Protocol and Statistical Analysis Plan: Cover Page

Monitoring Physical Activity in Hispanic Women With Chronic Neurological Disorders

HS-18-00993
NCT : not issued.
Date: March 24, 2021
Investigator: Dr Giselle M Petzinger
Email: petzinge@med.usc.edu

PROTOCOL NUMBER:

TITLE: Monitoring Physical Activity in Hispanic Women with Chronic Neurological Disorders

PRINCIPAL INVESTIGATOR(S):

Giselle Petzinger, MD USC. Dept. of Neurology
Address 1333 San Pablo, LA CA 90033
Telephone 323- 442-5710
Fax 323-442-5794

CO-INVESTIGATOR(S):

Alexander Garbin, DPT, Division of Biokinesiology
Janina Morrison, MD Medical Director of The Wellness Center
Jesus Diaz, PhD USC Dept. of Occupational Therapy
Lilyana Amezcua, MD Dept of Neurology
Charles Kaplan, PhD, USC Suzanne Dworak-Peck School of Social Work
Beth Fisher, PT, PhD, Dept of Neurology
Vy Bui, Dept of Neurology

Coordinator:

Vanessa Marroquin , The Wellness Center

Sponsor: USC Zumberge Diversity Grant

PARTICIPANTS/Locations:

The Wellness Center at The Historic General Hospital

1. BACKGROUND AND HYPOTHESIS

1.1. Physical Activity in Hispanic Women Population

In the last decade, regular physical activity (PA), particularly exercise, has been shown to play an important role in improving the disease course of many chronic neurological conditions, such as Parkinson's disease, Multiple Sclerosis, and headache. Unfortunately, the generalizability of these findings to other diverse populations is unclear since the vast majority of clinical research has been conducted in non-Hispanic men with affordable access to medical care. In addition, studies examining the population of people regularly engaged in physical activity in this country have indicated that lack of physical activity is particularly prevalent in Hispanic groups compared to non-Hispanic white individuals. In terms of gender, a significantly high percentage (74%) of Hispanic women do not participate in exercise activities and this number climbs with age. While there a number of reasons for this occurrence, a significant contributor includes lack of resources and accessibility to programs that promote PA and exercise.

1.2. Role of Physical Activity in Chronic Neurological Disorders

Neurological disorders, including stroke, headache, Parkinson's disease (PD) and multiple sclerosis represent the most common cause of disability world-wide[7]. While there are treatments available for many disorders, these medications often provide modest relief and are expensive with limited accessibility to this population we serve. There also remain no effective cures. In the last decade, published studies have supported the vital role of PA (particularly exercise) in many chronic neurological disorders by improving neurological outcomes, quality of life, and potentially modifying disease course[1,8]. A limitation is that the majority of studies have been conducted in non-Hispanic white populations. In addition, PA is known to be significantly lacking in the Hispanic population overall, particularly in Hispanic women. This application will begin to address this gap by examining the role of coaching and wearable devices in promoting PA in Hispanic women population with chronic neurological conditions.

1.3. The Wellness Center at the Historic General Hospital

The Wellness Center at the Historic General Hospital (TWC) located next to Los Angeles County/University of Southern California (LAC +USC) medical center, serves a large and diverse ethnic population, many of whom are Hispanic and live within close proximity to LAC+USC hospital. TWC serves as a community center and is also a referral for patients seen at the LAC/USC Outpatient Neurology Clinics. TWC offers an opportunity to engage this diverse ethnic population of patients in an educational exercise program, along with coaching and social support, factors that have been shown to promote behavioral change.

1.4. Hypothesis

The primary goal of this proposal is to demonstrate the feasibility of using a Fitbit charge to monitor and promote physical activity in a diverse population of Hispanic women with chronic neurological disorders. Hispanic women will also receive behavioral coaching using a Lifestyle Redesign approach (see below) to enhance physical activity in their daily lives. The secondary goal of this proposal is to investigate whether changes in physical activity are associated with (i) quality of life including perception of health and well- being and (ii)

frequency of hospital and county clinic visits.

2. OBJECTIVES AND PURPOSE

2.1 Primary Objective

This pilot study will provide feasibility on use of wearable technology for tracking and self-monitoring PA as well as preliminary data to support our overall approach for promoting PA and improving disease status in a Hispanic women population. A larger application will be submitted to the NIH, DoD, or other federal agency focused on investigating the impact of PA on chronic neurological diseases in a diverse and inclusive Hispanic population in LA County.

