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TITLE: Developing Personalized Medicine Strategies to Increase Physical Activity in Parkinson's Disease (PD) Through Digital Health Technology

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14. ABSTRACT Increasing physical activity levels in people with Parkinson's disease (PD) is a major unmet need. Objectives are to investigate whether: 1) Protocols using gamification to increase physical activity in patients with PD employing remote intervention and assessment will be feasible and acceptable to participants; 2) Individual NMS will predict responsiveness to a gamification intervention targeting physical activity levels—facilitating a personalized approach in future efficacy studies; 3) Changes in physical activity will be associated with changes in motor symptoms, measured using the wearable Parkinson's Kinetograph (PKG). This is a prospective observational study. Using administrative databases and review of medical records, we will identify and remotely enroll 85 Veterans with PD on stable medication regimens into a protocol. Personalized strategies using digital health technology to increase physical activity will be highly scalable, improving the symptoms and lives of countless people living with PD.					
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1. INTRODUCTION:

PD is a common, progressive and currently incurable neurodegenerative disease. Current treatments based on medications are the mainstay of PD management but are invariably associated with complications. Therefore, non-pharmacologic lifestyle modifications, including exercise, are of great interest. The symptomatic benefits of many different types of exercise for PD are indisputable and some evidence suggests that exercise could be a disease-modifying therapy that delays onset and/or slows progression. The benefits of exercise have mostly been observed in short, monitored clinical trials with directly supervised exercise programs. Despite evidence of the efficacy of exercise, physical activity levels of patients with PD in the community are typically low. Strategies that can increase physical activity in real life settings levels represent a major therapeutic opportunity and unmet need in PD research. This project aims to develop new approaches that 1) use “gamification”— applying rules of games like point scoring, achieving silver, gold or platinum levels and competition-- to overcome barriers to physical activity in PD; 2) identify individual characteristics of PD patients that limit or enhance response to gamification interventions; 3) use readily and commercially available (including Fitbits) digital health technologies to perform all recruitment, enrollment, intervention, assessment and analysis remotely, enabling a “touchless” study at a time where COVID19 has transformed the way in which clinical research can be done. All of the technologies used in the study are currently commercially available, and gamification interventions to increase physical activity will be immediately relevant to nearly all patients with PD. Future clinical trials can further refine personalized medicine approaches that tailor interventions for increasing physical activity to individual needs.

2. KEYWORDS:

Parkinson’s disease, exercise, lifestyle modification, gamification, wearable sensors

3. ACCOMPLISHMENTS:

What were the major goals of the project?

The major goals of this project, as defined in the Statement of work are:

- 1) Determine the feasibility and acceptability of a “touchless” intervention to increase physical activity in patients with PD using digital health technology and behavioral economics strategies
- 2) Determine whether non-motor features predict responsiveness to a behavioral economic-based gamification intervention to increase physical activity in patients with PD
- 3) Examine the relationship of change in physical activity to change in motor symptoms

What was accomplished under these goals?

Study Startup

The initial major activities during this first reporting period were devoted to study startup including obtaining necessary local regulatory approvals, contracting with collaborators (including the University of Pennsylvania for the Way to Health digital health platform and Global Kinetics Corporation for the use of Parkinson's Kinetographs), obtaining study supplies and hiring a study coordinator. All startup tasks were completed by or before the proposed deadline and we were able to begin recruitment in Dec 2021/Jan 2022.

Recruitment

Using an administrative data approach through the VA Corporate Data Warehouse as outlined in the project proposal, we have sent 775 letters to potentially eligible subjects. From those 775 invitations, 95 patients responded with interest, and 43 of those interested patients were found to meet eligibility criteria. After receiving further information about the study, 37 patients agreed and consented to participate in the study. After enrollment, 6 participants withdrew from the study (16%, projected attrition up to 20%), leaving 31 total enrolled participants, 20 of whom have completed all study activities. Based on our proposed milestones, we are ahead of recruitment goal (enrolled: 37 vs current target: 30, total goal: 85) and we have more than 3000 potential subjects available to contact if needed. Consistent with the goals of the NET-PD program, we included queries regarding service-related environmental exposures associated with PD (Agent Orange, Camp Lejeune Groundwater, Southwest Asia burn pits, TBI) in our initial study assessments. Of the initially enrolled cohort, 65% reported at least one exposure (most commonly Agent Orange followed by Camp Lejeune groundwater) and 22% reported multiple exposures.

