

# Collaborative-Care Rehabilitation to Improve Functional Outcomes after Dysvascular Amputation

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## *COMIRB Protocol*

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### ***Title: Collaborative-Care Rehabilitation to Improve Functional Outcomes after Dysvascular Amputation***

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V1.3

## **SYNOPSIS**

### Objectives

The objective of this study is to determine the efficacy of a collaborative-care, home-based rehabilitation program for improving functional outcomes following dysvascular transtibial amputation. The primary aim is to determine if the rehabilitation program improves performance-based and participant-report measures of physical function, compared to standard of care, for participants with dysvascular transtibial amputation. The secondary aim is to determine if the rehabilitation program improves daily physical activity, compared to standard of care, for participants with dysvascular transtibial amputation. Two exploratory aims are: 1) determine the efficacy of the intervention for promoting health self-management, measured as participant-reported self-efficacy for managing chronic disease, motivation for exercise, and health-care resource use and 2) identify factors at initial testing that are predictive of physical activity level and disability 24 weeks after intervention.

### Design and Outcomes

This will be a randomized, controlled clinical trial on the effects of 12 weeks of collaborative-care, home-based rehabilitation on physical function outcomes. Outcome variables include:

1. Performance-Based Physical Function Measures:
  - a. Timed Up-and-Go (TUG)<sup>1</sup>
  - b. Two-Minute Walk (2MW)<sup>2</sup>
  - c. Five-meter Walk (5mW)<sup>3</sup>
2. Self-Report Physical Function Measures:
  - a. Prosthesis Evaluation Questionnaire – Mobility Section (PEQ-MS)<sup>4</sup>
  - b. Houghton Scale<sup>5</sup>
  - c. Patient-Specific Functional Scale (PSFS)<sup>6</sup>
3. Activity Measurement:
  - a. Physical activity monitors (Actigraph) worn for 1 week following each test session (baseline, 12-week, 24-week). These monitors are valid tools for measuring relative level of activity (e.g., sedentary, light, moderate, vigorous) for various patient populations<sup>7-9</sup> and are valid and reliable spatiotemporal gait measures for patients with lower limb amputation.<sup>10,11</sup>
4. Self-Efficacy and Motivation:
  - a. Self-Efficacy in Managing Chronic Disease (SEMCD) questionnaire<sup>12,13</sup>
  - b. Intrinsic Motivation Inventory (IMI) Interest and Enjoyment Subscales<sup>14</sup>
  - c. Participant compliance with exercise will be tracked as number of exercise sessions missed/possible sessions.
5. Healthcare Use:

- a. Number of healthcare provider visits scheduled and attended; from electronic medical record.
- b. Number of hospital contacts (emergency department visits and hospital admissions); from electronic medical record.

#### Interventions and Duration

Forty-four participants will be randomly assigned to two groups: 1) experimental (EXP) or 2) control (CTL). The entire intervention period is 12 weeks, with the primary end point at 12 weeks. At 24 weeks after initiation of intervention, each group will be asked to return for a follow-up test session.

Evaluations will take place using the following schedule:

Baseline, 12 and 24 weeks: Physical Performance Tests, Self-Report Physical Function Measures, Activity Measurement, Self-Efficacy questionnaire, Motivation questionnaire, Health Status questionnaire, and healthcare use assessment.

Baseline only: At Baseline testing, participants will also complete the following tests/measures/forms: 1) Folstein Mini-Mental State Examination,<sup>15</sup> 2) Geriatric Depression Scale SF,<sup>16,17</sup> 3) Chakrabarty scoring of residual-limb quality,<sup>18</sup> 4) Residual limb length, 5) lower extremity sensory testing, 6) pre-amputation ambulatory status report, 7) type of prosthesis (socket, suspension, and foot), and 8) demographic information. Hemoglobin A1c measurements (for DM) and confirmation of PAD will be extracted from the participant medical records.

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 44 persons with recent transtibial amputation, resulting from PAD or DM complications.

Participants will be recruited from the University of Colorado Hospital and Denver Health.

