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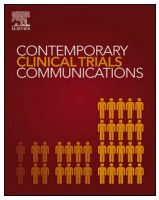

Protocol of a feasibility study of a virtual personalized (N-of-1) trial for increasing low-intensity physical activity in older adults via habit formation

Jerry Suls *, Ciarán P. Friel, Mark Butler, Joan Duer-Hefele, Patrick L. Robles, Frank Vicari, Thevaa Chandereng, Ying Kuen (Ken) Cheung, Karina W. Davidson

Institute for Health System Science Feinstein Institutes for Medical Research Northwell Health 130 East 59th Street, Suite 14C, New York, NY, 10022, USA

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ABSTRACT

Background: Personalized interventions that can be delivered remotely are needed to increase physical activity (PA) in older adults to reduce risk of CV disease and mortality. Prior research indicates that Behavioral Change Techniques (BCTs) (e.g., goal setting, self-monitoring, behavioral repetition) can instill a habit for increasing daily walking. However, past interventions relied on between-subject randomized clinical trials, which can only only be informative about response of the hypothetical average person. Personalized trial designs can identify the benefits of an intervention for a specific individual although extended periods are required for collecting frequent measurements within-subject. Advances in remote, virtual technologies (e.g., text messaging, activity trackers), integrated with automatic platforms, can meet these requirements because they capacitate delivery of BCT interventions, and collection of data during daily life without personal contact. This Stage I-b trial is designed test whether a virtual, personalized intervention is feasible and acceptable to older adults, can elicit participant adherence and exhibit preliminary evidence for efficacy.

Methods: A series of up to 60 single-arm, personalized trials, involving no personal contact, will recruit adults, 45–75 years of age, to wear an activity tracker during a 2-week baseline and a 10-week intervention. Five BCT prompts to execute a walking plan will be delivered on a daily basis during the intervention phase. Participants will rate satisfaction with personalized trial components and whether automaticity of the walking plan can be achieved. Step-counts, adherence to the walking plan and self-monitoring of step-count will also be recorded.

1. Introduction

This paper describes a study protocol for testing the feasibility, acceptability, adherence and preliminary efficacy of an innovative, virtual personalized trial approach for increasing habitual physical activity (PA) in older adults. The study is a first-step toward our goal to develop a single-patient, N-of-1 methodological approach that is automated and can be used at point-of-care to revolutionize how we interact with patients and set the stage for a truly transformative approach to precision therapeutics. In this feasibility study, we focus on the problem that sedentary behavior is a risk factor for cardiovascular disease [1,2], but few older adults engage regularly in even low-intensity activity (e.g., walking) [3]. Based on observational studies, older individuals who increased their steps by 1000 to 2000 per day had a lower mortality rate [4,5]. Between-subject randomized clinical trials (RCTs) find that PA interventions designed to increase walking can reduce deaths [6,7]. Although conventional between-subject RCTs involving behavioral change techniques (BCTs) [8,9] have had success increasing PA *on average*, not all participants show gains in PA and may instead show modest or no effects [5,10,11]. This heterogeneity of effects (HTEs) [10,11] reflects the fact that "… habit typically develops asymptotically and idiosyncratically, differing in rate across people, cues and behaviours" [12]. A focus on individual-level habit formation, however, can identify each person's rate and intensity of habit change, and benefits (if any) of an intervention [12,13]. A requirement of the within-subject design, however, is that behavior is monitored frequently over an extended period.

Experimental and observational personalized (N-of 1) trials can be designed to measure how behavioral strategies influence the acquisition and intensity of habit formation on an individual basis [12]. For example, a personalized trial involving behavioral prompts, tailored and personalized for each individual, and administered daily over an

* Corresponding author.
E-mail address: jsuls@northwell.edu (J. Suls).

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extended period (of weeks or months) can estimate improvements in step-count and side-effects quantitatively. With this approach, monitoring and collection of individual participant's responses allow the clinician and the individual to determine if a treatment has net benefit for that person, rather than trying to guess the benefit for the patient based on data obtained from other trial participants and averaged and summarized in published articles.