Preliminary results

As planned in the SOW, we performed an initial data pull after 10 completed subjects to ensure appropriate syncing of all digital health platforms/wearables and data fidelity. All systems performed as expected. We performed an additional limited data pull to examine step counts for the first 17 completed subjects to present preliminary data at the 2022 Congress of the International Congress of the Movement Disorders Society. Demographic characteristics of the preliminary cohort are outlined in the Table and are consistent with our prior experience recruiting Veteran PD subjects and measuring baseline activity levels. Of note, subjects resided more than 150 miles from the medical center, on average, highlighting the reach and scalability of this remotely implemented program. During the gamification intervention, average daily steps increased by 43%, and 65% subjects met their step goal on more than 50% of days (Figure). During the non-intervention followup period, step counts remained 26% higher than baseline and 47% of subjects remained compliant with steps goals on more than 50% of days. We did not attempt to examine associations with baseline predictors (Aim 2) or PD symptoms (Aim 3) because of the small preliminary sample, but we plan a prespecified analysis when approximately half of subjects have completed study activities.

Age (y)	71.5(6.6)
%male	94.1
Duration (y)	5.1(4.1)
Distance from VAMC (miles)	166(144)
Duration (y)	5.1
Baseline steps	4847 (691)

Table. Characteristics of the preliminary cohort (N=17). Data are mean (SD) unless otherwise indicated

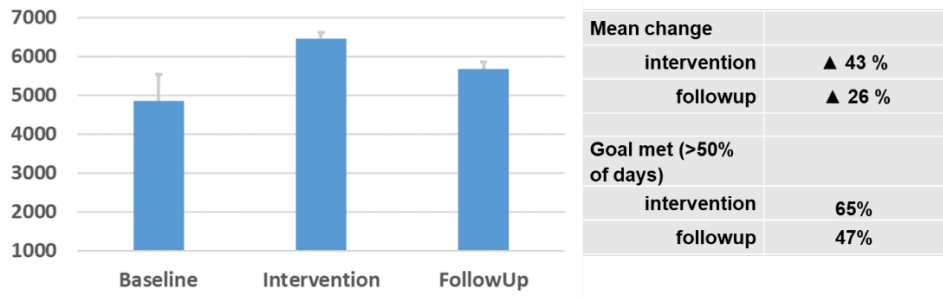


Figure. Average daily step counts and compliance with step goals during different study periods.

What opportunities for training and professional development has the project provided?

Nothing to report.

How were the results disseminated to communities of interest?

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

We plan to continue with current strategies for recruitment, enrollment and study assessments, as we have been fortunate to hit/stay ahead of prespecified milestones. As described above, we plan a data pull and preliminary analysis when approximately one half of subjects have completed study activities. Based on current trajectories, this is likely to occur toward the end of the next reporting period.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS:

Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them

Nothing to report.

Changes that had a significant impact on expenditures

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Nothing to report.

Significant changes in use or care of vertebrate animals

Nothing to report.

Significant changes in use of biohazards and/or select agents

Nothing to report.

6. PRODUCTS:

- **Publications, conference papers, and presentations**

Journal publications

Nothing to report.

Books or other non-periodical, one-time publications.

Nothing to report.

Other publications, conference papers and presentations.

Waddell, K.J., Patel, M.S., Wilkinson, J.R., Koganti, S, Wood, S, Morley, J.F.: Remote physical activity monitoring programs for Veterans with Parkinson's disease. 2022 INTERNATIONAL CONGRESS OF PARKINSON'S DISEASE AND MOVEMENT DISORDERS

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	<i>James Morley, MD, PhD</i>
Project Role:	<i>Principal Investigator</i>
Researcher Identifier (e.g. ORCID ID):	0000-0002-1950-9128
Nearest person month worked:	2.4
Contribution to Project:	<i>Dr. Morley has overseen all study activities and supervised study personnel.</i>
Funding Support:	
Name:	Kimberly Waddell, PhD, MS, OTR/L
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	0000-0002-8137-2900
Nearest person month worked:	1.8
Contribution to Project:	Dr. Waddell has performed work in the area of digital health platform setup, statistics and data analysis.
Funding Support:	
Name:	Madison Smith
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	12
Contribution to Project:	Ms. Smith has performed work in the area of daily study activities such as database management, recruitment, consent, subject contact and shipment of supplies.
Funding Support:	

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

The following pending award became active. There is no scientific or funding overlap with the DoD award.

Parkinson's Disease Biomarkers In Human Olfactory Cleft Mucus, National Institute on Deafness and other Communication Disorders, 4/2022-3/2024 (Morley/Wang, PI), annual direct costs, 10% effort (Role in grant: co-PI, This project will examine protein biomarkers derived from olfactory cleft mucus to distinguish between subjects with Parkinson's disease and healthy controls.)

What other organizations were involved as partners?

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

9. APPENDICES: