Supplement 1

Study Protocol

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1. Summary of changes to the protocol and statistical analysis plan

We made 3 minor changes to our initial protocol. The first, we initially stated the baseline period would be 1 week (7 days), which was an error. We submitted a modification to change the baseline period from 7 days to 14 days to be consistent with previous work. This was done before enrollment opened. Second, our initial protocol stated that we would exclude individuals with a history of cerebellar stroke. We removed this criteria as having a cerebellar stroke does not increase risk to participants. We also initially stated that we would include people up to 3 years post-stroke, however, we removed this upper limit as there was not scientific reason to exclude those who had experienced a stroke more than three years before enrollment. Lastly, we added the option to call participants for recruitment, in addition to sending an email, after discovering that some individuals did not have an email address listed within the Penn Medicine system.

There were not changes to the analysis plan.

2. Study Protocol

Using Behavioral Economics to Improve Mobility for Adults with Stroke

IRB Protocol

November 2020

Outline

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1. Introduction and Purpose

Stroke is the leading cause of complex, long-term disability.[1,2] Every year, the United States spends approximately $45 billion on direct and indirect stroke-related costs, a number projected to more than double to $95 billion over the next 15 years.[2,3] Over half of survivors fail to meet physical activity guidelines[4] and survivors average between 2608 and 4616 steps per day.[5,6] Regular physical activity after stroke can help prevent cardiovascular deconditioning, muscle loss, and secondary strokes,[4,7] but novel interventions to improve daily physical activity post-stroke are neither well-studied nor well-defined. The purpose of this proposed study addresses the above limitations by delivering a novel mobility intervention with daily step goals using wearable technology and the principles of behavioral economics to help improve mobility for adults with stroke. This pilot, randomized controlled trial utilizes the Way to Health platform to deliver a supportive partner and gamification intervention, leveraging social incentives, to help increase mobility. This medically complex population will likely vary in their overall mobility and responsiveness to the intervention as a result of individual and behavioral factors. The proposed study includes assessments to quantify the unique individual and behavioral factors that may influence responsiveness. Together, results from this project will provide important pilot data for a future clinical trial to improve mobility in adults with stroke.

2. Objectives

The overall objective of this study is to evaluate the feasibility of a connected health mobility intervention for community-dwelling adults with stroke. We will examine the outcomes of an 8 week mobility intervention on steps per day. Additionally, we will explore individual phenotypes as they relate to intervention responsiveness, which will inform a future clinical trial.

3. Aims

a. Primary outcome

The **primary outcome** variable will be the mean difference in change in daily steps between baseline and the 8 week intervention period.

b. Secondary outcome

The **secondary outcomes** will be the proportion of days the gamification arm participants met their step goal.

c. Exploratory outcomes

We will also assess indicators of acceptability and feasibility of our intervention including adherence to wearing the activity tracker and interacting with the Way to Health platform, and how behavioral and clinical factors may influence mobility.

4. Study design

a. *Design*

We will conduct a two-arm, prospective, pilot randomized controlled trial comparing a control group that uses a wearable device to track steps per day and selects a daily step goal they will be asked to reach throughout the study to a gamification arm that uses the same wearable device and receives a gamification/support partner intervention to adhere to a step goal program. All participants' step counts will be quantified using wearable devices (Fitbit) and stored securely via the Way to Health platform. Participants are not required to interact with the device in order for step data to be collected; however, they will need to sync the device with their smartphone periodically so they can see their step count and so that these data can be transmitted to the Way to Health platform.

Participants in the gamification arm will participate in a gamification/support partner intervention to improve mobility. There are three key components to this intervention. First, all intervention participants will be asked to sign an electronic pre-commitment pledge. This simple pledge asks participants to indicate they will strive to achieve their daily step goal during the study. Signing a pre-commitment pledge helps improve motivation.[8,9]

Second, at the beginning of every week, gamification participants will receive 70 points in a virtual account. For every day participants do not meet their step goal, 10 points will be deducted from their account. On days when participants meet their step goal, they will keep their points. At the end of the week, participants with at least 40 points will advance a level in the game. Consistent with previous work, there are 5 levels (blue, bronze, silver, gold, and platinum) and all participants will start at the silver level. Participants who do not have 40 points in their virtual account at the end of each week will drop a level in the game. Participants will receive a daily text message informing them if they met their step goal the previous day to provide immediate performance feedback.

