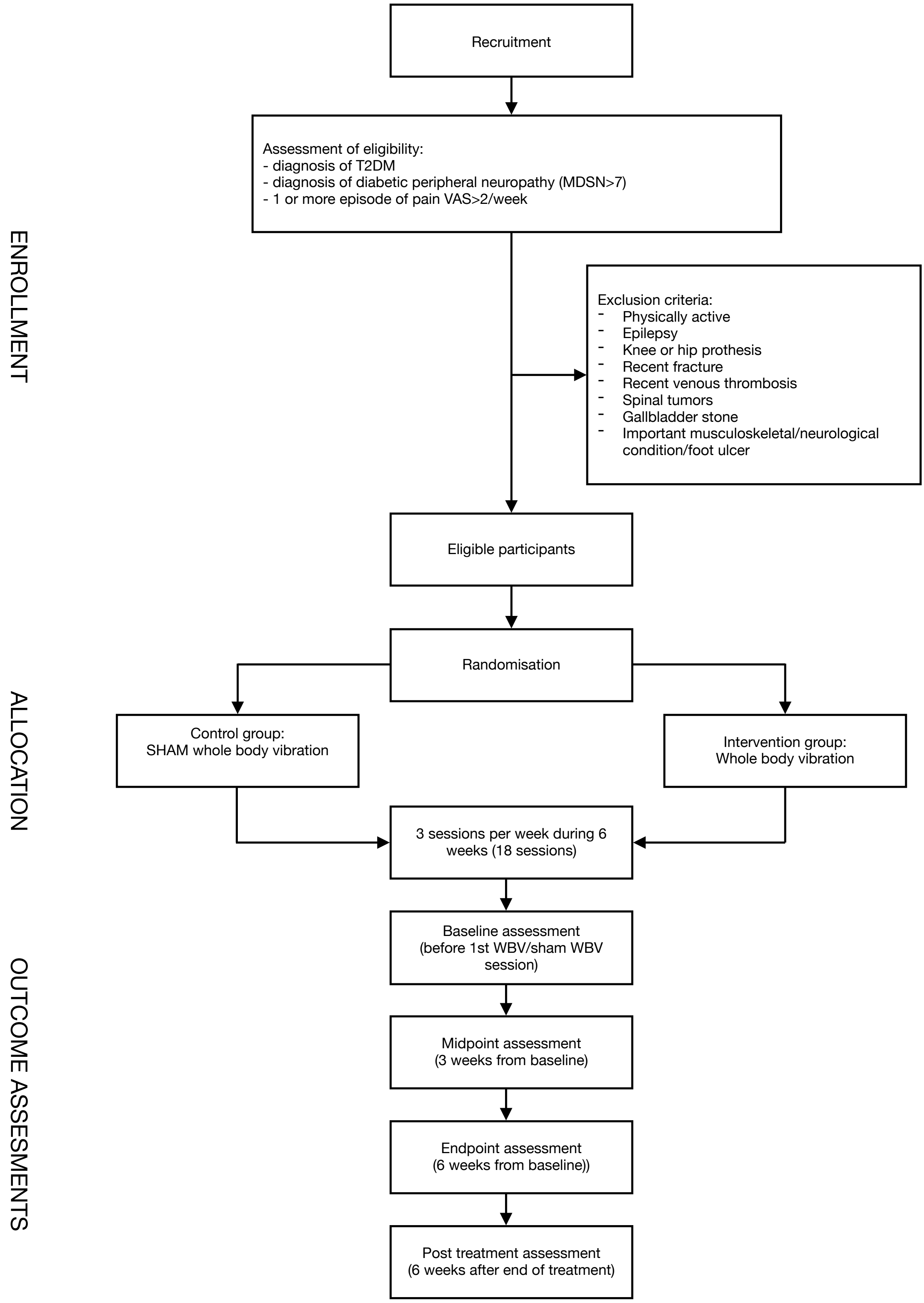
To demonstrate the benefits of WBV on pain in DPN patients.
To assess the impact of WBV on the following; quality of life, aerobic capacity, plantar sensitivity, glycemic profile, lower limb strength and balance in DPN populations.

VI. Method

1) Study Design

This study will be a double blind randomized control trial (RCT) with an allocation ratio of 1:1. It will compare the effects of WBV therapy with sham WBV on T2DM with painful peripheral neuropathy patients. The spirit guidelines will be followed to describe the procedure. Our trial will take place in multiple centers in and around Barcelona; Hospital clinic de barcelona, hospital de Bellvitge and Germans Trias i Pujol Hospital.

2) Flow diagram



3) Eligibility Criteria - Participants: Inclusion and Exclusion Criteria

The targeted population is adults over 50, who have been diagnosed with type 2 diabetes for at least 5 years and have an additional diagnosis of PN (caused by diabetes).
The diabetes diagnosis will be confirmed by a fasting plasma glucose of 7.0 mmol/l or more or the use of diabetic medication (56, 57). The DPN will be verified via the Michigan diabetic neuropathy score (MDNS) where participants must have a score of 7 or above (20, 58, 59). A neurologist will further confirm the diagnosis. Furthermore, the participants must be physically inactive (following the WHO guidelines) (60). Physical inactivity will be defined as doing less than 150 minutes of moderate intensity training or less than 75 minutes of high intensity training per week.
In the following table, we listed the exact inclusion and exclusion criteria. The exclusion criteria are mainly based on the contraindication for WBV (61).

To participate in the study, participants must fulfil the following:

Inclusion criteria	**exclusion criteria**
Adult>50 Diagnosis of T2DM > 5y (definition of ADA) MDNS>7 1 or more episode of pain VAS>2/week	Physically active (according to WHO) Epilepsy Knee or hip prothesis Recent fracture Recent venous thrombosis Spinal tumors Gallbladder stone Musculoskeletal/neurological condition/foot ulcer that do not allow locomotion

4) Procedures to obtain the Sample Size

Pain is our main outcome, it will be measured with the VAS. With the existing literature regarding DPN, we can estimate that the minimal clinically important difference (MCID) in the VAS is set at a 1 point difference. We will therefore consider that our intervention is meaningful if there is a difference of 1 or more in the VAS between the beginning and end of the WBV intervention (15, 51).

5) Outcomes

Our main outcome is pain. It will be assessed with the Visual Analogue Scale (VAS) (*See Annex 1).* VAS is one the most acceptable and well-known scale which allows to rate the intensity of pain from 0 (no pain) to 10 (worst imaginable pain). It is found in most studies involving DN (13, 51, 62, 63).

Regarding quality of life, we will use the NeuroQol which is a validated neuropathy-specific measurement system that can reliably assess neuropathic individual's quality of life, including DPN (62, 64, 65).
The instrument will consist of 57 items that will assess 7 domains separately; anxiety, depression, fatigue, lower extremity function, positive well being, sleep disturbance, as well as satisfaction with social roles and activities (*Annexes 2 to 8)*. These domains are chosen as they have been proven to be affected in painful DPN (66).
Each question is answered on a five point Likert scale (1= never; 5= all the time/very much).

Plantar sensitivity will be measured via the nylon Semmes-weinstein monofilament test (SWMT).
The SWMT determines impairment in pressure perception in T2DM and DPN (67, 68, 69) .
Following guidelines on diabetic foot, we will use a 5,07/10-g monofilament (70) (*annex 9)*.
An assessor will show the filament and demonstrate the sensation it causes by applying it to the arm of the subject. They explain to the participant the concept of the test: while the subject is lying down supine, barefoot and with their eyes closed, the assessor will touch the patients foot with the filament in different areas. The patient will have to say "yes" if he can feel the sensation of the filament on his foot.
The filament is pressured in 9 specific areas according to diabetic foot guidelines (on the big, the third and the fifth toe, the plantar aspect of the first, third, and fifth metatarsal heads, and 3 sites on the bottom of plantar aspect) (71). *Areas shown in annex 10.*
A score from 0 to 9 will be given in function of the number of sites the tested individual was able to feel.
Apart from giving the instructions and clearing any doubts, the assessor will not talk during the test.