## Title: Collaborative-care rehabilitation to improve functional outcomes after dysvascular amputation

### A. Abstract & Specific Aims

**The primary objective of this project is to determine the efficacy of a collaborative-care, home-based exercise program for improving physical function, activity level, and health self-management within the first year following dysvascular transtibial amputation.**

Over 1 million Americans currently live with lower limb amputation, and the number is expected to more than double by 2050.<sup>19</sup> The increasing amputation rate is attributed to an aging population and increased incidence of underlying causes such as peripheral artery disease (PAD) and diabetes mellitus (DM).<sup>19-22</sup> Unfortunately, under-representation of people with dysvascular amputation in rehabilitation research has led to a gap in knowledge of how to 1) optimize physical rehabilitation and 2) facilitate successful health self-management for these patients.<sup>23</sup>

Due to the lack of research on rehabilitation following *dysvascular* lower limb amputations, optimal physical rehabilitation is largely undefined.<sup>24</sup> Traditional rehabilitation goals focus narrowly on the episode of care surrounding amputation, emphasizing prosthetic function, mobility/gait training, and targeted remediation of physical impairments.<sup>24-27</sup> However, this approach neglects underlying comorbidities, chronic physical inactivity, and history of poor health self-management which are all risk factors and contribute to poor outcomes of dysvascular amputation. As a consequence, patients typically experience chronic function limitations.<sup>28-31</sup>

Considering the large, under-represented population with dysvascular transtibial amputation and evidence of poor long-term functional outcomes, there is an immediate need to address rehabilitation practice.

This intervention study will address impaired physical function, activity limitation, and health self-

management for people recovering from dysvascular transtibial amputation using innovative collaborative-care, home-based rehabilitation (Figure 1). Collaborative-care will pair the participant and therapist to promote responsibility in participant management of his/her physical rehabilitation and health. In addition, home-based intervention will promote carry-over of rehabilitation gains into the functional setting of the home.

Participants will self-monitor progress and communicate regularly with the research team to advance the intervention and address barriers to successful goal achievement. While outcome measures are standardized for all participants, intervention selection and incremental goals will be participant-tailored, within specific guidelines, with therapist collaboration to optimize rehabilitation progress.

Results of this study will quantify the effect size of the proposed intervention and inform future research designed to optimize intervention, focus examination based on the dominant pathophysiology (i.e., DM, PAD, or both), and examine efficacy in other populations (e.g., patients with trans-femoral amputation).

**Specific Aim 1:** The Primary Aim (PA1), on which this trial is powered, and the Primary Hypotheses (H1.1 and H1.2) are:

- a) PA1: Determine if the collaborative-care, home-based rehabilitation program improves performance-based and participant-report measures of physical function compared to standard of care for participants with dysvascular transtibial amputation.

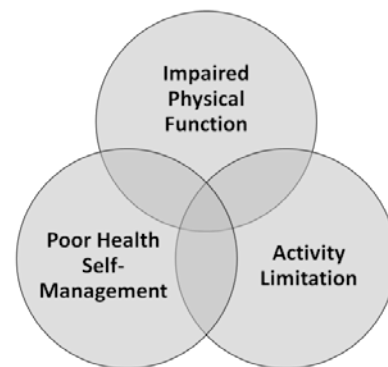


Figure 1. Outcome factors after amputation

- b) H1.1: The rehabilitation program will result in greater improvements in the performance-based measures of the Timed Up-and-Go, 2-Minute Walk, and 5-meter Walk tests than standard of care at 12 weeks (primary end-point) and persist at 24 weeks following initiation of intervention.
- c) H1.2: The rehabilitation program will result in higher ratings of participant-reported physical function on the Prosthesis Evaluation Questionnaire – Mobility Section, Houghton Scale, and Patient-Specific Functional Scale than standard of care at 12 weeks (primary end-point) and persist at 24 weeks following initiation of intervention.

**Specific Aim 2:** The Secondary Aim (SA) and Hypothesis (H2) are:

- a) SA: Determine if the collaborative-care, home-based rehabilitation program improves physical activity when compared to standard of care for participants with dysvascular transtibial amputation.
- b) H2: The rehabilitation program will result in greater increases in physical activity than standard of care at 12 weeks (primary end-point) and persist at 24 weeks following initiation of intervention.