Lastly, gamification participants will identify a support partner (spouse, friend, family member) who will receive weekly updates of their progress in the game. This leverages social incentives which can help improve motivation to reach goals. Participants will provide the name, email address, and phone number of their chosen support partner for the duration of the 8 week intervention. Prior to the intervention phase of the study, we will arrange a three-way phone call with the participant, support partner, and a member of the study team. During this phone call, we will explain the rules of the gamification intervention and ask the participant and support partner to create 3 goals or strategies for how the support partner can encourage and support the participant during the 8 week intervention. These 3 goals will be included in the weekly email to the support partner. Participants who are at the blue level in the game at week 4 (halfway through the intervention) will be contacted and asked to participate in an additional three-way phone call with their support partner and a member of the research team to discuss new ways the support partner can help the participant achieve their step goals. Participants who are unable to identify a support partner will be paired with a member of the research team.

The intervention will stop after 8 weeks. We will also arrange a one-time phone call with participants in the control group to discuss the study and answer any questions they may have prior to the 8 week intervention period.

b. Duration

This study is anticipated to take approximately 18 months to complete including study preparation, recruitment, participant interventions, data analysis, and dissemination of findings. The length of enrollment for individual participants will be approximately 10 weeks (slightly longer for participants who need an extended baseline period).

c. Target population

The target population for this study are adults ≥ 18 years of age who discharged from any Penn affiliated hospital >3 months after their initial stroke. Participants who ambulate in the community without assistance from another person (Life Space Assessment level 3) and sufficient cognitive ability will be included in this study. Sufficient cognitive ability will be determined using the Mini Montreal Cognitive Assessment (Mini MoCA), a validated, 5-minute telephone based assessment. Participants with a total score ≥ 11 points will be eligible to participate.

d. Accrual

This pilot will enroll 50 participants. A total of 25 participants will be randomized to the control group and 25 participants will be randomized to the gamification arm. The target population will be identified via PennChart using ICD-10 and stroke-related diagnosis related group (DRG) codes. A secondary approach includes a recruitment flyer posted within Penn Neurology Clinic and Penn outpatient physical rehabilitation centers.

e. Randomization procedures

Participants will be randomized in block sizes of 2 to the control or gamification arm using a stratified randomization approach. Participants will be stratified using age (>65 years) and baseline step count (1000-2499, 2500-4999 steps, 5000-7499 steps). Randomization will occur using the Way to Health platform.

f. Key inclusion criteria

1) Age 18 or older
2) Ability to provide informed consent
3) History of ischemic or hemorrhagic stroke (confirmed with ICD-10 or DRG code) at least 3 months prior to enrollment
4) Life Space Assessment mobility level 3
5) Ability to ambulate outside of their home (self-reported)
6) Owns a smartphone or tablet compatible with required applications for the wearable tracking device
7) Sufficient cognitive ability to participate (5-minute Montreal Cognitive Assessment Score ≥ 11 points)

g. Key exclusion criteria

1) Inability to provide informed consent, illiteracy or inability to speak, read, and write English
2) Self-reported history of falls within the last 3 months
3) Severe cognitive impairment (MoCA score ≤ 10 points)
4) Medical condition that may limit participation in physical activity program (e.g. metastatic cancer, end-stage renal disease)
5) Currently institutionalized in skilled nursing or long-term care facility
7) Baseline step count > 7500/day
8) Currently receiving physical therapy services

5. Subject recruitment

Eligible participants will be identified within the electronic health record and Penn Data Store, the health system's clinical data warehouse, by ICD-10 codes consistent with ischemic or hemorrhagic stroke (160, 161, 162, 163, 164) or stroke diagnosis related group (DRG, 061, 062, 063). Participants meeting the ICD-10 and DRG criteria will be invited to participate by email or phone. Additionally, we will post recruitment flyers within Penn Neurology clinics and Good Shepherd Penn Partners outpatient physical rehabilitation clinics. Interested participants will be allowed to take a flyer that provides instructions for what to do if interested in participating.

