Physical Activity Behavior Change for Older Veterans After Dysvascular Amputation

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Title: Physical Activity Behavior Change for Older Veterans after Dysvascular Amputation

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V 12-09-2015

SYNOPSIS

Objectives
This pilot study will use mobile-health technology to deliver an intervention designed for lasting physical activity behavior change. The study will be the first to assess the feasibility of using the PABC intervention for Veterans with dysvascular LLA. This evidence-based behavior change intervention will be delivered using a wearable activity sensor (FitBit, Inc.) and a home-based tablet to allow real-time activity feedback and video interface between participant and therapist. The use of home-based behavior change methods has successfully improved physical activity in healthy older adults[1, 2] and patients with chronic health conditions,[3-9] but a mobile-health PABC intervention has yet to be studied for people with dysvascular LLA.

Design and Outcomes
This will be a randomized, tester-blinded, crossover design pilot study assessing PABC intervention feasibility and effect size. Randomization will create two groups (GROUP1 and GROUP2) . GROUP1 will receive intervention during months 1-3, and GROUP2 will receive the PABC intervention during months 4-6 (Fig.1).

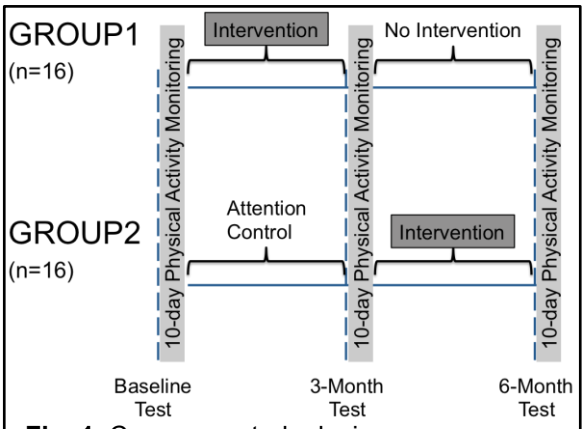

Fig. 1. Crossover study design.

Outcomes will be measured during in-home visits (Baseline, 3M, and 6M), instead of remotely, to promote safety and reduce fall risk during the test session. Aim 1 outcomes will be 1) participant retention rate, 2) dose goal attainment, 3) acceptability (Intrinsic Motivation Inventory – Interest/Enjoyment Subscale[10]), and Adverse & Serious Adverse Events (Timed Up-and-Go, Falls Efficacy Scale-International, Frequency of Events). Aim 2 outcomes, to assess effect size, will be average 10-day physical activity counts (ActiGraph monitors[2, 11]) and self-report disability (Late-Life Function and Disability Index (LLFDI)[12, 13]). In addition, Baseline descriptive measures include demographics, medications, cognition (Folstein Mini-Mental State Exam[14]), depression (Geriatric Depression Scale SF[15, 16]), residual limb quality (Chakrabarty Scale[17]), sensory testing (Michigan Neuropathy Screen[18, 19]), social support (Multidimensional Scale of Perceived Social Support), exercise readiness to change (Exercise Stages of Change[20, 21]), prosthesis description, and comorbidities (Functional Comorbidity Assessment[22]).

Interventions and Duration

Thirty-two participants will be randomly assigned to two groups: GROUP1 or GROUP2. The home-based study design is intended to reduce participant burden by removing transportation and time barriers. There will be two participation periods of three months (Months 1-3 and 4-6). PABC intervention will occur Months 1-3 for GROUP1 and Months 4-6 for GROUP2. GROUP2 will participate in a no-exercise, attention control in Months 1-3. GROUP1 will have a no contact, intervention "wash-out" period in Months 4-6.

Evaluations will take place using the following schedule:

Baseline only: At Baseline testing, participants will also complete the following tests/measures/forms:

1) Folstein Mini-Mental State Examination
2) Geriatric Depression Scale SF
3) Chakrabarty scoring of residual-limb quality
4) Michigan Neuropathy Screen
5) Prosthetic description and Demographic Form
6) Functional Comorbidity Index
7) Multidimensional Scale of Perceived Social Support

Baseline, 3 and 6 months:

1) Timed Up-and-go
2) Two Minute Walk Test
3) Five Meter Walk
4) Single Limb Stance Test
5) Falls Efficacy Scale-International
6) Activity Measurement
7) Self-Efficacy for Exercise Scale
8) Intrinsic Motivation Inventory (IMI) – Interest/Enjoyment Subscale
9) LLFDI
10) Exercise Stages of Change
11) Prosthesis Evaluation Questionnaire – Mobility Section

Continuously: Falls, Adverse Events (AEs), and Serious Adverse Events (SAEs) will be recorded and reported as needed.

