COMIRB Protocol

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Protocol #: 18-2783
Project Title: Optimizing Prosthetic and Bicycle Fit for Veterans with Transtibial Amputations

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I. Hypotheses and Specific Aims:

The purpose of the research study is to challenge the state-of-the-science by developing evidence-based prosthetic and bicycle fit guidelines that optimize the biomechanics (injury), metabolic costs (effort), efficiency (function), satisfaction, and comfort of Veterans with transtibial amputations (TTAs). Thus, the proposed research is highly relevant to the rehabilitation of Veterans with TTAs. Following a TTA, Veterans who wish to restore their physical function have limited options for exercise. For example, running while using a prosthesis may increase the risk of secondary injury due to asymmetric and high loading patterns. Low impact exercise such as bicycling could facilitate normative function after amputation by improving cardiovascular fitness, muscle strength, endurance, and quality of life without incurring the high loads typical for walking and running for Veterans with TTAs. Bicycling as exercise could also prevent the deleterious effects of vascular disease and diabetes by improving cardiovascular function, controlling body weight, decreasing the rate of re-amputation, and improving quality of life for Veterans with TTAs. However, to maximize comfort and improve adherence to exercise, Veterans with a TTA likely need to adapt the fit of their prosthesis and bicycle. Optimizing bicycling, as exercise, for Veterans with TTAs through changes in prosthetic and bicycle fit (i.e. pylon length (PL), pedal attachment position (PAP) beneath the prosthetic forefoot versus the pylon, and crank arm length (CAL)) would improve rehabilitation by minimizing injury risk and discomfort, and maximizing function, thus facilitating the return to an active lifestyle and/or active duty. We propose to vary PL, CAL, and PAP in Veterans with unilateral TTAs. Then, we will develop evidence-based guidelines that optimize prosthetic/bicycle fit for Veterans with TTAs. These guidelines will allow Veterans with TTAs to enhance their physical function and quality of life by using bicycling for exercise.] Moreover, evidence-based prosthetic/bicycle fit guidelines will allow clinicians to more effectively fit Veterans with lower extremity amputations to bicycles, leading to shorter appointment times and fewer revisits due to enhanced function and reduced comorbidities.

Specific Aim 1. We will study 15 Veterans with unilateral TTAs to determine the effects of systematically varying PL, PAP beneath the prosthetic forefoot versus the pylon, and CAL for the affected leg (AL) on bicycling biomechanics, metabolic cost, and comfort/satisfaction. **Hypothesis 1.** A taller PL and shorter CAL for the AL compared to the unaffected leg (UL) and a PAP beneath the pylon compared to beneath the forefoot, will maximize mechanical power symmetry and reduce metabolic cost and muscle activity, and thus maximize efficiency and comfort/satisfaction during bicycling in Veterans with unilateral TTAs. Veterans with unilateral TTAs will ride a stationary bicycle ergometer at a fixed power output (1.5 W/kg) and complete a series of experimental trials over 2 days. On Day 1, we will perform a custom bike fit for each subject according to a protocol developed by Retül for non-amputees (Specialized Bicycle Components Inc., Boulder, CO). When fitting riders with TTAs, we will adjust the PL in combination with the socket and prosthetic foot of the AL to match the shank and foot length of the UL. Using this protocol, we will systematically vary saddle height and fore-aft position, handlebar vertical and fore-aft position, and alter cleat placement within the shoe for a forefoot PAP, using a conventional CAL of 172 mm. Then, we will measure the biomechanics (motion, forces, and muscle activity) and metabolic rates while subjects ride using the initial fit and three taller PLs for the AL in increments of 6.8 mm using a PAP beneath the prosthetic forefoot. Then, using the optimal (most efficient) PL, we will measure the biomechanics and metabolic rates while subjects ride using three shorter CALs for the AL in decrements of 6.8 mm using a PAP beneath the prosthetic forefoot. On Day 2, we will repeat the protocol of Day 1, but have riders use a PAP beneath the pylon for their AL. We will randomize the order of days and trials within a day. [Because a prosthetic foot cannot flex and extend in a manner similar to the biological ankle, shortening CAL for the AL compared to the UL will reduce the geometric asymmetries between the AL and UL in bicyclists with a TTA. Childers and Kogler estimated that the UL shank and foot have 19.8 mm of displacement throughout the pedal stroke. Moreover, previous studies found differences in biomechanics and metabolic costs during bicycling based on CAL changes of 7.5-15 mm. Thus, we elected to measure the effects of four different CALs within a 19.8 mm range (0 mm, -6.6 mm, -13.2 mm, -19.8 mm) to establish how different prosthetic/bicycle configurations affect biomechanics and metabolic costs across CAL changes. To our knowledge, previous studies have not assessed the effects of changing PL. Thus, we chose to vary PL by the same magnitudes as CAL. We chose to increase PL and decrease CAL because if we lowered PL or increased CAL this would require us to lower the seat height for subjects to reach the bottom pedal position with their AL.