To measure the aerobic capacity, a peak oxygen uptake (VO2max) test will be taken (72).
This will be done during a graded exercise protocol using a cycle ergometer *(Annex 11)*. An open-circuit spirometry will be used to monitor oxygen uptake (VO2).

The test will consist of 2 minutes stages where workload gradually increases until maximal effort is reached (20W increase at each stage starting at 60W in the first stage) .
Maximal effort is defined as a respiratory exchange ratio of/greater than 1.0.
Heart rate (HR), blood pressure and rating of perceived exertion (RPE) will also be measured throughout the test. An exercise physiologist will always be there to attend the assessment. They will stop the test if participants are put at risk (hypotension, hypertension, electrocardiogram abnormalities, angina, intense dyspnea or fatigue).
The VO2max obtained will be used as the outcome measure to describe aerobic capacity.

The glycemic profile will be evaluated with a fasting blood glucose test that will measure current glucose control (68). A glycosylated hemoglobin test will also be done in order to determine the average blood glucose level for past 2/3 months.

For the strength, we will do a sit to stand test (73, 74).
Participants will have to sit and stand off a chair as many times as possible in 30 seconds without the use of their hands, this will evaluate their lower leg strength in a functional context.

Finally, the berg balance scale will serve to assess balance of the participants (74, 75) *(Annexes 12-14).*
The berg balance scale assesses functional tasks in subjects. It is a validated 14 items-instrument to measure effectiveness of interventions on balance in adults and elders. Each item is given a score from 0 to 5 by the assessor depending on the quality of the task execution. A total score lower than 46 indicates impairments and risk of fall. The maximum obtainable score is 56.

6) Assessments

The outcomes will be assessed multiple times during the study. First at baseline (T0), second at the middle of the intervention (3 weeks- T1) and third at the end, 6 weeks from baseline (T2). The last assessment will be made at follow up (T3) which will happen 6 weeks after the end of the intervention.
Regarding pain, we will have a more thorough assessment in order to better see potential acute effects:
Participants will orally communicate their VAS score before and after each WBV or sham WBV sessions.

7) Ethics

In order to conduct our study, it will have to be approved by the ethics committees of the Hospital clinic de barcelona, hospital de Bellvitge and Germans Trias i Pujol Hospital. They will make sure our study follows the Declaration of Helsinki guidelines. If any changes are made to the study protocol, it will have to be evaluated again by the ethics committees. In case of unpredicted or severe side affects, the committees will be informed.

*Informed consent (in Annexes, page 41)

8) Recruitment

We will identify potential participants through local private practices, clinics, hospitals, rehabilitation centres and diabetic support groups. They will be contacted by our team in charge of recruitment who will explain the study and see if there are any evident exclusion criteria. The interested eligible individuals will then be met to further discuss the study protocol and be given the written informed consent sheet. Potential subjects who decide to participate will undergo further screening to confirm diagnosis as well as the absence of exclusion criteria. If the battery of test confirms the the individual has the fitting profile for the study, they will then sign the consent sheet.

9) Randomisation

An external physician that took no part in recruitment or coordination will be in charge of the randomisation. They will not participate in the intervention afterwards either.
The physician will put all the participant's name into a computerised program. This program will then randomly allocate each individual to a group A or B (control intervention or intervention group) with a ratio of 1:1. To ensure concealment of allocation, the physician will not be aware of which intervention is represented by the letters A and B. They will print out the 2 lists in a sealed opaque envelope and send it to the research coordinator. This information will be hidden from the assessors, only the physiotherapist who will supervise WBV sessions will be aware of the group allocation.

10) Blinding

Our study will be double blinded, the assessors as well as the participants will be blinded. The assessors will not know in which group the participants are in when they evaluate the outcomes. For the participants, they will not know if they are receiving the sham or the real WBV. The sham group's WBV machine will be turned on to negligible parameters that do not produce effective vibrations. The participants will be told that the vibrations of the machine have magnitudes that are small and most likely cannot be physically perceived. Furthermore, a sound will be emitted from a speaker put under the machine in order to make it seem more believable.
The physicians giving the lifestyle recommendations will be the same for both groups, they will be unaware of the group allocation.

11) Intervention

The participants of our trial will be divided into one of two groups: the intervention group, which will undergo real WBV treatment and the sham control group, that will take part in the sham WBV treatment.

At the beginning of the study, both will receive recommendations based off of the American Diabetes Association (ADA) "standard of medical care in diabetes" guideline (76). They include diet, physical activity and behavioural therapy advice which are all supported by evidence. Their main aim is to create an energy deficit in individuals in order to make them lose weight.
This will be done by a nurse, a physical trainer and a nutritionist whom are all specialised in diabetes care.

Pharmacological treatment will be tracked. To minimise medication co-intervention, letters will be sent to the participant's therapists asking not to alter medication intake during the intervention period unless if deemed medically necessary.

Subjects will be allowed to take part in physical activity outside of the trial, however they will be asked to document any training that they undergo.

a. Intervention group

In order to be replicable, we will describe this WBV intervention following specific WBV research guidelines (54).

The WBV machine used will be the Galileo 2000 (Novotec Medical GmBH, Germany) *(Annex 15).* The vibrations will be synchronous (77).
A mechanic will verify the machine's parameters and make sure all of our WBV machines are equal.
Parameters include frequency; the number of impulses delivered per second, amplitude; the extent of vertical displacement and magnitude; the acceleration power/force of the movement.

The parameters will be initially set at 15 Hz for frequency and 3mm for amplitude (74).
The frequency will gradually increase over the course of the study. 15 Hz the first week, 20 Hz the second and third, 25 Hz the forth and fifth, finishing at 30 Hz the sixth. Therefore peak acceleration (magnitude) obtained during the last week can be calculated at 5,6g (78).

The participants will be standing with knees slightly bent (30°) and asked to contract their lower limb muscles. This will allow a reduction of vibration transmission to the head which can be detrimental. They will be asked to keep their arm at the side and not use hand support, however a railing will be there in case the subjects lose balance. They will be barefoot and their weight will be equally distributed on their whole foot. Skidding will be prevented.

The WBV sessions will take place in a private room in the hospital. The participants will be alone with a researcher. The sessions will be done 3 times per week (with at least 1 day rest in between) during the 6 weeks of intervention. Before starting the WBV, each participants will undergo 5 minutes of warm up on a stationery ergometer. The WBV sessions consist of 4 bouts of 3 minutes each on the WBV machine (15, 51) . There will be 1 min break in between each bouts where participants will be allowed to sit.

A trained physician will always be there to supervise, make sure the patient is correctly placed and turn the machine on and off.
They will remind how the sessions will take place and clear any doubts before each WBV intervention.
They will also keep track of attendance.

An assessor blinded to the intervention will see each subject in another room before and after their sessions to receive their VAS scores.

b. Control group

The control group will not know that they are undergoing the sham WBV intervention.
They will come to the hospitals at the same frequency as the intervention group; 3 times per week.
Before starting the sham WBV, each participants will also undergo 5 minutes of warm up on a cycle ergometer. They will do 4 bouts of 3 minutes each on the WBV machine with 1 minute break in between. The machine will be turned on to a negligible parameters that do not provide effective stimulus. The participants of this group will be told that the vibrations are of too small magnitudes to be physically felt. Furthermore, a speaker that emits a vibration like sound will be activated by the supervising physician to make the treatment more believable.
Attendance will be tracked.

An assessor blinded to the intervention will see each subject in another room before and after their sessions to receive their VAS scores.

12) Data Analysis

As each of our outcomes can be measured in quantitative variables, we will use the student t-test to compare results between the WBV group and the sham group for each outcome (51). This test will be applied at the different assessment points.
To evaluate difference between the beginning and the end of our intervention in each individual group, the paired t-test will be used.
To know whether our results will be statistically significant or not, we will set alpha at 0,05.

In order to make results more reliable, only the data of participants attending to 80% or more of WBV/sham WBV sessions will be used for in analysis.