Sample Size and Population

The target sample is 32 persons with transtibial or transfemoral amputation, resulting from PAD or DM complications within the past one to five years.

Participants will be recruited from the Denver VA Medical Center

A. Abstract & Specific Aims:

The primary objective of this pilot study is to determine the feasibility of using a physical-activity behavior-change (PABC) intervention targeting improved physical activity and reduced disability in Veterans 1-5 years following dysvascular lower-limb amputation (LLA).

This pilot study will use mobile-health technology to deliver an intervention designed for lasting physical activity behavior change. The study will be the first to assess the feasibility of using the PABC intervention for Veterans with dysvascular LLA. This evidence-based behavior change intervention will be delivered using a wearable activity sensor (FitBit, Inc.) and a home-based tablet to allow real-time activity feedback and video interface between participant and therapist. The use of home-based behavior change methods has successfully improved physical activity in healthy older adults[1, 2] and patients with chronic health conditions,[3-9] but a mobile-health PABC intervention has yet to be studied for people with dysvascular LLA.

Over 1 million Americans currently live with LLA and the number is expected to more than double by 2050.[23] The increasing population of patients with LLA is attributed largely to an aging population with chronic vascular conditions, such as DM and PAD. Such dysvascular amputations in older adults account for the majority of LLA (>80%).[23-25]

There is an immediate need to identify effective methods for improving physical activity and disability outcomes after dysvascular LLA. Current VA/DoD Clinical Practice Rehabilitation Guidelines describe a comprehensive approach, including community reintegration after LLA.[26] However, no intervention strategies target the physical inactivity that often contributes to the initial dysvascular LLA. This is a problem, since people with dysvascular LLA have chronic low physical activity and high rates of disability.[27-30] This pilot study will address the gap in current practice guidelines by advancing community reintegration with specific PABC intervention.

We will recruit older Veterans with dysvascular LLA (1-5 years after LLA) to participate in the PABC intervention, which uses established VA Health Care system technology and evidence-based intervention methods. The five key dimensions of feasibility to be assessed are whether Veterans: 1) can successfully participate in the intervention (practicality), 2) tolerate physical activity progression (implementation feasibility), 3) are interested and enjoy the intervention (acceptability), 4) complete the intervention safely (safety), and 5) respond to the intervention with increased activity and decreased disability (responsiveness).[31, 32] Measures of physical activity and disability will be used to establish effect size estimates for the PABC intervention, with the intention of planning a future clinical efficacy trial. Testing will occur at baseline (pre-intervention), three months (end of intervention), and six months, using a two-group randomized crossover design.

Primary Aim: Determine feasibility of using the PABC intervention with older Veterans who have dysvascular LLA by assessing: 1) practicality (measured by retention rate), 2) implementation feasibility (measured by dose goal attainment), 3) participant acceptability (measured by the Intrinsic Motivation Inventory (IMI) – Interest / Enjoyment Subscale), and 4) safety (measured with Adverse and Serious Adverse Events).
Hypothesis 1.1: Retention rate will be at least 85% over the PABC intervention period (i.e., ≤15% attrition).
Hypothesis 1.2: At least 75% of participants will meet the dose goal of a 3% average increase in daily steps per week, across the three months of intervention.
Hypothesis 1.3: Participants will indicate PABC intervention acceptability with a mean score of ≥ 5/7 on the IMI – Interest / Enjoyment Subscale.
Hypothesis 1.4: There will be similar rates of study related (definitely, probably, possibly) adverse events between groups during the first three months (period of direct comparison of intervention versus control).
Secondary Aim: Establish effect size estimates of the PABC intervention (responsiveness)

using physical activity and self-report disability outcomes.

Hypothesis 2.1: The PABC group will have increased activity counts and less self-reported disability than the control group at Month 3, each with effect size estimates ≥ 0.80 (Cohen's d).

Hypothesis 2.2: Mean and standard deviation values for activity counts (accelerometer-based activity monitors) and disability (Late-Life Function and Disability Index) will allow for sample size estimates for the subsequent larger efficacy trial.