N-of-1 trials have been successfully applied to such conditions as fatigue, depression and preventive behaviors [14,15], but have been seldom used in clinical practice [16]. As noted earlier, the N-of-1 within-subject design requires the effortful (often manual) engagement of clinicians and patients for instruction, monitoring behavior and collecting health outcomes daily (or weekly) over extensive time periods. Until recently, no automated, sustainable, user-friendly technology platform was available to make conduct of such a trial facile for researchers, clinicians or participants [17]. Recent advances in computing and technology, however, have created platforms [17], which integrate smartphones, texting, e-mail, activity tracker and remote sensors, capable of delivering behavioral interventions and obtaining real-world data at home or work without personal contact. Texts and e-mails can deliver instructions and surveys; activity trackers can remotely and continuously monitor and record step-counts, heart rate, etc. These features will figure prominently in this feasibility study.

Despite the availability of these virtual technologies, questions remain whether automated personalized instruction, data collection and intervention involving no direct personal contact are feasible and acceptable to participants. This study protocol used an observational N-of-1 design [18] to test the feasibility and acceptability to older patients of a virtual personalized trial delivering a set of behavioral change prompts to make a walking habit an automatic response pattern.

According to Habit Formation Theory [12], behavioral change strategies (i.e., BCTs) should prompt repetition of a walking plan in the presence of contextual cues to strengthen a mental cue-behavioral association [12,19], to the point that the cue triggers a mental representation eliciting the action with minimal conscious oversight. In this test of the study protocol, a primary aim was to determine the feasibility that a person can reach automaticity of a daily walking routine, involving an increase of 2000 steps more than their baseline, by virtual (no personal contact) BCT delivery. Automaticity is considered the mechanism of action (MoA) by which behavioral intervention strategies (e.g., prompting repetition) increase low-intensity walking [12,19–22].

The acquisition of automaticity over the course of BCT administration was measured with a brief daily self report questionnaire about the participant's agreement-disagreement with statements like, "Today, going on my walk was something … I did automatically," [23]. When a participant's daily score leveled out and reached a set criterion on more than 7 consecutive days, automaticity was deemed to be achieved [12]. The day on which automaticity was reached is considered the *asymptote*. An asymptote is considered to be a prolonged period of stable measures, in this case a prolonged period of high level of automaticity scores. Asymptotes are often utilized in habit formation theory to judge when a habit has been formed [20,24]. A primary aim was to determine whether it is feasible for a proportion of participants to achieve an asymptote (i.e., automaticity) for a daily walking routine during a virtual 10-week intervention phase.

The BCTs chosen for the trial were identified in a review finding 40 strategies were associated with improving PA [8]. A subset of five were chosen for the trial protocol on the basis of several considerations: (a) hypothesized to change automaticity [22]; (b) associated with large effect sizes from the extant multi-BCT interventions; (c) relevant to walking; (d) required only low resource intensity; e) implemented easily via text; and (f) could be delivered repeatedly. The following BCTs in Michie et al.'s taxonomy [9], developed on the basis of expert consensus and information science, met these criteria: Goal Setting (BCT 1.1), Action Planning (BCT 1.4), Self-Monitoring of Behavior (BCT 2.3), Behavioral Practice/Rehearsal (BCT 8.1), and Behavioral Repetition (BCT 8.3). These BCTs will be delivered via text messages five days per week during a ten-week intervention.

In addition to assessing the feasibility of a virtual trial to achieve walking routine automaticity, a second primary aim was to assess whether participants find the overall personalized trial and its components to be satisfactory, a descriptive variable relevant to feasibility. Participant satisfaction with the virtual, automated protocol indicates whether it is feasible to scale-up the intervention for a larger study. At the conclusion of their trial, participants will complete a questionnaire about their satisfaction with text messaging (for data collection), the BCTs, video explanations and demonstrations of study devices and procedures, etc.