2.1.1 Specific Aim 1

Specific Aim 1 establishes feasibility of this approach by measuring adherence and change in PA using a Fitbit Alta HR activity monitor in Hispanic women with chronic neurological diseases. Adherence will be determined through: (i) the average hours/day of use; and (ii) the length of time (percent of total study days) of usage throughout the 16-week study. Adherence defined as (i) 5 or more days/week of use and (ii) 10 or more hours of use during the day.

2.1.2 Specific Aim 2

Specific Aim 2 tests the hypothesis that an increase in physical activity will be correlated with a decrease in LA County (LAC) Facilities health care use (hospital and clinic visits). Physical activity will be assessed by change in either: (i) the average number of steps/week; and (ii) average time spent in sedentary, light, or moderate to vigorous intensity based on MET (metabolic expenditure) of physical activity/week. Methods: Changes in PA outcome metrics over the 16-week period will be correlated with the total number of hospital/outpatient clinic visits. Total hospital use will be determined through the LAC/DHS (Department of Human Services) electronic medical records and will include outpatient provider visits, emergency room and urgent care visits, total hospitalizations, and days spent in hospital.

2.1.3 Specific Aim 3

Specific Aim 3a tests the hypothesis that increase in physical activity is associated with an increase in the quality of life (QOL). Physical activity will be measured through: (i) the average number of steps/week; and (ii) average intensity of physical activity/week. QOL will be determined through measures of self-rated health and well-being. These Spanish validated surveys will include illness perception questionnaire and health and well-being questionnaire

3.0 STUDY DESIGN

3.1 Overall Study Design

This is a 16-week single group study of PA promotion and monitoring along with its effect

on Neurological Health. Twenty Hispanic women seen at LAC/USC Neurology clinic will be referred to TWC and invited to participate in a physical activity (PA) study for 16 weeks. Participants will receive individualized Fitbit Charge activity monitors at baseline and instructed on its usage and maintenance. Adherence to activity monitor use and amount and level of PA will be determined. All assessments that include quality of life, exercise behaviors, and self-rated health and mood will be made at baseline and at 16 weeks at TWC. Educational/coaching will take place through (i) individualized instruction on exercise at baseline and at the end of week 4 at TWC and (ii) weekly calls from TWC to promote PA goal setting as well as Fitbit use. At the end of week 1, participants will be asked to return to the TWC to review instructions on Fitbit App use and to receive further education on the benefits of exercise through a brief Power Point presentation. Patient may also receive text messages throughout the study to remind them of upcoming appointments or deadlines. General Neurological Health status will be determined through use of Electronic medical records to determine hospital and outpatient clinic visits through the 16 weeks. At study completion, participants will be allowed to keep their Fitbit activity monitor and will receive a 3-month follow up post-study call to assess the continued usage of the Fitbit charge activity monitor and a quality of life questionnaire.

3.2 Enrollment Plan

Twenty (20) Hispanic women with a chronic neurological disorder will be recruited from our LAC/USC Neurology Clinic. We expect to achieve this goal by 2 months from study start.

3.3 Participant Identification and Informed Consent

For this study, Drs. Petzinger or Morrison will screen all potential participants according to the list of inclusion/exclusion criteria. This will include talking to the referral neurology doctor from the neurology clinic to determine there are no limitations to physical activity/exercise (see exclusion below) .The principal investigators and members of the research team will explain the purpose, risks, procedures, and date of the study. If the subject is interested in participating, she will be given the Informed Consent to read or if they cannot read, our coordinator will read the informed consent to her. Subjects and their family members will be allowed sufficient time to read and/or think about the Informed Consent Form and be given the opportunity, and encouraged, to ask questions before signing the document. Following the patient giving informed consent (signing the document) she will be able to participate in the study. If the investigator or study team members have any reason to suspect that the subject does not fully comprehend the informed consent or the study, the individual will not be considered as a possible participant of the study. The study will be conducted after having Institutional Review Board (IRB) approval at USC.

