Abstract

Outcome measures can be utilized to assess physical function in controlled settings, but do not provide a comprehensive view of free-living mobility for individuals with transtibial amputation (TTA). We sought to expand upon established clinical-based outcome measures by developing and cross validating two equations for predicting daily steps. The relationship between health state predictors and performance on 1) the Timed Up and Go (TUG) Test, and 2) the Prosthetic Limb User's Survey of Mobility (PLUS-M) was also assessed via the model predictions. Adults with TTA were assigned activPAL and Fitbit accelerometers to wear for seven days. Participant data were randomly separated into training (n = 80) and testing (n = 26) groups. LASSO regression with 3-fold cross validation was implemented to construct each equation according to a participant's health state, TUG Test, L Test of Functional Mobility, and PLUS-M data. Each equation's validity was assessed in the testing group. An inverse relationship was noted between daily steps and TUG Test performance and higher PLUS-M T-scores were associated with greater daily steps. The equation overestimated steps for those with significantly low daily steps and underestimated steps for those with significantly high daily steps, which is to be expected given the nature of linear regression. We also assessed the validity of the Fitbit Inspire 3 for assessing steps among individuals with TTA. Daily step data were compared between the Fitbit Inspire 3 and the activPAL 3. The Fitbit overestimated physical activity by estimating higher daily steps compared to the activPAL. Because of the significant mean differences between the devices, the activPAL and Fitbit are not interchangeable for estimating steps in this group. The results will be interpreted and explored in the context of prosthetic rehabilitation and underscore the importance of personalized mobility assessments and interventions aimed at improving the free-living mobility of individuals with TTA.

DEVELOPMENT AND CROSS-VALIDATION OF A PREDICTION EQUATION FOR ESTIMATING STEP COUNT IN INDIVIDUALS WITH TRANSTIBIAL AMPUTATION

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Dedication

I dedicate this dissertation to my wife, Kylee. This truly has been a long, strange trip. Thanks for always sticking with me during the ride. I love you.

Acknowledgements

"So toss away stuff you don't need in the end,

but keep what's important and know who's your friend."

- *Theme from the Bottom, Phish*

There are many people who helped make this dissertation possible. First and foremost, I would like to acknowledge the participants who devoted their time and energy towards data collection efforts. Each participant was eager to help not for themselves, but for the future individuals who may benefit from this work.

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A very special thank you to my mom, dad, and the rest of my friends and family. My academic journey has taken me all over the country and has been the most arduous thing I've ever done. Through these transitions and challenges, you have all been supportive and willing to assist me in any way possible. Your consistent encouragement and steadfast belief that I could do this has been a pillar of my success.

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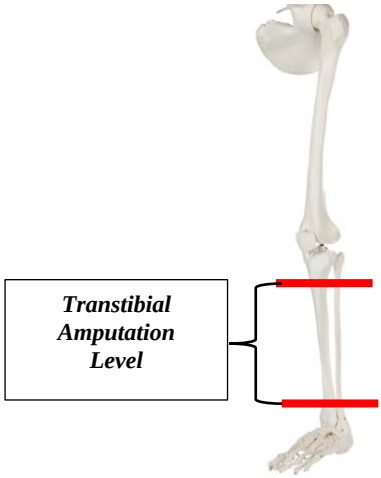
Key Concepts

Transtibial Amputation: An amputation occurring through the tibia of the lower leg, below the level of the anatomical knee. This is the second most common amputation level and is considered the most common "major" amputation. Type 2 diabetes, trauma, sarcomas, and peripheral vascular disease may contribute to transtibial amputation. Procurement of a transtibial prosthesis is a common rehabilitative practice after amputation and may increase an individual's mobility.



Type 2 Diabetes: A metabolic disorder affecting over 30 million Americans. Type 2 diabetes impairs how the body regulates and utilizes insulin, resulting in a myriad of systemic comorbidities. Type 2 diabetes is a contributing factor in over half of all amputations that occur in modern, industrialized nations. Individuals with amputation and concurrent type 2 diabetes are at risk for decreased mobility which may result in increased all-cause mortality.

Physical Activity: Defined broadly by the World Health Organization as any bodily movement produced by skeletal muscles that requires energy expenditure. Physical activity encompasses all movements including those executed during leisure time, for transport, or as part of a person's vocational/avocational activities. Both moderate- and vigorous-intensity physical activity improve health. Current recommendations encourage adults to participate in at least 150 minutes of moderate-intensity physical activity, 75 minutes of vigorous-intensity physical activity, or a combination of both, per week to attain health benefits.

Mobility: Refers to the ability to move freely from one place to another and is a strong predictor of quality of life after amputation. Restoration of mobility after amputation is often a primary rehabilitative goal. Valid and reliable physical and patient-reported outcome measures are available to assess the mobility of individuals with amputation.

Accelerometer: A device used to objectively measure physical activity, sedentary behavior, and sleep in humans. Accelerometers operate by measuring acceleration along a given axis, using technologies including piezo–electric, micro–mechanical springs, and/or changes in capacitance. A single monitor can be equipped with multiaxial sensors, permitting the device to track movement in multiple movement planes. During movement, an internal sensor converts motion into electrical signals proportional to the muscular force producing movement. These counts are summed over a specified epoch and stored. Commercially available devices including the Fitbit and research-grade devices including the activPAL have been used in research featuring individuals with amputation.

Outcome Measures: Instruments used to determine compensation for a healthcare entity, evaluate prognosis, plan patient placement, estimate care requirements, assist in choosing specific types of care, and determine change in status secondary to intervention. Additionally, outcome measures are often utilized to assess the effectiveness of a rehabilitation program and evaluate mobility. Patient-reported, clinical-based functional mobility tests, and objective accelerometry-based outcome measures represent three constructs for assessing mobility among individuals with amputation.

Validity: Pertains to the accuracy of a measurement or tool. Validity can be described as the degree to which an object measures what it is intended to measure. To assess concurrent validity, the device, algorithm, or model must be compared to a criterion or "gold standard" that has been thoroughly tested and supported within the scientific evidence base.

Non-Technical Summary

What is known?

The ability to walk drastically influences quality of life and overall satisfaction after amputation. Outcome measures are often used to assess one's mobility after receiving a prosthesis. Activity trackers can expand on outcome measures commonly performed in clinical or research settings by providing information regarding an individual's mobility within their home environment. This information can be used to better understand the relationship between clinical-based, self-reported, and objective mobility measures.

Because of mobility's influence on quality of life, an improved understanding of how performance on clinical or self-reported assessments of mobility translates into daily steps is needed. This relationship is worth investigating because it can provide clinicians with more information regarding the effectiveness of a specific treatment or rehabilitation program while also expanding the usefulness of existing, clinical-based outcome measures. Accordingly, the purpose of this project was to develop and validate two equations for estimating mobility, and to examine the relationships between daily steps and clinical-based outcome measures.

A second purpose of this project was to assess the validity of the Fitbit Inspire 3 for measuring daily steps among prosthesis users. Findings from this aim are important because the

Fitbit Inspire 3 is more accessible than research grade accelerometers such as the activPAL 3. Because of this, the Fitbit may be a better option for clinicians and prosthesis users who are interested in monitoring daily steps.

What is new and noteworthy from our results?

Study 1: Functional mobility tests including the Timed Up and Go (TUG) Test are used to assess the physical function of individual with transtibial amputation (TTA). We developed an equation to predict daily steps based on health characteristics and functional mobility test performance for individuals with TTA. The relationship between step count and TUG Test completion time was also assessed with the prediction model. An inverse relationship was noted between the TUG Test and daily steps, suggesting that the speed at which someone completes the TUG Test may be related to how much they walk each day. Additionally, people with a diagnosis of type 2 diabetes had substantially fewer daily steps than those without diabetes. On an individual level, the equation could predict daily steps with some degree of accuracy, but it overestimated steps for participants that walked very little and underestimated steps for participants with very high daily steps. Future research focusing on leveraging existing wearable technologies, implementing advanced statistical models, and/or the inclusion of additional predictors is needed to optimize the equation for individuals with TTA.

Study 2: The PLUS-M is a patient-reported outcome measure used to evaluate mobility after an individual with an amputation receives a prosthesis. We established and validated a second equation to expand the usefulness of the PLUS-M and examined the relationship between the PLUS-M and daily steps. We found that higher PLUS-M scores were associated with greater

daily steps and that lower PLUS-M scores were associated with fewer daily steps. We also found an inverse relationship between age and daily steps. Despite these important findings, the model produced notable individual-level differences and overestimations of steps, indicating the need for further refinements to improve prediction accuracy.

Study 3: The Fitbit Inspire 3 is less costly and more user friendly than research-grade devices such as the activPAL 3, but its validity for measuring steps among individuals with TTA had not previously been evaluated. We found that the Fitbit Inspire 3 and activPAL 3 were highly correlated, but the Fitbit Inspire 3 overestimated physical activity by predicting significantly more daily steps compared to the activPAL 3. This indicates that while the two devices may measure activity levels similarly, they may not be used interchangeably or provide similar results in terms of step counts.

Implications

Our findings suggest that a relationship exists between clinical-based functional and patient-reported outcome measures and daily steps, and that Fitbit Inspire 3 may over-predict steps for individuals with TTA. These results provide valuable information regarding a patient's free-living mobility and add value to established mobility constructs. Clinicians who treat individuals with TTA can use this information to offer more personalized care to their patients. The prediction equation will require modifications to better estimate steps for individuals with TTA who walk a lot or very little during the day. Collecting additional information about each participant and/or adjusting the equation to better fit the data may improve the model's predictions and represent areas for future research.

Table of Contents

List of Illustrative Materials

Figures

Tables

Chapter 1: Introduction

It is estimated that over two million Americans are living with an amputation, a number expected to reach 3.6 million by 2050.[1] Amputation of the lower extremity is considered a major health event that can profoundly affect one's quality of life, general well-being, and mobility.[2] After amputation, numerous factors contribute to diminished mobility, even after prosthesis procurement. Type 2 diabetes (T2D) is a contributing factor in 54% of all major amputations in the United States and has been linked to diminished physical capacity due to the disease's deleterious impact on numerous body systems.[1,3] Peripheral vascular disease, stroke, and mental health concerns are also common among individuals with amputation and may be predictive of decreased mobility in prosthesis users.[4] In addition to health state influences, biomechanical deficiencies, prosthetic socket satisfaction, and pain associated with amputation may negatively impact mobility in this population.[5,6] Given the positive association between mobility and enhanced quality of life, mobility restoration should be a primary goal of prosthetic rehabilitation.[7]

Clinical-based functional mobility tests and patient-reported outcome measures (PROMs) have been developed to assess mobility among individuals with lower extremity amputation. These outcome measures provide a wealth of information regarding a patient's progress through a rehabilitation program, including an intervention's impact on mobility.[8] However, these measures only reflect performance or perception on a particular occasion in an artificial setting (i.e., the clinic/laboratory). Wearable technologies (wearables) represent a third construct for evaluating mobility and have the capacity to expand on traditional, clinical-based constructs by capturing mobility in the free-living environment.[9]

In recent years, the healthcare industry has increasingly emphasized the importance of quantifying the degree of change associated with a given intervention. This can be accomplished by using one or more appropriate outcome measures. When the primary clinical goal concerns mobility, clinical-based functional mobility tests and PROMs represent two constructs for assessing mobility outcomes within the clinic or the laboratory setting. Accelerometry-based wearables represent a third construct that facilitates objective movement assessment outside the clinic and therefore may provide a more holistic perspective of an individual's mobility profile.

Clinical-based functional mobility tests, including the Timed Up and Go (TUG) Test, have been utilized in studies featuring prosthesis users.[10–13] The TUG Test is a reliable functional mobility test with acceptable concurrent validity for assessing mobility in individuals with amputation.[13] A normative TUG Test completion time of 8 ± 2 (mean ± SD) seconds has been reported for able-bodied, community-dwelling older adults.[14] In comparison, reference times of 23.1 ± 23.0 seconds and 28.3 ± 12.2 seconds have been reported among older adults with transtibial amputation (TTA) and transfemoral amputation (TFA), respectively.[13]

The L Test of Functional Mobility (L Test) is a second functional mobility test designed to assess physical function, including dynamic balance ability in individuals with amputation.[11] Normative L Test values for able-bodied, community-dwelling older adults have been reported to be 20.1 ± 3.1 seconds.[15] Reference times of 29.5 ± 12.8 seconds and 41.7 ± 16.8 seconds have been reported among adults with TTA and TFA, respectively.[11]

PROMs are commonly used to capture a patient's perception of their health condition, mobility, goals, and other unique factors pertaining to their care. The Prosthetic Limb Users Survey of Mobility 12 Item Short Form (PLUS-M) is a PROM for assessing the self-reported mobility levels of adults with lower extremity amputation who have experience using a

prosthesis.[16] The PLUS-M is scored using a standardized T-score ranging from 21.8-71.4, with higher T-scores indicating increased perceived mobility. Trained clinicians typically administer the TUG Test, L Test, and PLUS-M within a controlled, clinical or research environment, though the survey can also be completed electronically.

Accelerometry-based wearables have been used to collect quantitative mobility data since the 1980s.[17] Most wearables are innocuous and allow for objective mobility measurement by monitoring daily step counts. These devices provide a more realistic view of behavior patterns within the free-living environment versus what may be self-reported or demonstrated during functional mobility testing in the clinical setting. This information may be beneficial for evaluating progress through a rehabilitative intervention.[18,19] The activPAL is a research-grade, triaxial accelerometer capable of classifying time spent lying, sitting, standing, and stepping.[20] Because of these capabilities, the activPAL has been used extensively to measure mobility in various populations.[21–24] Fitbits are commercially available wearables intended to monitor physical activity (PA), heart rate, and sleep. Fitbits are readily available to the general public and may represent a more user-friendly, cost-effective method for tracking mobility compared to research-grade devices.[25]

Previous studies have utilized the activPAL and Fitbit to quantify daily steps among individuals with lower extremity amputation.[26–31] However, small, often homogeneous, samples prohibit the establishment of machine learning algorithms that can be used to predict daily steps based on clinical-based and patient-reported mobility constructs. As such, the ability to estimate daily step count based on outcome measure performance and clinical presentation is currently limited.

Because of mobility's influence on quality of life, an enhanced understanding of the relationship between clinical and patient-reported mobility constructs and free-living daily steps is warranted. This relationship merits investigation because it may provide more objective information regarding a patient's mobility profile while also adding value to established clinical-based constructs. Accordingly, this dissertation aims to develop and cross-validate two models for estimating free-living mobility (operationally defined as daily step count) among individuals with TTA, and to evaluate the relationship between clinical-based outcome measures, health state predictors, and daily steps. This information may be used to inform clinical decisions and provide more customized care to individuals with TTA.

The second aim of this dissertation is to determine the validity of the commercially available Fitbit Inspire 3 accelerometer for measuring daily step count for individuals with TTA. Potential findings from this specific aim may have clinical importance because the Fitbit Inspire 3 is more accessible to the general public than other research-grade accelerometers. Accordingly, this device may represent a more realistic option for individuals with TTA who are interested in monitoring daily steps.

This project strengthens the link between ambulatory capacity, functional mobility, and perceived mobility among individuals with TTA. By developing and validating two models to predict step count according to TUG and L Test performance, PLUS-M responses, and health state predictors, practitioners may have a more practical way of assessing free-living mobility. Furthermore, evaluating the relationship between daily steps, clinical-based outcome measure performance, and health state predictors may result in a broadened appreciation of ambulatory movement by providing more objective feedback regarding the effectiveness of a rehabilitation program or prosthetic prescription.

Purpose:

The purpose of this dissertation is to create and cross-validate two models using Least Absolute Shrinkage and Selection Operator (LASSO) regression to predict daily step count based on clinical-based and patient-reported mobility constructs and health state predictors. The equation will also be used to examine the relationships between daily steps and TUG Test performance, PLUS-M responses, and various health state covariates. The first prediction equation was created to determine the degree to which TUG and L Test performance and health state predictors could predict daily step count, and to examine the relationship between daily steps and TUG Test performance. The second prediction equation was created to determine the degree to which patient-reported PLUS-M T-scores and health state predictors may predict daily steps, and to examine the relationship between daily steps and the PLUS-M. Data from this study were also used to examine the validity of the commercially available Fitbit Inspire 3 for assessing daily steps among individuals with TTA, compared with the research-grade activPAL 3 accelerometer.

Specific Aims:

Mobility drastically impacts quality of life and overall satisfaction among prosthesis users.[32] Clinical-based functional mobility tests and PROMs represent two constructs for assessing mobility within the clinical setting. These constructs offer information pertaining to mobility characteristics and factors that may impact the quality of life and satisfaction of prosthesis users.[8] Accelerometry-based wearables represent a third construct that facilitates the objective assessment of mobility in the free-living environment. Thus, wearables have the

capacity to expand on traditional constructs of mobility assessment and may strengthen the link between clinical-based, patient-reported, and accelerometry-based mobility measures.

It has been reported that PA is positively correlated with increased mobility in prosthesis users.[33] Regular PA may also improve functional performance, quality of life, and longevity among individuals with amputation.[34] Additionally, a strong relationship exists between mobility and patient-reported quality of life and satisfaction.[32] Given the influence of mobility on these factors, free-living mobility assessment via wearables is merited to enhance the value of established clinical-based constructs.

The specific aims of this dissertation are as follows:

Aim 1a: *Develop and cross-validate a LASSO model to estimate daily step count according to TUG and L Test performance and health state predictors; examine the relationship between TUG Test performance and daily steps according to model predictions.*

To address Aim 1a, participants completed two standard clinical-based functional mobility measures (TUG and L Tests) while wearing an activPAL accelerometer for seven days. A LASSO regression model was developed to predict daily step count based on TUG Test completion time, L Test completion time, sex, ethnicity, cause of amputation, age, BMI, time since amputation, years of prosthesis utilization, age of current prosthesis, and T2D status. Separate testing data were then used to validate the skill of the LASSO model by comparing the model-predicted step count values with actual step count data collected from the activPAL accelerometer. The relationships between TUG Test performance, health state predictors, and daily steps were assessed according to the model predictions.

Aim 1b: *Develop and cross-validate a LASSO model to estimate daily step count according to PLUS-M responses and health state predictors; examine the relationship between the PLUS-M and daily steps according to model predictions.*

To address Aim 1b, the same cohort of participants from Aim 1a were asked to complete the PLUS-M 12 Item Short Form and wear an activPAL accelerometer for seven days. LASSO regression was utilized to predict daily steps based on a participant's PLUS-M T-score, sex, ethnicity, cause of amputation, age, BMI, time since amputation, years of prosthesis utilization, age of current prosthesis, and T2D status. Separate, testing data were then used to validate the skill of the LASSO model by comparing model-predicted step count values with actual step count data collected from the activPAL accelerometer. The relationships between PLUS-M, health state predictors, and daily steps were assessed according to the model predictions.

The second aim of this study was to determine the validity of the commercially available Fitbit Inspire 3 for measuring daily steps among individuals with TTA. Potential findings from this specific aim have clinical importance because the Fitbit Inspire 3 is more accessible to the general public than other research-grade accelerometers. As such, this device represents a more realistic option for individuals with amputation who are interested in monitoring their daily steps.

Aim 2: *Investigate the validity of the Fitbit Inspire 3 to assess daily step count among individuals with TTA in the free-living environment.*

To address Aim 2, at least four valid days of step count data collected via the Fitbit Inspire 3 were compared with the activPAL (criterion) accelerometer.

This dissertation is comprised of three studies, each designed to address one of the aforementioned specific aims. These studies build upon previous research pertaining to

functional and patient-reported mobility constructs and strengthen the link between ambulatory capacity, functional mobility, and perceived mobility among individuals with TTA. Potential findings from this dissertation are significant because they may provide a more practical framework for assessing intervention outcomes within the free-living environment, while informing more personalized rehabilitative interventions.