Specific Aim 2. We will synthesize and disseminate our findings from Specific Aim 1 into practical, evidence-based quantitative prosthetic/bicycle fit guidelines for Veterans with TTAs through a multiple regression and principal component analysis. These analyses will take into consideration the body mass, femur lengths, and UL shank and foot dimensions. We will disseminate our guidelines to prosthetists and clinicians in peer-reviewed public-access journals and through conferences/seminars.

II. Background and Significance:

Healthcare costs in the United States (US) now exceed $3.2 trillion per year and many of the healthcare conditions at the root of these costs, such as Type 2 diabetes, are preventable through exercise. Due in large part to the prevalence of diabetes and recent military conflicts, there are over one million people in the United States who have a lower extremity amputation [1] and this number continues to grow. The incidence of diabetes is much greater in Veterans compared to the civilian population [2]; nearly one million Department of Veterans Affairs (VA) patients (1 of 5 patients) have diabetes. Over 25% of Veterans with an amputation attributable to vascular disease/diabetes will need an additional amputation [3]. It is projected that the number of people with diabetes who are living with limb loss will nearly triple and that the prevalence of limb loss will more than double by the year 2050 [4]. In addition, recent military conflicts such as Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) have accounted for more than 1800 major limb amputations [5]. Due to functional impairments resulting from a lower extremity amputation, it is extremely important to advance rehabilitation practices that optimize the use of leg prostheses and increase exercise adherence so that Veterans and Service members with TTAs can regain the greatest possible level of health, function, and physical activity.

Due in part to the increased prevalence of amputations in Veterans and Service members, the Department of Defense (DoD) and VA Rehabilitation Directive has put forth an initiative that aims to dramatically improve and restore function in wounded Service members so that they have the choice to return to active duty or productive civilian employment. Our proposed research and development of optimized prosthetic/bicycle fit guidelines will enable VA prosthetists to improve rehabilitation, physical activity level, injury risk, and comfort of Veterans following amputation, thus helping to fulfill this initiative and having high potential impact. Our research addresses the *Prosthetics and Limb Loss* focus area within the Rehabilitation Research and Development service. This focus area serves to integrate advances in technology and rehabilitation to improve the lives of Veterans with an amputation. The utilization of evidence-based prosthetic/bicycle fit guidelines that optimize comfort, exercise adherence, and function will directly benefit Veterans with an amputation and the VA. More effective and optimized prosthetic and bicycle fitting will result in greater power output symmetry, reduced metabolic costs and injury risk, improved efficiency, and increased comfort. We aim to provide the best rehabilitation outcomes data regarding prosthetic devices and related clinical interventions.