6. Subject compensation

All participants will be compensated $30 for participating in the study via Greenphire Clin Card. All participants will receive $30 at the end of the intervention period. Financial payments will be sent to the participant via Greenphire ClinCard using the Way to Health platform.

Additionally, all participants will be allowed to keep their Fit Bit device.

7. Study procedures

a. Consent

Eligible participants will be contacted via email,phone, or recruitment flyer.

Individuals who are interested in learning more about the study will be directed to the Way To Health web portal. Upon reaching the portal, potential participants will be asked to create an account and will then be informed of the details of the study, including its objectives, duration, requirements, and financial payments. If participants are still interested in participating, the Way To Health portal will take them through an automated online informed consent. The consent document will be divided into sections and potential participants will have to click a button to advance through each section. This is to help ensure that participants read the consent form thoroughly by breaking down the form into manageable blocks of text. Each section will have a button allowing the user to contact a researcher via email or by telephone if they have questions about the consent form. Successive screens will explain the voluntary nature of the study, the risks and benefits of

participation, alternatives to participation, and that participants can withdraw from the study at any time. On the final consent screen, potential participants who click a clearly delineated button stating that they agree to participate in the study will be considered to have consented to enroll. Participants will be provided with details regarding how to contact the research team via email or phone at any time if they subsequently wish to withdraw from the study. This contact information will remain easily accessible via the participants' individual Way To Health web portal dashboards throughout the study.

b. Procedures

After providing informed consent, participants will complete an online screening assessment where we will ask about their current mobility level and history of falls. Participants who pass the initial online screen will then complete a demographics form. We will call participants to administer the Mini MoCA assessment to assess cognition as the final screening procedure. Participants with sufficient cognitive ability will then complete the baseline questionnaires via the Way to Health platform. Participants who do not pass the initial screen will be contacted by a member of the study team to discuss their screening results and explain ineligibility.

After enrollment and the completion of baseline questionnaires, participants will be mailed a wearable device with detailed instructions for set-up. We will also provide contact information for the study team so participants can contact us with set-up questions. Participants will be instructed to wear the device for 14 days as the baseline period. We will calculate a baseline step value for all participants. Participants will then be randomized into the control or gamification arm.

The control arm will participate in a one-time phone call with a member of the study team, prior to the 8 week intervention period, to review the study and answer any questions. Additionally, participants in the control arm will select a daily step goal at the beginning of the study and be able to see their daily steps using the Fitbit application. The control arm will receive no further communication during the intervention period. Participants in the gamification arm will have an individualized step goal and participate in a gamification/support partner intervention, to help meet their daily step goal. Gamification uses game design elements such as points and levels to help increase motivation for behavior change.[10–12] Consistent with previous work, we will have 5 levels (blue, bronze, silver, gold, and platinum), and all participants will start at the silver level. At the beginning of each week, participants will receive 70 points in a virtual account. During the week, if a participant does not meet their step goal they will lose 10 points and if they meet their step goal, they keep their points. At the end of each week, participants with at least 40 points in their account will advance a level while participants with less than 40 points will drop a level. We will send a weekly e-mail message to the support partner at the end of every week updating that person on their loved one's progress in the game. Additionally, we will arrange a three-way phone call prior to the start of the intervention with the participant, their support partner, and a member of the research team to discuss the study. During

this call, the participant and their support partner will be asked to identify three goals or strategies for how the support partner can support the participant during the study. These three goals will be included in the weekly email to each support partner. This leverages social incentives, which can help improve motivation to meet goals or change behavior. Participants who are at the blue level at week 4 (halfway through the intervention) will be contacted by the study team to arrange a three-way phone call with the participant and the support partner to discuss new goals or strategies for how the support partner can help support the participant to meet their goals over the final 4 weeks of the study. Participants who are unable to identify a support partner will be paired with a member of the research team.