**Exploratory Aims:**

1. Exploratory Aim 1 (EA1) and Hypotheses (H3 & H4) are:

- a) EA1: Determine if the collaborative-care, home-based rehabilitation program influences the health self-management factors of self-efficacy for managing chronic disease, motivation for exercise, and healthcare use.
- b) While the study will likely be under-powered to find differences related to this aim, the, if trends in group differences are seen, data will provide a means for performing a statistical power analysis to determine sample size for future study. The hypothesized trends for group differences are:
  - (1) H3: The rehabilitation program group will tend to have greater positive change in ratings on the Self-Efficacy in Managing Chronic Disease (SEMCD) questionnaire and Intrinsic Motivation Inventory (IMI) Interest and Enjoyment Subscales, compared to the standard of care group at 12 and 24 weeks following initiation of intervention.
  - (2) H4: The rehabilitation program group will tend to have higher numbers of attended healthcare provider appointments and lower numbers of hospital contacts at 12 weeks and 24 weeks, compared to the standard of care group.

2. Exploratory Aim 2 (EA2) and Hypothesis (H4) are:

- a) EA2: Identify factors predictive of physical activity level and disability measured by activity monitors and self-reported disability (World Health Organization Disability Assessment Schedule 2.0), respectively.
- b) H5: Significant predictors of physical activity and disability will be identified from the categories of demographic/anthropometric, activity/mobility, health behaviors, physical health, amputated-limb health, contralateral-limb health, cognitive/affective health, and healthcare use factors for participants at 24 weeks following intervention, regardless of group assignment.

## **B. Background and Significance**

**B1. Significance.** Limitations in physical function are common following dysvascular major lower limb amputation.<sup>28,29,31</sup> This is a significant issue considering that dysvascular amputation is becoming increasingly more common in the United States. Dysvascular amputation is operationally defined as amputation resulting from severe PAD with critical limb ischemia or severe DM with dense distal sensory and motor neuropathy leading to a non-healing wound (or a combination of these two related, but separate pathophysiologies). The projection of 2.3 million people living with amputation in the United States by the year 2050 represents an increase of nearly 100% from current values.<sup>19</sup> As a result, dysvascular amputation has become a major healthcare issue in the U.S, including an economic problem.<sup>32</sup>

Compounding the problem of increasing prevalence and cost is that rehabilitation following dysvascular amputation is neither well-defined nor well-studied.<sup>24</sup> While the majority of lower limb amputations (>80%) are dysvascular,<sup>20</sup> available research evidence on functional outcomes is largely based on relatively younger populations with traumatic, congenital, or cancer-related amputations. This study bias limits the knowledge needed to develop rehabilitation guidelines for people following dysvascular amputation.<sup>23,24,33</sup>

**B2. Clinical Importance.** Traditional rehabilitation emphasizes prosthetic function, mobility/gait training, and targeted remediation of physical impairments,<sup>24-27,34</sup> neglecting the underlying comorbidities and poor health self-management that contribute to dysvascular amputation. While physical impairments and functional limitation can show modest improvement across the course of rehabilitation after amputation,<sup>35</sup> long-term functional outcomes are poor.<sup>28,29,36-40</sup> **For example, 40-50% of patients are not community ambulators 1 year following dysvascular lower limb amputation.<sup>28,41</sup> These poor functional outcomes are likely linked to pre-existing comorbidities and poor vascular health self-management.<sup>40,42</sup>**

Patients typically receive treatment to manage chronic vascular problems prior to and concurrent with physical rehabilitation following dysvascular amputation. However, health management is not typically coordinated with physical rehabilitation and is often *prescriptive*, rather than *collaborative* between patient and health-care provider. The presence of vascular comorbidities that lead to amputation is an indication in itself of poor patient health self-management. Using a patient/therapist collaborative intervention approach may improve upon current standard of rehabilitation following dysvascular amputation. Evidence indicates collaborative approaches to promoting health self-management improve vascular risk factor outcomes.<sup>43,44</sup> In addition, home-based intervention can effectively improve physical function and activity in people with chronic health problems.<sup>45,46</sup> As an example, Vernooij and colleagues<sup>44</sup> found patient/provider collaboration for managing vascular risk factors led to reduced risk factors over a 12 month period for people with atherosclerosis.