Impact: This pilot study addresses an understudied and growing population of older Veterans characterized by complex health conditions, compounded by chronic low physical activity and high levels of disability. This novel trial will be the first to specifically target chronic physical inactivity behavior for Veterans living with dysvascular LLA. The outcome will significantly advance current research by 1) characterizing the feasibility of using the PABC intervention and 2) establishing an intervention effect size estimate to guide future trials.

B. Background and Significance:

B.1. Significance

This pilot study is significant for Veterans with dysvascular LLA, based primarily on: 1) a high prevalence of dysvascular LLA, 2) poor long-term physical activity outcomes, 3) limited evidence-based physical activity rehabilitation strategies, and 4) barriers to accessing rehabilitation clinicians.

Dysvascular Amputation: Amputation caused by severe diabetes mellitus (DM) with dense sensory and motor neuropathy leading to a non-healing foot wound or severe peripheral artery disease (PAD) with critical limb ischemia (or a combination of these two related but separate pathophysiologies).

High prevalence of dysvascular amputation

The number of Veterans with dysvascular LLA is increasing. The number of people living with amputation in the United States is projected to be 2.3 million in 2050 (≈100% increase from current value), due to an aging population and increased prevalence of underlying causes such as DM and PAD.[23] Although there is a current trend of decline in total amputation rate among Veterans, there is a growing population of Veterans with dysvascular LLA. For example, from 2000 to 2004 there was a 34% decrease in relative amputation rate (amputation/DM Veteran population).[33] However, due to an increase in number of Veterans with DM during the same time period, the population of Veterans with diabetes and initial LLA increased by 23%.[33]

Poor long-term physical activity and disability outcomes

Physical limitations are well documented following dysvascular LLA.[27, 28] Patients with dysvascular LLA participate in dynamic walking activities half as much as healthy people of similar age[34] and only 33% of Veterans with major LLA achieve pre-amputation mobility one year after LLA.[30] Importantly, patients with PAD and DM have lower physical activity and greater disability than healthy peers.[35, 36] In addition, LLA of any etiology leads to lower physical activity and disability.[30, 34, 37] The combination of chronic vascular conditions and LLA make physical activity and disability a critical target for improved health in this population.

Limited evidence-based physical activity rehabilitation strategies

Rehabilitation strategies to improve physical activity after dysvascular LLA are neither well-defined nor well-studied,[38] despite patients with LLA being well below recommended levels of physical activity.[39] While the majority of LLAs (>80%) are dysvascular,[25] available functional outcomes research is largely based on relatively younger populations with traumatic, congenital, or cancer-related LLAs. This study bias limits the knowledge needed to develop rehabilitation strategies following dysvascular LLA.[38, 40] In addition, physical activity is not currently targeted with interventions following LLA. Yet, physical activity interventions for older adults with chronic

diseases, including DM and PAD, have known benefits including decreased fall risk and improved health outcomes.[3, 4, 41, 42] For example, a recent study of older adults in Medicare-sponsored physical activity programs found that patients in the programs had significantly reduced risk of falls.[41] However, activity interventions for patients with chronic vascular disease in addition to LLA have not been addressed.

Barriers to accessing rehabilitation clinicians

For many Veterans with dysvascular LLA, long-term access to rehabilitation providers is difficult. While supervised exercise programs for patients with chronic health conditions can create short-term improvements in physical activity,[3, 43-45] such programs have high patient burden (e.g., transportation and time). This burden is especially relevant to Veterans living in remote or rural areas.[46] In addition, supervised exercise programs for patients with chronic health conditions have limited success in maintaining long-term changes in walking activity.[47, 48] Mobile-health interventions are a promising alternative to traditional direct supervised intervention to decrease patient burden and improve long-term activity behavior.[2-5, 8, 9]

B.2. Innovation

Innovation 1: This is the first study using evidence-based physical activity behavior change for older adults with dysvascular LLA. Traditional rehabilitation focuses on physical impairments, neglecting physical activity behaviors that often exist prior to dysvascular LLA. Chronic inactivity behavior compounds the insult of LLA, resulting in dangerously low activity levels after LLA.[34, 49, 50] However, health benefits of being physically active are well established, with higher levels of physical activity linked to improved health and quality of life in patients with chronic disease.[39, 51]This study will implement behavior change techniques, proven successful for other chronic disease populations,[3-5, 9] to target physical inactivity following dysvascular LLA.