Chapter 2: Literature Review

It is estimated that approximately two million people are living with limb loss in the United States.[1] Amputations secondary to vascular etiology comprise over 70% of all nontraumatic lower extremity amputations and are often associated with additional comorbidities, including peripheral vascular disease, diabetic foot ulcers (DFUs), obesity, and type 2 diabetes (T2D); all of which may negatively impact mobility.[35] Individuals with T2D are 10 times more likely to require lower extremity amputation than their non-diabetic counterparts.[36] Additionally, among Medicare recipients, it has been reported that four per 1,000 persons with T2D will require lower extremity amputation annually.[36] The presence of one or more DFUs further increases the likelihood of amputation among this group. Given the increased prevalence of metabolic diseases (including T2D and its associated comorbidities), it is expected that amputation rates will nearly double by the year 2050.[1]

After amputation, mobility limitations decrease one's ability to independently complete activities of daily living, which negatively impacts self-sufficiency and quality of life.[37] Reduced mobility may also decrease PA, which elevates the risk of cardiovascular disease and all-cause mortality.[38] Therefore, restoring mobility to improve independence, physical activity (PA), and cardiovascular health is essential.[39]

Mobility is a central component of everyday living and the ability to move in and around the home is a strong indicator of independence.[40] Even with moderate assistance from family or social services, an individual with lower extremity amputation must have the capacity to perform 600 steps throughout the day to function inside a one-level house or apartment.[41] This indoor walking ability, albeit limited, may allow an individual with amputation to transfer from a

wheelchair to the bed or toilet facilities which may increase autonomy and self-esteem. Further improvements in ambulatory capacity may permit outdoor walking, which could promote PA within the local community.

Given the importance of ambulatory capacity post-amputation, clinical-based functional mobility tests and patient reported outcome measure (PROMs), including the Timed Up and Go (TUG) Test, L Test, and Prosthetic Limb User's Survey of Mobility (PLUS-M) have been validated for use among individuals with amputation. Although these outcome measures provide valuable information regarding an individual's mobility status in the clinical setting, objective assessment of mobility in the free-living environment is often more complex. However, it may provide a more transparent picture of one's overall ambulatory profile.

Amputation Pathophysiology

Approximately 150,000 amputations are performed in the United States each year.[42] Non-healing DFUs, diabetic peripheral neuropathy, peripheral vascular disease, and ischemia stemming from uncontrolled T2D represent leading contributing factors towards lower extremity amputation (Figure 2.1). T2D and its comorbidities are a major public health problem. Projections indicate that the global prevalence of T2D will

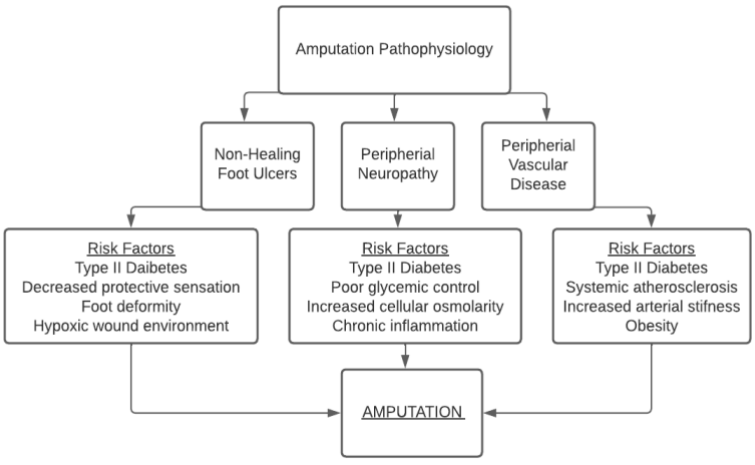


Figure 2.1: Amputation pathophysiology conceptual model. Non-healing diabetic foot ulcers, peripheral neuropathy, and peripheral vascular disease form the "classic triad" of risk factors associated with amputation.

increase to 7,079 per 100,000 people by 2030, representing a 16.8% increase from 2017 estimates.[43] Moxey et al. reported that people with T2D are nearly 30 times more likely to require lower extremity amputation compared to those without T2D, translating to an economic healthcare burden of over $4.3 billion in annual costs in the United States.[44]

DFUs are a leading contributing factor for amputation among individuals with T2D. It is estimated that over 80% of amputations among individuals with T2D are preceded by a DFU and that 19%-34% of individuals with T2D will eventually develop a DFU.[45,46] Diabetic peripheral neuropathy, peripheral vascular disease, and ischemia are also common among individuals with T2D. These comorbidities result in decreased protective sensation and restricted blood flow while creating a hypoxic wound environment, which is inconducive to healing.[47] Non-healing DFUs combined with diabetic peripheral neuropathy, peripheral vascular disease, and ischemia frequently result in infection, gangrene, and amputation.

After amputation, one in four individuals with T2D will require more proximal amputation of the ipsilateral limb or contralateral limb amputation.[48] After bilateral amputation, further decreases in quality of life, health status, and mobility are typically observed. These declines result in a more sedentary lifestyle and the development of other metabolic disorders.[49] Studies have reported overall survival rates of 69.7% and 34.7% at one and five years, respectively, after major lower extremity amputation.[50] Therefore, restoring mobility and promoting PA is paramount.

Diabetic Foot Ulcer Pathophysiology

DFUs are among the most common comorbidity accompanying T2D.[51] Though the cause of DFUs is multifactorial, diabetic peripheral neuropathy, peripheral vascular disease, and

ischemia constitute the "classic triad" of contributing risk factors.[52] Decreased protective sensation combined with altered gait biomechanics and/or foot deformity may increase the likelihood of DFU development.[52] Once a DFU has developed, hyperglycemia, decreased perfusion, and a chronically hypoxic wound environment weaken wound-healing processes, often resulting in infection, gangrene, and amputation. Non-healing DFUs are a leading cause of amputation among individuals with T2D. After wound development, diabetic peripheral neuropathy, peripheral vascular disease, and ischemia contribute to delayed healing, which can lead to infection and amputation. Mortality rates are high after initial amputation and increase further after subsequent bilateral amputation.[53] As such, wound care techniques such as debridement and offloading are often recommended to treat DFUs.

Diabetic Peripheral Neuropathy

Diabetic peripheral neuropathy often contributes to the pathogenesis of DFUs and resulting amputation. Evidence suggests that nearly 50% of individuals with T2D will develop diabetic peripheral neuropathy during their lifetime.[54] Diabetic peripheral neuropathy impacts the nervous system's motor, autonomic, and sensory components. Poor glycemic control among individuals with T2D contributes to the development of diabetic peripheral neuropathy. Individuals with hyperglycemia experience increased cellular osmolarity, which can disrupt the hexosamine pathway.[55] This disruption can inhibit neuronal activity, alter transcription factors that function in neural preservation, and induce an inflammatory cascade, culminating in nerve impairment.[56]

Diabetic peripheral neuropathy-induced nerve impairment can decrease the affected extremity's strength and range of motion.[57] Damaged intrinsic foot nerves can further lead to

intrinsic muscle denervation, causing altered gait biomechanics and foot deformities that contribute to skin breakdown. In a study conducted by Muller et al., individuals with T2D and diabetic peripheral neuropathy exhibited significantly decreased ankle plantar flexion power (diabetic: 1.05 w/kg vs. non-diabetic: 1.95 w/kg), strength (diabetic: 49.80 Nm vs. non-diabetic: 90.20 Nm), and range of motion (diabetic: 22.1° vs. non-diabetic: 30.6°) during gait compared to non-diabetic controls.[58] These deficiencies and gait deviations result in repetitive trauma to the diabetic foot, increasing the likelihood of DFUs and eventual amputation.

In addition to diabetic peripheral neuropathy-induced foot deformity, Chung and Pin found that obesity, hypertension, and cardiovascular disease accompanying T2D may compromise thermoregulatory mechanisms controlled by the autonomic nervous system.[59] Luo et al. also found that poor glycemic control and autonomic neuropathy negatively impact sweat glands, causing the skin to become dry and susceptible to fissures and infection.[60] As a result, individuals with T2D and diabetic peripheral neuropathy commonly present with increased foot temperature which may indicate underlying tissue damage and impending DFU development.[61]

In addition to altered lower extremity thermodynamics, sensory dysfunction resulting from diabetic peripheral neuropathy often leads to decreased protective sensation on the plantar foot. Local paresthesia over prominent, high-pressure areas of the foot can contribute to tissue breakdown, DFUs, and amputation. Due to decreased sensation, an individual with diabetic peripheral neuropathy-induced sensory dysfunction may be unaware of the damage to the foot or the presence of an open wound which may result in delayed treatment.

Peripheral Vascular Disease

Diabetic peripheral neuropathy is often accompanied by peripheral vascular disease. A 2009 population-based study conducted by Setacci et al. reported that up to 30% of individuals with T2D would develop peripheral vascular disease.[62] The same study also concluded that nearly 25% of individuals with T2D and peripheral vascular disease would develop a DFU during their lifetime.[62] Based on these risk factors, peripheral vascular disease has become a leading cause of lower extremity amputation, with peripheral vascular disease-related amputation rates close to eight times higher than amputations attributed to trauma.[63]

A systemic proliferation of atherosclerosis is the underlying mechanism contributing to peripheral vascular disease. Atherosclerosis causes a narrowing and hardening of the arterial walls, which can restrict blood flow and oxygen (O_2) delivery. Insulin resistance, hyperglycemia, and dyslipidemia are common in individuals with T2D and may lead to the progression of atherosclerosis and peripheral vascular disease.[64]

Inflammation also plays a central role in the pathophysiology of peripheral vascular disease. Obesity concomitant with T2D is closely related to insulin resistance, which up-regulates free fatty acids and inflammatory mediators.[65] This up-regulation increases reactive oxygen species and systematic inflammation.[65] Increased inflammation may also impair insulin binding and activity response, resulting in endothelial dysfunction.[66]

Increased circulating levels of pro-inflammatory cytokines stimulating tumor necrosis factor (TNF)-α and interleukin-6 have also been reported.[67] TNF-α and interleukin-6 bind to endothelial cell surface receptors and activate nuclear factor (NF)-κβ. This process promotes the binding of leukocytes and platelets to the endothelial surface, stimulating thrombogenesis.[64] In addition, increased leukocyte proliferation enhances arterial plaque accumulation, which diminishes vascular remodeling and elevates the risk of vessel rupture, clot formation, and

obstruction.[68] This process retards blood flow to structures distal to the blockage, which diminishes O_2 delivery and increases the likelihood of tissue necrosis and amputation.

Angiogenesis is also impaired in individuals with T2D and peripheral vascular disease, resulting in delayed healing after trauma. It is hypothesized that angiogenesis is triggered by endothelial shear stress within the vessel wall.[69] A study by van Globe et al. illustrated that hyperglycemia associated with T2D negatively impacts the adaptive angiogenic response by impairing or inhibiting shear-induced vasodilation, outward collateral vessel growth, and monocyte chemotaxis.[70] As a result, the formation of new blood vessels is prohibited, and blood flow redistribution is reduced.

The combination of inflammation-induced occlusion and diminished angiogenesis can restrict blood flow to the lower extremity and contribute to amputation. O_2-carrying red blood cells, leukocytes, and platelets are necessary for wound healing. As such, DFUs are often slow to heal because of decreased blood supply to the wound. Prolonged healing increases the likelihood of infection, which can result in amputation.

Ischemia

As peripheral vascular disease severity worsens, the likelihood of developing ischemia increases. Ischemia is an advanced form of peripheral vascular disease that occurs when blood flow is critically restricted. Diminished blood flow secondary to ischemia can reduce the level of O_2 necessary for cellular metabolism and removal of metabolic waste products including nitrogen, carbon dioxide, and phosphates.[71]

Critical limb ischemia is the most severe form of ischemia. Critical limb ischemia is characterized by recurring ischemic pain, an ankle systolic pressure of < 50 mmHg, or ulceration

and/or gangrene of the foot/toes with similar hemodynamic parameters.[72] Prognosis after critical limb ischemia diagnosis is poor. Studies have reported that nearly half of all individuals diagnosed with critical limb ischemia will require major lower extremity amputation, and more than one quarter will not survive one year post-diagnosis.[73]

Amputation, Mobility, and Physical Activity

Mobility is highly related to quality of life and is often reduced after lower extremity amputation.[74] PA is a crucial indicator of mobility that may influence the quality of life of an individual with lower extremity amputation.[33] Regular PA has many positive effects on overall health and is typically recommended for managing T2D and cardiovascular disease.[75] Individuals with amputation who participate in suggested levels of PA report increased perceived mobility and decreased all-cause mortality.[76] Health benefits ascribed to regular PA among individuals with amputation and concurrent T2D include decreased glycated hemoglobin (HbA1c) levels and body mass index (BMI).[77] Furthermore, PA also positively impacts mental health, which is a primary determinant of quality of life after amputation.[78–80]

Current recommendations from the United States Department of Health and Human Services encourage adults to participate in at least 150 minutes of moderate-intensity PA, 75 minutes of vigorous-intensity PA, or a combination of both per week to attain health benefits.[81] In addition to these recommendations, daily step count has been referenced in the literature as a proxy for PA, with 10,000 steps per day being an often-cited (though controversial) recommendation for general health.[82–85] Despite the health benefits ascribed to regular PA, many individuals with lower extremity amputation fail to achieve recommendations, primarily due to restricted mobility.[31,86] Individuals with transfemoral (TFA) and transtibial amputation (TTA)

have been shown to take an average of 3,553 and 5,087 steps per day, respectively, which is well below recommendations for healthy individuals and averages typically observed in individuals with T2D (approximately 6,000 steps).[87–89] Given the positive effects of PA on overall health, individuals with amputation should be encouraged to participate in regular PA, and restoration of mobility should be of chief concern among clinicians.

Physical Activity and Mobility After Amputation

The attainment of pre-surgery PA and mobility levels is an important rehabilitation goal following lower extremity amputation. Restoring mobility can have physical, psychological, and social health benefits for a prosthesis user.[90] Despite these benefits, several studies indicate that individuals with lower extremity amputation undertake low levels of PA and are less physically active than individuals without amputation.[91–96]

While walking is the most commonly performed PA among older adults, physical and biomechanical requirements associated with prosthesis utilization necessitate additional skill, strength, and proprioceptive capabilities of the prosthesis user.[97,98] Further mobility challenges may exist because of coexisting chronic illnesses and difficulties in procuring a prosthesis.[99,100] In addition to these challenges, psychosocial limitations, including a fear of falling, body image anxiety, and a lack of social support, negatively influence one's ability to meet daily PA goals.

A retrospective analysis of 12 months of daily step activity revealed that participants with TFA averaged 1,540 steps per day and that daily step counts were largely influenced by the patient's Medicare Functional Classification Level (K Level).[92] Table 2.1 describes each Centers for Medicare and Medicaid K Level and provides mobility characteristics associated with each classification.[101]

K Level	Medicare Functional Classification Level Description
K0	Does not have the ability or potential to ambulate or transfer safely with or without assistance and a prosthesis does not enhance their quality of life or mobility.
K1	Has the ability or potential to use a prosthesis for transfers or ambulation on level surfaces at fixed cadence, typical of the limited and unlimited household ambulator.
K2	Has the ability or potential for ambulation with the ability to transverse low level environmental barriers such as curbs, stairs, or uneven surfaces. This level is typical of the limited community ambulator.
K3	Has the ability or potential for ambulation with variable cadence, typical of the community ambulator who has the ability to transverse most environmental barriers and may have vocational, therapeutic, or exercise activity that demands prosthetic utilization beyond simple locomotion.
K4	Has the ability or potential for prosthetic ambulation that exceeds the basic ambulation skills, exhibiting high impact, stress, or energy levels typical of the prosthetic demands of the child, active adult, or athlete.

Table 2.1: Medicare Functional Classification Levels and associated mobility characteristics. Adapted from Centers for Medicare and Medicaid Services.

Although limited by a small, homogeneous sample (n = 17 individuals with TFA), the findings suggest that individuals with TFA are limited in their PA and overall mobility. Participants were also less physically active during extreme temperatures associated with the summer and winter months, suggesting that the external environment and season may also impact mobility. These conclusions underscore the importance of continued rehabilitative care after prosthesis procurement, especially for individuals living in areas with extreme climates or with lower K Level classifications.

Littman et al. also reported that among a sample of 158 older veterans with TTA or TFA, 57% of the participants were not considered physically active.[93] Self-reported history of regular PA prior to amputation was positively associated with elevated levels of PA post-amputation. Further, family support and financial assistance to obtain a gym membership positively impacted mobility. Low income, excessive (> 5 h/day) television watching, pain, and limited community

resources were cited as common barriers. These findings exemplify the importance of family support and community resources for maintaining PA.

A comparative study also indicated that individuals with TTA are less physically active than their non-amputated counterparts.[96] Specifically, Bussmann et al. assessed differences in the percentage of daily dynamic activities, heart rate, heart rate reserve, and body motility during walking during a 48-h period between individuals with and without TTA.[96] Individuals with TTA showed a significantly lower percentage of dynamic ambulatory activities (6.0% vs. 11.7%) and body motility during walking (0.14 g vs. 0.18 g,) compared to individuals without TTA. Conclusions from the study demonstrate that although an individual may become a proficient prosthesis user, decreased PA and increased physical strain may persist secondary to increased energy expenditure inherent with prosthesis utilization. These findings further emphasize the importance of effective rehabilitation strategies to optimize prosthetic gait kinetics and kinematics.

Health Impacts of Physical Activity and Mobility

Adopting a physically active lifestyle can improve overall health.[102,103,75] Although regular PA elicits numerous positive systemic effects, PA's influence on cardiovascular health may be the most beneficial. Individuals with amputation are at an increased risk for cardiovascular disease, which is strongly related to disability and mortality.[104,105] Individuals with lower extremity amputation and cardiovascular disease are more likely to experience adverse mobility outcomes and increased difficulty using a prosthesis.[104] Siriwardena and Bertrand reported decreased walking ability index (operationally defined as the ability to walk

for a distance of 10 feet on a flat surface) among individuals with lower extremity amputation and cardiovascular disease, which ultimately lead to a more sedentary lifestyle.[106]

Regular PA reduces resting blood pressure by decreasing systemic peripheral resistance throughout the cardiovascular system. This reduction in peripheral resistance results from neurohormonal and structural responses with reductions in sympathetic nerve activity and an increase in arterial lumen diameters, respectively.[107] In addition to resting blood pressure, studies have consistently demonstrated the beneficial effects of PA on individuals with established cardiovascular pathologies, including hypertension.[108–110] A systematic review and meta-analysis by Cornelissen and Smart concluded that regular PA resulted in up to a seven mmHg reduction in systolic and diastolic blood pressure among individuals with preexisting hypertension.[110] This reduction in blood pressure places less stress on working cardiac muscle and improves contractility efficiency.

Other proposed PA-induced cardiovascular benefits include favorable changes in endothelial function, arterial compliance, and nitric oxide production. The endothelium is the thin layer of cells lining the blood vessels. The endothelium interacts with vascular smooth muscle to constrict or dilate blood vessels, depending on the blood flow requirements.[111] Endothelial cells also release nitric oxide, which is a potent vasodilator. The release of nitric oxide by endothelial cells further increases blood flow during PA. This increase in perfusion permits O_2 transport to active muscles and facilitates adenosine triphosphate production. PA improves endothelial function by increasing the action of nitric oxide synthase and superoxide dismutase, both of which enhance production and prevent the breakdown of nitric oxide.[111]

While increased levels of PA positively effect cardiovascular health, increased sedentary time has less favorable effects. Decreased PA may contribute to endothelial dysfunction,

occlusion, and atherosclerosis which can reduce the distribution of blood throughout the body. A study by Gertz et al. illustrates these phenomena.[112] In the study, mice participating in daily PA exhibited long-term upregulation of nitric oxide and endothelial progenitor cells in the spleen and bone marrow, resulting in enhanced blood flow, angiogenesis, and decreased blood pressure.[112] However, the protective effects of PA were eliminated once mice were treated with nitric oxide inhibitors. Findings from the study illustrate the importance of PA for maintaining blood pressure and perfusion throughout the body.