Secondary outcomes will include self-reported daily adherence to the (2000 step) walking plan and adherence to self-monitoring and recording of the daily step count. These questions will be sent 30 min after the time scheduled for the daily walking routine via an automated text message. Step-counts will be available to the participant from the Fitbit activity tracker that participants wear throughout the study. Acceptability (or level of agreement) with elements of protocol implementation will assessed with an eleven item questionnaire sent to participants at the conclusion of the study. These items will be used to identify the acceptability of individual elements of the trial, thereby facilitating additional revisions and adjustments to future implementations of the intervention.

Table 1 lists the relationship between each aim and the outcome assessments, including how each is measured. (More details are

Table 1
Connection between aims and outcome assessments.

Aim	Outcome	Assessment
Primary aims		
Feasibility of virtual trial to achieve participant walking plan automaticity	Proportion of participants who achieve automaticity for a daily walking plan, reported on self-rated scale (24)	Within-person change in self-reported automaticity scale ratings. When ratings level out and reach a score of 8 or more on more than 7 consecutive days; the participant is judged to have reached asymptote at this point in time
Feasibility/acceptability of the personalized trial overall and its components satisfactory	Participants' satisfaction with the overall trial and eight components	Ratings of satisfaction on 4-point Likert scales completed at end of trial (e.g., text messaging, video instructions, Fitbit)
Secondary aims		
Feasibility that participants adhere to a scheduled daily walking plan	Proportion of days during the intervention period that participants' adhered to daily walking plan	Response to e-mail, post-walk survey, delivered via e-mail, "Did you walk according to your walking plan today?" Yes/No
Feasibility that participants adhere to self-monitoring of their step-count during their planned walk	Proportion of days during the intervention period that participants adhered to self-monitoring of step-count during the planned walk	Response to email, post-walk survey, delivered via e-mail, "How many steps did your Fitbit say you took during your planned walk?" along with a space to provide the count.
Acceptability of personalized trial implementation	Participants' agreement/disagreement about elements of implementation	Ratings of agreement on 11 items rated on 7-point scales about trial implementation (" … I knew what was coming next; " … I found my personalized trial to be burdensome."
Did intervention produce within-person changes in step-count from baseline to intervention?	Fitbit-assessed daily steps during 2-week baseline versus 10-week intervention	Average step-count during baseline and intervention will be analyzed with GLM analyses

provided about assessment in the Methods section.)

2. Methods

2.1. Design

This will be a virtual series of up to 60 single-arm trials involving a personalized intervention design. Each potential participant will engage in a 2-week baseline phase to gauge both their adherence to wearing an activity tracker for 10-h or more per day and responding to automated text messages. Those who are deemed adherent will be moved to the 10-week intervention phase and continue to wear the activity tracker 10-h or more each day. The 2-week baseline will also provide step-counts affording the ability to compare baseline steps with step-counts achieved during intervention. Upon starting the intervention phase, each participant will receive text message prompts to respond to 5 behavior change techniques on 5 successive days of each week. Prior to baseline, participant will already have selected the 5 days each week they will receive the text prompts. Primary outcome measures will include daily self-reports of the automaticity with which the participant executes the walking plan, to assess the feasibility that virtual delivery of BCTs can produce automaticity. Collected at study completion, another primary outcome important for feasibility will inquire about participants' level of satisfaction with components of the personalized trial, such as instructions delivered via e-mail, text or video's, wearing the Fitbit, answering survey questions, etc. Secondary outcomes will consist of daily self-reports about adherence to the daily walking plan and to daily self-monitoring of daily step count. In addition, Fitbit-assessed step-counts collected during baseline will compared with step-counts during intervention. Also, ratings of acceptability of 11 aspects of personalized trial implementation (e.g., instructions were easy to follow, enjoyed receiving daily text message prompts and surveys on my cell phone) will be collected at study completion. The project (20–1182) received IRB approval from Northwell Health on April 16, 2021. The protocol was registered with clinicaltrial.gov at https://clinicaltrials.gov(NCT04869644) on May 3, 2021, and last updated on June 13, 2022.