Innovation 2: This study advances current physical rehabilitation by using home-based intervention to build on inpatient and outpatient rehabilitation success. While physical function improves across the course of rehabilitation,[52, 53] long-term functional outcomes after LLA are poor.[28, 30, 54, 55] Traditional physical rehabilitation focuses narrowly on care immediately following LLA, emphasizing prosthetic function, mobility/gait training, and targeted remediation of physical impairments.[38, 56] Once Veterans complete traditional outpatient rehabilitation, continued physical activity intervention is often not practical, especially for Veterans living in rural areas with unique barriers to healthcare access.[46] Improved long-term physical activity outcomes may result from practical behavior changes through home-based intervention to supplement clinic-based rehabilitation.

Innovation 3: This study adds value to emerging mobile health technology currently used for Veteran populations with various other complex health conditions. The proposed mobile-health technology in this pilot study is currently used in the VA system to promote psychological health,[57] diabetes monitoring,[58] and pharmacological management of cardiovascular disease.[59] This proposed study will provide added value to the VA mobile-health technology by using the technology for promoting physical activity behavior change in a population of Veterans at high risk for physical inactivity and high disability.

Innovation 4: The integration of PABC intervention, wearable activity sensors, and mobile-health tablets is novel. We will combine a proven behavior change approach with technologies to both track physical activity and guide behavior change. Accelerometer-based wearable sensors combined with tablet applications will provide accurate physical activity tracking and real-time feedback to guide the intervention. Accurate activity measurement using accelerometer-based sensors are essential, compared to relying solely on the subjective measures traditionally used in studies of physical activity following dysvascular LLA.[27, 30, 55] Subjective reports of physical activity are typically higher than accelerometer measures,[60-62] which could misinform the participant and therapist as they work to change activity behavior. The tablet also provides a video interface for direct interactions between participant and

therapist. By integrating wearable sensors with the mobile-health tablets, the intervention can be delivered with critical real-time participant feedback and a video conduit to allow collaborative action planning, tailored feedback, problem solving, and participant encouragement.

B.3. Approach

Seven characteristics of successful physical activity behavior change interventions, based largely on Social-Cognitive and Control Theories of behavior change, are central to the PABC intervention (Tab.1).[6, 7, 63-66] This evidence-based behavior change intervention will be delivered using a wearable activity sensor (FitBit, Inc.) and a home-based tablet to allow real-time activity feedback and video interface between the participant and therapist. The use of mobile-health technology with theory-based behavior change methods have successfully improved physical activity in healthy older adults[1, 2] and patients with chronic health conditions.[2-9] This pilot study will determine if targeted PABC, remote intervention is feasible for Veterans with dysvascular LLA.

Table 1. The PABC intervention components.

Intervention Characteristic	Theoretical Framework
1. Education	Social-Cognitive Theory
2. Action Plan (Collaborative)	Social-Cognitive Theory
3. Self-Monitoring	Control Theory
4. Tailored Feedback	Control Theory
5. Barrier Identification	Social-Cognitive Theory
6. Promotion of Problem Solving	Social-Cognitive Theory
7. Encouragement	Social-Cognitive Theory

C. Preliminary Studies:

The study team has experience in design and implementation of rehabilitation research involving older adults with activity limitations and disability.[67-71] Four studies are most directly related to the proposed pilot.

C.1. Activity and mobility limitations related to dysvascular amputation

Our research team has worked with outpatient rehabilitation clinics in four regional hospitals on the front-range of Colorado, including the Denver VAMC, to develop and implement a standardized battery of rehabilitation outcome measures for patients with LLA. In our recent analysis, patients with dysvascular LLA at all hospitals improved physical function with rehabilitation.[53, 72] Despite improvements, functional outcomes remained below clinically important cut-off scores. For example, gait speeds <0.8 m/s indicate low life expectancy and poor ability for community ambulation.[73, 74] In our sample (n=42) at rehabilitation discharge, 45% of patients had gait speeds <0.8 m/s. Additionally, Timed Up-and-Go (TUG) test times >19 s indicate high risk for multiple falls after LLA.[75] Thirty-two percent of participants had discharge TUG times >19 s. These results demonstrate that despite improvements during rehabilitation, the risks of inactivity and falls are high following dysvascular LLA.