13) Calendar

	Study period						
							Follow-up
	Enrollment	Allocation	Baseline			Post-intervention	
Timepoint	-T1		T0	T1	T2		T3
ENROLLMENT							
Eligibility screen	x						
Informed consent	x						
Allocation		x					
INTERVENTIONS							
WBV intervention group			—	—	—		
ShamWBV control group			—	—	—		
ASSESMENT							
Pain			x	x	x		x
QoL			x	x	x		x
Glycemic profile			x	x	x		x
Plantar sensitivity			x	x	x		x
Aerobic capacity			x	x	x		x
LL strength			x	x	x		x
Balance			x	x	x		x

Pain assessed before/after every session (VAS)

14) Role of the Investigators

There will be a recruitment team composed of investigators who's role will be to search for potential participants in different establishments and then call them. They will conduct the interviews to see who exactly is eligible for the study. A nurse and neurologist will also be part of recruitment to confirm the diabetes and PN diagnosis.
An external physician who is fully blind to the study hypothesis will do the randomisation process for group allocation. He will take no further part in the study.
The researchers who conduct assessments will be fully blinded. They will not know group allocation. The participants will be asked not to discuss their treatment with their assessors.
There will be different assessors for each group in order to reduce potential bias. They will all undergo a meeting/training before the study begins in order to standardise as much as possible the assessments.
The researchers who apply the WBV intervention will be physiotherapists. They will be aware of group allocation as they will be the one to turn on the WBV machine or fake turn on the WBV machine. They will be different physiotherapists for the 2 groups.
Finally the coordinator will have an overview on the study, they will make sure everything is going smoothly and be the one to end up with all the collected data once the trial finishes.

15) Resources

Non fungible:
- Chair
- Timer
- neuroQoL sheet
- Berg balance scale sheet
- Open circuit spirometry
- Ergometer (Monark LC7TT)
- Whole body vibrations platform (Galileo 2000)

Fungible:
- Nylon Semmes-weinstein monofilaments

Human resources:
- 1 recruitment nurse
- 1 neurologist
- 1 dibetes specialised nurse

- 1 diabetes specialised nutritionist
- 1 diabetes specialised physical trainer
- 2 physical therapists (intervention)
- 2 exercice physician (assesors)
- 1 external physician for randomisation
- 2 research coordinators

16) Limitations

Although steps will be put in place to keep the participants blinded from knowing their treatment, it is important to take into account that, considering the WBV machine is physically felt when turned on, some participants of the study might figure out or at least be very suspicious regarding their group allocation.

Another limitation of our study is the lack of preceding standardised research on WBV, and even more in our study population. This lack of standardisation makes it complicated to know exactly which parameters can or should be used. For example, many studies do not detail if they are using synchronous or side alternating vibrations.

Even though our study population is not active and any training done during the study will be tracked, it is possible some participants will be more physically active than others therefore altering the results of our study. Furthermore, apart from asking medication to not be altered, we did not stop participants from getting any additional/alternative treatment on the side. This could have a large impact on our results, however we did not find it ethical to prohibit participants from seeking ways to relieve their symptoms.

VII. References

1. World Health Organization. Diabetes [Internet]. World Health Organization. 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/diabetes

2. International Diabetes Federation. IDF Diabetes Atlas 9th edition 2019 [Internet]. diabetesatlas.org. 2021. Available from: https://diabetesatlas.org

3. Pan B, Ge L, Xun Y, Chen Y, Gao C, Han X, et al. Exercise training modalities in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis. *International Journal of Behavioral Nutrition and Physical Activity* [Internet]. 2018 Jul 25 [cited 2019 Dec 6];15(1). Available from: https://ijbnpa.biomedcentral.com/track/pdf/10.1186/s12966-018-0703-3

4. Khursheed R, Singh SK, Wadhwa S, Kapoor B, Gulati M, Kumar R, et al. Treatment strategies against diabetes: Success so far and challenges ahead. *European Journal of Pharmacology*. 2019 Nov;862:172625.

5. Harding JL, Pavkov ME, Magliano DJ, Shaw JE, Gregg EW. Global trends in diabetes complications: a review of current evidence. *Diabetologia*. 2018 Aug 31;62(1):3–16.

6. Beagley J, Guariguata L, Weil C, Motala AA. Global estimates of undiagnosed diabetes in adults. *Diabetes Research and Clinical Practice* [Internet]. 2014 Feb [cited 2019 Sep 10];103(2): 150–60. Available from: https://www.sciencedirect.com/science/article/pii/S0168822713003847

7. Pop-Busui R, Boulton AJM, Feldman EL, Bril V, Freeman R, Malik RA, et al. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. *Diabetes Care* [Internet]. 2016 Dec 20;40(1):136–54. Available from: https://care.diabetesjournals.org/content/40/1/136

8. Hicks CW, Selvin E. Epidemiology of Peripheral Neuropathy and Lower Extremity Disease in Diabetes. *Current Diabetes Reports*. 2019 Aug 27;19(10).

9. Davies M, Brophy S, Williams R, Taylor A. The Prevalence, Severity, and Impact of Painful Diabetic Peripheral Neuropathy in Type 2 Diabetes. *Diabetes Care* [Internet]. 2006 Jun 26;29(7): 1518–22. Available from: https://care.diabetesjournals.org/content/29/7/1518

10. Pop-Busui R, Ang L, Boulton A, Feldman E, Marcus R, Mizokami-Stout K, et al. Diagnosis and Treatment of Painful Diabetic Peripheral Neuropathy. *ADA Clinical Compendia* [Internet]. 2022 Jan [cited 2022 Dec 12];2022(1):1–32. Available from: https://diabetesjournals.org/compendia/article/2022/1/1/147001/Diagnosis-and-Treatment-of-Painful-Diabetic?searchresult=1

11. Sadosky A, Schaefer C, Mann R, Bergstrom F, Baik R, Parsons B, et al. Burden of illness associated with painful diabetic peripheral neuropathy among adults seeking treatment in the US: results from a retrospective chart review and cross-sectional survey. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*. 2013 Feb;79.

12. Gimbel JS, Richards P, Portenoy RK. Controlled-release oxycodone for pain in diabetic neuropathy: A randomized controlled trial. *Neurology* [Internet]. 2003 Mar 25 [cited 2019 Sep 10]; 60(6):927–34. Available from: https://n.neurology.org/content/60/6/927

13. Harati Y, Gooch C, Swenson M, Edelman S, Greene D, Raskin P, et al. Double-blind randomized trial of tramadol for the treatment of the pain of diabetic neuropathy. *Neurology*. 1998 Jun 1;50(6):1842–6.

14. Bril V, England J, Franklin GM, Backonja M, Cohen J, Del Toro D, et al. Evidence-based guideline: Treatment of painful diabetic neuropathy: Report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. *Neurology* [Internet]. 2011 Apr 11 [cited 2020 Jan 13];76(20):1758–65. Available from: https://n.neurology.org/content/76/20/1758.long

15. Kessler NJ, Hong J. Whole body vibration therapy for painful diabetic peripheral neuropathy: A pilot study. *Journal of Bodywork and Movement Therapies.* 2013 Oct;17(4):518–22.

16. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *The New England journal of medicine*. 2002;346(6):393–403.

17. Tatikola SP, Natarajan V, Desai VK, Asirvatham AR, Rajsekhar H. Effect of various exercise protocols on neuropathic pain in individuals with type 2 diabetes with peripheral neuropathy: A systematic review and meta-analysis. *Diabetes & Metabolic Syndrome* [Internet]. 2022 Sep 1 [cited 2022 Dec 12];16(9):102603. Available from: https://pubmed.ncbi.nlm.nih.gov/36049390/

18. Ogle T, Alexander K, Miaskowski C, Yates P. Systematic review of the effectiveness of self-initiated interventions to decrease pain and sensory disturbances associated with peripheral neuropathy. *Journal of Cancer Survivorship.* 2020 Feb 20;

19. Holmes CJ, Hastings MK. The Application of Exercise Training for Diabetic Peripheral Neuropathy. *Journal of Clinical Medicine.* 2021 Oct 28;10(21):5042.