Participants will complete the study at the end of the 8 week intervention and there are no follow-up visits.

8. Analysis plan

All analyses will be performed using intention-to-treat. Data can be missing for any day if the participant did not use the activity-tracking device, did not upload data, or have a daily step count that is less than 1000 steps. For the main analysis, we will use multiple imputation for step values that are missing. We will perform five sets of imputations and results will be combined using Rubin's standard rules. To test of the robustness of our findings we will also evaluate models using collected data without imputation.

The primary analysis will fit linear mixed effect regression models to evaluate changes in physical activity from baseline during the intervention period between the gamification and control group, using study day as a fixed effect and participant as a random effect to take into account clustering from repeated observations of participant step counts. We will compare differences in the average steps per day between the control and intervention group. Generalized linear models will be used to test the difference in proportion of days participants in the intervention arm met their step goal, compared to the control group. Our exploratory analyses will fit mixed effect regression models adjusted for other variables of interest such as participant characteristics (social support, balance confidence). We will test for changes in self-efficacy and balance confidence from pre-intervention to post-intervention using a paired samples t-test.

9. Investigators

Ryan Greysen, MD, MHS, MA is the Principle Investigator (PI). He is Chief of the Section of Hospital Medicine in the Division of General Internal Medicine and an Assistant Professor of Medicine at the Perelman School of Medicine at the University of Pennsylvania. He has past experience leading studies of older, hospitalized adults focused on functional vulnerability and outcomes including hospital readmission. He currently spends 75% of his effort on research and 25% on clinical and administrative activities.

Mitesh Patel, MD, MBA, MS (Co-Investigator) is an Assistant Professor of Medicine and Health Care Management at the Perelman School of Medicine and

The Wharton School at the University of Pennsylvania. He has past experience leading six clinical trials using the Way to Health Platform to deploy interventions using financial and social incentives to promote weight loss and increased physical activity. He currently spends 80% of his effort on research and 20% on clinical and teaching activities.

Kimberly Waddell, PhD, OTR/L is an advanced postdoctoral fellow at the Crescenz VA Medical Center and the Penn Medicine Nudge Unit. She has nine years' experience as an occupational therapist and has extensive experience with recruiting individuals with stroke for research studies. She currently spends 100% of her effort on research.

10. Human research protection

a. *Data confidentiality*

Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study. Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords. Wherever feasible, identifiers will be removed from study-related information. Precautions are in place to ensure the data are secure by using passwords and encryption, because the research involves web-based surveys.

b. *Subject confidentiality*

Research material will be obtained from participant surveys, from the wearable devices, and from the electronic health record. The data to be collected include demographic data (e.g., age, sex, self-identified race), outcome data, and daily activity data collected by the wearable device. Research material that is obtained will be used for research purposes only. The same procedure used for the analysis of automated data sources to ensure protection of patient information will be used for the survey data, in that patient identifiers will be used only for linkage purposes or to contact patients. The study identification number, and not other identifying information, will be used on all data collection instruments. All study staff will be reminded to appreciate the confidential nature of the data collected and contained in these databases. The Penn Medicine Academic Computing Services (PMACS) will be the hub for the hardware and database infrastructure that will support the project and is where the Way to Health web portal is based. The PMACS is a joint effort of the University of Pennsylvania's Abramson Cancer Center, the Cardiovascular Institute, the Department of Pathology, and the Leonard Davis Institute. The PMACS provides a secure computing environment for a large volume of highly sensitive data, including clinical, genetic, socioeconomic, and financial information. Among the IT projects currently managed by PMACS are: (1) the capture and organization of complex, longitudinal clinical data via web and clinical applications portals from cancer patients enrolled in clinical trials; (2) the integration of genetic array databases and clinical data obtained from patients with cardiovascular disease; (3) computational biology and cytometry database management and analyses; (4) economic and health policy research using Medicare claims from over 40 million Medicare beneficiaries. PMACS requires all users of data or applications