**This study will use a collaborative-care rehabilitation program combining traditional physical rehabilitation goals with patient self-management techniques to improve functional outcomes following dysvascular amputation.** In addition to the potential for improving long-term physical function, this study is designed to shift current practice paradigm by using a collaborative-care, home-based approach to promote physical function, activity and patient health self-management.

### C. Preliminary Studies

**C1. Clinical Research Experience.** Dr. Cory Christiansen (PI) has experience in design, implementation, and publication of clinical research studies involving older adult patients with activity limitations related to a variety of age- and health-related problems.<sup>47-52</sup> Dr. Christiansen is the PI of an ongoing randomized controlled trial involving outpatient and home intervention for patients following total knee arthroplasty, and has successfully completed all intervention and data collection phases.<sup>49,53</sup> In addition, he is currently the PI of an ongoing pilot study examining activity and mobility limitations related to dysvascular amputation (Section C2). Dr. Christiansen is also currently serving as co-investigator in a nearly-complete study examining physical activity and biomechanical outcome measures for patients following traumatic transtibial amputation.<sup>54,55</sup>

**C2. Physical Function Outcomes Related to Prosthetic Rehabilitation after Dysvascular Transtibial Amputation** (PI: Christiansen). This in-progress pilot study examines physical function recovery early (first 3 months) after dysvascular transtibial amputation. The study involves collaboration between rehabilitation clinics at five large regional hospitals in Colorado (The University of Colorado Hospital, Denver Health, The VA, Memorial Hospital, and Poudre Valley Hospital); with the PI coordinating from CU Anschutz Medical Campus. This pilot study has 1) demonstrated the PI's ability to coordinate a multi-site study for a population similar to

the proposed study and 2) begun to characterize physical function over the course of rehabilitation following dysvascular transtibial amputation. Initial data illustrate that patients with dysvascular transtibial amputation achieve meaningful gains in physical function measures with standard of care rehabilitation (Table 1). Yet, gains are not typically maintained; reported function is significantly lower 1-3 years after amputation.<sup>29,36-40</sup>

The pilot study also examines the comorbidity profile and rehabilitation dose for patients. Data collected to this point have guided development of the proposed intervention (Table 2).

#### D. Research Design and Methods

Table 2. Standard of care interventions following dysvascular transtibial amputation (n = 14)

Category	Specific Interventions
Gait Training	<ul style="list-style-type: none"> <li>•Level-ground walking</li> <li>•Parallel-bar walking</li> <li>•Community walking</li> <li>•Stair ascent/descent</li> <li>•Treadmill walking</li> </ul>
Neuromuscular Re-education	<ul style="list-style-type: none"> <li>• Variable techniques</li> </ul>
Therapeutic Exercise	<ul style="list-style-type: none"> <li>•Hip muscle strengthening</li> <li>•Knee muscle strengthening</li> <li>•CV/Endurance training</li> <li>•Hip stretching exercise</li> <li>•Knee stretching exercise</li> <li>•Trunk/Core strengthening</li> </ul>
Prosthetic Don & Doff / ADL	<ul style="list-style-type: none"> <li>•Don/doff prosthesis</li> <li>•Basic ADL training</li> </ul>
Standing Balance / Pre-Gait Training	<ul style="list-style-type: none"> <li>•Standing weight-shifts</li> <li>•Step-ups</li> <li>•Side-steps</li> <li>•Bilateral standing balance</li> <li>•Single-leg standing balance</li> </ul>
Mobility Training	<ul style="list-style-type: none"> <li>•Supine-sit mobility</li> <li>•Sit-stand mobility</li> <li>•Simulated community &amp; home mobility training</li> </ul>

Note: Specific categories listed in order of frequency during rehabilitation and specific interventions listed in order of frequency within each category.

initial test session at their home (or the research lab, whichever is more convenient for the participant) and be randomized to group: 1) experimental (EXP) or 2) control (CTL), stratified by sex.