20. Dixit S, Maiya A, Shastry B. Effect of aerobic exercise on quality of life in population with diabetic peripheral neuropathy in type 2 diabetes: a single blind, randomized controlled trial. *Quality of Life Research* [Internet]. 2013 Dec 11 [cited 2019 Nov 19];23(5):1629–40. Available from: https://link.springer.com/article/10.1007%2Fs11136-013-0602-7

21. Yoo M, D'Silva LJ, Martin K, Sharma NK, Pasnoor M, LeMaster JW, et al. Pilot Study of Exercise Therapy on Painful Diabetic Peripheral Neuropathy. *Pain Medicine (Malden, Mass)* [Internet]. 2015 Aug 1 [cited 2021 May 6];16(8):1482–9. Available from: https://pubmed.ncbi.nlm.nih.gov/25800666/

22. Hamed NS, Raoof NALA. Effect of high intensity interval training on diabetic obese women with polyneuropathy: a randomized controlled clinical trial [Internet]. 2014. Available from: http://dx.doi.org/10.7243/2055-2386-1-4

23. Fisher M, Langbein W, Collins E, Williams K, Corzine L. Physiological improvement with moderate exercise in type II diabetic neuropathy. [Internet]. europepmc.org. 2007. Available from: https://europepmc.org/article/med/17375878

24. Zhao G, Ford ES, Li C, Mokdad AH. Compliance with physical activity recommendations in US adults with diabetes. *Diabetic Medicine.* 2008 Feb;25(2):221–7.

25. Thomas D, Elliott EJ, Naughton GA. Exercise for type 2 diabetes mellitus [Internet]. *Cochrane Library.* 2006. Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD002968.pub2/full

26. Jenkins DW, Jenks A. Exercise and Diabetes: A Narrative Review. The Journal of foot and ankle surgery : official publication of the American College of Foot and Ankle Surgeons [Internet]. 2017;56(5):968–74. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28842107

27. Marinho FS, Moram CBM, Rodrigues PC, Leite NC, Salles GF, Cardoso CRL. Treatment Adherence and Its Associated Factors in Patients with Type 2 Diabetes: Results from the Rio de Janeiro Type 2 Diabetes Cohort Study [Internet]. *Journal of Diabetes Research.* 2018. Available from: https://www.hindawi.com/journals/jdr/2018/8970196/

28. L. Hudson J, Bundy C, A. Coventry P, Dickens C. Exploring the relationship between cognitive illness representations and poor emotional health and their combined association with diabetes self-care. A systematic review with meta-analysis. *Journal of Psychosomatic Research*. 2014 Apr; 76(4):265–74.

29. Bemben D, Stark C, Taiar R, Bernardo-Filho M. Relevance of Whole-Body Vibration Exercises on Muscle Strength/Power and Bone of Elderly Individuals. Dose-Response. 2018 Oct 1;16(4): 155932581881306.

30. Zaidell LN, Mileva KN, Sumners DP, Bowtell JL. Experimental Evidence of the Tonic Vibration Reflex during Whole-Body Vibration of the Loaded and Unloaded Leg. Woloschak GE, editor. PLoS ONE. 2013 Dec 30;8(12):e85247.

31. Rittweger J. Vibration as an exercise modality: how it may work, and what its potential might be. *European Journal of Applied Physiology*. 2009 Dec 12;108(5):877–904.

32. Park S-Y, Son W-M, Kwon O-S. Effects of whole body vibration training on body composition, skeletal muscle strength, and cardiovascular health. *Journal of Exercise Rehabilitation*. 2015 Dec 29;11(6):289–95.

33. Corum M, Topkara B, Kokce M, Ozkan M, Bucak OF, Ayture L, et al. The reflex mechanism underlying the neuromuscular effects of whole-body vibration: Is it the tonic vibration reflex? *Journal of Musculoskeletal & Neuronal Interactions* [Internet]. 2022 [cited 2022 Dec 12];22(1):37–42. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8919650/

34. Kholvadia A, Baard ML. Whole body vibration improves body mass, flexibility and strength in previously sedentary adults : original research. *South African Journal of Sport Medicine.* 2012 May 1;24(2).

35. Mingorance JA, Montoya P, Vivas Miranda JG, Riquelme I. A Comparison of the Effect of Two Types of Whole Body Vibration Platforms on Fibromyalgia. A Randomized Controlled Trial. *International Journal of Environmental Research and Public Health* [Internet]. 2021 Jan 1 [cited 2022 Dec 12];18(6):3007. Available from: https://www.mdpi.com/1660-4601/18/6/3007/htm

36. Dong Y, Wang W, Zheng J, Chen S, Qiao J, Wang X. Whole Body Vibration Exercise for Chronic Musculoskeletal Pain: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Archives of Physical Medicine and Rehabilitation.* 2019 Nov;100(11):2167–78.

37. Qiu C, Chui ECS, Chow SKH, Cheung W-H, Wong RMY. The Effects of Whole-body Vibration Therapy on Knee Osteoarthritis: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Journal of Rehabilitation Medicine.* 2022 Feb 17;

38. Wong ML, Widerstrom-Noga E, Field-Fote EC. Effects of whole-body vibration on neuropathic pain and the relationship between pain and spasticity in persons with spinal cord injury. *Spinal Cord* [Internet]. 2022 Nov 1 [cited 2022 Dec 12];60(11):963–70. Available from: https://www.nature.com/articles/s41393-022-00806-w

39. Sá-Caputo DC, Paineiras-Domingos LL, Oliveira R, Neves MFT, Brandão A, Marin PJ, et al. Acute Effects of Whole-Body Vibration on the Pain Level, Flexibility, and Cardiovascular Responses in Individuals With Metabolic Syndrome. Dose-Response. 2018 Oct 1;16(4): 155932581880213.

40. Guadarrama-Molina E, Barrón-Gámez CE, Estrada-Bellmann I, Meléndez-Flores JD, Ramírez-Castañeda P, Hernández-Suárez RMG, et al. Comparison of the effect of whole-body vibration therapy versus conventional therapy on functional balance of patients with Parkinson's disease: adding a mixed group. *Acta Neurologica Belgica.* 2020 Jul 11;121(3):721–8.

41. Moggio L, de Sire A, Marotta N, Demeco A, Ammendolia A. Vibration therapy role in neurological diseases rehabilitation: an umbrella review of systematic reviews. *Disability and Rehabilitation.* 2021 Jul 5;1–9.

42. Kitamoto T, Saegusa R, Tashiro T, Sakurai T, Yokote K, Tokuyama T. Favorable Effects of 24-Week Whole-Body Vibration on Glycemic Control and Comprehensive Diabetes Therapy in Elderly Patients with Type 2 Diabetes. *Diabetes Therapy.* 2021 May 12;12(6):1751–61.

43. Zhang L, Weng C, Liu M, Wang Q, Liu L, He Y. Effect of whole-body vibration exercise on mobility, balance ability and general health status in frail elderly patients: a pilot randomized controlled trial. *Clinical Rehabilitation*. 2013 Jul 17;28(1):59–68.

44. Wu S, Ning H-T, Xiao S-M, Hu M-Y, Wu X-Y, Deng H-W, et al. Effects of vibration therapy on muscle mass, muscle strength and physical function in older adults with sarcopenia: a systematic review and meta-analysis. *European Review of Aging and Physical Activity.* 2020 Sep 17;17(1).

45. Lam FMH, Lau RWK, Chung RCK, Pang MYC. The effect of whole body vibration on balance, mobility and falls in older adults: A systematic review and meta-analysis. *Maturitas*. 2012 Jul;72(3): 206–13.

46. Betik AC, Parker L, Kaur G, Wadley GD, Keske MA. Whole-Body Vibration Stimulates Microvascular Blood Flow in Skeletal Muscle. *Medicine & Science in Sports & Exercise.* 2020 Aug 21;Publish Ahead of Print.

47. Gomes-Neto M, de Sá-Caputo D da C, Paineiras-Domingos LL, Brandão AA, Neves MF, Marin PJ, et al. Effects of Whole-Body Vibration in Older Adult Patients With Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Canadian Journal of Diabetes*. 2019 Oct;43(7):524-529.e2.