on PMACS servers to complete a PMACS-hosted cybersecurity awareness course annually, which stresses federal data security policies under data use agreements with the university. The curriculum includes Health Insurance Portability and Accountability Act (HIPAA) training and covers secure data transfer, passwords, computer security habits and knowledge of what constitutes misuse or inappropriate use of the server. We will implement multiple, redundant protective measures to guarantee the privacy and security of the participant data. All investigators and research staff with direct access to the identifiable data will be required to undergo annual responsible conduct of research, cybersecurity, and HIPAA certification in accordance with University of Pennsylvania regulations.

Data will be stored, managed, and analyzed on a secure, encrypted server behind the University of Pennsylvania Health System (UPHS) firewall. This server was created for projects conducted by the Penn Medicine Nudge Unit related to physician and patient behavior at UPHS. All study personnel that will use this data are listed on the IRB application and have completed training in HIPAA standards and the CITI human subjects research. Data access will be password protected. Whenever possible, data will be de-identified for analysis.

c. *Subject privacy*

Enrollment will include a description of the voluntary nature of participation, the study procedures, risks and potential benefits in detail. The enrollment procedure will provide the opportunity for potential participants to ask questions and review the consent form information with family or caregivers prior to making a decision to participate. Participants will be told that they do not have to answer any questions if they do not wish and can drop out of the study at any time, without affecting their medical care or the cost of their care. They will be told that they may or may not benefit directly from the study and that all information will be kept strictly confidential, except as required by law. Subjects will be given a copy of the consent document. All efforts will be made by study staff to ensure subject privacy.

d. *Data disclosure*

The following entities, besides the members of the research team, may receive protected health information (PHI) for this research study: -Wells Fargo, the company which processes study-related payments. Patient addresses and account balances will be stored on their secure computers. –Fit Bit, the company that designs and manufactures the wearable devices used in the study to track participant physical activity. -Twilio, Inc., the company which processes some study-related messages. Twilio will store patients' phone numbers on their secure computers. -Qualtrics, Inc., the company which processes most study-related surveys. Qualtrics will house de-identified answers to these surveys on their secure servers. -The Office of Human Research Protections at the University of Pennsylvania -Federal and state agencies (for example, the Department of Health and Human Services, the National Institutes of Health, and/or the Office

for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes.

e. Data safety and monitoring

At the time of enrollment, all patients will be given anticipatory guidance on when to seek medical attention (e.g. when to call their doctor should they feel dizzy, short of breath, chest pain, lightheaded, unstable, or otherwise unwell while ambulating). In addition, participants will be asked to report to the study team any episodes of these symptoms that occur during the study period (the research assistant/study coordinator will check in periodically with enrolled patients to ensure devices are working properly and troubleshoot any issues encountered by patients/caregivers). Patients/caregivers will also be reminded that they can always contact the study team by phone or email at any time (contact information will be given at the beginning of the study and will also be posted on the Way to Health platform, which can be accessed at any time by the participant). If any concerns of a participant event are identified, the study coordinator will reach out to the participant and complete the event reporting form. This form will be reviewed with the study PI to determine if any action is needed and if the participant can continue safely in the study. Any identified adverse events will be reported to the Institutional Review Board.

11. Risk/benefit

a. Potential study risks

The major potential risk of this study is a breach of participant confidentiality. We will minimize this risk of confidentiality breach by linking individual identifying information with participant ID numbers only in one single secure file that will only be accessed by the study team in the case of an adverse medical event, participant dropout, or if otherwise deemed necessary by the Principal Investigator. All other identifying information will be discarded after initial contact with the Study Coordinator. All other members of the research team will be able to view only participant ID numbers. Additionally, participants will receive guidance from the research coordinator on when to seek medical attention (call for their nurse or doctor in the hospital) if they experience discomfort or increased fatigue with physical activity. While unexpected, another potential risk for this study is a risk for falls. We have mitigated this risk by recruiting a sample that can ambulate within the community without physical assistance without history of a recent fall. Our target population is higher functioning, which has been previously shown to have a low fall risk compared to individuals who are moderate to severely impaired.[13,14]