**D4. Intervention.** Experimental (EXP) Group: **Objectives for the collaborative-care, home-**

Table 1. Physical function rehabilitation outcomes following dysvascular amputation

	Initial Exam	Discharge
TUG (s)	26.4 (15.3)	12.4 (3.9)
Gait Speed (m/s)	0.57 (0.34)	1.16 (0.33)
TMW (m)	76.8 (22.8)	125.2 (22.4)
PEQ-MS (0-4)	2.4 (1.0)	2.8 (0.7)
PSFS (0-10)	3.5 (2.0)	5.9 (1.1)

Note: TUG: Timed Up-and-Go, TMW: Two-Minute Walk, PEQ-MS: Prosthesis Evaluation Questionnaire – Mobility Section, PSFS: Patient-Specific Functional Scale

N = 14, Rehab Duration = 8.3 (5.8) weeks. All values are mean (SD).

**D1. Subjects.** Forty-four participants with dysvascular transtibial amputation.

**D2. Inclusion/Exclusion Criteria.** Inclusion criteria: 1) DM and/or PAD, 2) unilateral transtibial amputation < 6 months prior to baseline testing, 3) household ambulation using definitive prosthesis prior to baseline testing, 4) participation in physical rehabilitation at time of baseline testing and 5) live within 45 minutes of a participating clinic.

Exclusion criteria: 1) require wheelchair for mobility (use prosthesis only for transfers), 2) ankle-level or above amputation on contralateral limb, 3) traumatic or cancer-related amputation, 4) uncontrolled heart condition, 5) acute systemic infection, 6) pregnancy, 7) decisionally challenged, and 8) prisoners.

Confounding variables will be tracked to allow better delineation of the “dysvascular amputation” population in future studies including: medications, cognitive function (Folstein Mini-Mental State Examination<sup>15</sup>), depression (Geriatric Depression Scale SF<sup>16,17</sup>), residual limb quality (Chakrabarty scoring of residual-limb quality<sup>18</sup>), residual limb length, ankle-brachial index of the non-amputated limb, lower extremity sensory testing, pre-amputation ambulatory status (self-report), and type of prosthesis (socket, suspension, and foot). A Comorbidity Assessment tool<sup>56</sup> will be used to document and account for comorbidities.

**D3. Screening.** Participants will be recruited at the rehabilitation site and screened with a phone call interview. After consent, participants will have an

based rehabilitation program are to: 1) improve physical impairments with targeted exercise, 2) increase physical activity through a home walking program and 3) optimize patient health self-management. The collaborative-care, home-based rehabilitation program was developed based on self-management programs for patients with chronic disease,<sup>45,46,57</sup>

Table 3. EXP Group Rehabilitation Program

Category	Specific Components
Impairment-Based Exercise	<p>A. <u>Strengthening* (3x/week)</u></p> <ul style="list-style-type: none"> <li>Hip Extensors</li> <li>Hip Abductors</li> <li>Hip Adductors</li> <li>Knee Extensors</li> <li>Knee Flexors</li> <li>Ankle Plantar Flexors (intact limb)</li> <li>Trunk Stabilization</li> </ul> <p>B. <u>Stretching (3x/week)</u></p> <ul style="list-style-type: none"> <li>Hip Flexors</li> <li>Knee Flexors</li> </ul>
Activity-Based Intervention	<ul style="list-style-type: none"> <li>• Walking Program (3x/week)</li> </ul>
Health Self-Management	<ul style="list-style-type: none"> <li>• Participant-tailored goals</li> <li>• Participant self-tracking of exercise and activity</li> <li>• Participant education on problem-solving skills for managing health</li> </ul>

\* List of options for strengthening program, priority muscles to be included in the program based on patient-researcher collaboration, with input from primary PT.

common physical impairments and functional limitations following dysvascular transtibial amputation,<sup>36,58-62</sup> published standard of care guidelines based on professional opinion,<sup>34,63,64</sup> and clinician input from the participating hospital systems (Table 3). Physical impairments and functional limitations will be individually identified at initial testing and interventions chosen with collaboration of participant and researcher. Participants will be contacted once/week via phone to discuss progress toward individual intervention goals. Barriers to achieving goals will be discussed and new goals created on a weekly basis during the phone or home visits.