Improved body composition may also be observed with regular PA. PA can increase lean body mass via hypertrophy of the skeletal muscles used to perform the task. In turn, fat mass is reduced, resulting in favorable changes in body composition. Increased capillary and mitochondrial density have also been reported in individuals who participate in regular PA, and may be attributed to changes in body composition.[113] Hermansen and Wachtlova reported that individuals participating in regular PA presented with higher capillary density (1 fiber supplied with approximately 1.5 capillaries) compared to more sedentary individuals (1 fiber supplied with approximately 1 capillary). The increased capillary density observed in physically active individuals was partially attributed to larger muscle cells and overall muscle mass.[113] These findings support that improved body composition secondary to PA results in improved metabolic health and oxidative capacity in skeletal muscle.

Substantial decreases in subcutaneous abdominal and visceral fat among individuals participating in regular PA have also been reported.[114,115] Broeder et al. found that individuals who participated in a 12 week PA program experienced significant decreases in fat mass and percent body fat compared to a control group.[115] In the study, participants were assigned a 12-week progressive walking program that required them to walk for 40 continuous minutes at

increasing intensities. Hydrostatic body fat measurements were taken prior to and post-intervention. Findings indicated that participants within the PA group experienced a significant decrease in relative body fat percentage (pre-treatment: 18.4 ± 7.9 vs. post-treatment 16.5 ± 6.4) and fat weight (kg) (pre-treatment: 14.4 ± 7.9 vs. post-treatment 12.8 ± 7.1).[115]

Individuals with amputation are especially susceptible to deleterious metabolic changes after amputation surgery. Eckard et al. measured muscle mass, fat mass, and weight within the first 12 weeks after amputation and at six, nine, and 12 months after amputation.[116] A significant increase in weight and BMI among individuals with unilateral amputation between baseline and all follow-up visits was reported. Further, increases in both total fat mass and trunk fat mass were noted among participants. Muscle atrophy, loss of lean body mass, metabolic changes secondary to psychological stress, and decreased PA were offered as potential explanations for alterations in body composition.

PA has a profound effect on overall health in individuals with and without amputation. Furthermore, it is apparent that individuals with amputation often engage in less PA than their non-amputated counterparts, primarily due to decreased mobility. As a result, the likelihood of developing additional comorbidities post-amputation is elevated. Considering the relationship between mobility, PA, and overall health, early and effective rehabilitation strategies are warranted to optimize patient outcomes.

Amputation and Outcome Measures

A standardized, methodological appraisal of an individual's rehabilitation following lower extremity amputation is required to determine the effectiveness of a treatment intervention. Outcome measures are instruments developed to monitor progress and provide a rationale for

clinical decision-making. According to Feinstein et al., the purposes of outcome measures are to: (1) determine compensation for a facility, (2) predict prognosis, (3) plan placement, (4) estimate care requirements, (5) assist in choosing specific types of care, and (6) determine a change in status secondary to an intervention.[117] Valid and reliable outcome measures have the capacity to measure the magnitude and sensitivity of change over time ascribed to a particular intervention.[118] An outcome measure should be selected after first identifying an individual's functional level, goals, and clinical objectives. Utilizing outcome measures to guide clinical decisions is an essential aspect of patient care and should be incorporated into prosthetic treatment paradigms.[119]

Outcome measures can be classified into clinical-based functional mobility tests, PROMs, and accelerometry-based objective constructs. Figure 2.2 outlines various examples of common functional mobility tests, PROMs, and accelerometry-based wearables that have been utilized to assess mobility among prosthesis users.

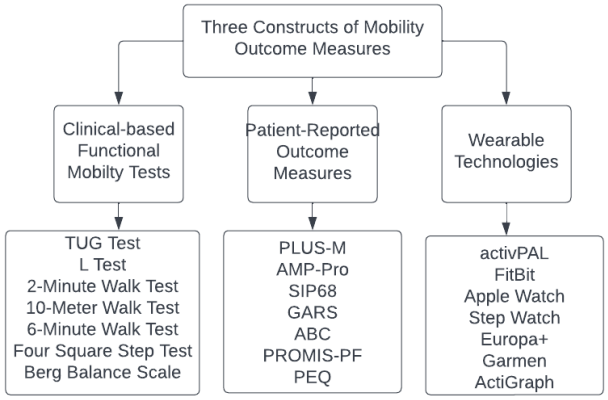


Figure 2.2: Three constructs of mobility and common outcome measures conceptual model.

Clinical-based functional mobility tests are performance-based instruments typically administered by trained professionals in the clinical or laboratory settings. Clinical-based functional mobility tests are objective and often require the execution of a set of movements or functional tasks. Clinical-based functional mobility tests scores are frequently based on quantitative measures, including (but not limited to) time to complete a specific task. These

measures provide valuable information regarding the effectiveness of a rehabilitative intervention, but only provide a cross-sectional representation of a performance in an artificial setting (i.e., the clinic/laboratory).

PROMs are self-reported measures where an individual responds to a series of questions designed to classify a clinical characteristic or personal perception. The questions are typically scored by applying a predetermined point system or algorithm to the responses.[16] PROMs reflect an individual's perspective of the benefits of a treatment program or their current functional level. While PROMs are subjective in nature, they are inexpensive, easy to administer, and provide a first-hand account of the respondent's opinion or perception.

Accelerometry-based measures via wearable devices permit the objective assessment of mobility by monitoring PA and sedentary time. These devices provide a more realistic view of mobility in a natural environment compared to what a patient may self-report or be capable of demonstrating during clinical testing. This information may be beneficial as the clinician tracks a patient's progress through a rehabilitative intervention.[18,19] Despite the potential benefits of accelerometry-based objective measures, their practical application among individuals with TTA is currently limited, primarily due to methodological constrains in many experimental protocols.

Clinical-based Functional Mobility Outcome Measures

The TUG Test is a clinical-based functional mobility test that has been used to assess mobility and fall risk.[11–13,15] A schematic of the TUG Test is depicted in Figure 2.3. To complete the TUG Test, participants are instructed to sit in a chair with their back against the chair, arms resting on the chair's arms, and if applicable, assistive device in hand. The participant is then

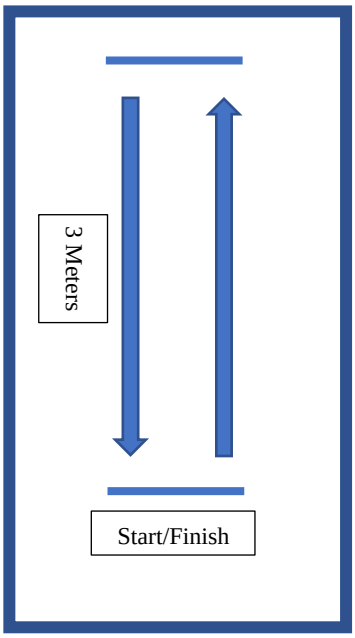


Figure 2.3: TUG Test schematic. The TUG Test requires a participant to start in a seated position, walk three meters, turn around, and walk three meters back to their chair.

instructed upon hearing the word "go," to arise from the chair, and walk at a normal, comfortable pace to a line on the floor three meters away, turn around, return to the chair, and sit down again.

The TUG Test was developed to identify mobility and balance impairment in elderly adults but has since been used to assess mobility outcomes in a myriad of clinical populations, including individuals with amputation.[120] Schoppen et al. concluded that the TUG Test exhibited good inter- and intrarater reliability (r = 0.96 and r = 0.93, respectively) for measuring mobility in older adults with lower extremity amputation.[13] The same study also confirmed the validity of the TUG Test after comparing performance measures between the TUG Test and Sickness Impact Profile, 68-item version (SIP68), and the Groningen Activity Restriction Scale (GARS) criterion measures. Based on the findings, it was determined that the TUG Test was a reliable instrument with adequate concurrent validity for assessing mobility among individuals with lower extremity amputation.

The TUG Test has been used to predict fall risk, overall mobility, and prosthesis nonuse/abandonment among individuals with TTA.[121,122] In a study by Dite et al., individuals with TTA (n = 47) completed the TUG Test at discharge and were then retested (n = 40) six months later.[121] Participants were classified as either "multiple fallers" or "non-fallers" based on the frequency of self-reported falls experienced within the six-month window. Significant differences in TUG Test performance were noted between the two groups, and TUG Test

completion times ≥ 19 seconds were associated with increased fall prevalence and decreased mobility. The findings suggest that a positive relationship exists between higher TUG Test completion times and fall risk, and an inverse relationship exists between higher TUG Test completion times and mobility. In addition to increased fall likelihood, Roffman et al. found that individuals taking ≥ 21.4 seconds to complete the TUG Test were at an increased risk for prosthetic nonuse and/or abandonment 12 months after procurement.[122] Findings from the study highlight the importance of effective, early rehabilitation, and demonstrate the TUG Test's utility for predicting successful prosthesis utilization after amputation.

The impact of amputation level and duration of prosthesis usage on TUG Test performance has also been investigated.[123] Specifically, Newton et al. determined that, on average, individuals with TFA take longer to complete the TUG Test compared to participants with TTA.[123] Potential explanations for this observation may be attributed to inferior standing balance, muscle asymmetries, and increased metabolic costs associated with utilizing a transfemoral prosthesis.[124] Furthermore, an inverse relationship was noted between years of prosthesis utilization and TUG Test times, suggesting that practice and extended rehabilitation may positively influence mobility.

While the use of the TUG Test for assessing mobility outcomes among individuals with amputation has clearly been described, potential ceiling effects may exist for higher functioning individuals with amputation.[125] As such, a modified version of the TUG Test was designed to ameliorate ceiling effects associated with the TUG Test. The L Test is a 20-meter test of mobility that involves two transfers and four turns, making it longer and more complex than the TUG Test.[11]

The L Test of Functional Mobility is a functional mobility test that can be used to assess physical function, including dynamic balance ability. A schematic of the L Test is depicted in Figure 2.4. To complete the L Test, the participant begins in a seated position with his or her back against the chair, arms resting on the chair's arms, and if applicable, assistive device in hand. Upon hearing the word "go," the participant is instructed to stand up from the chair, walk to a line three meters away, turn 90 degrees, and walk to a second line located seven meters away. The participant turns 180 degrees, return to the chair, and sit down again.

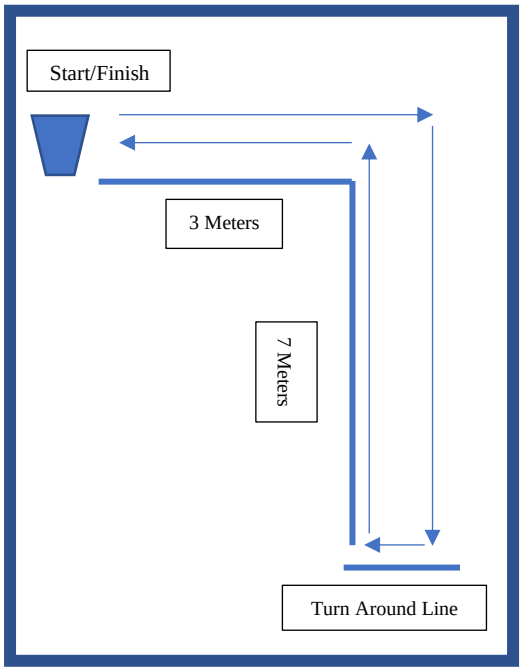


Figure 2.4: L Test schematic. The L Test involves walking a total of 20 meters and completing two turns.

The validity and reliability of the L Test for assessing mobility among individuals with amputation have been investigated by Deathe and Miller.[11] In the study, 93 individuals with unilateral TTA (74%) or TFA (26%) were recruited to complete the L Test and a series of additional functional mobility outcome measures (TUG Test, 2-Minute Walk Test, and Activities-Specific Balance Confidence Scale (ABC)) during two visits. The L Test was highly correlated with all measures, indicating high concurrent validity. Further, intraclass correlation coefficients (ICC) were 0.96 and 0.97 for interrater and intrarater reliability, respectively. This suggests that the L Test is a valid functional mobility instrument to assess mobility outcomes among higher-functioning individuals with amputation. In addition, the study provides evidence that the L Test minimizes the ceiling effect that may occur in the TUG Test. Based on these

findings, incorporating both the TUG and the L Test into an experimental protocol featuring individuals with amputation may allow the quantitative assessment of mobility capabilities among a full range of functional levels.

Patient-Reported Outcome Measures

The PLUS-M is one of the most common PROMs for assessing function among individuals with lower extremity amputation. The PLUS-M V1 includes 44 mobility questions that have been calibrated to an item response theory model using mobility data from over 1,000 individuals with lower extremity amputation.[126] Two short forms (12- and 7-item) and accompanying scoring tables have also been developed for use in clinical care and research.[16] Normative data obtained from a sample of over 1,000 individuals with amputation are available to facilitate score interpretation.[16] The PLUS-M utilizes a standardized T-score derived from population means.[127] Computerized versions of the PLUS-M have been developed to limit administrative burden while maintaining the psychometric qualities of the original instrument.[128]

Hafner et al. assessed the construct validity of the PLUS-M.[129] A total of 199 prosthesis users were assessed before receiving replacement of a full prosthesis, prosthetic socket, and/or prosthetic knee unit. Convergent construct validity was examined through correlation analysis by comparing a participant's PLUS-M T-score with their scores on the Amputee Mobility Predictor (AMP),[130] TUG Test, Patient Reported Outcomes Measurement Information System-Physical Function (PROMIS-PF),[131] Prosthesis Evaluation Questionnaire-Mobility Subscale (PEQ-MS),[132] and ABC outcome measures. Conclusions from the study indicated that the PLUS-M demonstrated a moderate positive relationship ($r = 0.54$, $p < 0.001$) and a moderate negative relationship ($r = -0.56$, $p < 0.001$) with AMP scores and TUG Test times, respectively. Strong

positive relationships were noted between PLUS-M and PEQ-MS scores ($r = 0.78$, $p < 0.001$), ABC scores ($r = 0.81$, $p < 0.001$), and PROMIS-PF T-scores ($r = 0.81$, $p < 0.001$).

The PLUS-M has also been used to assess the relationship between mobility, quality of life, and general satisfaction among prosthesis users.[32] A retrospective chart analysis by Wurdeman et al. analyzed PLUS-M T-scores and PEQ responses from 509 individuals with lower extremity amputation. Mobility was found to be positively correlated with quality of life ($r = 0.51$, $p < 0.001$) and general satisfaction ($r = 0.47$, $p < 0.001$). Given this relationship, it may be inferred that a rehabilitation paradigm focused on optimizing mobility may result in greater quality of life and general satisfaction among prosthesis users. Results from the study also underscore the necessity of designing a rehabilitation paradigm that maximizes an individual's mobility.

The PLUS-M has also been used to develop a logic tree designed to predict functional potential for ambulation among prosthesis users.[133] Retrospective analysis of outcomes data for 2,770 individuals with lower extremity amputation was utilized to create a classification and regression tree for predicting ambulatory capacity.[133] To create the logic tree, predictor variables including gender, age, height, weight, amputation-adjusted BMI, amputation level, cause of amputation, comorbidities, and PLUS-M T-scores were entered into the model. A participant's ambulatory level was defined by dichotomizing his/her K-Level functional status into either an "unlimited community ambulator" (K3 or K4) or a "limited community/household ambulator" (K1 or K2). The logic tree accurately classified 81.6% of the model's testing group. Age, PLUS-M T-score, cause of amputation, and body weight were determined to be accurate predictors and were retained within the logic tree. These findings are clinically relevant because they provide

healthcare professionals with a tool to help predict ambulatory capacity based on the patient's clinical characteristics.

Accelerometry-based Objective Measures

Accelerometry-based wearable technologies provide a quantitative tool for assessing mobility in the free-living environment. The activPAL is a research-grade accelerometer that produced reliable and valid measurements of PA in healthy adults and individuals with amputation.[134,135] Ryan et al. conducted one of the first studies to determine the reliability and validity of the activPAL to measure daily step count in healthy adults.[134] Findings from the study indicated excellent inter-device reliability for the activPAL (ICC (2,1) > 0.99) for both step count and cadence when compared to the Yamax Digi-Walker SW-200 and Omrion HJ-109-E pedometers. Furthermore, authors noted that the pedometers' accuracy decreased as gait cadence decreased, but the activPAL was not impacted. These findings are particularly important among individuals with amputation, who typically ambulate more slowly than those without amputation.

The reliability and criterion-related validity of the activPAL for measuring PA among individuals with lower extremity amputation was assessed by Deans et al.[135] In the study, 15 adults with unilateral lower extremity amputation completed various simulated activities of daily living tasks in a laboratory setting that were retrospectively scored after video analysis. During these tasks, accelerometry data were obtained via an activPAL worn on the participant's sound and prosthetic limb. The activPAL demonstrated acceptable reliability (ICC = 0.77-0.88) during the activities of daily living when worn on the prosthetic side. While conclusions demonstrate the activPAL's reliability for monitoring step count during activities of daily living, noteworthy methodological limitations exist. Specifically, the study was limited by a small sample size.

Further, the simulated activities of daily living were conducted in the laboratory setting, which may impact the external validity of the overall findings.

A second study by Salih et al. examined the activPAL's validity for measuring step count among prosthesis users in the inpatient setting during initial rehabilitation.[136] Participants in the study utilized an activPAL on the prosthetic and sound limb while performing a walking task and two seated wheelchair transfers. A research clinician timed each task and observed times were compared with data collected via the activPAL. Sensitivity between the activPAL and observed times was 90.5% and 86% for the sound and prosthetic sides, respectively. The results further support the activPAL's use for monitoring the mobility of individuals with amputation in the clinical setting.

While the studies by Deans and Salih et al. assessed the validity and reliability of the activPAL in the clinical setting, Buis et al. utilized the activPAL to assess daily stepping activity over one week while detailing physical activity in 24-hour epochs.[30] A total of 48 individuals with TTA were fit with either a total surface bearing or patellar tendon bearing prosthetic socket, which was instrumented with the activPAL. The authors reported high consistency between devices (ICC = 0.99) over a 24-hour period, indicating strong reliability. Surprisingly, the authors also reported that participants were physically active throughout the week, taking an average of 8,000 steps daily. This increase in daily step count was attributed to successful prosthetic treatment and rehabilitation.

Chapter 3: Development and Cross-Validation of a Model for Predicting Daily Steps Based on Functional Mobility Test Performance in Adults with Transtibial Amputation

Abstract

Restoring mobility after amputation has a positive impact on quality of life. Clinical-based functional outcome measures provide insightful mobility information within a controlled environment. Incorporating accelerometers can facilitate objective measurement of free-living mobility and provide a more holistic view of one's ambulatory profile. **Objectives:** This study sought to expand the utility of functional mobility tests by developing and validating an equation for predicting daily steps and examining the relationship between TUG Test time and daily steps. **Methods:** Health state information was collected. Each participant completed the TUG and L Test and wore an activPAL accelerometer for seven days. LASSO regression with three-fold cross-validation was used to build a prediction model in a training data set (n = 80). The model's validity was examined by comparing steps generated by the equation with actual steps collected via the activPAL in a testing data set (n = 26). **Results:** Participant age, BMI, T2D status, and TUG Test completion time were identified as significant predictors. Model evaluation in the testing sample indicated a moderately high correlation (r = 0.60) and no significant mean difference between actual vs. predicted steps (t_{25} = 0.74, p = 0.461). A root mean squared error (RMSE) of 2,294 steps was noted between methods and equivalence testing revealed that equivalency could not be claimed. **Conclusion:** Participants taking longer to complete the TUG Test tended to have lower daily steps. The model overestimated steps for those with significantly low steps and underestimated steps for those with significantly high steps. Further refinement is necessary to improve the model fit for individuals with extreme step counts.