48. Runge M, Rittweger J. Whole-Body Vibration in Geriatric Rehabilitation. Manual of Vibration Exercise and Vibration Therapy. 2020;255–68.

49. Robinson CC, Barreto RPG, Plentz RDM. Effects of whole body vibration in individuals with diabetic peripheral neuropathy: a systematic review. *Journal of Musculoskeletal & Neuronal Interactions* [Internet]. 2018 Sep 1 [cited 2022 Dec 12];18(3):382–8. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6146195/

50. Sohrabzadeh E, Kalantari KK, Naimi SS, Daryabor A, Akbari NJ. The immediate effect of a single whole-body vibration session on balance, skin sensation, and pain in patients with type 2 diabetic neuropathy. *Journal of Diabetes & Metabolic Disorders*. 2021 Nov 25;21(1):43–9.

51. Kessler NJ, Lockard MM, Fischer J. Whole body vibration improves symptoms of diabetic peripheral neuropathy. *Journal of Bodywork and Movement Therapies.* 2020 Apr;24(2):1–3.

52. Jamal A, Ahmad I, Ahamed N, Azharuddin M, Alam F, Hussain ME. Whole body vibration showed beneficial effect on pain, balance measures and quality of life in painful diabetic peripheral neuropathy: a randomized controlled trial. *Journal of Diabetes & Metabolic Disorders.* 2019 Dec 21;19(1):61–9.

53. Waheed A, Azharuddin M, Ahmad I, Noohu MM. Whole-body vibration, in addition to balance exercise, shows positive effects for strength and functional ability in patients with diabetic peripheral neuropathy: A single-blind randomized controlled trial. *Journal of Diabetology.* 2022 Jan 12;12(4):456–63.

54. van Heuvelen MJG, Rittweger J, Judex S, Sañudo B, Seixas A, Fuermaier ABM, et al. Reporting Guidelines for Whole-Body Vibration Studies in Humans, Animals and Cell Cultures: A Consensus Statement from an International Group of Experts. *Biology*. 2021 Sep 27;10(10):965.

55. Rauch F, Sievanen H, Boonen S, Cardinale M, Degens H, Felsenberg D, et al. Reporting whole-body vibration intervention studies: Recommendations of the International Society of Musculoskeletal and Neuronal Interactions. *JOURNAL OF MUSCULOSKELETAL & NEURONAL INTERACTIONS* [Internet]. 2010 Sep 1 [cited 2022 Dec 12];10. Available from: https://e-space.mmu.ac.uk/595958/

56. Castaneda C, Layne JE, Munoz-Orians L, Gordon PL, Walsmith J, Foldvari M, et al. A Randomized Controlled Trial of Resistance Exercise Training to Improve Glycemic Control in Older Adults With Type 2 Diabetes. *Diabetes Care.* 2002 Dec 1;25(12):2335–41.

57. American Diabetes Association. Diagnosis | ADA [Internet]. diabetes.org. 2022. Available from: https://diabetes.org/diabetes/a1c/diagnosis

58. Feldman EL, Stevens MJ, Thomas PK, Brown MB, Canal N, Greene DA. A Practical Two-Step Quantitative Clinical and Electrophysiological Assessment for the Diagnosis and Staging of Diabetic Neuropathy. *Diabetes Care.* 1994 Nov 1;17(11):1281–9.

59. Feldman EL, Callaghan BC, Pop-Busui R, Zochodne DW, Wright DE, Bennett DL, et al. Diabetic neuropathy. *Nature Reviews Disease Primers* [Internet]. 2019 Jun 13;5(1). Available from: https://www.nature.com/articles/s41572-019-0092-1

60. WHO. Global recommendations on physical activity for health [Internet]. www.who.int. 2010. Available from: https://www.who.int/publications/i/item/9789241599979

61. Cardinale M, Rittweger J. Vibration exercise makes your muscles and bones stronger: fact or fiction? *British Menopause Society Journal*. 2006 Mar;12(1):12–8.

62. Tesfaye S, Boulton AJM, Dyck PJ, Freeman R, Horowitz M, Kempler P, et al. Diabetic Neuropathies: Update on Definitions, Diagnostic Criteria, Estimation of Severity, and Treatments. *Diabetes Care.* 2010 Sep 28;33(10):2285–93.

63. Kluding PM, Pasnoor M, Singh R, Jernigan S, Farmer K, Rucker J, et al. The effect of exercise on neuropathic symptoms, nerve function, and cutaneous innervation in people with diabetic peripheral neuropathy. *Journal of Diabetes and its Complications.* 2012 Sep;26(5):424–9.

64. Cella D, Lai J - S, Nowinski CJ, Victorson D, Peterman A, Miller D, et al. Neuro-QOL: Brief measures of health-related quality of life for clinical research in neurology. *Neurology*. 2012 May 9;78(23):1860–7.

65. Vileikyte L, Leventhal H, Gonzalez JS, Peyrot M, Rubin RR, Ulbrecht JS, et al. Diabetic Peripheral Neuropathy and Depressive Symptoms: The association revisited. *Diabetes Care*. 2005 Sep 26;28(10):2378–83.

66. Girach A, Julian TH, Varrassi G, Paladini A, Vadalouka A, Zis P. Quality of Life in Painful Peripheral Neuropathies: A Systematic Review. *Pain Research and Management*. 2019 May 23;2019:1–9.

67. Tütün Yümin E. Plantar Sensation and Balance in Patients with Type 2 Diabetes Mellitus with and without Peripheral Neuropathy. *Acta Clinica Croatica*. 2021;

68. Kanchanasamut W, Pensri P. Effects of weight-bearing exercise on a mini-trampoline on foot mobility, plantar pressure and sensation of diabetic neuropathic feet; a preliminary study. *Diabetic Foot & Ankle.* 2017 Jan;8(1):1287239.

69. Ahn S, Song R. Effects of Tai Chi Exercise on Glucose Control, Neuropathy Scores, Balance, and Quality of Life in Patients with Type 2 Diabetes and Neuropathy. *The Journal of Alternative*

and Complementary Medicine [Internet]. 2012 Dec [cited 2019 Nov 7];18(12):1172–8. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3513979/

70. Feng Y, Schlösser FJ, Sumpio BE. The Semmes Weinstein monofilament examination is a significant predictor of the risk of foot ulceration and amputation in patients with diabetes mellitus. *Journal of Vascular Surgery* [Internet]. 2011 Jan 1 [cited 2020 Feb 26];53(1):220-226.e5. Available from: https://www.sciencedirect.com/science/article/pii/S0741521410014953?via%3Dihub

71. Costa T, Coelho L, Silva MF. Automatic Segmentation of Monofilament Testing Sites in Plantar Images for Diabetic Foot Management. *Bioengineering.* 2022 Feb 22;9(3):86.

72. Kokkinos P, Kaminsky LA, Arena R, Zhang J, Myers J. A new generalized cycle ergometry equation for predicting maximal oxygen uptake: The Fitness Registry and the Importance of Exercise National Database (FRIEND). *European Journal of Preventive Cardiology.* 2018 Apr 25;25(10):1077–82.

73. Mullerpatan R, Kanjirathingal J, Nehete G, Raghuram N. Effect of yogasana intervention on standing balance performance among people with diabetic peripheral neuropathy: A pilot study. *International Journal of Yoga*. 2021;14(1):60.

74. Lee K, Lee S, Song C. Whole-Body Vibration Training Improves Balance, Muscle Strength and Glycosylated Hemoglobin in Elderly Patients with Diabetic Neuropathy. *The Tohoku Journal of Experimental Medicine*. 2013;231(4):305–14.

75. Song CH, Petrofsky JS, Lee SW, Lee KJ, Yim JE. Effects of an Exercise Program on Balance and Trunk Proprioception in Older Adults with Diabetic Neuropathies. *Diabetes Technology & Therapeutics.* 2011 Aug;13(8):803–11.