*The exercise program* will be tailored to each participant and includes targeted exercise to strengthen trunk, hip, knee, and ankle musculature (Table 3). Weakness in these muscle groups is identified in the literature<sup>36,65</sup> and by collaborating clinicians for this study. Therapists treating the participant prior to enrollment will help prioritize the targeted muscle groups for each participant, based

on participant-specific muscle weakness identified during rehabilitation. The participant (along with researcher collaboration) will then identify specific exercises from a menu of progressive exercises to target each muscle. Exercises will be performed at home independently by the participant, assessed weekly and advanced through participant-researcher interaction, with the goal of performing strengthening exercises 3 days/week for 20 minutes/session.

Other exercises target hip and knee joint contracture prevention, two common joint mobility problems for patients with transtibial amputation.<sup>63</sup> Presence of contractures of the hip and/or knee are predictors of poor physical rehabilitation outcome.<sup>35</sup> Included are static stretches (e.g., prone lying and seated with knee propped into extension) performed 2-3 X/week for 2 minutes each (total 4 minutes).

*The walking program* will be performed all 12 weeks, with the goal of walking at least 3X/week. Initial walk duration will be determined at the first visit and goals set weekly by the participant with a guideline of at least 5 minutes of increased walking weekly. Once 30 minute duration is achieved, intensity will be progressed based on targeted heart rate or other health-specific parameters such as claudication intensity. Similar programs have improved symptoms, walking distance, and quality of life for people with PAD.<sup>45,46</sup>

*Health self-management* will be promoted in 3 primary ways: 1) action plan development with participant-directed goal setting, 2) participant self-tracking of activity (pedometers and exercise diary), and 3) participant education on problem-solving skills to manage chronic health conditions. Participants will also monitor their individual health condition (e.g., heart rate, time to claudication with walking, blood sugar, and blood pressure). These data will focus the weekly discussions (home or phone) over the 12-weeks.<sup>44,66,67</sup>

**Control (CTL) Group:** CTL group participants will be contacted at the same interval (phone and home visits) as the EXP group (Figure 2) to ensure attention control between groups. Visits will



consist of recording problems reported by the participant. If health or rehabilitation questions arise that require professional advice during participant-researcher visits, the participant will be referred to his/her healthcare provider.

**D5. Data Analysis.** Data will be managed using REDCap (Research Electronic Data Capture; which is HIPAA compliant).<sup>68</sup> Primary analysis will be group differences in TUG times (primary outcome) at the 12-week time point. As a pilot feasibility study, data will only be analyzed for participants with sufficient intervention exposure, defined as six weeks. For participants who withdraw at or beyond six weeks of intervention, an early termination test will be performed and carried forward as the end-point. Participants who withdraw before completing six weeks will be lost to follow-up and no imputation will be performed for missing data. Attempts will be made to test all participants at 24-weeks. However, missing 24-week data will not be imputed from the 12 week measurement, as this would bias the effect following the primary end-point (i.e., it is expected that both groups would have worse 24- compared to 12-week outcomes). Group differences will be based on a linear model with TUG as the outcome and explanatory variables being primary medical diagnosis (PAD, DM, or both), rehabilitation site, treatment group, and baseline TUG. Group differences will be determined by this single test to protect against Type I error ( $\alpha$  level: 0.05).

Secondary analyses will include differences at 12-weeks in the other outcomes (2MW, 5mW, PEQ-MS 12/5, Houghton Scale, PSFS, Activity level, number of healthcare provider visits, and number of hospital encounters) using the same method as for the primary outcome. A mixed-effects model with time as a fixed covariate across baseline, 12-, and 24-weeks will be used to evaluate long-term outcomes (24-week) and make inferences regarding the effectiveness of the intervention up to 12-weeks after intervention is complete. As with the other analyses, evaluation of the time trajectory will be conditioned on stratification variables and baseline values of the outcome measure. Also the mixed-effects model will not include data from subjects who drop prior to 6 weeks.