C.2. Functional training and participation-based rehabilitation following dysvascular LLA: a case series

We have conducted a prospective case-series (n=3) examining progressive outpatient rehabilitation after dysvascular LLA. The aims of the case-series were to: 1) describe progressive functional training and participation-based rehabilitation after dysvascular LLA, 2) describe the complex medical conditions of patients with dysvascular LLA, and 3) determine the persistence of functional improvements across the first year after LLA. Each patient in this case series had large functional gains during rehabilitation. However, all three patients rated their physical function lower (10-50%) at a seven-month follow-up than at the time of rehabilitation discharge. In addition, two of the three patients developed a new diabetic foot ulcer on the limb opposite the amputation by the seven-month follow-up. These poor functional outcomes are consistent with other studies,[27, 30, 76] further supporting the need to identify strategies to improve long-term function and activity.

C.3. Collaborative-care, home intervention for improving physical function following dysvascular LLA

An ongoing randomized controlled trial (RCT) examines efficacy of a collaborative-care, home-based intervention to improve functional outcomes within the first six months after dysvascular LLA. The primary outcomes are performance-based (TUG, Two-Minute Walk Test) and participant-report (Prosthesis Evaluation Questionnaire, Houghton Scale) measures of function. The RCT intervention uses home visits and phone calls, with no mobile-health technology. Veterans account for just over 60% of the participants enrolled to date. The RCT includes a 3-month intervention beginning when participants complete physical rehabilitation (≈6 months after LLA). The RCT will complete in 16 months and currently only 1 of 23 participants has been lost to follow-up. This ongoing RCT differs from the proposed PABC pilot study in that the PABC study focuses on physical activity behavior, conducts intervention completely remotely, uses mobile-health technology, and intervenes 1-5 years after LLA. This ongoing RCT demonstrates the ability of the study team to effectively conduct an intervention study for Veterans with dysvascular LLA.

C.4. Collaborative-care intervention to promote physical activity after total knee arthroplasty
An ongoing study examines efficacy of physical activity feedback using face-to-face group meetings compared to a standard of care control group, for patients with total knee arthroplasty. The collaborative-care intervention involves real-time activity tracking using FitBit wearable sensors in combination with monthly group meetings. Primary outcomes are physical activity and physical function. Four months remain in this two-year RCT and 36 of 40 participants have been enrolled. Preliminary data analysis indicates a 14% mean increase in physical activity per week with intervention, with no unexpected adverse events. Besides focusing on a different population of patients (LLA vs. total knee arthroplasty), the currently proposed PABC study differs from this total knee arthroplasty trial as an individualized intervention, conducted completely remotely, using mobile-health technology for delivery, and targeting physical activity and disability outcomes. This study demonstrates the ability of the study team to conduct an intervention study targeting physical activity behavior change.

D. Research Design and Methods:

The proposed pilot study is a randomized, tester-blinded design assessing PABC intervention feasibility (Aim 1) and effect size (Aim 2). Randomization (n=32) will create two groups (GROUP1 or GROUP2) using computer-generated random blocks of 2 and 4, stratified by amputation level (transtibial and transfemoral). An investigator not involved with testing or intervention (Stevens-Lapsley) will conceal group allocation. A crossover design is used to simultaneously accomplish the aims and optimize recruitment (Fig.2). The PABC Intervention will be delivered to both groups (GROUP1 during Months 1-3 and GROUP2 during Months 4-6). The crossover design provides n=32 for assessing Aims 1 and 2. Intervention effect retention will be tested at six months for GROUP1 (n=16).

D.1. Setting

The study will occur at the VA Geriatric Research Education and Clinical Center (GRECC), where Drs. Christiansen and Stevens-Lapsley have dedicated positions (Dr. Robert Schwartz (GRECC Director)). Intervention delivery will occur with the participant at home and therapist at a VA site with access to tablet interface software (e.g. VA Jewell Motion Analysis Lab or VA Clinical Building South, using VA-supplied and approved mobile-health tablets and wearable activity sensors (FitBit).

D.2. Participants

Thirty-two participants will be recruited from the Denver VAMC. The target sample is older Veterans diagnosed with PAD and/or DM, who have major LLA. We expect <15% attrition, with a goal of 26 participants completing.

D.3. Eligibility Criteria

Inclusion criteria: ≥ 50 years of age, LLA 1-5 years prior, Type II DM and/or PAD, and

ambulatory without human assistance, in the home or better using a prosthesis, with assistive device as needed, with assistive device as needed. Exclusion criteria: wheelchair as primary form of locomotion, trauma or cancer-related etiology of the LLA, unstable heart condition, uncontrolled hypertension, acute systemic infection, cancer, recent stroke (within 2 years), or lower extremity wound or ulcer that limits ambulation.