2.2. Participants, recruitment, and screening

The intended participants will be volunteers who are employed by the Northwell Health System. Potential participants will be recruited using e-mail newsletters and lists of those who have previously expressed an interest in participation in a personalized trial with the Center for Personalized Health. Flyers will also be shared within the Northwell Health network and Northwell Health employee social media (Facebook) site. The e-mail/flyer will solicit persons interested in participating in a personalized trial to increase low-intensity physical exercise.

Those who express interest will be directed to a series of webpages and short videos that describe study aims and procedures; if they indicate continued interest they will be asked to complete an initial online screening measure containing questions regarding study inclusion and exclusion criteria. The on-line screening questionnaire will ask: "Do ALL of the following apply to you?: I am at least 45 years old and I'm no more than 75 years old; I can read and understand English; I have a smart phone capable of receiving text messages; I have never been told by a health care provider that I should not participate in a walking program; I have never been diagnosed with bi-polar disorder or a severe mental illness; I am not pregnant." Followed by "ALL of the above statements apply to me." with response option, "Yes," and "No."

Study staff will review responses to the initial on-line screening measure. Anyone responding "No" will be ruled as ineligible and notified within two business days.Those who are eligible will receive the following message: "You ARE ELIGIBLE to participate in research activities related to personalized trials to promote low-intensity walking. Please proceed to the next page for more detailed study information and to provide your contact information." In the case of high demand, the participant will receive an email informing them they will be waitlisted.

2.3. Consent process

Persons who are eligible to participate after the screening will receive a message from study staff with a link to access a short video explaining key details of the study protocol and an electronic copy of the informed consent form. A 4-question screening measure will follow to assess participant understanding of the protocol and consent process. The automatic platform will monitor whether any of the true/false questions are answered incorrectly. An incorrect answer will prompt a red pop-up saying "Incorrect. Please try again."

Consent is then obtained electronically, in accordance with all regulatory guidelines, and a copy of the signed consent form will be mailed to the participant along with printed study instructions and an activity tracker device. Signed consent forms will be stored electronically on a Health Insurance Portability and Accountability Act (HIPAA)–compliant, Northwell Health-approved shared drive accessible only to the IRB-approved study staff.

2.4. Participation compensation

Participants will be compensated as follows: After completing all aspects of the study, participants will receive a $100 payment card. As a thank you for participation, they will be able to keep the activity monitor (Fitbit Charge 4™, a value of $150).

2.4.1. Sample size and statistical power

Sample size was based on the primary outcome of automaticity. Results from previous research show levels of automaticity prior to intervention are generally low (with automaticity of health behaviors ranging from 0 to 20% for participants) [20]. Assuming that most participants entering the trial will not have automaticity in their walking behavior, we predict 15% of the sample will display automaticity of walking behavior prior to the intervention. Following PA interventions, automaticity has ranged between 62% and 81% in intervention samples [20]. Assuming a conservative intervention effect, we feel that it is reasonable that 66% of the sample will display automaticity for walking upon completion of the trial. With a sample size of 60 and an alpha level of 0.05 (one-sided), we should have 83% power to detect intervention effects using a one-sample z-test of proportions.

2.5. Procedures

If participants provide consent, they will receive a "Demographics and Contact Information Survey." Once research staff confirm the participant meets the screening criteria, an initial study kit, including a Fitbit Charge 4 activity tracker and printed materials to guide the participant through the study, will be shipped to the participant. Written instructions will direct participants to download an app to their personal phone to use the Fitbit and how to charge the Fitbit and sync it to their phone. Anonymous study accounts will be created to protect privacy of the participant.

2.5.1. Baseline phase

An email will follow to confirm the study start date. A text message will be sent the day the study begins that reminds the participant that during the first two weeks, they will be asked to wear the Fitbit for a minimum of 10 h per day and at night, even while sleeping, if it is possible and respond to a daily acknowledgement survey ("Today is a baseline day? Yes/No"). Minute-level heart rate data from the Fitbit will provide an indication of adherence to wear. The Fitbit will provide a measure of the participant's usual physical activity patterns (i.e., step-count). Additional text messages may be sent to remind participants to sync their Fitbit or respond to the acknowledgement surveys if staff

notices non-adherence. Those persons who adhere to wearing the device and responding to text messages at a rate of 80% or more over the first 10 days of baseline will then be contacted about when to start the 10-week intervention phase. An 80% adherence criterion was adopted to try to insure that those moving to the intervention phase would be sufficiently exposed to the protocol and sufficiently adherent to assess the feasibility of key elements of the virtual protocol. Eighty-percent or higher adherence is a general standard in the literature [25,26]. Applying the 80% adherence criterion should identify the proportion of individuals actively engaged with the intervention and also ensure sufficient power for analyses of the primary outcome.