Introduction

The utilization of outcome measures has long been recommended to justify and inform clinical decision-making. More recently, there has been a heightened emphasis on collection and reporting of patient outcomes within the field of prosthetics and orthotics, as evidence-based medicine becomes the standard in healthcare.[137] When appropriately selected and administered, performance-based outcome measures can offer valuable insights into an individual's current functional level and predict future capabilities.[138] For individuals with a lower extremity amputation, clinical-based functional mobility tests can serve as effective tools for measuring changes over time and evaluating the efficacy of rehabilitation programs. In addition, prosthetists and other healthcare professionals are increasingly encouraged or mandated to include patient outcomes to fulfill clinical documentation obligations in order to receive third-party reimbursement.[139] The inclusion of patient outcome measures plays an important role in assuring high-quality care and optimizing the overall experience of a prosthesis user.

Clinical-based functional mobility tests are physical outcome measures intended to evaluate an individual's performance while completing various mobility tasks such as transferring, turning, or walking. Clinical-based functional mobility tests, including the Timed Up and Go (TUG) and L Test of Functional Mobility (L Test) have been used extensively in research and clinical settings to assess the mobility of lower extremity prosthesis users.[11–13,15,123] These instruments are cost-effective and have been shown to be reliable and valid tools for measuring ambulatory capacity within this population.[11,13] While the TUG and L Test provide a cross-sectional view of mobility in a controlled environment, full appreciation of an individual with amputation's free-living ambulatory profile is often more complex.

Information collected from self-reported walking time and/or inferences drawn from physical performance measures completed in controlled settings has traditionally been utilized to estimate free-living mobility among prosthesis users.[130,140] The ability to objectively measure daily physical activity (PA) has become more feasible with the introduction of wearable technologies (wearables) equipped with accelerometers.[141,142] Wearables, including the research grade activPAL accelerometer, have been used to measure PA in a myriad of special populations and represent a method for objectively assessing free-living mobility among prosthesis users.[9,23,30,143] The small, unobtrusive nature of the activPAL makes it an attractive tool for objectively monitoring mobility external to the controlled laboratory or clinical environments. As such, these devices may provide a more holistic view of an individual's free-living ambulatory profile and may be used to expand upon clinical-based mobility outcome measures, including the TUG and L Test.

After amputation, mobility is frequently limited, impacting safety and quality of life.[144] The ability to safely walk and perform daily activities while wearing a lower extremity prosthesis is essential for regaining independence and returning to work, social, and recreational activities. Furthermore, a significant positive correlation has been noted between mental health status and locomotor capability index in individuals with lower extremity amputation.[145] Thus, free-living daily step count assessment should be considered a fundamental clinical care metric after the procurement of a prosthesis. While wearables may be well suited to accomplish this, only a limited number of studies have explored the use of such technology to assess free-living mobility in special populations. Further, to the best of our knowledge, no studies have specifically examined the relationship between the TUG Test and step count among individuals with transtibial amputation (TTA). This represents a potential gap in clinical care.

Because of the profound impact of mobility on quality of life and the significance of functional outcome measures in rehabilitation, an enhanced understanding of how clinical-based functional mobility test performance may translate into daily step count is warranted. This relationship merits investigation because it can provide clinicians with more objective insights regarding the effectiveness of interventions within a patient's natural setting. Additionally, it can augment the value of established clinical-based outcome measures of mobility such as the TUG Test. By developing and cross-validating an equation that predicts daily step count based on performance on clinical-based functional mobility outcome measures, clinicians can have a practical tool for assessing activity levels outside of the clinical setting while also gaining a broadened appreciation of ambulatory movement within the home environment.

Accordingly, the purpose of this study was to develop and cross-validate a prediction model that estimates free-living mobility (operationally defined as daily step count) based on performance on two commonly employed clinical-based functional outcome measures and health-state covariates in a representative sample of individuals with TTA. Additionally, the study examined the relationship between daily step count and performance on the TUG Test, utilizing the equation developed in the prediction model.

Materials and Methods

Participants

Adults with a unilateral transtibial amputation were recruited from a network of orthotic/prosthetic clinics located throughout the United States. The identification process began with their respective treating prosthetist, who initially referred potential participants. Subsequently, the individuals were provided with a medical history screening form to complete.

The inclusion and exclusion criteria for the participation were determined based on the evaluation of the responses provided in the self-reported medical history questionnaire.

Inclusion Criteria

All enrolled participants were over the age of 18, had a unilateral TTA, and had at least three months of experience using a prosthesis before study enrollment. It is estimated that 28.2% of amputations occur at the transtibial level, making it the second most common amputation type, trailing only toe/partial foot amputation (33.2%).[146–148] Thus, decision was made to limit recruitment to individuals with TTA to increase recruitment feasibility compared to focusing on individuals with amputations at other, less common levels (i.e., hip disarticulation, knee disarticulation, etc.). All participants utilized their existing transtibial prosthesis during the protocol.

Exclusion Criteria

The same medical history questionnaire was used to determine if participants had any additional movement disorders that may have drastically impacted mobility (i.e., stroke, Parkinson's disease, spinal cord injury, traumatic brain injury, etc.). Any participants that self-reported a movement disorder that may have impacted their mobility were excluded. This criterion was established as various movement disorders may be associated with decreased mobility.[149,150] Therefore, additional movement disorders that impact mobility may have confounded the results.

Study Design

All participants provided written informed consent in accordance with Syracuse University's Institutional Review Board approved protocol. Figure 3.1 provides a conceptual overview of the study protocol. The protocol was completed during one clinic encounter where each participant received prosthetic care. During the encounter, participants completed a health and demographics survey, the Prosthetics Limb User's Survey of Mobility (PLUS-M) 12-Item Short Form, and the TUG and L Test. Participants were provided with activPAL 3 and Fitbit Inspire 3 accelerometers to wear for seven full days. Data collected from the Fitbit Inspire 3 were used in a subsequent follow-up device validation study and not used to build the prediction equation or assess the relationship between actual step count and functional mobility test performance. Participants were asked to return the devices to the same location where they completed the protocol or through the postal service via a self-addressed stamped envelope.

Demographics and Health State Metrics

A survey collected information about each participant's ethnicity, sex, age, and type 2 diabetes (T2D) status. The same survey was used to obtain information concerning each participant's cause of amputation, amputation date, years of prosthesis utilization, and age of their current prosthesis. The participant's height and weight were measured with a stadiometer and electronic scale, respectively, and amputation-level adjusted BMI was calculated.[151]

TUG Test completion time, L Test completion time, sex, ethnicity, age, T2D status, cause of amputation, time since amputation, years of prosthesis utilization, age of current prosthesis, and BMI served as predictor variables within the statistical model. The decision to include these predictor variables was made as each factor (sans ethnicity) has been shown to independently impact mobility among individuals with amputation.[152–154] Specifically, Jayakaran et al. reported

that individuals who underwent amputation surgery secondary to dysvascular etiology reported significantly fewer MET-hours/day compared to those with traumatic amputation (13.2 ± 12.7 vs. 27.0 ± 23.2).[152] Johnson et al. also reported that individuals with amputation secondary to T2D complications reported reduced mobility after amputation.[153] The same study also concluded that age significantly predicted mobility regardless of amputation etiology.[153] Studies have also concluded that the level of independence and mobility a prosthesis user achieves are strongly related to time since amputation and years of prosthesis utilization.[154,155]

Timed Up and Go (TUG) Test

The TUG Test is a functional mobility test with high intrarater (r = 0.93), interrater (r = 0.96), and test-retest (ICC = 0.83-0.97) reliability for assessing mobility in individuals with TTA.[13,156] The TUG Test's concurrent validity for measuring mobility in individuals with lower extremity amputation has also been confirmed by Schoppen et al.[13] In the study, authors reported moderate relationships between the TUG Test and the Groningen Activity Restriction Scale (ρ = 0.39) and the "Mobility Control" subscale of the Sickness Impact Profile, 68-item version (ρ = 0.46).[13]

The TUG Test was completed in accordance with published guidelines.[13,156] To complete the TUG Test, the participant was instructed to sit in a chair with their back against the chair, arms resting on the chair's arms, and assistive device in hand (if applicable). Upon hearing the word "go," participants were instructed to stand from the chair, walk to a reference line three meters away from the chair at a normal, comfortable pace, turn around, return to the chair, and sit down again. Each participant completed three trials (one practice and two test trials). Completion times from trials two and three were averaged and used for analysis.

L Test of Functional Mobility

The L Test is a functional mobility test for assessing physical function and dynamic balance ability in individuals with amputation.[11] The L Test has demonstrated high intrarater (r = 0.96), interrater (r = 0.97), and test-retest (r = 0.98) reliability for assessing mobility in individuals with TTA.[11,157] High correlations between the L Test and other standard functional mobility tests, including the TUG Test (r = 0.93), 2-Minute Walk Test (r = -0.86), and 10-Meter Walk Test (r = 0.97) have also been reported in this population, indicating strong concurrent validity.[11]

The L Test was completed following published guidelines.[11,156] To complete the L Test, the participant began in a seated position with their back against the chair, arms resting on the chair's arms, and assistive device in hand (if applicable). Upon hearing the word "go," the participant stood from the chair, walked to a line three meters away, turned 90 degrees, and walked to a second line seven meters away. The participant then turned 180 degrees, returned to the chair, and sat down again. Each participant completed three trials (one practice and two test trials). Completion times from trials two and three were averaged and used for analysis.

activPAL 3 Wearable

Each participant was provided an activPAL 3 accelerometer. The activPAL 3 is a triaxial accelerometer with a sampling frequency of 20 Hz with a dynamic range of ± 2 gravitational units.[20] The device weighs 20 g (5 cm x 3.5 cm x 0.7 cm) and estimates sitting, standing, walking, and daily step count using proprietary algorithms based on acceleration measurements. A previous study measuring observed versus activPAL-measured walking activity in a sample of

individuals with TTA reported a sensitivity of 86% and 90.5% for the amputated and non-amputated limb, respectively.[136] These findings suggest that the activPAL is a valid tool for continuous ambulation monitoring in individuals with amputation.

The activPAL 3 was attached to each participant's non-amputated thigh with Hypafix tape per recommendations by Deans et al.[135] Written and verbal donning/doffing instructions were provided to each participant. Participants were instructed to wear the activPAL at all times for seven full days, only removing it when in contact with water. A minimum of four valid days (three weekdays and one weekend day) of step count data were required for participants to be included in the analysis. Based on recommendations from Edwardson et al., a valid day was defined as a 24-hour period in which at least 10 hours of accelerometer wear time data were observed during typical waking hours after visually inspecting the data within the PALanalysis software suite.[158] Daily step count values from the valid days were averaged, resulting in a single step count value for each participant.

Statistical Analysis and Model Building

Statistical Assumptions

All statistical analyses were performed using R (R Core Team (2023)), Minitab (Minitab 17 Statistical Software, State College, PA) and SPSS Statistics (version 29; IBM Corp., Armonk, NY, USA). Prior to constructing the predictive model, statistical assumptions for regression were evaluated. Linear relationship and monotonicity between the dependent (daily step count) and predictor variables (TUG Test, L Test, and non-categorical covariates) were evaluated by examining scatter plots.

After fitting the model, leverages and Cook's distances for each observation were examined, and unusually high values were flagged for further analysis. Residuals were then plotted against the fitted values, and the degree of variability across the range of fitted values was visually assessed. A Q-Q plot of the residuals against theoretical quantiles of residuals was established to evaluate normality, and residuals were plotted against the leverage of each observation to further identify potentially extreme values.

Model Building with Least Absolute Shrinkage and Selection Operator (LASSO) Regression

LASSO linear regression is an L1 regularization technique where a penalty proportional to the absolute value of the magnitude of coefficients ($|\beta_j|$) is added, thereby reducing the likelihood of model overfitting associated with other forms of linear regression (Equation 1).[159]

Equation 1 $$\sum_{i=1}^{n}(y_i - \sum_{j} x_{ij}\beta_j)^2 + \lambda \sum_{j=1}^{p} |\beta_j|$$

In LASSO regression, *n* represents the number of data points in the dataset, *p* represents the number of features (predictors), y_i is the observed value of the dependent variable for the *i*-th data point, and x_{ij} is the *i*-th data point's value for the *j*-th feature. The tuning parameter lambda (λ) is implemented to control the strength of the L1 regularization penalty. Through this mechanism, LASSO regression selects only the most important variables for predicting the outcome (daily step count) by shrinking the regression coefficients associated with the least essential predictors to zero. This technique produces a more parsimonious model, which improves the overall prediction quality compared to predictions based on models fit via unpenalized maximum likelihood.[159]

In the present study, the '*glmnet'* package in R was utilized to develop a LASSO model for predicting the mean daily step count within the sample. The data underwent preparation for

model training and evaluation by randomly dividing the sample into training (n = 80) and testing (n = 26) sets. Dummy variables were then assigned to each categorical predictor. The categorical predictors included sex (male or female), ethnicity (White, Black, Latino), cause of amputation (T2D/vascular, trauma/injury, infection (without diabetes), cancer/tumor, congenital/birth, other), and T2D status (yes or no).

Three-fold cross-validation, which divides the training data into three blocks and analyzes each block against each other, was executed using the *'trainControl'* function to estimate the model's performance and to select the optimal tuning parameter (λ). Subsequently, the LASSO model was then trained using the *'train'* function. In this study, the response variable was the daily step count measured using the activPAL 3. The predicators included in the model were TUG Test completion time, L Test completion time, sex, ethnicity, cause of amputation, age, BMI, time since amputation, years of prosthesis utilization, age of current prosthesis, and T2D status.

A grid of tuning parameters (α and λ) for the LASSO model was established using the *'tuneGrid'* function. The optimal λ value was selected based on the three-fold cross-validation performance. The LASSO regression model coefficients representing the estimated association of each predictor with mean daily step count were analyzed. Next, the LASSO model was created using the selected predictors and the best tuning parameter (λ) obtained from the training data. The same model was used to generate new predictions for the holdout (testing) data.

Model Validation

Model validation was conducted on the testing data (n = 26). The relationship between activPAL-measured and LASSO model-predicted (actual vs. predicted) daily step count was

examined using Pearson's Correlation.[160] Based on previously published standards, observed correlation coefficients between 0.40 and 0.59 were considered moderate. Correlation coefficients between 0.60 and 0.79 were considered moderately high, and correlations between 0.80 and 1.00 were considered high.[160]

A paired samples t-test was conducted to identify differences between actual and LASSO model-predicted daily step count. Given that the testing data were randomly selected, the expected difference between the actual versus predicted daily steps was presumed to be zero. Root mean squared error (RMSE) was calculated to further examine the differences between methods.

To assess the equivalency between the predicted mean daily step values obtained from the LASSO model and the criterion values measured by the activPAL, equivalence testing using the confidence interval method was performed. Equivalence testing is an alternative approach to testing for significant differences between means.[161] Equivalence testing requires pre-defined equivalence zones and permits comparisons between the values. If the full 95% confidence interval range lies within the equivalence zone, it can be concluded that the predicted value is equivalent to the criterion value. In the current study, the mean daily step values obtained from the two methods were statistically equivalent ($p < 0.05$) if the 95% confidence intervals of the predicted mean daily step value fell within an equivalence zone set at ±10% of the actual step count data.

Results

Participants

Descriptive characteristics for the training data, testing data, and entire sample are presented as means ± SD in Table 3.1. The model training and testing sample included 106 adults with TTA (27 females and 79 males). The group's average age was 57.6 ± 13.9 years. The average daily step count was 4,488 ± 2,869 steps per day among the total sample. The average time to complete the TUG and L Test among the entire sample was 13.3 ± 5.6 and 30.2 ± 12.9 seconds, respectively (Table 3.1).

The training data set included 80 out of the 106 participants (21 females and 59 males). The group's average age was 57.4 ± 13.6 years. The average daily step count among the training sample was 4,385 ± 2,923 steps per day. The average time to complete the TUG and L Test among the training sample was 13.5 ± 8.3 and 30.9 ± 14.0 seconds, respectively (Table 3.1).

The testing data set included 26 out of the 106 participants (6 females and 20 males). The group's average age was 58.2 ± 15.1 years. The average daily step count was 4,806 ± 2,724 steps per day among the testing sample. The average time to complete the TUG and L Test among the testing sample was 13.0 ± 4.7 and 28.2 ± 8.7 seconds, respectively (Table 3.1).

Model Development

Beta coefficients (β) indicating the strength and direction of the relationship between each predictor variable and the outcome variable (daily step count) were calculated via LASSO regression. The LASSO model identified the following predictor variables and their corresponding estimated β coefficients: age (β = -8.33), BMI (β = -0.10), T2D diagnosis (β = -425.68), TUG Test completion time (β = -154.98). The remaining variables had their coefficients shrunk to zero, indicating their removal from the model. The model coefficients and intercept

value are displayed in Table 3.2 and Equation 2. The following equation was established to predict step count based on the β values predicted from the LASSO model:

$$SC = 7169.49 + (-8.33) \cdot Age + (-0.10) \cdot BMI + (-425.68) \cdot T2D + (-154.98) \cdot TUG$$

Equation 2

where *SC* represents predicted daily step count and *TUG* represents TUG Test completion time.

Model Evaluation

The relationship between the actual versus predicted daily step count values is presented in Figure 3.2. For predicting daily step count, evaluation of the LASSO model in the testing set indicated a RMSE of 2,294 steps and a moderately high correlation (r = 0.60). The paired samples t-test was not statistically significant at the $p < 0.05$ level, indicating no significant difference between methods ($t_{25} = 0.74$, $p = 0.461$) (Table 3.3).

Based on the equivalence plot depicted in Figure 3.3, the predicted step count values did not fall within the equivalency range of ±10% of the actual mean daily step count values (CI: -480.67, 480.67 steps; $p > 0.05$); thus, equivalency between methods could not be claimed.

Discussion

The current study aimed to develop and cross-validate a LASSO regression prediction equation to estimate daily steps and to use the equation to evaluate the relationship between step count and the TUG Test. This is important because accurately predicting step count can provide valuable information for monitoring free-living PA among individuals with TTA. The prediction equation may also be valuable for expanding upon existing functional outcome measures and assessing the effectiveness of mobility and prosthetic rehabilitation interventions.

While a moderately high correlation was noted between the actual and predicted step counts, the prediction accuracy, as indicated by the RMSE and equivalency analyses, suggests room for improvement. It should be noted that when considering the equivalency analysis, accurately estimating daily steps within a precision of ±10% requires a larger and more representative sample size and careful consideration of data quality and variability due to the inherent noise and variability associated with step count data.

The predicted individual step counts had a notable deviation from the actual values, indicating that the LASSO model may not accurately estimate daily steps within a clinically meaningful range for individuals with TTA with exceptionally high or low actual daily steps. Further model refinements and/or consideration of additional variables may be necessary to enhance its predictive performance and improve the agreement between the predicted and actual step counts.

On an individual level, the prediction equation tended to overestimate participants with low daily steps and underestimate participants with high daily steps, which is an inevitable limitation given the nature of linear regression and the imperfect information about the participants. When estimating daily steps (or any other variable in a population), there are inherent uncertainties due to various factors. These uncertainties arise from individual differences, unobserved variables, and random fluctuations, making it challenging to precisely predict or estimate a behavior or clinical characteristic for an entire population.

An individuals' unique characteristics, preferences, and behaviors may influence their daily PA and mobility.[162] Some individuals with TTA may have inherently higher PA levels due to their lifestyle, occupation, or personal habits, while others may have lower PA levels due to comorbidities or personal constraints. While capturing these individual differences may improve

model prediction capabilities, the observation of overestimates for participants with low daily steps and underestimates for participants with high daily steps should be expected given the overall heterogeneity of this population.