D.4. Recruitment Strategies

All participants will be recruited from the Denver VA Medical Center (VAMC) or Veterans that are receiving care outside of the VA system in our core-group of regional hospitals. Dr. Stephenson and Dr. Fields will use the Amputation Clinic database and meet with the rehabilitation teams to obtain names of Veterans meeting the inclusion criteria. A research team member will then contact the potential participant in person or by letter and ask for permission to explain and complete a brief screening form to determine the Veteran's eligibility. We will increase the recruitment pool for this study from our previous studies, by allowing participants with both transfemoral and transtibial amputation. Recruitment from the Denver VAMC is expected to be feasible based on Denver VAMC data (47 new Veterans seen in rehabilitation for new major LLA in last 18 months).

D.5. Intervention

The home-based study design is intended to reduce participant burden by removing transportation and time barriers. There will be two participation periods of three months (Months 1-3 and 4-6). PABC intervention will occur Months 1-3 for GROUP1 and Months 4-6 for GROUP2 (Fig.1). GROUP2 will participate in a no-exercise, attention control in Months 1-3. GROUP1 will have a no contact, intervention "wash-out" period in Months 4-6.

Study Initiation. A physical therapist will initially meet with the participant at the participant's home to: 1) obtain informed consent and authorization, 2) deliver and orient the participant to wearing an activity monitor (ActiGraph Inc. Pensacola FL), and 3) assess the prosthetic fit and function (Prosthetic Evaluation Questionnaire). If prosthetic fit and function concerns are identified, the participant will be given recommendations for seeing his/her prosthetist, which must be met before beginning the intervention. The participant will wear the ActiGraph monitor for 10 days after the initial visit. The ActiGraph monitor will be used only for outcome data (not intervention) and provides no feedback to participants. Following the initial visit, participants will be randomized (GROUP1 and GROUP2).

Table 2. PABC Intervention Overview

Technique	*General Content of Weekly Visit**
Education	*1. Specific weekly educational message* *2. Participant feedback on message* *3. Therapist clarification as needed*
Self Monitoring	*1. Promote self-monitoring using FitBit* *2. Self-monitoring goal creation*
Tailored Feedback	*1. Direct feedback from FitBit application*
Barrier Identification	*1. Participant input on barriers* *2. Therapist assists identification* *3. Falls & adverse events recorded*
Promotion of Problem Solving	*1. Ideas for addressing barriers* *2. Participant and therapist provide input*
Action Planning	*1. Collaborative weekly action plan* *2. Guideline: 3% ↑ in weekly steps* *3. Goals based on individual needs*
Encouragement	*Therapist ends session by:* *1. Reviewing the "take home" message* *2. Reviewing action plan for next week* *3. Acknowledging achievements*

Physical-Activity Behavior-Change (PABC) Intervention. The PABC intervention will occur during Months 1-3 for GROUP1 and Months 4-6 for GROUP2 (Fig.1). The intervention begins with a home visit in which the therapist delivers and outlines the PABC intervention and use of equipment (FitBit wearable sensor (FitBit Inc., Boston MA) and FitBit application on the tablet). The FitBit wearable sensor is designed specifically to provide user feedback through an

application on the home-based tablet. (FitBit Use Handout)

The first intervention week will be an accommodation period for the participant to interact with the equipment and establish baseline activity feedback. After the first week, an individualized participant action plan will be developed and the therapist will deliver the intervention following a semi-structured script (Tab.2). Weekly video-based interactions between participant and therapist (30 minutes) will occur during the 3-month intervention (12 visits) using the mobile-health tablets. The PABC intervention will require daily participant interaction with the tablet application. The tablet application is commercially available through FitBit and will provide feedback on number of steps taken and progress toward activity goals. Participants' activity will guide the goals for each week and barriers to reaching goals will be identified. The therapist will guide the participant in reasoning how to address any identified barriers to activity progression.

Each week will include scripted education delivered by the therapist during the video interaction, on a relevant intervention topic (e.g., fall prevention, monitoring blood sugar and diet relative to increasing activity, etc.) (10 minutes). The initial education topic will be fall prevention, to minimize fall risk during the study period.

No-Exercise Attention Control Period. During Months1-3, GROUP2 will weekly have weekly video interactions with a therapist using the mobile-health tablets, in a no-exercise control period. These meetings will provide health and safety education on non-exercise topics pertaining to older Veterans (e.g., fall prevention, diet, medication management, retirement issues, etc.). Physical activity recommendations will not be discussed. Each week will include scripted education on one topic (10 minutes) and a brief period of light upper and lower extremity range of motion tasks led by the therapist with the video interface and participants seated in a chair (20 minutes). As in the PABC intervention period, the initial education topic for the Control period will be fall prevention, to minimize fall risk during the study period. The rationale for the no-exercise control period is to determine the natural change in physical activity and disability without PABC intervention, while accounting for any potential benefit from contact with the physical therapist (i.e., attention control).