Differences in demographic characteristics (age, sex, race, ethnicity) will be tested between adherent versus non-adherent participants with chi-square analyses. Any obtained differences may indicate that results of the intervention phase may not adequately represent individuals from of certain demographic groups.

2.5.2. Preparation for intervention phase

Following day 10 of baseline, if eligible to continue, the participant will receive an email message asking them to form a plan (i.e., time and location) for walking 2000 steps more than their (2-week) baseline. "You are about to begin the 10-week intervention portion of your study. During the intervention portion, you will receive BCT text messages tailored to the specifics of your walking plan for 10 weeks. To tailor your walking plan to your daily schedule, please complete the following form (accessible via the email)." Participants have the final 4 days to formulate their walking plan.

The form will remind the participants that the "goal of your walking plan is to find time for habitually walking 2000 steps more than your baseline. Please keep that in mind as you fill out your walking plan." Instructions will direct participants to indicate on what days of the week they could walk, the general time of day (morning, afternoon, evening), followed by specific 1-h blocks. A final question will inquire about where they can walk consistently with a parenthetical note that "The average person needs to walk 1 mile, or for about 20 min, to achieve 2000 steps." This information will be used by research staff to program the timing and tailored content of messages to be sent to individual participants during the 10-week intervention.

2.5.3. Intervention phase

Participants will receive a "pre-intervention text" the day before the intervention begins: "This text is a reminder that you will begin your intervention period tomorrow. The intervention period goes on for ten weeks. During the intervention period, please wear your Fitbit as much as possible and respond to the daily post-walk surveys, which we will text you. During your baseline period, you walked an average of (XXXX) steps per day. Your goal is to walk 2000 more steps during your planned walk, so that you walk more than your baseline average on as many of the five days that you selected."

Five BCTs will be delivered across the course of the intervention phase: Goal Setting-the behavior to be achieved; Action Planning-detailed planning of the behavior; Behavioral Practice/Rehearsal-at a time different from the scheduled walk when performance may not be necessary, in order to increase habit and skill; Self-Monitoring-a method to monitor the behavior; and Behavioral Repetition/Habit Formation-prompt rehearsal and repetition of behavior in the same context so the context elicits the behavior [12].

Based on the walking plan schedule each participant selected, they will receive the 5 BCTs in two text messages per day on five successive days for ten weeks. The first message will be sent 30 min ahead of their intended walking time (per their walking plan): "This (time of day), your plan is to walk an extra 2000 steps (Goal) on the way to: (location) (Action Planning). Try leaving your sneakers and water bottle by the door for your walk (Behavioral Practice/Rehearsal). Be sure you start walking (Behavioral Repetition/Habit Formation) and, after your walk, write down how many steps were measured by your Fitbit (Self-Monitoring) on the electronic survey you will soon receive."

A second message (email) with a link will be sent approximately 30 min after the scheduled walk should have ended. The "Post-Walk Survey" will inquire: "Did you walk according to your walking plan today? Yes/No," a measure of adherence to the walking plan. Another item will ask: "How many steps did your Fitbit say you took during your planned walk?" along with a space to provide the count (Self-Monitoring). Four automaticity subscale items adapted from the Self-Report Behavioral Automaticity Index (SRBAI) will be presented as the final part of the "Post-Walk Survey" [23]. Each item is rated on 4-point scale with agree-disagree as end-points. For example, following the phrase, "Today, going on my walk was something …," participant indicates level of agreement with the following four statements: "I did automatically," "I did without having to consciously remember," "I did without thinking," and "I started doing before I realized I was doing it." By tracking each participant's automaticity ratings across ten-weeks, the N-of-1 method can identify what proportion of participants achieve automaticity of the walking plan and at what point in time. These data will also shed light on individual heterogeneity in reaching automaticity [10,12].