The exploratory aim of identifying predictors of physical activity and disability will be analyzed by regression analysis. First, variables will be grouped into demographic/anthropometric, activity/mobility, health behaviors, physical health, amputated-limb health, contralateral-limb health, and cognitive/affective health, and healthcare use factors. A hierarchical process will be used to screen variables within each group of factors to identify the best predictors within each group. Finally, the best predictor variables from each group will be entered into a regression model to determine models containing subsets of the variables that predict the outcome, based on  $R^2_{adj}$ . The most parsimonious model will be identified by comparing the 10 best models, using partial F-tests

**D6. Sample Size Estimate.** Sample size was estimated using TUG means and variances at discharge from the ongoing pilot study. In addition, literature was used to estimate long-term (> 3 months post-amputation) TUG scores for the population.<sup>60-62,69,70</sup> Using 12.4 (3.9) seconds mean (SD) TUG time at rehabilitation discharge from the first 14 participants in the pilot study and 19.3 seconds as the average of TUG time reported for patients several months to years after amputation, a group difference of approximately 6.0 seconds was expected in TUG times at the 12-week time-point (primary end-point). With this group difference and an estimated SD of 6.0 (effect size = 1.0), 17 participants per group would provide 80% power to identify differences. The assumption is the EXP group will maintain or improve TUG times after the 12-week intervention and the CTL group will decline toward levels reported in the literature. A 3.4 second change in TUG represents a minimal detectable change for patients with lower limb amputation.<sup>69</sup>

The goal is to enroll 44 participants and graduate 17 participants per group (n=34) at the 12-week test point. Based on data from the four participating hospitals, 150 patients will complete rehabilitation and achieve functional ambulation following dysvascular transtibial amputation

over the next 3 years. Based on the pilot study (Section C2), 60% of these patients are expected to meet inclusion/exclusion criteria (n = 90) and 50% of those will agree to participate (n = 45). A 20% loss to follow-up at 12 weeks (n=34) is estimated, which is twice the observed rates of studies with 12-week end-points that the PI has been involved with for other patient populations.

**D7 Outcome Measures.** Participants will have three test sessions of 1.5 hours each (initial, 12-week (primary end-point), 24-week) beginning within three weeks of completing outpatient rehabilitation. All sessions will occur at the participant's home or Interdisciplinary Movement Science Lab (IMSL), whichever is more convenient for the participant, using standardized protocols by research assistants.

- **Physical Function Outcomes:** Three physical performance tests will be used: the Timed Up-and-Go (TUG)<sup>1</sup>, 2-Minute Walk (2MW)<sup>2</sup>, 5-meter Walk (5mW)<sup>3</sup>, and Single-Limb Stance tests. Self-report measures of physical function include the Prosthesis Evaluation Questionnaire – Mobility Section (PEQ-MS)<sup>4,71</sup>, Houghton Scale<sup>5</sup>, Patient-Specific Functional Scale (PSFS)<sup>6</sup>, and the World Health Organization Disability Assessment Schedule 2.0. Each of these are reliable and valid measures for people with chronic disease.<sup>4,62,69,72-76</sup>
- **Activity Measurement:** Physical activity will be assessed with physical activity monitors (Actigraph) worn for 1 week following each test session. These monitors are valid tools for measuring relative level of activity (e.g., sedentary, light, moderate, vigorous) for various patient populations<sup>7-9</sup> and are valid and reliable spatiotemporal gait measures for patients with lower limb amputation.<sup>11,77</sup>
- **Self-Efficacy and Motivation:** Self-efficacy and exercise motivation will be used as descriptive measures related to health self-management. The Self-Efficacy in Managing Chronic Disease (SEMCD) questionnaire has been used as an outcome for self-management of various chronic diseases.<sup>12,13</sup> The Intrinsic Motivation Inventory (IMI) Interest and Enjoyment Subscale measures participant-reported interest and enjoyment related to the intervention.<sup>14</sup> Participant compliance with daily health monitoring will be tracked as number of days missed/possible days.

Procedural reliability is critical to the success of the proposed and future studies with multiple clinical sites. The PI will oversee standardization and implementation of testing and intervention. The PI will provide 2-3 training sessions, including a training manual, for each designated tester. If procedural reliability is below 0.90, additional training sessions will be scheduled.

#### E. Study Timeline and Enrollment Goals

Task	Year 1				Total	Year 2				Total	Year 3				Total
Training of Personnel															
Screening & Enrollment		3	3	4	n=10	5	5	5	5	n=30	5	5	4		n=44
Intervention															
Data Collection															
Data Reduction & Analysis															
Dissemination															

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