Only 32-37% of people with TTAs engage in enough vigorous physical activity to elicit health benefits compared to 60% of non-amputees [6, 7]. Engagement in physical activity following an amputation is much lower than that of pre-amputation levels, and there are more barriers than motivations for adopting and maintaining a physically active lifestyle in people with TTAs [6]. Generally, people with TTAs who return to recreational or sports activities choose to participate in less strenuous activities where a prosthesis is not required or the person is not functionally dependent on it. The barriers to engaging in physical activity include pain and physical limitations [6, 7]. Throughout rehabilitation, it has been suggested that clinicians and prosthetists should repeatedly encourage people with TTAs to stay/become physically active and provide information about strategies to reduce environmental barriers to sports participation, which could help people using assistive devices to overcome these barriers [8]. An optimal prosthetic/bicycle fit would reduce pain, physical limitations, and environmental barriers to exercise and could thus promote physical activity in Veterans with TTAs. Low impact aerobic exercise such as bicycling could facilitate normative function after amputation by improving cardiovascular fitness, muscle strength, endurance, and quality of life for Veterans with TTAs without incurring the high joint and tissue loads inherent in walking and running [9]. Bicycling for exercise could also prevent the deleterious effects of vascular disease and diabetes by improving cardiovascular function, controlling body weight, decreasing the rate of re-amputation, and improving quality of life for Veterans with TTAs. However, a previous study estimated that only 11.5% of Veterans with TTAs use bicycling for exercise [7]. It is likely that bike and socket discomfort/pain and the increased potential for secondary musculoskeletal injury due to the lack of a proper bike fit discourage Veterans with TTAs from using bicycling for rehabilitation and exercise.

Riding a bicycle with a TTA presents novel challenges compared to non-amputees. People with TTAs lack the muscles that plantarflex and dorsiflex the ankle joint to assist them in the pedaling motion of bicycling. These muscles act to stabilize the ankle and transfer force and energy to and from the pedal [9]. Bicyclists with TTAs have increased muscle activity variability in the two-joint muscles of both legs and a longer duration of gastrocnemius activity in the unaffected leg (UL) compared to non-amputees [9]. Although the role of the ankle in bicycling is disputed, research has shown that the ankle position throughout the pedal cycle influences the application of mechanical power generated by the leg [10]. Pierson-Carey et al. [10] immobilized the ankle in non-amputees and found that during the down-stroke of the pedaling cycle, power output decreased compared to a fully mobile biological ankle joint. The application of force on each bicycle pedal influences mechanical power production, and therefore affects overall efficiency. Thus, optimizing PL, PAP, and/or CAL would improve mechanical power output symmetry and efficiency in individuals with TTAs during bicycling.

Research that examines the underlying changes in biomechanics and metabolic costs that are elicited by people with TTAs when bicycling with different prosthetic/bicycle configurations would facilitate improved rehabilitation [9] and exercise adherence. Changes in body positioning due to changes in PL, CAL, and PAP likely affect the overall function, comfort, and injury risk of bicyclists, but the effects of these changes are complex and likely more complicated due to different limb geometry in bicyclists with TTAs [9]. The asymmetric structural differences between the legs of bicyclists with a TTA result in dramatically asymmetric torque and mechanical work during bicycling; mechanical work asymmetry can be up to 7x greater in bicyclists with a TTA compared to non-amputees [9]. Presumably, the magnitude of force asymmetry between the AL and UL of people with unilateral TTAs is influenced by leg length discrepancies and the loss of the muscles that act across the ankle joint. To our knowledge, no previous research has systematically varied PL and determined the effects on bicycling biomechanics and performance. Because a person with a TTA does not have a functional ankle joint, the PL combined with prosthetic foot build height may need to be taller than the height of the foot and shank of the UL to improve mechanical power symmetry and lower metabolic cost. Further, despite previous research, it remains unclear how alterations to a bicycle's CALs affect the efficiency of people without and with TTAs [9]. When manipulating CALs for both legs of non-amputee cyclists, Morris & Londeree [11] found that each individual had a specific CAL that resulted in the greatest efficiency. However, with a relatively small sample size (n=6), they were unable to determine any relationships between the rider's leg lengths and optimal CALs. Koutny et al. [12] investigated the effects of using three different CALs (160, 167.5, and 175 mm) on one high-caliber cyclist with a TTA and found that at a fixed mechanical power output, the rider's leg muscle activity was minimized with the medium CALs (167.5mm), but the average torque applied to the cranks was unchanged across CALs. It is unclear whether Koutny et al. manipulated CALs for both legs or just changed the CAL for the affected leg (AL). Regardless, reduced muscle activity suggests a lower metabolic cost and thus improved efficiency during bicycling. Childers and Kogler [13] compared the knee and hip joint kinematics and kinetics of 8 cyclists with TTAs with CALs of 172 mm for each leg compared to a CAL of 172 mm for the UL and a CAL of 162 mm for the AL. With asymmetric CALs, knee and hip joint angles and range of motion were more symmetric between legs, but joint kinetics (torque and work) did not change. They suggest that a CAL of 160 mm for the AL would be advantageous for joint angle and range of motion symmetry. However, it is not clear if Childers and Kogler [13] matched the AL height of the pylon and the prosthetic foot to the UL height of the shank and biological foot. Shortening the CAL for the AL could reduce the geometric asymmetry between legs and thus result in more symmetric knee and hip joint angles.] A pilot study (n=3) by Childers et al. [9] found that a 15 mm shorter CAL for the AL versus UL may improve the force symmetry of people with TTAs and thus improve their power output symmetry. They reported that shortening the CAL for the AL versus UL reduced mechanical work asymmetry by 53% [9]. Further, with a shortened CAL on the AL compared to UL, riders reported improved comfort [9]. [Previous studies that varied the anterior-posterior position of the bicycle cleat (PAP) found no effects on metabolic costs for non-amputees, but did find a reduction in gastrocnemius, soleus, and tibialis anterior muscle activations with a forefoot position compared to a heel placement. Childers et al. [9] suggest that the effective prosthetic length, the distance from the knee center to the pedal spindle, should be equivalent between legs in cyclists with unilateral TTAs to minimize kinematic asymmetries. However, no studies to date have determined the optimal PAP or calculated the optimal effective prosthetic length.