One noteworthy finding from this study was the moderately high relationship between daily step count and TUG Test performance. The negative coefficient for the TUG Test time predicted by the LASSO model indicates an inverse relationship between TUG Test completion time and daily step count. Results from the LASSO model indicate that for every one-unit increase in TUG Test completion time, a decrease of 154.98 daily steps might be expected, holding other variables constant. This suggests that individuals with TTA who take longer to complete the TUG Test tend to take fewer daily steps and those who complete the TUG Test faster may be expected to have a higher daily step count. These findings are supported by previous work by Uesugi et al., who also found that higher levels of vocational and avocational PA were associated with lower TUG Test completion times in middle-aged and older adults.[163] Similarly, Paxton et al. reported that PA was inversely related to the time required to perform the TUG Test for individuals with T2D and lower extremity amputation and individuals with T2D but without an amputation.[34]

The negative relationship between the TUG Test and daily step count indicates that maintaining mobility and functional abilities after prosthesis procurement is crucial for achieving higher free-living daily steps. Individuals who can perform the TUG Test quickly, indicating better mobility and functional abilities, are more likely to engage in higher levels of PA and accumulate a more significant number of steps throughout the day.[120,164,165] As such, strength and balance exercises or rehabilitation programs targeting improvements in mobility and functional performance may positively impact daily step count and overall PA levels in this population.

Additionally, longitudinally monitoring changes in TUG Test completion time may provide valuable information regarding an individual with TTA's response to interventions and free-living daily step count. By regularly assessing and monitoring these measures, clinicians can evaluate the effectiveness of a rehabilitative paradigm and make necessary adjustments to optimize mobility outcomes.

The LASSO model also predicted that the presence of T2D may significantly relate to daily step count. The LASSO model predicted that the presence of T2D was associated with 425.68 fewer estimated daily steps compared to individuals with TTA but without T2D. The substantial negative coefficient associated with a T2D diagnosis implies that individuals with T2D and TTA tend to take fewer daily steps compared to individuals with TTA without T2D. Similar findings have been reported in the evidence base. Specifically, Miller et al. reported that individuals with lower extremity amputation secondary to dysvascular etiology, including T2D, took an average of 1,450 ± 1,309 (mean ± SD) steps per day.[166] These findings highlight the importance of promoting PA interventions specifically tailored for individuals with TTA and T2D to improve their daily step count, as regular PA is critical for managing diabetes and reducing associated health risks.[3,77]

Findings from the current study suggest that behavioral strategies aimed at promoting PA adherence should be incorporated into prosthetic rehabilitation management plans. These strategies include goal setting, self-monitoring of step counts, providing feedback and encouragement, and addressing potential barriers and motivators. Collaborative efforts between healthcare professionals and individuals with TTA and T2D can help establish realistic goals and develop approaches to overcome challenges, ultimately improving daily step count, T2D management, and overall mobility in this population.

While findings from the LASSO model provide valuable information regarding the relationship between TUG Test performance and the influence of T2D on mobility, the model's utility for predicting daily steps for participants with unusually high or low step counts requires further investigation. Predicting daily steps in advance can be challenging, especially when accounting for unusually high or low step counts. While predictive models can make use of historical data and patterns, there are inherent limitations to predicting individual behaviors with absolute precision. Future investigations should focus on elucidating human factor variables that may influence step count among individuals with TTA. Furthermore, analyzing daily measures of step counts may improve the understanding of individual variations and capture real-time fluctuations that predictive models may omit. Daily monitoring serves as a potential method for capturing the real-time dynamics of daily PA and enables the discovery of underlying patterns or triggers that might not be evident from occasional or less frequent measurements.

LASSO regression models, including the one created in this study, provide a valuable but limited perspective on explaining the free-living ambulatory characteristics of all individuals with TTA. While the TUG Test completion time, age, BMI, and T2D status variables included in the model provide clinically relevant information and appear to be associated with daily step count among individuals with TTA, it should be acknowledged that other factors can also contribute to individual behaviors and may strengthen the prediction model. Human behavior is complex and influenced by various personal, environmental, and social factors, which may not be fully captured by the predictors included in the model. Among individuals with TTA, factors such as mental health, prosthesis comfort, and overall prosthesis satisfaction have been shown to influence daily step count but were not included in the current model.[76,93,167–169] This is reflected

in a study by Diment et al., where it was found that perceived prosthetic socket fit was correlated (r = 0.49) with PA levels among a sample of individuals with lower extremity amputation.[169]

In addition to these individual-level factors, the using of a linear regression model assumes a linear relationship between the predictor variables and the response variable. However, the relationship between variables may only sometimes be strictly linear. Nonlinear relationships can exist, and a linear model may not adequately capture these complexities, limiting the model's predictive ability. Furthermore, the sample size used for model building (n = 80) and validation (n = 26) may have been relatively small, which could affect the stability and generalizability of the prediction equation. Addressing these limitations through future research with larger, more diverse samples, may enhance the reliability and applicability of the equation for predicting daily step count in individuals with TTA on an individual level.

It is vital to interpret the results and limitations of the model within these frameworks. While the model provides valuable insights and explains a certain amount of variability in daily step count, it does not account for all the factors that influence human behavior. Other unmeasured variables, such as personal motivations, social support, environmental factors, and individual preferences, may also play significant roles in determining daily step count.

Therefore, it is essential to recognize the model's limitations and consider the results as part of a larger framework. Incorporating additional variables, larger sample sizes, and exploring non-linear relationships can potentially improve the model's predictive ability and provide a more comprehensive understanding of factors influencing daily step count. Future research should be conducted to explore these aspects to enhance the accuracy and applicability of predictive models in explaining and promoting behaviors related to free-living step count among individuals with TTA.

Conclusions

This study aimed to develop and validate a LASSO regression equation for predicting daily step count in a large sample of individuals with TTA in free-living conditions. Additionally, the study evaluated the relationship between step count and performance on clinical-based functional outcome measures. The findings of the study indicated a moderately strong inverse relationship between free-living daily step count and performance on the TUG Test. Individuals who took longer to complete the TUG Test tended to have a lower daily step count. This finding suggests that poorer mobility, as measured by the TUG Test, may be associated with reduced PA in individuals with TTA. Clinically, this highlights the importance of assessing mobility and balance as potential indicators of PA levels.

A moderately strong inverse relationship between daily step count and the presence of T2D was also observed. This finding emphasizes the significance of PA in managing and preventing T2D among individuals with TTA. Increasing daily step count could be a valuable target for interventions to improve glycemic control and overall health in individuals with TTA and T2D.

Despite these noteworthy findings, the model overestimated steps for individuals taking significantly lower steps than the group mean and underestimated steps for individuals taking steps significantly higher than the group mean. This suggests the equation may not accurately predict step counts in extreme cases due to unexplained variance within the sample. The exclusion of certain human factors and non-linear relationships between the dependent variable (step count) and predictors may partially explain these discrepancies. Clinicians and researchers should be aware of these limitations when using the equation to estimate step counts in

individual cases. Future investigations should focus on advanced methods for optimizing the prediction equation for individuals with TTA with very high and low daily step counts.

Table 3.1: Demographic, clinical characteristics, average daily step count, TUG, and L Test times for the full sample, training group, and testing group (mean ± SD).

Characteristic	**Value**		
	Complete (n = 106)	*Training (n = 80)*	*Testing (n = 26)*
Age	57.6 ± 13.9	57.4 ± 13.6	58.2 ± 15.1
Sex	27 Female	21 Female	6 Female
Ethnicity			
Black or African American	16	13	3
Hispanic or Latino	8	4	4
White	82	63	19
Amputation Cause			
Vascular Disease/Diabetes	54	39	15
Injury/Trauma	33	29	4
Infection (Without Diabetes)	12	7	5
Cancer/Tumor	3	2	1
Congenital/Birth	4	2	2
BMI	30.7 ± 5.8	31.1 ± 6.3	29.3 ± 3.8
Years of prosthesis utilization	12.2 ± 14.5	12.6 ± 15.0	11.0 ± 13.4
Age of current prosthesis	2.13 ± 1.9	2.1 ± 1.7	2.2 ± 2.3
Daily Step Count (steps)	4,488 ± 2,869	4,385 ± 2,923	4,806 ± 2,724
TUG Test (seconds)	13.3 ± 5.6	13.5 ± 8.3	13.0 ± 4.7
L Test (seconds)	30.2 ± 12.9	30.9 ± 14.0	28.2 ± 8.7

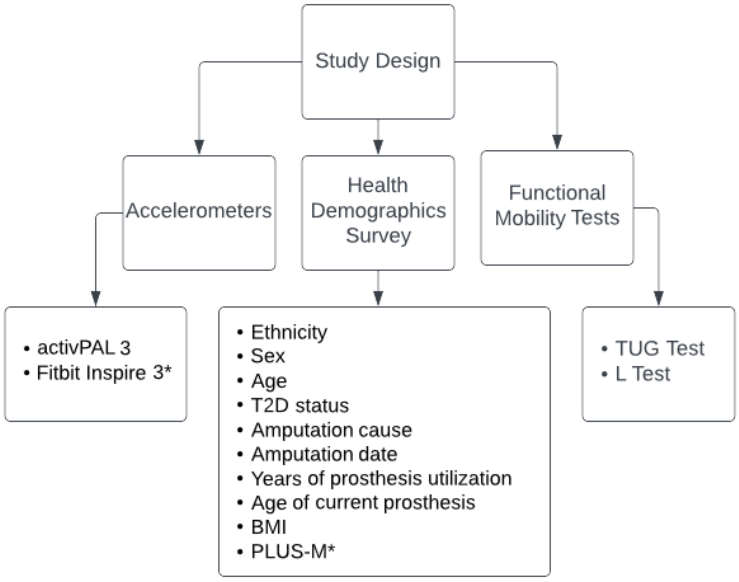
Table 3.2: LASSO regression model coefficients for predicting daily step count.

Characteristic	
Intercept (steps)	7,169
Age (years)	-8.33
Sex	0
Ethnicity	
Black or African American	0
Hispanic or Latino	0
White	0
Amputation Cause	
Vascular Disease/Diabetes	0
Injury/Trauma	0
Infection (Without Diabetes)	0
Cancer/Tumor	0
Congenital/Birth	0
Other	0
T2D Status (Yes)	-425.68
BMI	-0.10
Years of prosthesis utilization	0
Years since amputation	0
Age of current prosthesis (years)	0
TUG Test Time (seconds)	-154.98
L Test time (seconds)	0

Table 3.3: Model validation statistics for actual daily step count measured via the activPAL 3 versus LASSO model predicted daily step count.

	RMSE	**Correlation**	***t***	***p***
Actual vs. Predicted step count	2,294 steps	$r = 0.60$	0.74	= 0.41

Figure 3.1: Overview of experimental protocol.



* Data collected and utilized for future investigations and not included in prediction model.

Figure 3.2: Relationship between predicted and actual daily step count values.

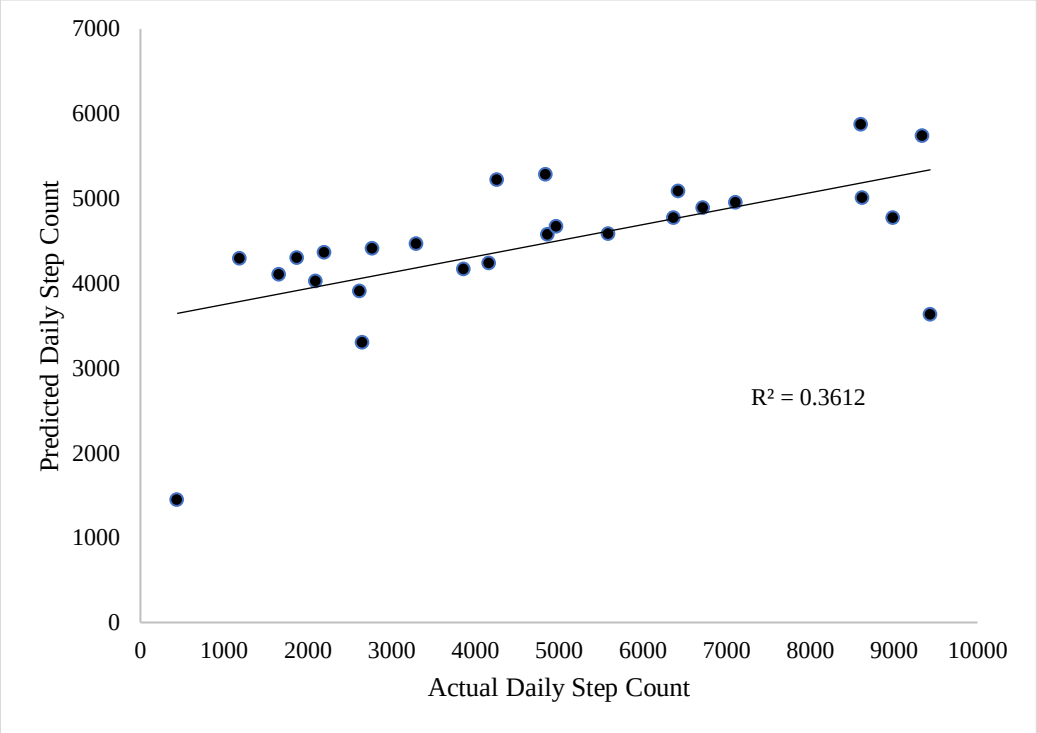
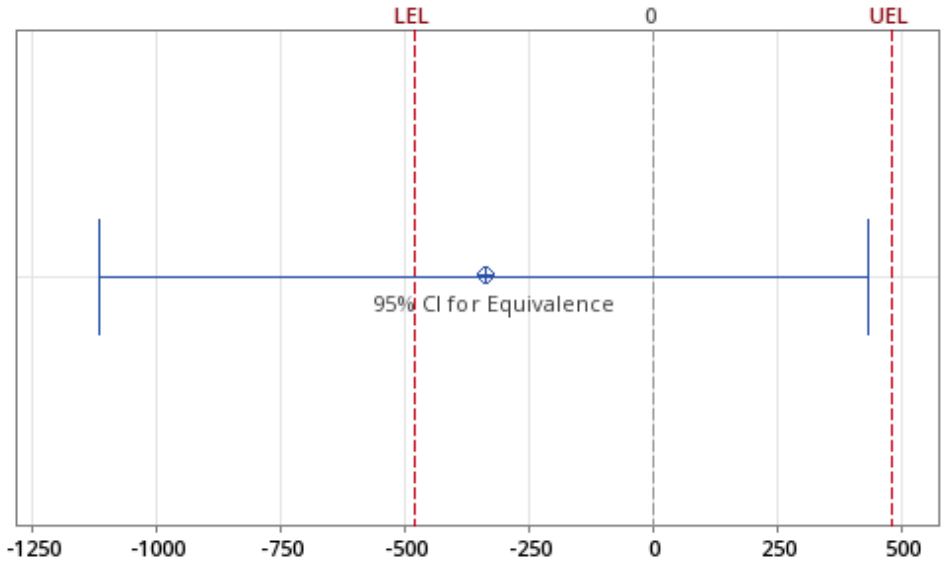


Figure 3.3: Equivalency outcomes for activPAL- and LASSO- predicted daily step count. The 95% CI for equivalence was not within the equivalence interval set at ±10% of the mean activPAL-measured steps. Therefore, equivalence cannot be claimed.



Chapter 4: Development and Cross-Validation of a Model for Predicting Daily Steps Based on PLUS-M Responses in Adults with Transtibial Amputation

Abstract

Patient reported outcome measures (PROMs) are used to evaluate mobility after prosthesis procurement, but only provide insight into one aspect of a patient's clinical presentation. Accelerometers can enhance the utility of PROMs by permitting objective, free-living measurements of mobility, thus facilitating more accurate assessment of ambulatory capacity for individuals with transtibial amputation. **Objectives:** This study sought to expand the utility of the PLUS-M by developing and validating an equation for predicting daily steps and examining the relationship between the PLUS-M and daily steps. **Methods:** Health state information was collected. Each participant completed the PLUS-M and wore an activPAL accelerometer for seven days. LASSO regression was used to build a prediction model in a training data set (n = 80). The model's validity was examined by comparing daily steps predicted by the equation with actual daily steps collected via the activPAL 3 in holdout data (n = 26). **Results:** Age, BMI, T2D status, and PLUS-M T-score were identified as significant predictors. A moderately high correlation (r = 0.77) was noted between actual vs. predicted steps. Paired samples t-test revealed a significant mean difference between methods (t_{25} = -2.09, p = 0.046) and equivalence testing revealed that equivalency could not be claimed. A RMSE of 1,380 steps was noted between methods. **Conclusion:** Higher PLUS-M T-scores were associated with greater daily steps. Additionally, the model identified an inverse relationship between age and daily step count. However, there were notable individual-level differences and overestimations of steps in the testing sample, indicating the need for further model refinement to improve prediction accuracy.

Introduction

It is estimated that 185,000 amputations occur in the United States each year and that over two million Americans are currently living with limb loss.[1,170] Amputation of the lower extremity results in impairments to mobility and the ability to traverse environmental barriers.[171,172] After amputation, a prosthesis offers an individual with lower extremity amputation a tool to reestablish mobility and independence. To optimize the likelihood of successful prosthesis utilization, a multidisciplinary team is often assembled to restore physical function and independence.

A strong, positive relationship exists between mobility and both quality of life and general satisfaction.[32] This relationship has been thoroughly investigated and described in the evidence base.[79,173,174] Suckow et al. conducted a series of interviews with 26 individuals with lower extremity amputation secondary to vascular etiologies and concluded that 65% of the participants considered mobility the primary factor in their quality of life.[79] In a second study, Pell et al. utilized the Nottingham Health Profile Questionnaire to investigate the effects of amputation on quality of life by comparing responses between individuals with and without lower extremity amputation.[174] Findings indicated that perceived level of mobility was the only component that differed significantly between the two cohorts. This suggests that proficient prosthesis utilization is of primary importance for maintaining a high quality of life.

Patient reported outcome measures (PROMs) are often administered to understand the effects of rehabilitative outcomes on mobility and satisfaction. PROMs provide insight into self-perceived performance, making them especially important for evaluating clinical decisions and intervention effectiveness. When properly selected, PROMs have the capacity to compliment clinical observations, resulting in a more comprehensive approach to patient care.

The Prosthetic Limb Users Survey of Mobility (PLUS-M) is a population-specific PROM developed for adults with lower extremity amputation who utilize a prosthesis.[16] The PLUS-M 12-Item Short Form is comprised of 12 questions which require the respondent to assign a value (1 = "unable to do" to 5 = able to do "without any difficulty") to their self-perceived ability to complete various mobility tasks. The resulting raw score is converted to a T-score and associated percentiles, where higher values indicate better mobility.[16] A T-score above or below 50 indicates that the respondent is above or below the mean with respect to the reference sample, respectively.[16] Given its ease of use and strong psychometric performance, the PLUS-M is one of the most widely used PROMs for assessing mobility among prosthesis users.[175]

PROMs, including the PLUS-M, are a key component of the patient-centered care continuum but only provide insight into one aspect of a patient's overall clinical profile. A systematic review by Campbell et al. reported that PROMs were perceived by some clinicians to reduce complex conditions to simple numeric scores while failing to consider factors including clinical expertise, experience, and other more objective measures.[176,177] Additional patient-level challenges associated with PROMs include recall limitations or, in the case of electronically administered PROMs, technological proficiency difficulties.[178] A lack of knowledge of how to incorporate PROM findings into practice and inadequate IT infrastructures also represent potential barriers to PROM implementation.[178,179] Given these challenges, the importance of interpretating PROM data in combination with physical, objective outcome measures has been stressed.[180]

Wearable technologies (wearables) designed to track daily steps represent a potential method to enhance the usefulness of PROMs, including the PLUS-M. Wearables allow objective measurements of mobility within the free-living environment. By accomplishing this, clinicians

may ascertain a more accurate picture of a prosthesis user's ambulatory profile compared to what may be self-reported in a controlled setting.