3.4 Fitbit Charge HR2 Activity Monitor

Participants will be provided a Fitbit Alta HR and wall charger. Each participant will be given a unique ID# that will be assigned at baseline and used to set-up the Fitbit data acquisition. The Fitbit app will also be set up on their smartphone to allow self-monitoring of activity. The Fitbit device includes both an accelerometer and heart rate monitor and is capable of continuous measuring and storing data at up to a 1-second sampling rate for up to 5 days. Fitbit data will be passively downloaded through either a WiFi and/or smartphone connection

to Fitabase. Fitabase (Fitabase, San Diego, Ca) is a research friendly application programming interface and comprehensive data management program that allows the device data from all users to be identified through a uniquely assigned ID# and transmitted in a secure fashion to the data acquisition and integration center.

The Fitbit Alta will be worn on the wrist every day during the course of the 16-week study. While the Fitbit is water resistant, participants will be asked not to wear the device while bathing or swimming. Participants will be instructed on self- monitoring, usage and maintenance of the Fitbit at the baseline visit. Participants will be monitored for Fitbit compliance by (i) weekly phone calls; and (ii) monitoring of passively downloaded Fitbit data through Fitabase data collection server. Further instructions will also be given 1 week into the study, to ensure proper compliance. Participants will be allowed to keep their Fitbit monitor at the end of the study. Follow-up phone call at 3-months post-study will assess continued use of the Fitbit activity monitor.

3.5 Educational/Behavioral Coaching on Exercise (Lifestyle Redesign)

Participants will receive individualized goal setting and a guide to increase exercise at the beginning of the study (baseline) and at week four (week four visit) at TWC. The Occupational therapist (OT) will administer a well published approach for promoting PA called Lifestyle Redesign which addresses physical, psychosocial and environmental barriers to health and incorporate self-care strategies and goal setting. Coaching will be administered by a bilingual OT (Dr. Jesus Diaz) and in language (Spanish or English) preferred by participant. Based on studies examining PA and brain health, the Occupational Therapist (OT) will guide the participant through a goal setting process for moderate to vigorous intensity of physical activity including a specific guide plan to achieve these goals of 10,000 steps per day and/or 150 minutes/week of moderate to vigorous activity. Participants will also receive weekly calls from the TWC (supervised by OT) to review PA and goal setting for each week over the course of the 16-week study.

3.5.1 Motivation to Exercise

Participants will be given a brief Power Point presentation titled “Promoviendo un Cerebro Sano En las Enfermedades Neurologicas, el Rol Del Ejercicio”. The purpose of this presentation is the educate participants on the importance of exercise for brain health and increase motivation throughout the study. This presentation will be given at baseline visit, week 1, and week 4 follow up.

3.6 Primary Outcome Measures

3.6.1 Baseline Demographic Data

Following inclusion and exclusion and after obtaining informed consent, baseline demographic data will be obtained which will include age, recent healthcare visit frequency, medical history, medication, years of education, and tobacco use.

3.6.2 Physical Activity, Adherence Assessment

Data gathered from Fitbit based device will be stored, visualized and aggregated through a commercially available service (Fitabase Inc, Https:/www.Fitabase.com). Fitabase is a research friendly application

programming interface that allows the device data from all users to be identified through a uniquely assigned ID# and transmitted in a secure fashion to the data acquisition and integration center. Data is downloaded from Fitabase in a de-identified matter and is ready for statistical analysis (i.e. CSV files that are SPSS ready). The Fitabase one-time set-up process (taking approximately five minutes) will take place at the wellness center to establish a continuous, passive and secure data stream of all measures. The following measures will be obtained during the course of the study: (i) step count, (ii) time spent in sedentary, light, moderate, and vigorous activity, and (iii) length of wear.

3.6.3 Determination of LA County Facilities Health Care Use

We will utilize electronic medical record (EMR) system of LA County Department of Health Services (DHS) to determine the number of hospital visits including Emergency room and urgent care visits, outpatient clinic visits, hospital stays and days within the hospital. HIPPA guidelines will be followed.

3.7 Secondary Outcome Measures (scales in Spanish and English)

All scales will be offered to patient in their preferred language of Spanish or English. For patients who are illiterate, the coordinator will read the scales to the patient and record their answer.

3.7.1 Quality of Life (QOL)

This measure assessed participants' views of their health, how well they feel, and well they are able to complete their usual activities.

3.7.2 Spanish Acculturation

The purpose of this questionnaire is to assess the level to which participants acculturate or adopt the attitudes, values, customs, beliefs, and behaviors of another culture.