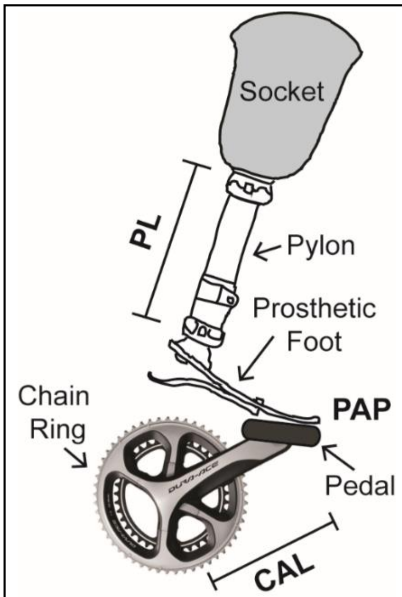

Figure 1. A pylon connects the socket of the affected leg of a cyclist with a transtibial amputation to the prosthetic foot, which attaches to the pedal. The crank arm links the pedal to the chain ring, allowing power transmission to the rear wheel. Adjustments to pylon length (PL), pedal attachment position (PAP) and crank arm length (CAL) likely affect mechanical power output, metabolic cost and comfort/satisfaction.

Moreover, it is unclear how changes in each prosthetic and bicycle configuration, such as PL, PAP beneath the prosthetic forefoot versus the pylon, and CAL (Fig. 1) affect the biomechanics, metabolic cost, and comfort/satisfaction of Veterans with TTAs. Thus, we will quantify the effects of systematic changes in PL, PAP, and CAL on the bicycling performance of Veterans with unilateral TTAs to develop novel evidence-based guidelines that optimize prosthetic and bicycle fit. The proposed analysis is innovative in that we will assess and optimize the effects of each geometrical change in the same person and use the overall results to develop guidelines for bicycle/prosthetic fit. Further, we will examine the underlying mechanisms, such as changes in joint kinematics and kinetics, and muscle activity magnitude and timing that elicit these effects to determine the unique adaptations made by bicyclists with TTAs. Optimized prosthetic and bicycle fit guidelines will allow Veterans with TTAs to ride longer with less effort, pain/discomfort, and injury risk, which would lead to improved rehabilitation and quality of life. Reducing the metabolic cost required for bicycling is clinically significant because an excessive sense of effort and fatigue discourages physical activity [14]. The prosthesis/bike fit guidelines resulting from our research will also determine the configuration that maximizes symmetry between legs, which could reduce injury risk and pain, and maximize function through improved mechanical power output and efficiency. Moreover, evidence-based prosthetic/bicycle configuration guidelines will allow clinicians to more effectively treat Veterans with TTAs, leading to shorter appointment times and fewer revisits due to enhanced function and reduced comorbidities.