Given mobility's influence on quality of life and the significance of PROMs in rehabilitation, an enhanced understanding of the relationship between PROM scores and daily step count is warranted. This relationship merits investigation because it may enhance the utility of established PROMs while also providing clinicians with more objective information regarding free-living mobility after prosthesis procurement.

Currently, few studies have utilized wearables to assess free-living mobility among individuals with transtibial amputation (TTA). This prohibits the establishment of an equation to predict daily steps and the capability to evaluate the relationship between the PLUS-M and free-living mobility. Developing an equation to predict daily steps according to PLUS-M responses represents a potential method to ameliorate shortcomings associated with solely utilizing PROMs to assess mobility, as it may provide a more quantitative assessment of free-living mobility. Accordingly, the purpose of this study was to develop and cross-validate a prediction model for estimating free-living mobility (operationally defined as daily step count) based a participant's PLUS-M responses and health-state characteristics, and to evaluate the relationship between daily steps and PLUS-M T-score among individuals with TTA.

Materials and Methods

Participants

The daily step count prediction equation was developed and tested in a sample of adults with TTA recruited at seven prosthetic clinics located in Syracuse, NY, East Syracuse, NY, Geneva, NY, Elmira, NY, Denver, CO, Houston, TX, and Annapolis, MD. All participants

provided written informed consent in accordance with Syracuse University's Institutional Review Board approved protocol. All participants were first identified by their treating prosthetist. Inclusion/exclusion criteria were then confirmed after evaluating responses on a self-reported medical history questionnaire.

Inclusion Criteria

All participants were over the age of 18, had a unilateral TTA, and had at least three months of experience using a prosthesis prior to study enrollment. All participants were free of any additional movement disorders that may have drastically impacted mobility. This criterion was established as various movement disorders (stroke, Parkinson's disease, spinal cord injury, etc.) may be associated with decreased mobility.[149,150] Therefore, additional movement disorders that impact mobility may have confounded the prediction equation. All participants used their existing transtibial prosthesis during the study protocol.

Exclusion Criteria

Participants were excluded if they reported any additional movement disorders on the medical history questionnaire that could have significantly impacted their mobility. Participants were also excluded if they had an amputation of the contralateral limb or an amputation at any level other than transtibial.

Study Design

The protocol was completed during one encounter at the participant's local prosthetic clinic. During the encounter, participants completed a health and demographics survey, the

PLUS-M 12-Item Short Form, and two clinical-based functional mobility tests. Participants were provided with activPAL 3 and Fitbit Inspire 3 accelerometers to wear concurrently for seven full days. Data collected from the Fitbit Inspire 3 were used in a subsequent, follow up device validation study and were not used to build the prediction equation. Participants were asked to return the devices to the same location that they completed the protocol, or through the postal service via a self-addressed stamped envelope.

Demographics and Health State Metrics

A survey was used to collect information regarding each participant's ethnicity, sex, age, and type 2 diabetes (T2D) status. The same survey was used to obtain information concerning each participant's cause of amputation, amputation date, years of prosthesis utilization, and the age of their current prosthesis. The participant's height and weight were measured with a stadiometer and electronic scale, respectively, and amputation-level adjusted BMI was calculated.[151]

PLUS-M T-score, sex, ethnicity, age, T2D status, cause of amputation, time since amputation, years of prosthesis utilization, age of current prosthesis, and BMI served as predictor variables within the statistical model. The decision to include these predictor variables was made as each factor has been shown to independently influence mobility among individuals with amputation.[152–154]

The Prosthetic Limb Users Survey of Mobility

Each participant completed the PLUS-M 12 Item Short Form. Developed by Hafner et al., the PLUS-M is a self-report instrument for measuring the mobility of adult prosthesis users.[16]

The PLUS-M encompasses various aspects of mobility and functional performance, including activities related to daily living, mobility aids, community participation, and psychosocial factors. The PLUS-M assesses an individual's perceived level of difficulty or ease in performing specific tasks and activities by using a modified Likert scale.

The PLUS-M questionnaire has been used in research and clinical settings to evaluate the impact of prosthetic interventions, assess functional outcomes, and gather patient-reported data regarding mobility, prosthesis satisfaction, and quality of life.[32,129,181–183] The survey provides valuable insight into the challenges faced by individuals with amputation and helps to identify areas for improvement in prosthetic design, rehabilitation strategies, and overall patient care. The PLUS-M Short Form is scored using a standardized T-score ranging from 21.8-71.4, where higher T-scores indicate increased levels of mobility. The PLUS-M 12 Item Short Form is depicted in Figure 4.1.

activPAL Wearable

Each participant was provided with an activPAL 3 accelerometer. The activPAL 3 is a triaxial accelerometer with a sampling frequency of 20 Hz and a dynamic range of ± 2 gravitational units.[20] The device weighs 20 g (5 cm x 3.5 cm x 0.7 cm) and estimates sitting, standing, walking, and step count using proprietary algorithms based on measurements of acceleration. A previous study measuring observed versus activPAL-measured walking activity in a sample of individuals with TTA reported a sensitivity of 86% and 90.5% for the amputated and non-amputated limb, respectively.[136] These findings suggest that the activPAL is a valid tool for continuous ambulation monitoring in individuals with lower extremity amputation.

The activPAL 3 was attached to each participant's non-amputated thigh with Hypafix tape, per recommendations by Deans et al.[135] Written and verbal donning/doffing instructions were provided to each participant. Participants were instructed to wear the activPAL at all times for seven days, only removing it when in contact with water. A minimum of four valid days (three weekdays and one weekend day) of step count data were required for participants to be included in the analysis. Based on recommendations from Edwardson et al., a valid day was defined as a 24-hour period in which at least 10 hours of accelerometer wear time data were observed during typical waking hours after visually inspecting the data within the PALanalysis software suite.[158] Daily step counts from the valid days were averaged, resulting in a single step count value for each participant.

Statistical Analysis and Model Building

Statistical Assumptions

All statistical analyses were performed using R (R Core Team (2023)), Minitab (Minitab 17 Statistical Software, State College, PA), and SPSS Statistics (version 29; IBM Corp., Armonk, NY, USA). Prior to constructing the prediction model, statistical assumptions for regression were evaluated. Linear relationship and monotonicity between the dependent (daily step count) and predictor variables (PLUS-M T-score, and covariates) were evaluated by examining scatter plots.

After fitting the model, leverages and Cook's distances for each observation were examined, and unusually high values were flagged for further analysis. Residuals were then plotted against the fitted values and the degree of variability across the range of fitted values was visually assessed. A Q-Q plot of the residuals against theoretical quantiles of residuals was

established to evaluate normality, and residuals were plotted against the leverage of each observation to further identify potentially extreme values.

Model Building with Least Absolute Shrinkage and Selection Operator (LASSO) Regression

LASSO regression was utilized to develop the daily step count prediction equation and to evaluate the relationship between the PLUS-M and daily steps. PLUS-M T-scores and health-state variables from the health history questionnaire were used to predict activPAL 3-measuered daily steps. The model was fit using the following predictor variables: PLUS-M T-score, sex, ethnicity, cause of amputation, age, BMI, time since amputation, years of prosthesis utilization, age of current prosthesis, and T2D status. Dummy variables were assigned to each categorical predictor (sex (male or female), ethnicity (White, Black, Latino), cause of amputation (T2D/vascular, trauma/injury, infection (without diabetes), cancer/tumor, congenital/birth, other), and T2D status (yes or no)) using the *'as.numeric'* function in R.

To prepare the data for model training and evaluation, the sample was divided into training (n = 80) and testing (n = 26) sets using random sampling procedures in R. The '*glmnet'* package in R was used to predict daily steps among the sample in the LASSO model.

LASSO regression applies constraints on model parameters proportional to the absolute value of the magnitude of coefficients ($|\beta_j|$), effectively shrinking coefficients towards zero (Equation 1).[159] This process helps to exclude unnecessary predictor variables from the model,

Equation 1 $$\sum_{i=1}^{n}(y_i - \sum_{j} x_{ij}\beta_j)^2 + \lambda \sum_{j=1}^{p} |\beta_j|$$

facilitating model selection and parsimony. In the LASSO regression equation, *n* represents the number of data points in the dataset, *p* represents the number of features (predictors), y_i is the observed value of the dependent variable for the *i*-th data point, and x_{ij} is the *i*-th data point's

value for the *j*-th feature. The tuning parameter lambda (λ) is implemented to control the strength of the L1 regularization penalty. The λ value plays a crucial role in the shrinkage procedures of LASSO regression, as it limits the complexity of the model. A 3-fold cross-validation approach was utilized to determine the optimal λ value. The purpose of LASSO regression is to identify the variables and coefficients that minimize model prediction error and prioritize the best combined prediction of the outcome, rather than focusing on interpreting the contributions of individual variables.[184]

Model Validation

Using the testing data set (n = 26), the model's performance was assessed through Pearson's Correlation, null hypothesis significance testing (paired samples t-test), root mean squared error (RMSE), and equivalence testing.

The relationship between activPAL-measured and LASSO model-predicted (actual vs. predicted) daily step count was assessed with Pearson's Correlation.[160] Based on previously published standards, observed correlation coefficients between 0.40 and 0.59 were considered moderate. Correlation coefficients between 0.60 and 0.79 were considered moderately high, and correlations between 0.80 and 1.00 were considered high.[160]

A paired samples t-test was conducted to identify differences between the actual versus model-predicted daily step count. RMSE was calculated to further examine differences between methods.

Equivalence testing was conducted using the confidence interval method. Equivalence testing requires pre-defined upper and lower equivalence zones that permit comparisons between the values.[161] If the full 95% confidence interval range lies within the equivalence zone, it can be

concluded that the predicted and criterion values are equivalent. In the current study, the mean daily step values obtained from the two methods were determined to be statistically equivalent if the 95% confidence intervals of the predicted mean daily step counts fell within an equivalence zone set at ±10% of the mean activPAL 3 data.

Results

Participants

Descriptive characteristics for the training data, testing data, and full sample are presented as means ± SD in Table 4.1. The model training and testing samples included 106 adults with TTA (27 females and 79 males). The group average age was 57.6 ± 13.9 years. The average daily step count was 4,488 ± 2,869 steps per day among the full sample. The average PLUS-M T-score among the full sample was 53.98 ± 8.12 (Table 4.1).

The training group included 80 of the 106 participants (19 females and 61 males). The group average age was 58.03 ± 14.52 years. The average daily step count was 4,808 ± 2,967 steps per day among the training sample. The average PLUS-M T-score among the training sample was 54.18 ± 7.80 (Table 4.1).

The testing group included 26 of the 106 participants (8 females and 18 males). The group average age was 56.35 ± 12.10 years. The average daily step count was 3,503 ± 2,327 steps per day among the testing sample. The average PLUS-M T-score among the testing sample was 53.36 ± 9.17 (Table 4.1).

Model Development

Beta coefficients (β) indicating the strength and direction of the relationship between each predictor and the outcome variable (daily step count) were calculated via LASSO regression. The predictor variables and corresponding estimated β coefficients retained in the LASSO model were as follows: age (β = -27.59), BMI (β = -8.18), T2D diagnosis (β = -440.18), PLUS-M T-score (β = 65.04). The coefficients of the remaining variables were shrunk to zero, tantamount to removal from the model. The model coefficients and intercept value are displayed in Table 4.2. The following equation was established to predict step count (Equation 2):

$$SC = 3{,}089 + (-27.59) \cdot Age + (-8.18) \cdot BMI + (-440.18) \cdot T2D + 65.04 \cdot PLUSM$$

Equation 2

where *SC* represents daily step count, *T2D* represents type 2 diabetes diagnosis (yes or no), and *PLUSM* represents PLUS-M T-score.

Model Evaluation

The relationship between the actual and model-predicted step count values are plotted in Figure 4.2. For predicting daily steps, evaluation of the LASSO model in the testing set indicated a RMSE of 1,380 steps and a moderately high correlation (r = 0.77). The paired samples t-test was statistically significant at the $p < 0.05$ level, indicating a significant difference between the actual vs. predicted steps (t_{25} = -2.09, p = 0.046) (Table 4.3). Based on the equivalence plot depicted in Figure 4.3, the predicted step count values did not fall within the equivalency range of ±10% of the actual mean daily step count values (CI: -411.88, 411.88 steps; $p > 0.05$), thus, equivalency between the methods could not be claimed.

Discussion

The purpose of this study was to develop and cross-validate a prediction equation for estimating daily steps using LASSO regression. The relationship between step count, PLUS-M T-score, and health state predictors was also assessed according to the LASSO model's estimations. The findings suggest a potential application for machine learning in predicting daily steps among individuals with TTA and have implications for practitioners providing care for this population.

The model-predicted step counts exhibited a moderately high correlation with the actual step counts measured by the activPAL 3 in the testing sample. However, there were noteworthy individual-level differences between the predicted and actual step values. Specifically, the model tended to overestimate steps compared to the actual values. Furthermore, a high RMSE and a lack of equivalency between the methods also suggests that further refinements are necessary to enhance the model's prediction accuracy.

Data limitations, including unaccounted variables, and inherent noise and variability associated with step count data may partially explain the incongruencies resulting from the current model and lack of equivalency noted in the equivalence test. LASSO regression relies on the available data for model training and prediction. If the training data utilized to develop the model do not adequately represent the population (i.e., all individuals with TTA), or if the predictors lack diversity, the model may not capture the full range of variability associated with daily step count. As a result, the model may suboptimally generalize to new or "unseen" data, leading to under- or overpredictions.

In LASSO regression, the predictor variables are selected based on their predictive power and less influential variables are penalized by the λ coefficient, shrinking their coefficients to zero.[184] However, given the heterogeneity of individuals with TTA, additional, unaccounted

variables or confounding factors that influence daily steps may have been excluded from the model. These excluded predictors add noise and reduce the variance explained by the model, which may result in overestimates. Potential explanations for this phenomenon may include (1) discrepancies in the baseline PA levels between the testing and training data (i.e., the participants included in the training data were more physically active than individuals in the testing data), (2) the values of the included predictors differ (i.e., the testing data was comprised of more individuals who responded favorably on the PLUS-M), or (3) the relationships with the included predictors differ (i.e., diabetes affected steps more strongly among individuals in the holdout data vs. the training data).

Additional variables such as specific prosthetic componentry, social support structure, psychological status, and lifestyle factors could strengthen the model by potentially explaining additional variability within the population. Considering these additional predictors in future studies and incorporating them into the LASSO model may provide a more comprehensive understanding of the factors that influence daily steps among individuals with TTA. This may result in improved model accuracy for step predictions.

Despite these individual-level limitations, a relationship between the PLUS-M and step count was noted. In the current model, PLUS-M T-score emerged as a significant predictor of daily steps. The positive estimated coefficient ($\beta = 65.04$) predicted by the LASSO model indicates that higher PLUS-M T-scores may be associated with higher daily steps.

The PLUS-M T-score is a measure of physical function that encompasses various factors such as strength, endurance, balance, and overall mobility.[16] A higher PLUS-M T-score suggests enhanced mobility and greater functional capacity for performing daily activities.[183] The positive relationship between the PLUS-M and daily steps implies that individuals with TTA with better

perceived function may be more likely to engage in higher levels of PA. These individuals likely possess greater mobility, which may facilitate a higher daily step count.

The relationship between the PLUS-M and step count highlights the clinical significance of physical function in determining mobility outcomes after TTA and prosthesis procurement. Further, this finding also expands the PLUS-M's utility for assessing mobility in the free-living environment. By considering the PLUS-M as a predictor, practitioners can identify individuals who may have higher daily step counts and better free-living functional performance. This can result in more individualized care and more optimal rehabilitative outcomes.

Interventions that aim to improve mobility, such as targeted exercise programs, prosthetic training, and gait rehabilitation, may be particularly beneficial for individuals with lower PLUS-M T-scores.[185] Findings from the current study suggest that lower PLUS-M T-scores may be indicative of decreased daily step count. As such, personalized rehabilitation programs tailored to the specific needs and abilities of individuals with lower PLUS-M responses may improve mobility, potentially resulting in increased daily steps. Such programs should focus on muscle strengthening, improving balance and coordination, and enhancing cardiovascular fitness. By addressing the specific areas of weakness or impairment identified through the PLUS-M, practitioners can design personalized interventions that target the individual's unique needs and limitations. This personalized approach ensures that the interventions are customized to address the specific challenges and barriers faced by individuals with TTA with lower PLUS-M T-scores. These interventions can assist individuals to overcome limitations, increase their mobility, and potentially achieve higher daily step counts.

In addition to the PLUS-M, a relationship between participant age and daily steps was identified. These findings mirror previous research reporting that older adults with lower

extremity amputation experience reduced mobility, regardless of amputation etiology or level.[181,186] Specifically, Davies et al. found that individuals with a lower extremity amputation who were over the age of 50 exhibited significantly reduced community ambulatory rates compared to younger adults with lower extremity amputation. In the current study, the LASSO model-estimated β coefficient of -27.59 for age provides evidence that age and daily step count may be inversely related and that older adults with TTA may take fewer daily steps compared to their younger counterparts.

Several factors may contribute to the inverse relationship between age and daily steps observed in this study. As age advances, humans experience age-related physiological changes such as decreased muscle strength, joint mobility, and balance, which can affect one's ability to engage in PA.[187–190] Older adults may also be more likely to have comorbidities, including T2D, which can further impact their mobility and PA levels.[191] In addition to these physiological factors, older adults with TTA often face challenges related to prosthesis usage, fear of falling, or lack of social support, which can influence their willingness and ability to engage in PA while utilizing a prosthesis.[144]

The relationship between age and daily steps noted in this study has implications for clinicians involved in designing rehabilitation interventions for this population. The inverse relationship between age and daily steps in this population highlights the importance of considering age-related factors when prescribing interventions to address the specific needs and limitations of older prosthesis users. Strategies such as gait training, assistive devices, and psychological support may be beneficial in promoting PA and enhancing mobility outcomes among older adults with TTA, which may ultimately result in increased daily steps.

While carefully conducted, there are several limitations associated with this study. First, the prediction equation included a specific set of predictor variables. While the variables were selected a priori and based on previous research, there may be additional relevant variables or confounding factors that were not considered in the model. Unaccounted variables can affect the accuracy of the predictions in LASSO regression. Furthermore, the LASSO model in this study may have excluded relevant predictor variables due to the nature of the L1 penalty, which shrinks some coefficients to zero. Ultimately, the selected predictors may not fully capture the complexity and variability of mobility among all individuals with TTA, leading to potential under- or overestimation of step counts.

Second, LASSO regression assumes a linear relationship between the predictors and the outcome variable. However, this assumption may not hold true in all cases. Nonlinear relationships or interactions between variables may exist, and if unaccounted for in the model, may impact prediction accuracy. The study did not explore or include nonlinear relationships or interactions in the analysis, which may have impacted the model's prediction accuracy.

Finally, the sample size used for model building (n = 80) and validation (n = 26) may have been relatively small, which could affect the stability and generalizability of the prediction equation. Addressing these limitations through future research with larger, more diverse samples, while exploring advanced nonlinear model-building techniques may enhance the reliability and applicability of the equation for predicting daily step count in individuals with TTA on an individual level.

Conclusions

The current study represents the first attempt to develop and cross-validate a prediction equation using LASSO regression to estimate daily steps among individuals with TTA. While the model-predicted step counts exhibited a moderately high correlation with the actual (activPAL-measured) step counts, there were notable individual-level differences and overestimations of steps in the testing sample. This indicates the need for further model refinement to improve prediction accuracy.

The limitations of the study, including unaccounted variables and potential bias introduced by the exclusion of relevant predictors, highlight the complexity and variability of mobility in individuals with TTA and humans in general. Incorporating additional physical and psychosocial predictors in future studies and refining the LASSO model to accommodate nonlinear relationships may enhance the understanding of factors influencing daily steps and improve prediction accuracy, respectively.