D.6. Outcomes

Outcomes will be measured during in-home visits (Baseline, 3M, and 6M), instead of remotely, to promote safety and reduce fall risk during the test session. Aim 1 outcomes will be 1) participant retention rate, 2) dose goal attainment, 3) acceptability (Intrinsic Motivation Inventory – Interest/Enjoyment Subscale[10]), and Adverse & Serious Adverse Events). Aim 2 outcomes, to assess effect size, will be average 10-day physical activity counts (ActiGraph monitors[2, 11]) and self-report disability (Late-Life Function and Disability Index (LLFDI)[12, 13]). In addition, Baseline descriptive measures include demographics, medications, cognition (Folstein Mini-Mental State Exam[14]), depression (Geriatric Depression Scale SF[15, 16]), residual limb quality (Chakrabarty Scale[17]), sensory testing (Michigan Neuropathy Screen[18, 19]), exercise readiness to change (Exercise Stages of Change[20, 21]), prosthesis description, and comorbidities (Functional Comorbidity Assessment[22]).

D.7. Data Management

The FitBit sensor will be used to guide the intervention and data from the sensors will NOT include personal health information; with generic accounts will be created for each user without participant-identifiable information. FitBit data will not be used as outcomes, but rather, only to guide the PABC intervention. Outcome data will be managed using the REDCap (Research Electronic Data Capture) platform. REDCap is a secure, web-based application designed to support research data capture, providing user-friendly case report forms, real-time data entry validation (e.g., data type and range checks), audit trails, transaction logs, and a de-identified data export to common statistical packages. The VA Eastern Colorado Health Care System has approved REDCap for research use. More detail is provided in the Human Subjects section.

D.8. Sample Size Estimate

The sample size estimate was based on evidence for activity change in patients with DM and PAD, which indicates a reasonable expected increase of 3% walking activity per week (e.g., steps, distance, time) over 3 months.[3, 12, 77, 78] A baseline mean (SD) of 2000 (900) steps/day was estimated based on data from our ongoing dysvascular LLA RCT (Section C.3.) and published LLA data.[49, 79, 80] A 3% weekly increase in steps during intervention, assuming no order effect, would provide an effect size of 0.8 (Cohen's d). Based on those assumptions, a sample size of 13 per group with a crossover design (total n=26) provides >95% power to detect an intervention effect (effect size=0.8, α=0.05, two-tailed paired t test). The study is generously powered intentionally, because the assumption of 'no order effect' will not likely hold. We will recruit 32 participants, and expect at least 26 to complete. This 15% attrition estimate is conservative, based on an historical attrition rate <15% in our intervention studies with other older adult populations[81, 82] and our current dysvascular LLA RCT.

D.9. Data Analysis Plan

Aim 1 (Feasibility of PABC Intervention): The analyses for Aim 1 are based on four hypotheses: H1.1) participant retention, H1.2) dose goal attainment, H1.3) intervention acceptability, and H1.4) safety.

- H1.1) Retention rate will be assessed using a cut off of 15% attrition (i.e., loss of >6 participants). Mean attrition rate will be compared to the null value of 15% using a one-sample t-test (α=0.05). This attrition rate is considered feasible based on previous activity change programs for patients with DM or PAD.[5, 83]
- H1.2) Dose goal attainment will be assessed by the proportion of participants achieving the goal of 3% average weekly increase in steps, based on activity gains in other intervention studies.[3, 12, 78] The ability to attain a 3% average weekly step increase for <75% of the participants will be considered a negative result. The proportion of participants attaining a 3% average weekly step increase will be reported (95% CI) and compared to the null value of 75% using a one-sample binomial proportions test (α=0.05).
- H1.3) Acceptability of the intervention will be measured with the IMI Interest and Enjoyment subscale, with a mean score of <5/7 considered a negative acceptability result.[10] Mean IMI Interest and Enjoyment score will be compared to the null value of 5.0 using a one-sample t-test (α=0.05).
- H1.4) Adverse and serious adverse event (AE/SAE) rates (events/participant) will be compared between groups for Months1-3 (PABC intervention for GROUP1, attention control for GROUP2). We expect similar AE/SAE rates between groups (assessed by Safety Officer and research team).