III. Preliminary Studies/Progress Report:

Our proposal represents a potentially high-risk project because we lack substantial preliminary data. However, we believe that the project is innovative and feasible. To support the feasibility of the project, we measured the average mechanical power output from both legs and each leg when one subject with a TTA rode on a cycle ergometer, which had fixed CALs (172 mm) (Table 1). We measured mechanical power output using PowerTap P1 pedals (PowerTap, Madison, WI). Across overall mechanical power outputs of 50-175 W, the AL provided ~40%, while the UL provided ~60% of the overall mechanical power output. Thus, the development of optimal prosthetic/bicycle configuration guidelines could improve biomechanical symmetry and maximize function in Veterans with TTAs, yet bicycles have not been effectively utilized in clinical settings. Bicycling as a form of exercise has been shown to greatly improve overall fitness, reduce obesity, and prevent cardiovascular health problems in non-amputees [15], yet <12% of Veterans with TTAs use bicycling for exercise. By systematically altering PL, PAP, and CAL, we expect to optimize function and comfort by reducing kinematic and kinetic asymmetries, reducing metabolic costs, and improving efficiency for Veterans with TTAs during bicycling. We expect that these improvements will increase the use of bicycling for exercise and thereby advance the rehabilitation and function of Veterans with TTAs.

Table 1. Total, affected leg (AL) and unaffected leg (UL) mechanical power (Watts) and cadence from the Lode bicycle ergometer for an athlete with a unilateral transtibial amputation. Each stage was 4 min and we averaged data from the last 3 min.

Total (W)	Cadence (RPM)	AL (W)	UL (W)
50	78.5	18.37	31.63
75	78.0	28.54	46.46
100	78.1	40.91	59.09
125	79.0	49.99	75.01
150	80.0	63.28	86.72
175	80.8	75.29	99.71

IV. Research Methods

The proposed study will be a repeated-measures within-subjects design. This is a multi-site study, and the VA Eastern Colorado Healthcare System and University of Colorado Boulder will be participating.

A. Outcome Measure(s):

During each trial, subjects will ride a stationary bicycle ergometer (Retül Müve, Specialized Bicycle Components Inc., Boulder, CO). Each trial will be 6 minutes long with at least 6 minutes rest between trials. At minutes 4 and 5, we will measure kinematics at 100 Hz, including joint angles, with a 10-camera 3D motion capture system (Vicon, Centennial, CO), kinetics at 1000 Hz, including mechanical power output, with motion capture and force-measuring pedals (Sensix, Poitiers, France) and muscle activity at 1000 Hz using electromyography (Noraxon, Scottsdale, AZ) for approximately 30 seconds. The key muscles that influence bicycling are the vastus lateralis, rectus femoris, biceps femoris, gluteus medius, gluteus maximus, tibilais anterior, soleus, and gastrocnemius [9]; thus we will calculate activation magnitudes and durations for these muscles during each trial, when possible. We will analyze these data with Visual 3D software (C-Motion, Germantown, MD) using a standard anatomical model and a custom software program (Matlab, Mathworks, Natick, MA). We will measure rates of oxygen consumption and carbon dioxide production at standard temperature and pressure dry (STPD) throughout each trial using indirect calorimetry (ParvoMedics TrueOne 2400, Sandy, UT). We will calculate average steady-state metabolic power (W) from minutes 3.5-5.5 of each trial using a standard equation [16]. In our experience, a 6-minute trial duration is sufficient for subjects to reach steady-state metabolic rates. We will adjust trial length as needed if 6 minutes is not sufficient. We will calculate efficiency by dividing the mechanical power (1.5 W/kg) by the average metabolic power in W/kg. We will calculate the degree of mechanical power output symmetry between legs for each configuration using the symmetry index (SI) as a percentage: $SI = \left|\frac{MechP_{UL} - MechP_{AL}}{0.5(MechP_{UL} + MechP_{AL})}\right| \times 100$, where MechP is the mechanical power for the UL and AL of subjects with a TTA. SI values closest to zero are the most symmetric. After each trial, we will ask all subjects to rate their comfort/pain with a Visual Analog Scale (VAS), and subjects with TTAs to rate their comfort/satisfaction with a modified

Prosthesis Evaluation Questionnaire (PEQ). We will use repeated measures analysis of variance (ANOVAs) (significance at $\alpha<0.05$) with Bonferroni corrections as needed for multiple comparisons to compare data between groups and between legs and determine the optimal PL/PAP/CAL combination (JMPIN, SAS Institute, Cary, NC). We will analyze results from Specific Aim 1 using linear mixed models. We will use a multiple regression and/or principal component analysis to develop optimal prosthetic/bicycle fit guidelines for Veterans with TTAs in Specific Aim 2.