The study revealed a significant relationship between the PLUS-M T-score and daily steps. Higher PLUS-M T-scores were associated with higher step counts, indicating that individuals with enhanced perceived function may engage in higher levels of PA. This finding underscores the importance of considering physical function when determining mobility outcomes for individuals with TTA and suggests that personalized rehabilitation programs and interventions targeting individuals with lower PLUS-M T-scores can improve mobility and increase daily step counts.

Additionally, consistent with previous research, the current study identified an inverse relationship between age and daily steps in individuals with TTA. Recognizing this negative association is crucial for healthcare professionals involved in rehabilitation and emphasizes the need to tailor interventions to address the specific needs and limitations of older prosthesis users.

Future research should include larger samples, explore advanced nonlinear model-building techniques, and consider additional variables to enhance the reliability and applicability of prediction equations for predicting daily step count in individuals with TTA. Through this, researchers and practitioners can advance the understanding of free-living mobility outcomes and design more effective interventions for individuals with TTA.

Table 4.1: Demographic, clinical characteristics, average daily step count, and PLUS-M T-score for the full sample, training group, and testing group (mean ± SD).

Characteristic	**Value**		
	Complete (n = 106)	*Training (n = 80)*	*Testing (n = 26)*
Age (years)	57.6 ± 13.9	58.0 ± 14.5	56.3 ± 12.1
Sex	27 Female	19 Female	8 Female
Ethnicity			
Black or African American	16	9	7
Hispanic or Latino	8	3	5
White	82	68	14
Amputation Cause			
Vascular Disease/Diabetes	54	38	16
Injury/Trauma	33	29	4
Infection (Without Diabetes)	12	7	5
Cancer/Tumor	3	3	0
Congenital/Birth	4	3	1
BMI	30.7 ± 5.8	30.3 ± 5.7	31.8 ± 6.1
Years of prosthesis utilization	12.2 ± 14.5	12.4 ± 14.9	11.6 ± 13.6
Age of current prosthesis	2.13 ± 1.9	1.9 ± 1.7	2.6 ± 2.3
Daily Step Count (steps)	4,488 ± 2,869	4,808 ± 2,967	3,503 ± 2,327
PLUS-M T-score	53.9 ± 8.1	54.1 ± 7.8	53.3 ± 9.1

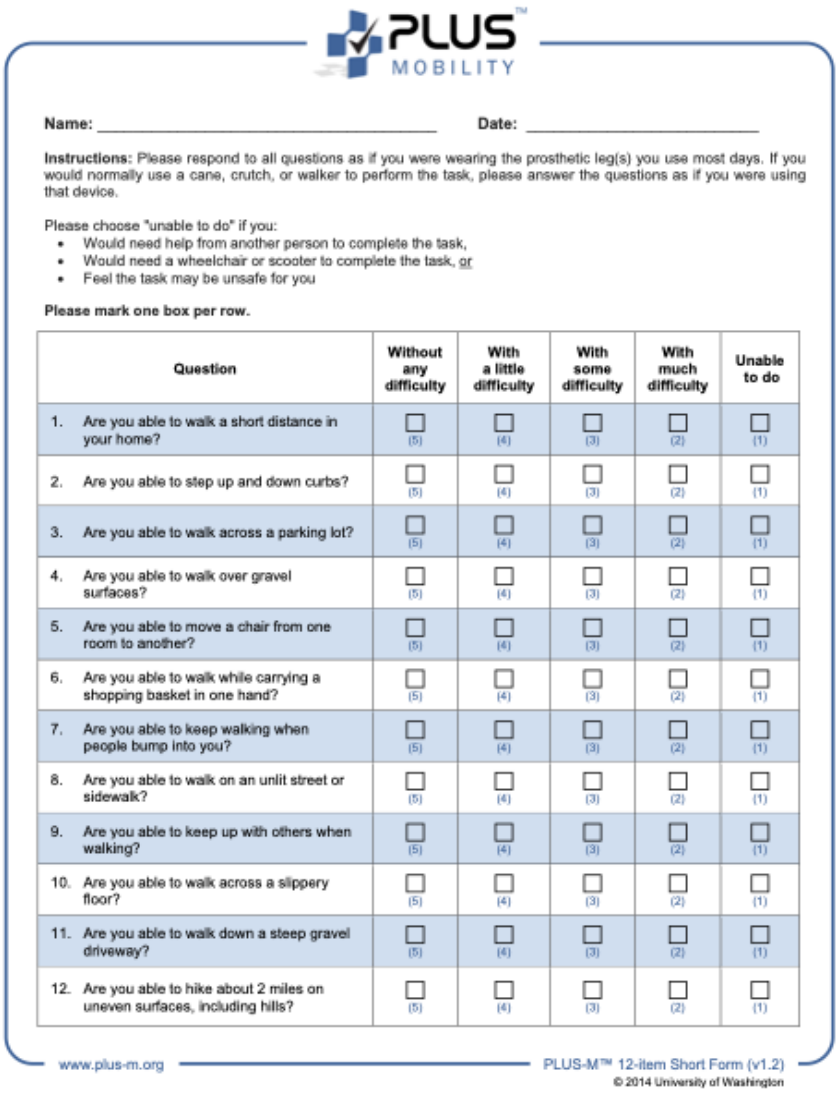
Table 4.2: LASSO Regression model coefficients for predicting daily step count.

Characteristic	
Intercept (steps)	3,089
Age (years)	-27.59
Sex	0
Ethnicity	
Black or African American	0
Hispanic or Latino	0
White	0
Amputation Cause	
Vascular Disease/Diabetes	0
Injury/Trauma	0
Infection (Without Diabetes)	0
Cancer/Tumor	0
Congenital/Birth	0
Other	0
T2D Status (Yes)	-440.15
BMI	-8.18
Years of prosthesis utilization	0
Years since amputation	0
Age of current prosthesis (years)	0
PLUS-M T-score	65.04

Table 4.3: Model validation statistics for actual daily step counts versus LASSO model predicted daily step count in the testing data.

	RMSE	Correlation	*t*	*p*
activPAL 3 vs. Predicted step count	1,380 steps	$r = 0.77$	-2.09	= 0.046

Figure 4.1: PLUS-M 12 Item Short Form



PLUS™ MOBILITY

Name: _____ **Date:** _____

Instructions: Please respond to all questions as if you were wearing the prosthetic leg(s) you use most days. If you would normally use a cane, crutch, or walker to perform the task, please answer the questions as if you were using that device.

Please choose "unable to do" if you:

- Would need help from another person to complete the task,
- Would need a wheelchair or scooter to complete the task, or
- Feel the task may be unsafe for you

Please mark one box per row.

Question	Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
1. Are you able to walk a short distance in your home?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
2. Are you able to step up and down curbs?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
3. Are you able to walk across a parking lot?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
4. Are you able to walk over gravel surfaces?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
5. Are you able to move a chair from one room to another?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
6. Are you able to walk while carrying a shopping basket in one hand?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
7. Are you able to keep walking when people bump into you?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
8. Are you able to walk on an unlit street or sidewalk?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
9. Are you able to keep up with others when walking?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
10. Are you able to walk across a slippery floor?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
11. Are you able to walk down a steep gravel driveway?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
12. Are you able to hike about 2 miles on uneven surfaces, including hills?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)

www.plus-m.org PLUS-M™ 12-item Short Form (v1.2)

Figure 4.2: Relationship between predicted and actual daily step count values.

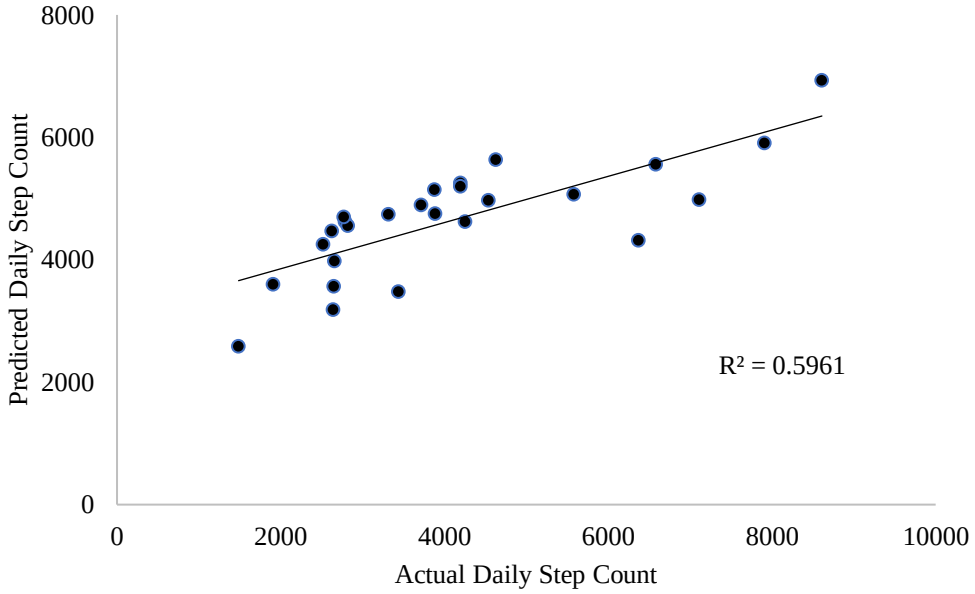
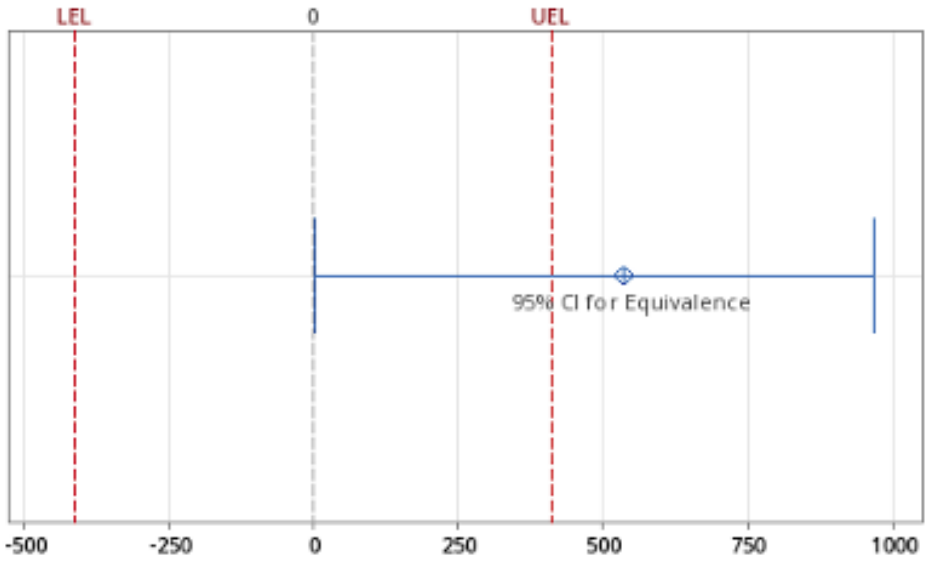


Figure 4.3: Equivalency outcomes for activPAL- and LASSO- predicted daily step count in the testing data. The 95% CI for equivalence was not within the equivalence interval set at ±10% of the mean activPAL-measured steps. Therefore, equivalency cannot be claimed.



activPAL-measured steps

Chapter 5: Validity of the Fitbit Inspire 3 to Predict Daily Steps in Adults with Transtibial Amputation

Abstract

Physical activity has significant positive effects on health. Accelerometers can be used to track daily physical activity. The Fitbit Inspire 3 is a commercially available accelerometer, but its validity for tracking mobility among individuals with transtibial amputation has not been examined. **Objective:** The purpose of this study was to evaluate the validity of the Fitbit Inspire 3 for assessing daily steps in adults with transtibial amputation. **Methods:** Participants (n = 79) completed a general health survey and were provided with a Fitbit Inspire 3 and activPAL 3 accelerometer to wear concurrently for seven days in their home environment. Relationships between the activPAL and Fitbit Inspire 3 were examined using Pearson's Correlation. Paired samples t-tests, mean absolute difference, and equivalence testing was conducted to identify mean differences between Fitbit Inspire 3- and activPAL 3-assessed daily steps. **Results:** A high correlation but significant mean difference was found between the activPAL 3 and Fitbit Inspire 3 (t_{78} = -6.83, p < 0.001, r = 0.93). The mean absolute difference between the devices was 1,347 ± 1,184 (mean ± SD) steps. On average, the Fitbit Inspire 3 predicted 1,094 ± 1,423 more daily steps than the activPAL 3. Equivalence testing revealed that equivalency could not be claimed between the devices. **Conclusions:** The Fitbit Inspire 3 overestimated physical activity by predicting higher daily step counts compared to the activPAL 3. Because of the significant mean differences and large mean absolute difference between the devices, the activPAL 3 and Fitbit Inspire 3 are not interchangeable for estimating physical activity in individuals with transtibial amputation.

Introduction

Regular physical activity (PA) has significant positive physical and mental health benefits. Meeting daily PA recommendations can result in decreased risk of metabolic diseases and all-cause mortality while improving overall quality of life.[90,192–194] Given the profound impact of PA on health and general well-being, encouraging PA after injury or disease is a primary goal of most rehabilitation interventions.[141] It is currently recommended that adults should participate in at least 150 minutes of moderate-intensity PA, 75 minutes of vigorous-intensity PA, or a combination of both, per week to attain health benefits.[81] Accelerometers are often utilized to determine the degree to which these daily PA recommendations are met. Accelerometers are simple, innocuous, wearable devices that can be used to monitor daily levels of ambulatory PA, and therefore represent feasible tools for assessing physical behaviors.[195]

Mobility and PA influence one's functional status, which is a primary determinate of independence and quality of life.[196] This is especially true among lower extremity prosthesis users, who often present with reduced mobility post-amputation. After lower extremity amputation, mobility limitations inherent with limb loss and prosthesis utilization typically manifest. Given these challenges, several studies have reported decreased PA among individuals with amputation.[96,197] Factors such as pre-amputation activity level, amputation etiology, and prosthetic component selection have been identified as strong predictors of PA after amputation.[152,198] Amputation level (i.e., transtibial vs. transfemoral) has also been shown to influence PA, as individuals with transfemoral amputation must compensate for the loss of additional degrees of freedom compared to individuals with transtibial amputation (TTA).[199]

Decreased PA among this population is problematic because it may result in increased sedentary time and the development of additional comorbidities. As such, assessing daily PA and

mobility within the home environment is a clinically relevant objective. Accurately measuring PA may help to identify an individual with TTA who may be at risk for further health deterioration after surgery. This information may also inform prosthetic rehabilitation efforts. Given these important factors, selecting the optimal PA measurement instrument should be considered. A device's cost, availability, and ease of use should be considered when selecting an accelerometer to monitor PA in special populations, including those with an amputation. In addition, the device's validity should be evaluated before interpreting data output that may be used to inform clinical decisions. The validity of a measurement represents the degree to which a device measures what it declares to measure.[200] Determining an accelerometer's validity is essential to ensure accurate elucidation of PA assessment and intervention effects.

The activPAL and Fitbit represent two accelerometers that have been used in research, clinical, and commercial settings to collect PA information. The activPAL is a triaxial accelerometer that has demonstrated reliability and validity in measurements of walking, sedentary behavior, and sleep activity in adults.[20,134] The activPAL has also been utilized in studies featuring individuals with amputation.[30,90,136] A study by Salih et al. tested the accuracy of activPAL for measuring walking activity among a sample of individuals with lower extremity amputation.[136] The authors reported that when comparing activPAL-logged and manually-assessed step counts, sensitivity levels of 90.5% and 86% were achieved for the non-amputated and amputated side, respectively. A second study by Deans et al. assessed the criterion-related validity of the activPAL for measuring various step parameters among a group of adults with unilateral lower extremity amputation.[135] In the study, the validity of the activPAL was compared with direct observation of steps taken during a series of laboratory-based tasks.

Findings supported that the activPAL was a valid instrument for detecting purposive stepping among prosthesis users within a laboratory setting.

While the activPAL has been used in various studies featuring individuals with amputation, the validity of the commercially available Fitbit Inspire 3 accelerometer has not been extensively tested in this group. The Fitbit Inspire 3 is a microelectromechanical triaxial accelerometer that can be purchased at many commercial retailers, making it more accessible to the general public than research grade devices such as the activPAL. In addition to greater accessibility, the Fitbit Inspire 3 is water resistant, less costly, and more user friendly than many research grade wearables. These features make the Fitbit a more attractive option for individuals with amputation who are interested in monitoring their daily PA.

The Fitbit has been validated in various clinical populations, but step count accuracy assessment is currently limited among individuals with TTA.[201–203] Assessing the Fitbit Inspire 3's validity among this group is important because Fitbits represent a more feasible, cost effective, and intuitive option for clinicians to assess rehabilitative outcomes outside the clinical setting. Additionally, the Fitbit may also serve as a motivation tool for a prosthesis user who is interested in enhancing their daily PA.

In consideration of these potential benefits, the purpose of this study was to investigate the validity of the Fitbit Inspire 3 for assessing free-living daily step count among individuals with TTA. To address this aim, daily step data collected via the Fitbit Inspire 3 were compared with the criterion, research-grade activPAL 3 accelerometer in adults with TTA.

Materials and Methods

Participants

A multicenter, cross-sectional design was used to investigate the validity of the Fitbit Inspire 3 to assess daily steps among individuals with TTA in their free-living environment. All participants were recruited from a network of orthotic/prosthetic clinics across the United States. Inclusion/exclusion criteria were determined after evaluating responses on a self-reported medical history questionnaire.

Inclusion Criteria

All participants were between the ages of 18 and 80 and had a unilateral TTA. All participants had used a prosthesis for at least three months prior to beginning the experimental protocol. It is estimated that 28.2% of amputations occur at the transtibial level, making it the second most common amputation type, trailing only toe/partial foot amputation (33.2%).[146–148] Thus, recruitment was limited to individuals with TTA to increase general applicability and recruitment feasibility.

Exclusion Criteria

Participants completed a medical history questionnaire to identify any additional movement disorders that may have drastically impacted their mobility (i.e., stroke, Parkinson's disease, spinal cord injury, traumatic brain injury, etc.). Any participant that self-reported a movement disorder that may have impacted their mobility was excluded. This criterion was established as various movement disorders may further perturb gait biomechanics beyond what is typically noted with prosthesis utilization, which may confound device validation efforts.[149,150]

Study Design

The experimental protocol was completed during one encounter at the clinic where the participant regularly received prosthetic care. During the encounter, participants completed a general health survey and were provided with activPAL 3 and Fitbit Inspire 3 accelerometers to wear concurrently for seven days in their home environment. Participants were asked to return the devices to the same location or send the devices via the postal service in a self-addressed stamped envelope.

Health Screening

All participants provided written informed consent in accordance with Syracuse University's Institutional Review Board approved protocol. Demographic information including ethnicity, sex, age, height (measured with a stadiometer), weight (measured with an electronic scale), and BMI were collected from each participant. Participants were then asked specific questions pertaining to their amputation and current prosthesis (cause of amputation, amputation date, years of prosthesis utilization, age of current prosthesis). Information regarding the participant's type 2 diabetes status, including date of diagnosis and treatment modality, were also collected during the initial screening.

activPAL 3 Assignment

Each participant was provided with an activPAL 3 accelerometer. The activPAL 3 is triaxial accelerometer with a sampling frequency of 20 Hz and a dynamic range of ± 2 gravitational units.[20] The device weighs 20 g (5 cm x 3.5 cm x 0.7 cm) and estimates sitting, standing, walking, and daily steps using proprietary algorithms based on measurements of acceleration. The activPAL was attached to the sound side (non-amputated) thigh with Hypafix

tape, per recommendations by Deans et al.[135] The activPAL's validity and accuracy for assessing walking activity among lower extremity prosthesis users has been evaluated and confirmed by Salih et at.[136]

Fitbit Inspire 3 Assignment

Each participant was also provided with a Fitbit Inspire 3. The Fitbit Inspire 3 is a microelectromechanical triaxial accelerometer that collects data in 60 second epochs and converts raw acceleration information to step counts using proprietary algorithms. The device weighs 23 g (14 cm x 17.6 cm x 1.4 cm) and measures step count, distance, active minutes, and sleep. The Fitbit Inspire 3 was worn on the non-dominant wrist, per the manufacturer's recommendation. Daily step count data recorded by the Fitbit Inspire 3 were extracted by logging into a research account and analyzing the software's daily step count log.