76. American Diabetes Association. 8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes—2022. *Diabetes Care*. 2021 Dec 16;45(Supplement_1):S113–24.

77. Kordi Yoosefinejad A, Shadmehr A, Olyaei G, Talebian S, Bagheri H, Mohajeri-Tehrani MR. Short-term effects of the whole-body vibration on the balance and muscle strength of type 2 diabetic patients with peripheral neuropathy: a quasi-randomized-controlled trial study. *Journal of Diabetes & Metabolic Disorders.* 2015 May 23;14(1).

78. Pollock RD, Woledge RC, Mills KR, Martin FC, Newham DJ. Muscle activity and acceleration during whole body vibration: Effect of frequency and amplitude. *Clinical Biomechanics.* 2010 Oct; 25(8):840–6.

79. Yale University. Visual Analogue Scale | Yale Assessment Module Training [Internet]. assessment-module.yale.edu. Available from: https://assessment-module.yale.edu/im-palliative/visual-analogue-scale

80. Northwestern University. HealthMeasures [Internet]. www.healthmeasures.net. [cited 2022 Dec 15]. Available from: https://www.healthmeasures.net/index.php?option=com_instruments&view=search&Itemid=977

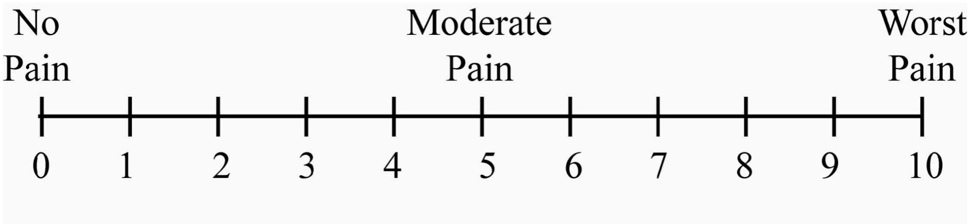
81. 5.07-10 G monofilament testing: Retractable & disposable [Internet]. Rainier Medical. [cited 2022Dec16]. Available from: https://www.rainiermeded.com/monofilament-5-07-to-10-gram-p/monofilament.htm

82. Monark LC7 TT novo time trial testing Bike Ergometer. [cited 2022Dec16]. Available from: https://www.hcifitness.com/Monark-LC7-TT-Testing-Bike-Ergometer

83. Berg KO, Wood-Dauphinee SL, Williams JI, Maki B. Measuring balance in the elderly: validation of an instrument. *Canadian Journal of Public Health = Revue Canadienne De Sante Publique* [Internet]. 1992 Jul 1;83 Suppl 2:S7-11. Available from: https://pubmed.ncbi.nlm.nih.gov/1468055/

84. Galileo® 2000 (product obsolete) [Internet]. Galileo® 2000 (product obsolete) - Technical data product detail —Novotec Medical and Stratec Medizintechnik. [cited 2022Dec16]. Available from: https://www.galileo-training.com/us-english/products/p39/galileo-2000---product-obsolete.html

VIII. Annexes



Annex 1: Visual Analogue Scale (79)

Neuro-QOL Item Bank v1.0 –Anxiety – Short Form

Anxiety – Short Form

Please respond to each question or statement by marking one box per row.

	In the past 7 days…	**Never**	**Rarely**	**Sometimes**	**Often**	**Always**
EDANX53	I felt uneasy………………………………	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX46	I felt nervous……………………………...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX48	Many situations made me worry………..	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX41	My worries overwhelmed me…………….	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX54	I felt tense………………………………....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX55	I had difficulty calming down…………...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX18	I had sudden feelings of panic……………	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQANX07	I felt nervous when my normal routine was disturbed…………………………..……	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

English
February 19, 2018

Page **1** of **1**

Annex 2: NeuroQoL Anxiety- short form (1 of 7) (80)

Depression – Short Form

Please respond to each question or statement by marking one box per row.

	In the past 7 days…	**Never**	**Rarely**	**Sometimes**	**Often**	**Always**
EDDEP29	I felt depressed…………………………...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDDEP41	I felt hopeless…………………………….	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDDEP09	I felt that nothing could cheer me up……..	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDDEP48	I felt that my life was empty……………...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDDEP04	I felt worthless……………………………	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDDEP36	I felt unhappy…………………………….	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDDEP39	I felt I had no reason for living…………...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDDEP45	I felt that nothing was interesting………....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Annex 3: NeuroQoL Depression- short form (2 of 7)

Lower Extremity Function (Mobility) – Short Form

Please respond to each question or statement by marking one box per row.

		Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
PFC45	Are you able to get on and off the toilet?...	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA30	Are you able to step up and down curbs?...	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA56	Are you able to get in and out of a car?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA45	Are you able to get out of bed into a chair?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA12	Are you able to push open a heavy door? ..	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA53	Are you able to run errands and shop?.......	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA31	Are you able to get up off the floor from lying on your back without help?...............	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
PFA23	Are you able to go for a walk of at least 15 minutes?	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

Annex 4: NeuroQoL Lower limb extremity function- short form (3 of 7)

Positive Affect and Well-Being - Short Form

Please respond to each question or statement by marking one box per row.

	Lately…	**Never**	**Rarely**	**Sometimes**	**Often**	**Always**
NQPPF14	I had a sense of well-being……………….	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQPPF12	I felt hopeful……………………………....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQPPF15	My life was satisfying………………….…	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQPPF20	My life had purpose………….……………	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQPPF17	My life had meaning……………………...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQPPF22	I felt cheerful………………….…………..	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQPPF19	My life was worth living……….…………	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQPPF16	I had a sense of balance in my life……….	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQPPF07	Many areas of my life were interesting to me………….………………………….....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Annex 5: NeuroQoL Positive affect and Wellbeing- short form (4 of 7)

Fatigue – Short Form

Please respond to each question or statement by marking one box per row.

	In the past 7 days…	Never	Rarely	Sometimes	Often	Always
NQFTG13	I felt exhausted…………………………...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQFTG11	I felt that I had no energy………………...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQFTG15	I felt fatigued……………………………..	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQFTG06	I was too tired to do my household chores.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQFTG07	I was too tired to leave the house………...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQFTG10	I was frustrated by being too tired to do the things I wanted to do…………………	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQFTG14	I felt tired…………………………………	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQFTG02	I had to limit my social activity because I was tired…………………………………	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Annex 6: NeuroQoL Fatigue- short form (5 of 7)

Sleep Disturbance – Short Form

Please respond to each question or statement by marking one box per row.

	In the past 7 days…	Never	Rarely	Sometimes	Often	Always
NQSLP02	I had to force myself to get up in the morning………………………………….	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQSLP03	I had trouble stopping my thoughts at bedtime…………………………………...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQSLP04	I was sleepy during the daytime………….	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQSLP05	I had trouble sleeping because of bad dreams…………………………………….	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQSLP07	I had trouble falling asleep………………..	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQSLP12	Pain woke me up………………………….	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQSLP13	I avoided or cancelled activities with my friends because I was tired from having a bad night's sleep…………………………..	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQSLP18	I felt physically tense during the middle of the night or early morning hours………...	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Annex 7: NeuroQoL Sleep disturbance- short form (6 of 7)

Satisfaction with Social Roles and Activities – Short Form

Please respond to each question or statement by marking one box per row.

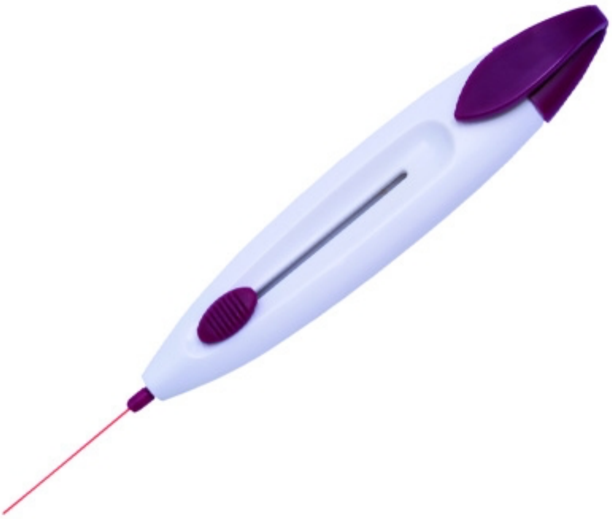
	In the past 7 days…	Not at all	A little bit	Somewhat	Quite a bit	Very much
NQSAT 03	I am bothered by my limitations in regular family activities	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQSAT 23	I am disappointed in my ability to socialize with my family………………....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQSAT14	I am bothered by limitations in my regular activities with friends..……………………	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
NQSAT11	I am disappointed in my ability to meet the needs of my friends	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

	In the past 7 days…	Not at all	A little bit	Somewhat	Quite a bit	Very much
NQSAT33	I am satisfied with my ability to do things for fun outside my home………………....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQSAT32	I am satisfied with the amount of time I spend doing leisure activities…………….	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQSAT47	I am satisfied with how much of my work I can do (include work at home).…………	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
NQSAT 46	I am satisfied with my ability to do household chores or tasks………..........	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

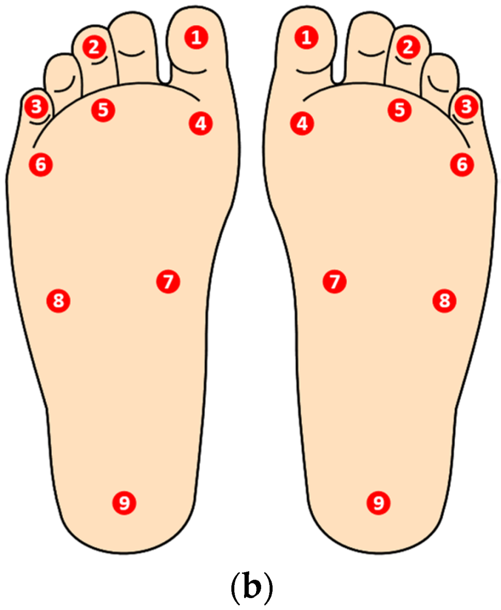
English
March 6, 2014

Page **1** of **1**

Annex 8: NeuroQoL Satisfaction with social role and activity- short form (7 of 7)



Annex 9: 5,07g monofilament used in Semmes-weinstein monofilament test (81)



Annex 10: Semmes-weinstein monofilament testing sites (71)

Annex 11: cycle ergometer used for assessment and warm up (Monark LC7TT) (82)

Berg Balance Scale

Name: ___________________________________ Date: ___________________

Location: _________________________________ Rater: ___________________

ITEM DESCRIPTION	SCORE (0-4)
1. Sitting to standing	________
2. Standing unsupported	________
3. Sitting unsupported	________
4. Standing to sitting	________
5. Transfers	________
6. Standing with eyes closed	________
7. Standing with feet together	________
8. Reaching forward with outstretched arm	________
9. Retrieving object from floor	________
10. Turning to look behind	________
11. Turning 360 degrees	________
12. Placing alternate foot on stool	________
13. Standing with one foot in front	________
14. Standing on one foot	________
Total	________

GENERAL INSTRUCTIONS
Please document each task and/or give instructions as written. When scoring, please record the lowest response category that applies for each item.

In most items, the subject is asked to maintain a given position for a specific time. Progressively more points are deducted if:

- the time or distance requirements are not met
- the subject's performance warrants supervision
- the subject touches an external support or receives assistance from the examiner

Subject should understand that they must maintain their balance while attempting the tasks. The choices of which leg to stand on or how far to reach are left to the subject. Poor judgment will adversely influence the performance and the scoring.

Equipment required for testing is a stopwatch or watch with a second hand, and a ruler or other indicator of 2, 5, and 10 inches. Chairs used during testing should be a reasonable height. Either a step or a stool of average step height may be used for item # 12.

Annex 12: Berg balance Scale (1 of 3) (83)

Berg Balance Scale

1. SITTING TO STANDING
INSTRUCTIONS: Please stand up. Try not to use your hand for support.
( ) 4 able to stand without using hands and stabilize independently
( ) 3 able to stand independently using hands
( ) 2 able to stand using hands after several tries
( ) 1 needs minimal aid to stand or stabilize
( ) 0 needs moderate or maximal assist to stand

2. STANDING UNSUPPORTED
INSTRUCTIONS: Please stand for two minutes without holding on.
( ) 4 able to stand safely for 2 minutes
( ) 3 able to stand 2 minutes with supervision
( ) 2 able to stand 30 seconds unsupported
( ) 1 needs several tries to stand 30 seconds unsupported
( ) 0 unable to stand 30 seconds unsupported

If a subject is able to stand 2 minutes unsupported, score full points for sitting unsupported. Proceed to item #4.

3. SITTING WITH BACK UNSUPPORTED BUT FEET SUPPORTED ON FLOOR OR ON A STOOL
INSTRUCTIONS: Please sit with arms folded for 2 minutes.
( ) 4 able to sit safely and securely for 2 minutes
( ) 3 able to sit 2 minutes under supervision
( ) 2 able to able to sit 30 seconds
( ) 1 able to sit 10 seconds
( ) 0 unable to sit without support 10 seconds

4. STANDING TO SITTING
INSTRUCTIONS: Please sit down.
( ) 4 sits safely with minimal use of hands
( ) 3 controls descent by using hands
( ) 2 uses back of legs against chair to control descent
( ) 1 sits independently but has uncontrolled descent
( ) 0 needs assist to sit

5. TRANSFERS
INSTRUCTIONS: Arrange chair(s) for pivot transfer. Ask subject to transfer one way toward a seat with armrests and one way toward a seat without armrests. You may use two chairs (one with and one without armrests) or a bed and a chair.
( ) 4 able to transfer safely with minor use of hands
( ) 3 able to transfer safely definite need of hands
( ) 2 able to transfer with verbal cuing and/or supervision
( ) 1 needs one person to assist
( ) 0 needs two people to assist or supervise to be safe

6. STANDING UNSUPPORTED WITH EYES CLOSED
INSTRUCTIONS: Please close your eyes and stand still for 10 seconds.
( ) 4 able to stand 10 seconds safely
( ) 3 able to stand 10 seconds with supervision
( ) 2 able to stand 3 seconds
( ) 1 unable to keep eyes closed 3 seconds but stays safely
( ) 0 needs help to keep from falling

7. STANDING UNSUPPORTED WITH FEET TOGETHER
INSTRUCTIONS: Place your feet together and stand without holding on.
( ) 4 able to place feet together independently and stand 1 minute safely
( ) 3 able to place feet together independently and stand 1 minute with supervision
( ) 2 able to place feet together independently but unable to hold for 30 seconds
( ) 1 needs help to attain position but able to stand 15 seconds feet together
( ) 0 needs help to attain position and unable to hold for 15 seconds

Berg Balance Scale continued…..