Besides these two messages per day, additional messages may be sent relating to reminders or study procedures (e.g., remaining duration of the study, Fitbit usage instructions).

2.6. Post intervention

Participants will receive a survey comprised of nine items to assess their level of satisfaction with the overall trial and its components. Each item will be rated on four-point scales with "satisfied" to "not all satisfied" as end-points. For item content, see "Measures and Analysis" section.

A report of each participant's trial results will be sent next, along with an email offering congratulations on completing the study. This report will summarize how the individual's data (i.e., automaticity and step-count) changed throughout the study. In addition, the rate of adherence to wearing the Fitbit, adhering to BCTs, and responding to texts/surveys will be provided. All feedback will be presented in narrative and in numerical form.

Finally, participants will be sent a completion survey text with a link to the "Participant Attitudes and Opinions toward Personalized Trials Survey." This survey consists of 11 items about personalized trial implementation rated on 7-point agree to disagree scales (e.g., "I felt like I knew what was coming next in my personalized trial"). (For all items, see "Measures and Analysis" section.)

3. Measures and analysis

3.1. Primary outcomes

3.1.1. Within-subject habit automaticity

An average daily automaticity score will be computed for each participant's ratings of the four-item SRBAI [23]. (See above for details.) The participant's ratings of agreement with each statement on a 4-point scale will be summed together to form a total score from 0 to 12 for each week of the intervention.

The within-person change in automaticity across the 10-week intervention will also be computed. Change in automaticity levels over the course of the intervention period will be examined until scores level out and reach a score of 8 (i.e., Two thirds of the maximum possible) or higher [24] on more than 7 consecutive days). (Consecutive days will be defined as days during which the participant had agreed to follow their walking plan.) Participants will be judged to have reached an asymptote at this point in time. Time-to-event analyses will be conducted to examine participant differences in reaching an asymptote for automaticity. Overall time-to-event will be represented using Kaplan-Meier curves [27]. Nearest-neighbor interpolation will be used to impute

missing data; that is, the value of the nearest data point will be used to impute missing data points [28]. Variability in the association between the personalized intervention and automaticity will be examined to identify whether future interventions may benefit from formalized N-of-1 trials of the intervention.

3.1.2. Satisfaction with the personalized trial

Participants will rate several statements on 4-point scales, with "Not at all satisfied" and "very satisfied," as endpoints. The following statements will be presented: "Overall satisfaction with the BCTs; Overall ease of using the BCTs; Overall effectiveness of the BCTs; Video explanations and demonstrations of study devices and procedures; Text messaging for reminders (e.g., sync your Fitbit); Text messaging for data collection (i.e., surveys); Use of the Fitbit to track activity and sleep; Study Communications; Presentation of your results." Means and standard deviations for each item, aggregated across participants, will be computed.

3.2. Secondary outcomes

3.2.1. Proportion of days participants adhered to walking plan

Proportion of days will be aggregated across participants and reported in terms of mean and standard deviation.

3.2.2. Proportion of days participants adhered to self-monitoring

Proportion of days for all participants will be calculated in terms of mean and standard deviation.

3.2.3. Attitudes and opinions about the personalized trial implementation

This survey will consist of nine 5-point Likert scales with responses ranging from "strongly disagree" to "strongly agree." Means and standard deviations for each item, aggregated across participants, will be computed.

The items are as follows: "I found the onboarding process (from the initial survey to getting my materials) for my personalized trial unnecessarily complex; I think my Fitbit device was easy to use; I think that I needed the support of a technical person to be able to successfully complete my personalized trial; The informational videos helped me understand how to participate in this study; The materials I received in the mail were clear and easy to follow; I enjoyed receiving daily text message prompts and surveys on my cell phone; I would imagine that most people would learn how to get started with their personalized trial very quickly; I have found my personalized trial to be very burdensome. I felt very confident starting my personalized trial: I felt like I knew what was coming next in my personalized trial; I needed to learn a lot of things before I could get going with my personalized trial."

3.2.4. Within-subject change in daily steps

Fitbit-assessed daily steps will be computed for the baseline assessment period (two weeks) and intervention (10 weeks). Average step-count during baseline and intervention will be analyzed with Generalized Linear Mixed Model analyses [29].

4. Limitations

A brief 2-week baseline will be used to identify participants who would be more likely to be adherent to the 10-week phase and also to collect baseline step-counts. However, a longer baseline may increase the precision of usual step-counts estimates. Similarly, a longer intervention phase and the addition of a post-intervention (no BCT prompts) phase may afford a more comprehensive assessment of longer term outcomes. Costs and concerns about attrition are perceived to be too high to consider these extensions. Another potential limitation is that we are not assessing satisfaction/acceptability of all elements of the trial which may inform feasibility. For example, we are not planning to systematically assess participant use or satisfaction with coordinator support (e.g., phone calls helping them to set up their Fitbit device). However, if systematic issues do arise in the course of trial implementation (e.g., all participants required long coaching sessions to utilize study devices), we will report these issues in the primary outcome manuscript. Another limitation is participant recruitment will be limited to employees of a large health care system; the degree to which our results will generalize to a more representative populations is unclear.

5. Future directions

If conduct of this protocol finds it is feasible to produce automaticity of a walking plan and patients express satisfaction with a no-contact, virtual approach for BCT delivery, monitoring and data collection, then the logical next step should be a within-subject control trial. Results from this protocol study will guide whether a larger randomized controlled trial, personalized N-of-1 trial, or revised pilot program should be the logical next step. If the BCT intervention successfully leads to the formation of a walking habit among older adults and the effect of the intervention is uniform across participants (i.e. not heterogeneous), then a large RCT will be the next step. If instead we detect significant HTEs, the next trial would take the form of a series of virtual multi-crossover, blinded, randomized single patient N-of-1 trials in which an individual tries two interventions (e.g., BCT intervention vs. no BCT intervention) multiple times, to determine if the BCT intervention improves automaticity, and the absence of the BCT intervention decreases automaticity. This type of trial design would also aid in identifying the heterogeneity of treatment effects (i.e., benefits, no gains or harms) across participants. If the current trial is not successful and/or the methods and design of the current trial are not satisfactory or feasible among participants, additional pilot testing may be required to refine the intervention. Thus, consideration of future trial designs is informed and consistent with the NIH Stage Model of Intervention, in considering next studies [30]. This study will serve our long-range goal to develop a single-patient, N-of-1 approach that is automated and can be used at point-of-care that could revolutionize how we interact with patients and set the stage for a truly transformative approach to precision therapeutics.

Author contributions

Jerry Suls was involved in project administration, conceptualization, design, methodology, interpretation, and writing. Ciarán Friel was involved in design, methodology and writing. Mark Butler was involved in design, methodology and writing. Patrick Louis Robles served as clinical research coordinator, engaged in investigation and data curation. Frank Vicari was involved in programming, investigation and data curation. Joan Duer-Hefele was involved in research supervision, management, design, methodology and writing. Thevaa Chandereng was involved in statistical design.Ying Kuen (Ken) Cheung was involved in conceptualization and statistical design. Karina Davidson was involved in conceptualization, design, methodology, and writing. All authors read and approved the final manuscript.

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Availability of materials

All relevant study materials (protocol, Informed Consent Form, statistical analysis plan, measures, data dictionary) will be made available

on the Open Science Framework (https://osf.io/registries), a free web application with no access restrictions, following study completion. Patient data will be de-identified and pooled when appropriate.

Ethics approval

Approval was granted by: Northwell Health Institutional Board (20–1182) on April 16, 2021.

NIH trial registration

https://clinicaltrials.gov(NCT04869644); Study protocol location: https://ClinicalTrials.gov; The protocol was registered with clinicaltrial.gov at https://clinicaltrials.gov(NCT04869644) on May 3, 2021, and last updated on June 13, 2022.

Consent for publication

Not applicable.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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