Description of Population to be Enrolled:

We will recruit 15 Veterans with unilateral TTAs who are at or above a K3 Medicare functional classification level (MFCL), and who are 18-55 years old from the VA Jewell Clinic, locally, and nationally. Subjects will give informed consent prior to participation. A K3 MFCL means that a person has the ability or potential for ambulation with variable cadence. A person at K3 MFCL is a typical community ambulator who has the ability to traverse most environmental barriers and may have vocational, therapeutic or exercise activity that demands prosthetic use beyond simple locomotion. Subjects will have no known neurological disease or disorder, and will have no musculoskeletal injuries beyond an amputation. These inclusion/exclusion criteria will minimize any potential confounding variables, thereby increasing the internal validity of the proposed studies. Any person matching the inclusion criteria of the study, regardless of race or gender, will be recruited to participate.

Women and/or minorities will be included in the proposed study. Anyone matching the inclusion criteria of the study, regardless of race, sex, or ethnicity will be recruited to participate.

B. Study Design and Research Methods

Before participants are enrolled in each study, we will complete a pre-screening form and each participant will be asked to give informed written consent. We will ensure that all participants understand the consent form and protocol prior to participation.

Subjects will be asked to complete two experimental sessions at the VA ECHCS/University of Colorado Applied Biomechanics Lab; each session on a separate day at the same time of day, and requiring approximately 2 hours of time. Subjects will be asked to ride a stationary bicycle ergometer (Retül Müve, Specialized Bicycle Components Inc., Boulder, CO) at a fixed power output (1.5 W/kg) and complete a series of experimental trials over two days. On each day, we will measure each subject's height, weight, and limb segment lengths. Then, we will place reflective markers on his/her legs and torso using double-sided tape. These markers will allow us to track his/her body position using our motion capture system. We will also record the forces subjects exert on each pedal using force-measuring pedals. Further, we will measure each subject's leg muscle activity using wireless electrodes that will be placed over his/her muscles using double-sided tape. Finally, we will measure each subject's metabolic rates from the air that he/she breathes out into a mouthpiece. Immediately after each trial, we will ask subjects to rate their satisfaction using a Visual Analog Scale and comfort, fit, effort, etc. with a questionnaire.

On Day 1, we will perform a custom bike fit for each subject according to a protocol developed by Retül for non-amputees (Specialized Bicycle Components Inc., Boulder, CO). Using this protocol, we will systematically vary saddle height and fore-aft position, handlebar vertical and fore-aft position, and alter cleat placement within the shoe for a prosthetic forefoot pedal attachment position, using a conventional crank arm length of 172 mm. Then, we will measure the biomechanics and metabolic rates while subjects ride using the initial fit and three taller pylon lengths for their affected leg in increments of 6.8 mm using a typical pedal attachment position beneath the forefoot. Then, using the optimal (most efficient) pylon length, we will measure the biomechanics and metabolic rates while subjects ride using three shorter crank arm lengths for their affected leg in decrements of 6.8 mm using a typical pedal attachment position beneath the prosthetic forefoot.

On Day 2, we will repeat the protocol of Day 1, but have subjects use a pedal attachment position beneath the pylon for their affected leg. We will randomize the order of days and trials within a day.

D. Description, Risks and Justification of Procedures and Data Collection Tools:

We propose to study healthy people who are familiar with using a prosthesis because this choice minimizes any potential confounding factors associated with novel prosthetic use. Bicycling requires moderate exercise intensity, yet poses no more than minimal cardiac risk for this population. We will restrict our patient age range to comply with the American College of Sports Medicine guidelines. The American College of Sports Medicine (ACSM) Guidelines for Exercise Testing and Prescription (Ninth edition, 2014) classify individuals of any age as having low or moderate risk to participate in an exercise program if they present no more than two of the following risk factors: males age ≥ 45 yrs, females age ≥ 55 yrs, first degree family history of coronary artery disease, cigarette smoking, sedentary lifestyle, obesity, hypertension, dyslipidemia (high cholesterol), and pre-diabetes. These guidelines further recommend that a medical exam and diagnostic exercise testing are not warranted prior to beginning a moderate exercise program for individuals at low to moderate risk. We are being conservative by including patients under 55 years of age (i.e. before their 55th birthday) who do not have any of the other risk factors listed above.

We will comply with Good Clinical Practices (GCPs) by upholding standards for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of our clinical studies, and by protecting the rights, safety, and well-being of human subjects. We will assure the quality, reliability, and integrity of data collected. We will maintain and monitor GCPs by obtaining Institutional Review Board (IRB)-approval, requiring informed consent, having a data-monitoring plan, reporting Adverse or Serious Adverse Events, having proper documentation, and validating our data collection and reporting procedures.

<u>Foreseeable risks:</u>

1. There is a potential risk of physical discomfort from wearing any type of prosthesis.
2. The adhesive used for motion analysis markers and electrodes may produce slight discomfort.
3. The metabolic analysis mouthpiece and nose clip may produce slight discomfort.
4. Confidential information about participants will be collected as part of this study; therefore, there is a risk of disclosure.

<u>Risk management (corresponds directly to the Foreseeable risks listed above):</u>

1. If you become fatigued, you may ask to rest or stop the study at any time.
2. Before participating in a study, you will be asked if you have any adhesive allergies and if you do, the reflective markers can be placed over tight-fitting clothing.
3. You may ask to remove the mouthpiece and nose clip, rest or stop at any time.
4. Significant efforts will be made to guard against the disclosure of confidential information. All data collected will be de-identified so that your identity is protected; however, the data collected poses no apparent risk to your privacy. We will implement a data and safety-monitoring plan to ensure your privacy. To de-identify your data, you will be given a unique code, and only the research team will have access to the key (linking the code to participant identifiers), which will be kept in a locked cabinet in a locked office. The key will be destroyed upon study completion.

E. Potential Scientific Problems:

Adjustments to PL, PAP, and CAL may not be significantly different from the standard prosthetic/bicycle configuration. In the unlikely event that we find the optimal configuration to be the same as the standard configuration, we will be more confident in the typical recommendations for bicycling and may not need to develop guidelines for optimizing efficiency and comfort. If we find this to be true, we will evaluate how robust this finding is across participants. Within our protocol, we will ask 15 patients with TTAs to complete a VAS and modified PEQ. We predict that use of different PLs, PAPs, and CALs will affect VAS and PEQ scores. We calculated a statistical power of >0.44 to detect a 10% difference in PEQ scores based on 15 participants and the largest standard deviations found in previous studies using the PEQ [23]. Therefore, we may not have adequate statistical power to detect a difference in comfort and fit.

F. Data Analysis Plan:

We predict that different PLs, PAPs, and CALs will affect biomechanics, metabolic costs, and comfort/satisfaction. We calculated effect sizes [17] >0.86, >0.995, 0.97, and >0.44 to detect 10% differences in efficiency (mechanical power/metabolic power), knee and hip joint range of motion, mechanical work output symmetry, and PEQ scores, respectively, based on 15 participants, a repeated measures design, α=0.05, and standard deviations found in previous studies [11, 13, 18, 19]. Thus, we feel we have an adequate sample size to detect biomechanical and metabolic differences in our proposed studies, but may not have adequate power to detect differences in PEQ scores.

G. Summarize Knowledge to be Gained:

The proposed research is highly relevant to and will benefit Veterans with transtibial amputations (TTAs). The goal of our research is to challenge the state-of-the-science by developing evidence-based prosthetic and bicycle fit guidelines that optimize the biomechanics, metabolic costs, efficiency and comfort/satisfaction for Veterans with TTAs. Optimizing these parameters through changes in prosthetic and bicycle configurations (i.e. pylon length (PL), pedal attachment position (PAP) beneath the forefoot versus the pylon, and crank arm length (CAL)) will improve rehabilitation and benefit Veterans with TTAs by minimizing injury risk and pain/discomfort, and maximizing physical activity and function; thus facilitating their return to an active healthy lifestyle and/or active duty.

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