Aim 2 (Effect Size and Preliminary Efficacy of PABC Intervention): Effect size of the PABC intervention will be calculated with Cohen's d using mean and standard deviation for change in activity counts and LLFDI scores. Statistical inference of group differences for calculation of sample size estimates will be based on linear models with activity counts and LLFDI scores as outcome variables. Explanatory variables in each model will include primary medical diagnosis (PAD, DM, or both), group, and baseline activity count or LLFDI score.

D.10. Expected Outcomes and Interpretation

Determining feasibility of the PABC intervention will set the stage for implementing a larger efficacy study. The expected result is that Veterans with LLA can be enrolled and retained in the PABC intervention with adherence to a 3% weekly increase in physical activity dose. In addition, the effect size is expected to be ≥ 0.80. While similar interventions have been feasible and successful for other chronic disease populations, this trial will be the first to target chronic physical inactivity behavior for Veterans living with dysvascular LLA.

D.11. Participant Safety

Anticipated adverse events include falls and medical complications due to DM and PAD. A Safety Officer (Dr. William Sullivan) for the study will meet with the PI quarterly to review study progress and adverse events. Dr. Sullivan is the Outpatient Medical Director for Rehabilitation Services at the Denver VAMC. Dr. Sullivan is also an Associate Professor in the Department of Physical Medicine and Rehabilitation at the University of Colorado. Beyond his clinical expertise, Dr. Sullivan has experience in outcomes research related to patients with LLA and functional exercise interventions. Fall risk will be monitored using the TUG test and Falls Efficacy Scale-International (FES-I) at all test points (baseline, 3M, 6M). Also, occurrence of falls will be recorded at each of weekly visit in both the intervention and control periods. Fall occurrences and other adverse events will be reported on a quarterly basis to the Safety Officer. The incidence of falls, defined as "inadvertently coming to rest on the ground, floor or other lower level, excluding intentional change in position",[84] will be of particular focus. All study-related falls (possibly, probably, or definitely) will be tracked. If the total number of falls reaches 4, the Safety Officer will review incidence by group. If the number of falls for the intervention group exceeds that of the control group by 3 (10% of enrollment) at any time, the study will be suspended until an evaluation of study relatedness for each incidence is performed by the Safety Officer.

D.12 Potential Pitfalls and Alternative Strategies

1. Recruitment feasibility: Recruiting 32 participants is challenging for a 2-year pilot study. The primary recruitment site will be the VAMC. Established relationships with 3 other regional hospitals will be used to expand recruitment, with a future protocol amendment as needed. In addition, recruiting Veterans with either transfemoral or transtibial LLA provides a larger recruitment pool than limiting the LLA to one specific level.
2. Functionality of the mobile-health technology: Durability and continued functionality is a concern when using any technology. The mobile-health tablets used in this study are used in standard of care for a variety of purposes in the VA Eastern Colorado Health Care system. If a tablet becomes dysfunctional, replacement units are available for immediate replacement. The VA will provide mobile-health technical support for the duration of the study (See letter of support from Dr. Bray-Hall). Finally, the PABC intervention is not dependent on equipment brand, so future changes in equipment will not necessitate change in intervention.
3. Long-term behavior change: Creating lasting change in physical activity behavior is a major challenge. We will collect data out to 6 months (GROUP1) to determine persistence of intervention effects. We expect activity changes may be reduced at the 6-Month time period compared to the 3-Month test point, but expect activity to remain higher than baseline, based on data from studies of patients with other chronic diseases.[2]
4. Transtibial and transfemoral LLA: Response to intervention may differ between Veterans with transfemoral and transtibial LLA. We have included both levels of amputation, as both are linked to low activity and high disability. We will protect against such differences by stratifying randomization by level of amputation.

E. Study Timeline and Enrollment Goals:

TASK	**Year 1**				Total (1)	**Year 2**				Total (2)	**TOTAL**
Personnel Training											
Screening											
Enrollment (n=32)	4	4	6	6	20	6	6			12	32
Data Collection, Processing & Analysis											
Abstracts/Manuscripts											

F. Future Investigation:

This pilot project is an important stepping-stone for a larger research line focused on optimizing physical activity and minimizing disability for Veterans with dysvascular LLA. Data from this pilot study will inform a larger intervention trial targeting mobile-health physical activity change (future VA Merit Review proposal).

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