b. Potential study benefits

Through participation in this study, each participant will have the potential to increase their physical activity, which could improve their health and reduce their risk for functional decline, secondary stroke, falls, nursing home placement, or hospital readmission. If this approach is effective, it could have tremendous benefits for society if adopted on a wide scale to help this vulnerable population increase their physical activity. It is expected that other people will gain

knowledge from this study and that participation could help understand how to effectively motivate people to become more physically active. Participants may also receive no benefit from their participation in the study.

c. *Risk/benefit assessment*

Anticipated risks of this study should be minimal and the risk/benefit ratio is very favorable. To minimize the chance for serious and unexpected adverse events, study participants will be screened through exclusion criteria. Participants that increase physical activity may improve their health and reduce their risk for functional decline, secondary stroke, or falls.

References

1. Adamson J, Beswick A, Ebrahim S. Is stroke the most common cause of disability? *J Stroke Cerebrovasc Dis*. 2004;13(4):171-177.

2. Benjamin Emelia J., Muntner Paul, Alonso Alvaro, et al. Heart Disease and Stroke Statistics—2019 Update: A Report From the American Heart Association. *Circulation*. 2019;139(10):e56-e528. doi:10.1161/CIR.0000000000000659

3. Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. *Circulation*. 2018;137(12):e67.

4. Rand D, Eng JJ, Tang PF, Jeng JS, Hung C. How active are people with stroke? Use of accelerometers to assess physical activity. *Stroke*. 2009;40(1):163-168.

5. Mudge S, Barber PA, Stott NS. Circuit-based rehabilitation improves gait endurance but not usual walking activity in chronic stroke: a randomized controlled trial. *Arch Phys Med Rehabil*. 2009;90(12):1989-1996.

6. Michael K, Goldberg AP, Treuth MS, Beans J, Normandt P, Macko RF. Progressive adaptive physical activity in stroke improves balance, gait, and fitness: preliminary results. *Top Stroke Rehabil*. 2009;16(2):133-139.

7. Billinger SA, Arena R, Bernhardt J, et al. Physical activity and exercise recommendations for stroke survivors: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45(8):2532-2553.

8. Ariely D, Wertenbroch K. Procrastination, deadlines, and performance: self-control by precommitment. *Psychol Sci*. 2002;13(3):219-224. doi:10.1111/1467-9280.00441

9. Rogers T, Milkman KL, Volpp KG. Commitment devices: using initiatives to change behavior. *JAMA*. 2014;311(20):2065-2066. doi:10.1001/jama.2014.3485

10. Edwards EA, Lumsden J, Rivas C, et al. Gamification for health promotion: systematic review of behaviour change techniques in smartphone apps. *BMJ Open*. 2016;6(10):e012447.

11. Kawachi I. It's all in the game—The uses of gamification to motivate behavior change. *JAMA Intern Med*. 2017;177(11):1593-1594.

12. Patel MS, Small DS, Harrison JD, et al. Effectiveness of Behaviorally Designed Gamification Interventions With Social Incentives for Increasing Physical Activity Among Overweight and Obese Adults Across the United States: The STEP UP Randomized Clinical Trial. *JAMA Intern Med*. 2019;179(12):1624-1632. doi:10.1001/jamainternmed.2019.3505

13. Wei WE, De Silva DA, Chang HM, et al. Post-stroke patients with moderate function have the greatest risk of falls: a National Cohort Study. *BMC Geriatr*. 2019;19(1):373. doi:10.1186/s12877-019-1377-7

14. Kerse N, Parag V, Feigin VL, et al. Falls after stroke: results from the Auckland Regional Community Stroke (ARCOS) Study, 2002 to 2003. *Stroke*. 2008;39(6):1890-1893.