3.7.3 Brief Illness Perception Questionnaire (BIPQ)

The purpose of this questionnaire is to assess participants' perceptions of their health and well-being.

3.7.4 Patient Activation Measure (PAM)

This measure assesses participants' knowledge, skill, and confidence for managing one's health and healthcare.

3.7.5 Spanish Physical Activity Questionnaire

This self-administered questionnaire determines total physical activity (MET-h week^{-1}) and total number of hours sitting down across a week to evaluate the levels of participants' physical activity and sedentary lifestyle.

3.7.6 FitBit Wear Technology Questionnaire

The purpose of this questionnaire is to ascertain the participants' opinions on how intuitive and useful the FitBit phone application and FitBit Alta HR activity monitor are and whether they think the device might be helpful in encouraging them to exercise or improve their physical fitness.

4.0 SELECTION AND WITHDRAWAL OF SUBJECTS

4.1 Inclusion Criteria

Inclusion Criteria includes (1) Women of Hispanic origin; (2) established patient of the neurology clinic defined as clinic visits at the LAC/USC Neurology Clinic that have spanned greater than one year; (3) age ≥ 30 (4) willing and able to utilize a Fitbit activity Monitor; (5) own a smart phone device; (6) ambulatory without assistance; (7) willing and able to provide informed consent; (8) within commuting distance to the wellness center and LAC/USC hospital; (9) reads or comprehends Spanish; (10) weekly internet access.

4.2 Exclusion Criteria

Exclusion Criteria includes (1) Clinically significant neurological or psychiatric illness including mental retardation, dementia or severe depression/anxiety; (2) any physical condition that precludes engagement in exercise, including significant heart disease.

4.3 Withdrawal Criteria

Participants may withdraw from the study at any time for any reason without affecting his/her care.

5.0 ASSESSMENT OF EFFICACY AND SAFETY

5.1 Potential Risks of the Proposed Research to the Subject

The potential risks are low and rare; however, the following are possible complications or adverse reactions related to study participation. Participation in this study may involve some discomfort. These include feelings of frustration or embarrassment which may occur while completing the outcome measures.

5.2 Protection Against Risk

All participants will be monitored by certified personnel throughout study visit to ensure subject safety. Research data collected from the study will be kept confidential in secure locked cabinets located in the Wellness Center.

5.3 Potential Benefits of the Study to the Participants and Others

Participants could potentially benefit from education on how to incorporate PA into their lifestyles and from learning how the FitBit Alta HR activity monitor can help in doing so. Findings from this study could support policies for establishing the overall need to educate, prescribe, and make available exercise programs and facilities to participants within LA County, such as wellness centers within communities and county health facilities. As collaborators on this study we gain important knowledge regarding best practices for our participants with neurological disorders and insight regarding how to help support and monitor physical activity in our patient population.

5.4 Adverse Event Reporting

All unexpected adverse events will be reported to the IRB. Serious adverse events (SAE) will be reported within 24 hours, first by phone and then followed by a written statement to the IRB. All serious adverse events will be followed to resolution and noted in the subject's chart. The following are defined as serious adverse events:

- Death
- Threat to life
- Inpatient hospitalization or prolongation of any existing hospitalization Persistent or significant disability/incapacity

6.0 CLINICAL EVALUATIONS AND STUDY CALENDAR

Parameter	Screening Visit	Baseline Visit	Weeks 1-4	Week 4	Weeks 5-16	Week 16	Week 28
Demographic Information		X					
Lifestyle Redesign Coaching		X		X			
Fitbit Charge Activity Monitor Instruction		X					
Quality of Life (QOL)		X				X	
Spanish Acculturation		X					
Brief Illness Perception Questionnaire (BIPQ)		X				X	
Patient Activation (PAM)		X				X	
Physical Activity Questionnaire		X				X	
FitBit Wear Technology Questionnaire						X	
Phone Call for FitBit Use		X	X	X	X	X	
Post-Study Phone Call on FitBit Use							X

7.0 DATA COLLECTION AND MONITORING

Data review will be ongoing by the study investigators to ensure scientific integrity of the study. A summary of study activity will be sent to the IRB annually with the continuing renewal submission. Quarterly reviews will take place to:

- determine whether all adverse events (if applicable) were appropriately reported
- check the Case Report Forms for legibility, accuracy and completeness
- validate the contents of the Case Report Forms against source
- oversee study progress and compliance
- verify that written Informed Consent and HIPAA authorization was obtained prior to patient's participation

8.0 STATISTICAL CONSIDERATIONS

8.1 Statistical Methods

Preliminary analyses will begin with an examination of the distribution of key variables to assess their characteristics (means, standard deviations, skewness, and kurtosis), to provide descriptive statistics of the study population. Continuous measures will be tested for normality and homogeneity of variance. Non-normally distributed variables will be transformed to meet the normal distribution assumption for linear statistical models.

8.1.1 Specific Aim 1

The percent of valid days of FitBit use and length of time will be calculated. We will then examine the percentage of participants who had acceptable adherence as defined as over 5 or more days/week of valid use and 10 or more hours/day length of time.

8.1.2 Specific Aim 2

Given the small sample size power to detect significant associations between physical activity and number of hospital visits will be low. Therefore, these analyses will purely exploratory. We will generate change scores from baseline to 16 weeks for both physical activity variables by subtracting week 16 scores from baseline scores. We will use Poisson regression analyses to examine the associations between changes in physical activity with our dependent variable hospital visit outcomes. Poisson regressions will be fit to account for the fact that our dependent variable (hospital visits) is a count variable and non-normally distributed. All regression models will adjust for baseline level of physical activity. Significance level will be set at 0.05.

8.1.3 Specific Aim 3

All analyses described for aim 3 are also exploratory in nature as the proposed analyses will be underpowered to detect a significant association. Change scores in Quality of life, symptoms of anxiety and depression will be calculated by subtracting week 16 scores from baseline scores. Linear regression analyses will be run examining the associations between change in PA and our dependent variable of change.

9.0 ETHICAL AND REGULATORY CONSIDERATIONS

All institutional and Federal regulations concerning the Informed Consent form will be fulfilled. The study will be conducted in adherence to ICH Good Clinical Practice.

10.0 REFERENCES

(1) Petzinger, G. M., B. E. Fisher, S. McEwen, J. A. Beeler, J. P. Walsh and M. W. Jakowec (2013) Exercise- enhanced neuroplasticity targeting motor and cognitive circuitry in Parkinson's disease, *Lancet Neurol* **12**:7, 716- 26.
(2) Motl, R. W. and B. M. Sandroff (2015) Benefits of Exercise Training in Multiple Sclerosis, *Curr Neurol Neurosci Rep* **15**:9, 585.

(3) Tan, C. O., W. P. Meehan, 3rd, G. L. Iverson and J. A. Taylor (2014) Cerebrovascular regulation, exercise, and mild traumatic brain injury, *Neurology*
(4) Ickes, M. J. and M. Sharma (2012) A systematic review of physical activity interventions in Hispanic adults, *J Environ Public Health* **2012**:156435.

(5) Clark, F., J. Jackson, M. Carlson, C. P. Chou, B. J. Cherry, M. Jordan-Marsh, B. G. Knight, D. Mandel, J. Blanchard, D. A. Granger, R. R. Wilcox, M. Y. Lai, B. White, J. Hay, C. Lam, A. Marterella and S. P. Azen (2012) Effectiveness of a lifestyle intervention in promoting the well-being of independently living older people: results of the Well Elderly 2 Randomised Controlled Trial, *J Epidemiol Community Health* **66**:9, 782-90.

(6) Lyons, E. J., Z. H. Lewis, B. G. Mayrsohn and J. L. Rowland (2014) Behavior change techniques implemented in electronic lifestyle activity monitors: a systematic content analysis, *J Med Internet Res* **16**:8, e192.
(7) Chin, J. H. and N. Vora (2014) The global burden of neurologic diseases, *Neurology* **83**:4, 349-51.
(8) Ahlskog, J. E., Y. E. Geda, N. R. Graff-Radford and R. C. Petersen (2011) Physical exercise as a preventive or disease-modifying treatment of dementia and brain aging, *Mayo Clin Proc* **86**:9, 876-84.

(9) Cadmus-Bertram, L., B. H. Marcus, R. E. Patterson, B. A. Parker and B. L. Morey (2015) Use of the Fitbit to Measure Adherence to a Physical Activity Intervention Among Overweight or Obese, Postmenopausal Women: Self-Monitoring Trajectory During 16 Weeks, *JMIR Mhealth Uhealth* **3**:4, e96.