8. REACHING FORWARD WITH OUTSTRETCHED ARM WHILE STANDING
INSTRUCTIONS: Lift arm to 90 degrees. Stretch out your fingers and reach forward as far as you can. (Examiner places a ruler at the end of fingertips when arm is at 90 degrees. Fingers should not touch the ruler while reaching forward. The recorded measure is the distance forward that the fingers reach while the subject is in the most forward lean position. When possible, ask subject to use both arms when reaching to avoid rotation of the trunk.)
( ) 4 can reach forward confidently 25 cm (10 inches)
( ) 3 can reach forward 12 cm (5 inches)
( ) 2 can reach forward 5 cm (2 inches)
( ) 1 reaches forward but needs supervision
( ) 0 loses balance while trying/requires external support

9. PICK UP OBJECT FROM THE FLOOR FROM A STANDING POSITION
INSTRUCTIONS: Pick up the shoe/slipper, which is place in front of your feet.
( ) 4 able to pick up slipper safely and easily
( ) 3 able to pick up slipper but needs supervision
( ) 2 unable to pick up but reaches 2-5 cm(1-2 inches) from slipper and keeps balance independently
( ) 1 unable to pick up and needs supervision while trying
( ) 0 unable to try/needs assist to keep from losing balance or falling

10. TURNING TO LOOK BEHIND OVER LEFT AND RIGHT SHOULDERS WHILE STANDING
INSTRUCTIONS: Turn to look directly behind you over toward the left shoulder. Repeat to the right. Examiner may pick an object to look at directly behind the subject to encourage a better twist turn.
( ) 4 looks behind from both sides and weight shifts well
( ) 3 looks behind one side only other side shows less weight shift
( ) 2 turns sideways only but maintains balance
( ) 1 needs supervision when turning
( ) 0 needs assist to keep from losing balance or falling

11. TURN 360 DEGREES
INSTRUCTIONS: Turn completely around in a full circle. Pause. Then turn a full circle in the other direction.
( ) 4 able to turn 360 degrees safely in 4 seconds or less
( ) 3 able to turn 360 degrees safely one side only 4 seconds or less
( ) 2 able to turn 360 degrees safely but slowly
( ) 1 needs close supervision or verbal cuing
( ) 0 needs assistance while turning

12. PLACE ALTERNATE FOOT ON STEP OR STOOL WHILE STANDING UNSUPPORTED
INSTRUCTIONS: Place each foot alternately on the step/stool. Continue until each foot has touch the step/stool four times.
( ) 4 able to stand independently and safely and complete 8 steps in 20 seconds
( ) 3 able to stand independently and complete 8 steps in > 20 seconds
( ) 2 able to complete 4 steps without aid with supervision
( ) 1 able to complete > 2 steps needs minimal assist
( ) 0 needs assistance to keep from falling/unable to try

13. STANDING UNSUPPORTED ONE FOOT IN FRONT
INSTRUCTIONS: (DEMONSTRATE TO SUBJECT) Place one foot directly in front of the other. If you feel that you cannot place your foot directly in front, try to step far enough ahead that the heel of your forward foot is ahead of the toes of the other foot. (To score 3 points, the length of the step should exceed the length of the other foot and the width of the stance should approximate the subject's normal stride width.)
( ) 4 able to place foot tandem independently and hold 30 seconds
( ) 3 able to place foot ahead independently and hold 30 seconds
( ) 2 able to take small step independently and hold 30 seconds
( ) 1 needs help to step but can hold 15 seconds
( ) 0 loses balance while stepping or standing

14. STANDING ON ONE LEG
INSTRUCTIONS: Stand on one leg as long as you can without holding on.
( ) 4 able to lift leg independently and hold > 10 seconds
( ) 3 able to lift leg independently and hold 5-10 seconds
( ) 2 able to lift leg independently and hold ≥ 3 seconds
( ) 1 tries to lift leg unable to hold 3 seconds but remains standing independently.
( ) 0 unable to try of needs assist to prevent fall

( ) TOTAL SCORE (Maximum = 56)

Annex 14: Berg balance Scale (3 of 3)

Annex 15: whole body vibration platform (Galileo 2000)
(84)

INFORMED CONSENT FORM

You are being asked to take part in a research study. Before you agree to participate in this study you must read this information sheet and make sure you understand the content and purpose of the study. Do not hesitate to ask questions to the researcher if you have any doubts.

PART I :
INTRODUCTION :

We are physiotherapist graduated from the university of EUSES Barcelona. We invite you to participate in our study called : The effects of whole body vibration on type 2 diabetes adults with painful peripheral neuropathies: a randomised controlled trial.
This information sheet will help you understand how the study will be carried out. It will provide a thorough explanation of the study's goals, methods, and potential side effects.

PURPOSE OF THE RESEARCH

We would like to study the effects of whole body vibration (WBV) on type 2 diabetes adults with painful peripheral neuropathies. We especially want to determine the effects this procedure has on pain as well as quality of life, balance, aerobic capacity, plantar sensation and strength.

To do so, the participants of our study will take part in either a WBV intervention or a sham WBV intervention in which the WBV machine will not be turned on.

TYPE OF RESEARCH INTERVENTION

The research involves the use of WBV as well as general lifestyle guidelines for diabetic patients. WBV is a therapy modality that consists of standing or doing exercise on a vibrating platform. In the case of our study, the participants will simply stand with bent knees on the platform. The vibrations created are believed to be beneficial for different clinical populations, including diabetics with neuropathies. They stimulate body tissues in a way that triggers muscle contraction and potentially improves sensations.

PARTICIPANTS SELECTION

The participants must meet the inclusion criteria to take part in the study. Furthermore they must be free of any exclusion criteria.

It is important that you are honest with the medical staff in regards to your health history.

Required criterias :

- Diagnose of T2DM
- Diagnose of peripheral neuropathy associated to diabetes
- 1 or more painful episode per week (VAS>4)

Exclusion criterias:

- Physically active
- Epilepsy
- Knee or hip prothesis
- Recent fracture
- Recent venous thrombosis
- Spinal tumors
- Gallbladder stone
- Musculoskeletal/neurological condition/foot ulcer that do not allow locomotion

VOLUNTARY PARTICIPATION

Your participation in this study is fully voluntary. You can choose whether you want to be a part of it or not. If you decide to take part in the study, you will be asked to sign the consent form. Even after the study has started and you have signed the consent form, you can still choose to withdraw at any moment and without giving a reason.

PROCEDURES AND PROTOCOLES

You will need to go to the hospital 3 times a week for 30 minutes each time. You will be expected to ;

- Do a 5 minutes warm-up
- Undergo 4x3 minutes of either SHAM WBV or real WBV (depending on your group allocation)
- Orally express your pain levels on a scale of 0-10 (VAS)

There will be audio recording to keep tract of the pain levels.
A supervising physician will always be there during your time in the hospital.

DURATION

The WBV treatment will be applied for 6 weeks. You will also be asked to come back to the hospital for the final assessment which will be done 6 weeks after the end of the treatment (12 weeks from baseline).

CONFIDENTIALITY

Your information will be kept anonymous and u only be sed for the purpose of this study. Participant data will not be shared except in the case of specific incidents during which the researchers are legally obliged to.

RIGHT TO REFUSE OR WITHDRAW

We remind you that your participation is voluntary and that you can withdraw at any moment during the research or the follow-up.

SIDE EFFECTS POTENTIAL RISKS

Unwanted side effects of WBV could include (78):
-Faintness
-Nausea
-Skin erythema (abnormal redness of skin)
-Oedema
-Pain
-Temporary loose of foot sensation

Measures will be put in place according to guidelines to reduce any potential side effect (position, time, parameters of the WBV machine).
There is the possibility of an accidental injury occurring during the assessment or during the WBV treatments. Physiotherapists and assessors will always be present to supervise the intervention.

BENEFITS

This intervention aims to relieve symptoms of diabetic neuropathy.

Benefits could include:
-reduction of pain
-improvement of quality of life
-improvement of strength and balance
-Improvement of plantar sensitivity
-improvement of aerobic capacity

Furthermore, the information obtained in this study will participate to an increase of knowledge regarding the subject of pain relief in diabetic neuropathies. This can be of help to all the individuals affected by the condition as well as the researchers studying it.

WHO TO CONTACT

Mrs Maelle Bernard
Direction : Carrer de la Feixa Llarga, s/n, 08907 L'Hospitalet de Llobregat, Barcelona
Email : mbernard.research@gmail.com
Phone : 978 664 §43

PART II :

CERTIFICATE OF CONSENT

I, ………………………………………………..………, guarantee that :

1. I have received a copy of the consent form. □yes □no
2. I have read and understood the consent form. □yes □no
3. I understand that my participation is voluntary. □yes □no
4. All my questions have been answered and I am satisfied with the answers. □yes □no
5. I understand that I can withdraw from the study at any moment. □yes □no
6. I am aware of the potential risks, benefits and side effects that may arise from my participation in the study. □yes □no
7. I understand that the researchers will keep my datas confidential. □yes □no
8. I consent to participate in the study. □yes □no

DATE AND PLACE :
NAME OF THE PARTICIPANT :
SIGNATURE OF THE PARTICIPANT