The Fitbit has been validated for overground walking among special populations. Fulk et al. reported that the Fitbit was a valid, low-cost option for measuring stepping activity in level, predictable environments for people with stroke (ICC = 0.73).[201] In a second study featuring individuals with obesity, McVeigh et al. found that the Fitbit had high agreement when compared with the ActiGraph GT3X+ (r = 0.94, ICC = 0.92) for assessing daily steps. These studies suggest that the Fitbit is a valid tool for assessing step count in these clinical populations.[21] The validity of the Fitbit Inspire 3 among individuals with TTA has not been assessed.

activPAL 3 and Fitbit Inspire 3 Wear Protocol

Written and verbal donning/doffing instructions were provided to each participant. Participants were instructed to wear both devices at all times for seven days, only removing when in contact with water. A minimum of four days was necessary for participants to be included in data analysis. activPAL 3 and Fitbit Inspire 3 data were manually matched for waking wear periods according to the activPAL 3 data using Microsoft Excel (Microsoft, Redmond, WA). Thus, only valid wear time during waking hours that were simultaneously recorded on both devices were included for statistical analyses. Once the same periods were identified across the same days, the average step count value (per day) from each device was compared. The daily step counts from at least four valid days were averaged, resulting in a single step count value for each participant for each device.

Statistical Analysis

The relationships between the activPAL 3 and Fitbit Inspire 3 were examined using Pearson's Correlation.[160] Based on previously published standards, an observed correlation coefficient between 0.40-0.59, 0.60-0.79, and 0.80-1.00 was considered moderate, moderately high, and high, respectively.[160]

A paired samples t-test was conducted to identify mean differences between the activPAL 3- and Fitbit Inspire 3-assessed step daily counts. Mean difference and mean absolute difference (MAD) were calculated to determine differences between methods.

Equivalence testing using the confidence interval method was conducted to compare activPAL 3 versus Fitbit Inspire 3 daily step counts.[204] Step values from the Fitbit Inspire 3 were determined to be statistically equivalent (at an $\alpha = 0.05$) if the 95% confidence intervals of the

mean step value fell within ±10% of the equivalence zone. The equivalence zone was set at ±10% of the mean activPAL 3 data.

A Bland-Altman plot was created using the scatter plot feature in IBM SPSS Statistics (version 29; IBM Corp., Armonk, N.Y., USA). Mean difference and upper and lower reference lines representing the 95% confidence interval for the measures were represented in the plot. All statistical analyses were conducted using SPSS, and the level of significance was defined as $p < 0.05$.

Results

A total of 79 adults with TTA (58.1 ± 14.8 years; 22 women) provided valid Fitbit Inspire 3 and activPAL 3 data; see Table 5.1 for summary demographics. A high correlation was found between the devices ($r = 0.93$) (Table 5.2). However, the paired samples t-test revealed a significant mean difference ($t_{78} = -6.83$, $p < 0.001$) (Table 5.2). The activPAL 3 predicted an average of 4,674 ± 3,081 daily steps, whilst the Fitbit Inspire 3 predicted 5,768 ± 3,750 daily steps. The mean difference and MAD between the activPAL 3 and Fitbit Inspire 3 was -1,094 ± 1,423, and 1,347 ± 1,184 steps, respectively (mean ± SD) (Table 5.2).

Equivalence testing was conducted to determine if the estimated step counts between the devices were equivalent. The results were outside of the 95% confidence interval for equivalency, indicating that equivalency could not be claimed (lower 95% confidence interval: $t_{78} = 9.75$, $p < 0.00$; upper 95% confidence interval: $t_{78} = 3.91$, $p > 0.99$) (Table 5.3). This result was expected, given the significant mean difference noted in the paired samples t-test.

Bland-Altman plots comparing activPAL 3 versus the Fitbit Inspire 3 yielded four data points outside the 95% limit of agreement (±1.96 SD) (Figure 5.1).

Discussion

Regular PA is an important component of health and wellbeing, particularly in individuals who present with decreased mobility, such as individuals with TTA.[96,205] Accurately measuring PA is fundamental for evaluating the effectiveness of rehabilitative interventions and understanding the impact of mobility on health outcomes. In this study, the validity and equivalency of two accelerometers for measuring PA were compared. The activPAL 3 and Fitbit Inspire 3 were highly correlated, indicating that both devices are related and capable of measuring similar constructs. However, the statistically significant paired samples t-test and large mean difference and MAD between the devices indicates that the activPAL 3 and Fitbit Inspire 3 may not be interchangeable for measuring free-living daily steps for individuals with TTA.

The Fitbit Inspire 3 recorded an average of 1,094 more daily steps than the activPAL 3, suggesting that it may be more sensitive when capturing steps. Accordingly, individuals with TTA using the Fitbit Inspire 3 may be at risk for overestimating their PA levels, which could have negative implications for health outcomes or rehabilitation paradigms focusing on mobility. These findings imply that while both devices can measure PA, caution should be exercised when comparing step count data between the activPAL 3 and Fitbit Inspire 3 to inform clinical decisions.

The lack of equivalency between the devices also highlights the importance of selecting the appropriate accelerometer for individuals with TTA. While the Fitbit Inspire 3 may be a more user-friendly, cost-effective option, the activPAL 3 may provide more accurate PA measurements for this group. Clinicians should consider these differences when selecting an

appropriate device for patients interested in monitoring their daily PA, as measurement inaccuracies could impact treatment outcomes.

One possible explanation for the observed differences may be attributed to each device's anatomical placement. In the current study, the Fitbit Inspire 3 was worn on the non-dominate wrist, while the activPAL 3 was worn on the thigh of the non-amputated limb. Although wrist-worn devices are popular for monitoring daily steps due to their convenience and wide availability, they may overestimate steps in certain situations, such as when the arms are moving and the lower extremities are stationary, or when an individual is handling or manipulating objects while in a seated or static standing position.[206–209] These phenomena are highlighted by Nelson et al., who reported that wrist-worn accelerometers can overestimate steps during free-living conditions by 10% to 35% when compared to devices worn on the lower body.[207] In contrast, thigh-worn devices are less prone to such inaccuracies, as the lower extremity is typically accelerating only during ambulatory activities.[134,210]

These observations are also supported by Montoye et al., who found that thigh-worn accelerometers more accurately predicted light- and moderate-intensity PA and sedentary behavior compared to wrist- and hip-worn devices.[211] In the study, participants completed three sedentary and 10 non-sedentary activities for 3-10 minutes each. Direct observation was used as the criterion measure of each activity, and a machine learning model was created for each accelerometer to predict the PA intensity category. The sensitivity and specificity were higher for the thigh-worn device compared to the wrist- and hip-worn accelerometers (> 99%). Ultimately, the thigh-worn device provided more accurate PA assessment under all conditions, while all other accelerometers overestimated PA.

In another study examining steps during completion of activities of daily living, a mean difference of 1,386 steps was noted between a wrist-worn and thigh-worn accelerometer in a sample of healthy individuals.[207] The step count discrepancy noted in the study was similar to the mean difference found in the current study (mean difference = 1,094), and further exemplifies the potential limitations of wrist-worn accelerometers and their tendency to overestimate steps.

It is important for individuals with TTA to engage in regular PA to maintain cardiovascular health, improve mobility, and prevent secondary health conditions. The accuracy of wearable activity monitors may impact the recommended intensity and duration of PA for individuals with TTA. It is well known that individuals with TTA face unique challenges pertaining to PA, including decreased mobility, increased energy expenditure, and altered gait biomechanics.[33,49,212] Individuals with TTA often walk at a slower cadence than healthy individuals, which may exacerbate discrepancies between wrist- and thigh-worn devices.[213] Hermodsson et al. reported that individuals with TTA secondary to vascular and traumatic etiology had significantly reduced walking speeds compared to healthy individuals during an overground walking test on an instrumented force platform (vascular: 0.85 ± 0.2 m/s; trauma: 0.99 ± 0.2 vs. healthy: 1.42 ± 0.2 m/s).[213] Given the decreased gait velocities exhibited by individuals with TTA, selecting an accelerometer that is capable of capturing slower movement signals is essential. The activPAL has been shown to be superior for capturing steps performed at a slower cadence, which may make it a more accurate option for tracking steps in individuals with TTA.[214] Specifically, Kanoun investigated the activPAL's accuracy for capturing steps during slow walking determined that the activPAL underestimated steps taken by less than 1% at 0.67, 0.90, and 1.33 m/s^{-1} and by 3.5% at 0.45 m/s^{-1}.[214] Given the slower walking speeds

common among individuals with TTA, these findings may further explain the significant mean differences observed in the current study.

Despite the significant mean differences, the devices were highly correlated. As such, decreasing the sensitivity of the Fitbit Inspire 3's proprietary step count algorithm may theoretically result in a more accurate daily step count estimation in individuals with TTA. Future research in this area should be focused on examining the sensitivity of the Fitbit Inspire 3 for tracking steps in this population.

Overall, the findings of this study suggest that individuals with TTA should be cautious when selecting and interpreting data from commercially available wearable activity monitors. Although these devices can be valuable tools for monitoring PA and tracking mobility progress, inter-device comparisons may be nuanced and not always provide accurate and/or interchangeable data. These limitations should be carefully considered before selecting the most appropriate option for clinical populations. This study highlights the importance of acknowledging the incongruities between commercially available and research-grade accelerometers.

Although carefully conducted, there are noteworthy limitations to the current study. One potential limitation is that the sample was only comprised of individuals with TTA. Future studies featuring individuals with amputations at additional levels (transfemoral, hip disarticulation, etc.) are needed to determine the accuracy and equivalency of the activPAL 3 and Fitbit Inspire 3 for more diverse populations. Additionally, the study did not explore the potential factors that could contribute to the differences in step count estimates between the two devices, such as differences in placement, attachment, or algorithm sensitivity. Future studies should be conducted to examine these factors.

Conclusions

The present study provides important insights into the validity of the Fitbit Inspire 3 for estimating step count for individuals with TTA. While a strong relationship was found between the activPAL 3 and Fitbit Inspire 3, both devices may not be equivalent or interchangeable in this population. Therefore, researchers and clinicians should consider these findings when selecting a device to monitor step count for individuals with TTA.

Table 5.1: Demographic and clinical characteristics of participants (mean ± *SD*).

Characteristic	Value
Age	58.1 ± 14.8
Sex	22 Female
Ethnicity	
Asian	2
Black or African American	12
Hispanic or Latino	2
White	63
Amputation Cause	
Vascular Disease/Diabetes	39
Injury/Trauma	26
Infection (Without Diabetes)	7
Cancer/Tumor	3
Congenital/Birth	3
Other	1
BMI	30.7 ± 6.0
Years of prosthesis utilization	11.8 ± 13.9
Age of current prosthesis	2.13 ± 1.9

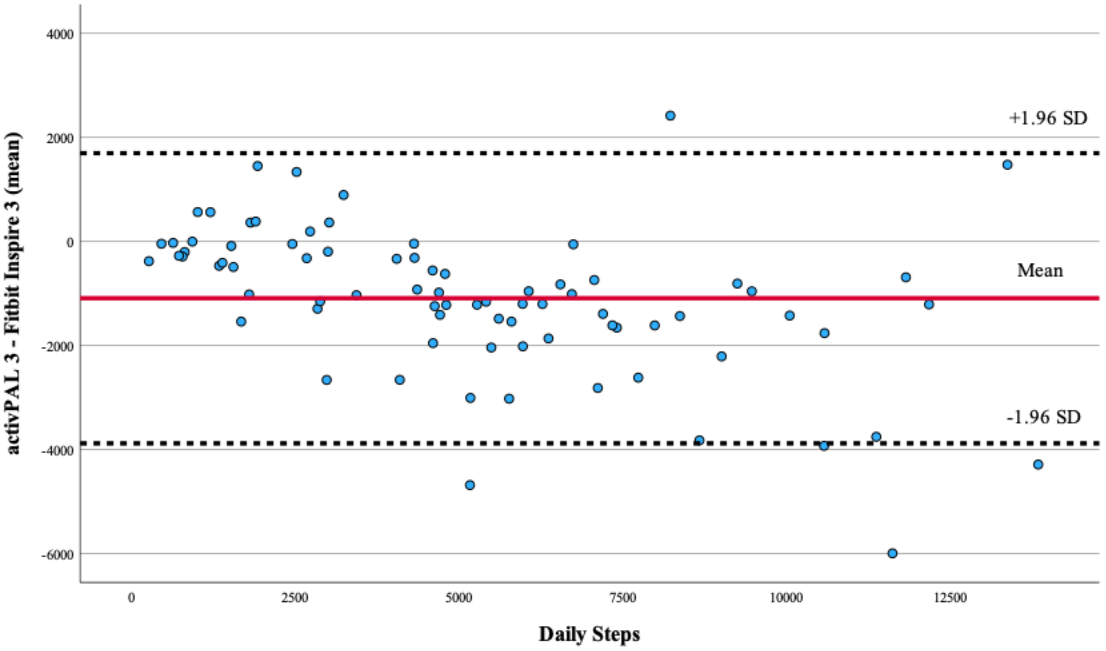
Table 5.2: Analysis results for activPAL 3 and Fitbit Inspire 3 daily step count (mean ± *SD*).

Device	Mean Step Count	Difference (steps)	Absolute Difference (steps)	Correlation	*t*	*p*
activPAL 3	4,674 ± 3,081	-1,094±1,423	1,347±1,184	0.93	-6.83	<.001
Fitbit Inspire 3	5,768 ± 3,750					

Table 5.3: Equivalency tests between activPAL 3 and Fitbit Inspire 3

	t		***p***		
	Lower	Upper	Lower	Upper	Equivalent
activPAL 3 vs. Fitbit Inspire 3	3.91	9.75	$p < 0.001$	$p > 0.99$	No

Figure 5.1: Bland-Altman plot of activPAL 3- and Fitbit Inspire 3-predicted daily step count values. Bland-Altman plots comparing activPAL versus the Fitbit Inspire 3 yielded four participant data points outside the 95% limit of agreement (±1.96 SD).



Chapter 6: Summary, Future Directions, and Conclusions

Mobility has a profound impact on independence and quality of life. As such, restoring mobility is often a primary rehabilitative concern after transtibial amputation (TTA).[215] Clinical-based functional and patient-reported outcome measures can be used to assess mobility and the effectiveness of a rehabilitation program after an individual with TTA receives a prosthesis. These traditional, clinical-based outcome measures provide a practitioner with valuable information, but their scope is typically limited to controlled environments. Wearable technologies have emerged as a means to assess free-living mobility, which can expand the utility of established mobility constructs by offering a more holistic perspective of an individual with TTA's ambulatory profile. This information can lead to a more customized approach to prosthetic rehabilitation.

This study sought to investigate the relationship between clinical-based outcome measures and daily steps in adults with TTA. This was accomplished through the development and validation of two prediction models constructed utilizing Least Absolute Shrinkage and Selection Operator (LASSO) regression with three-fold cross validation. This study also investigated the validity of the Fitbit Inspire 3 for assessing daily steps in individuals with TTA.

Two separate LASSO regression models were established to predict daily steps and evaluate the relationships between the predictors and daily step count. The predictors in Model 1 included Timed Up and Go (TUG) Test completion time, L Test completion time, sex, ethnicity, cause of amputation, age, BMI, time since amputation, years of prosthesis utilization, age of current prosthesis, and type 2 diabetes (T2D) status. The predictors in Model 2 included Prosthetic Limb User's Survey of Mobility (PLUS-M) T-score, sex, ethnicity, cause of

amputation, age, BMI, time since amputation, years of prosthesis utilization, age of current prosthesis, and T2D status. Age, BMI, and T2D status were identified as significant predictors in both models. TUG Test completion time and PLUS-M T-score were identified as significant predictors in Model 1 and Model 2, respectively.

A negative relationship between the TUG Test and daily steps was noted in Model 1. The model-estimated β coefficient of -154.98 indicated that for every unit increase in TUG Test completion time (i.e., one second increase), daily step count may be expected to decrease by an average of 154.98 steps. This suggests that individuals with TTA who take longer to complete the TUG Test are likely to take fewer daily steps than those with faster TUG Test completion times.

A positive relationship between the PLUS-M and daily steps was identified in Model 2. The positive β coefficient estimated for this predictor indicates that for every unit increase in PLUS-M T-score, daily steps are projected to increase by an average of 65.04 steps. This suggests that participants with higher PLUS-M T-scores are likely to have higher daily step counts compared to those with lower scores. In addition to these findings, a correlation of r = 0.77 was noted between the PLUS-M and daily step count, indicating a moderately high relationship between the clinic-based, patient reported outcome measure of mobility and free-living daily steps.

The presence of T2D emerged as a significant predictor in both LASSO models. β coefficients of -425.68 and -440.18 for T2D were noted in Model 1 and Model 2, respectively. This indicates that a strong, negative relationship exists between T2D and daily steps and that individuals with TTA and T2D should be expected to have lower levels of physical activity (PA). This finding may be attributed to the impact of T2D on mobility and overall health.[216,217]

On an individual level, moderately high correlations between the model-predicted and actual daily steps were found in Model 1 and Model 2. However, noteworthy individual-level differences between the predicted and actual steps were observed in both models. The LASSO equation predictions tended to overestimate steps for participants with remarkably low daily step counts and underestimate participants with remarkably high daily step counts, as any reasonable predictive equation would. Clinicians and researchers should be cognizant of these limitations when using the equation to estimate daily steps for very active or very sedentary individuals with TTA.

To improve predictions for individuals with TTA with very high daily steps, the model requires additional features or predictors that can capture information pertaining to each individual's mobility profile. This may include information pertaining to one's exercise routines, exercise frequency, and duration of each exercise session; all of which may provide valuable insight into one's PA levels.[218] Additionally, measuring caloric expenditure through metabolic rate assessment and heart rate monitoring may also provide insight into how much energy one is exerting through PA. Additional objective measures of physical fitness such as maximum oxygen uptake (VO_2 max) or performance in endurance tests may also help identify highly active individuals and better inform the prediction model specific to individuals taking significantly more steps than the mean.[219]

To improve predictions for individuals with TTA with very low daily steps, variables such as sitting time and screen time may be useful for identifying inactive individuals. Environmental factors including access to parks, recreational facilities, and walkable neighborhoods may also influence PA, and could add valuable information to the prediction equation and help distinguish individuals who may be less physically active. This information

may better inform the prediction model specific to individuals taking significantly less steps than the mean.

The validity of the Fitbit Inspire 3 for assessing daily steps among individuals with TTA was also assessed. The Fitbit Inspire 3 is a more cost-effective, user-friendly wearable accelerometer compared to research-grade devices such as the activPAL. In the study, participants wore a Fitbit Inspire 3 and activPAL 3 concurrently for seven days. Daily step data were compared between the devices. The Fitbit Inspire 3 and the activPAL 3 were highly correlated, but a significant mean difference was observed. On average, the Fitbit Inspire 3 overestimated PA by predicting higher daily steps compared to the activPAL 3 (Fitbit Inspire 3: 5,768 ± 3,750; activPAL 3: 4,674 ± 3,081 steps). The mean absolute difference between the devices was also considerably high (MAD: 1,347 ± 1,184 steps). Consequently, the Fitbit Inspire 3 and activPAL 3 are not interchangeable for estimating PA in individuals with TTA. These findings highlight the need for further research and the development of more accurate, commercially available, population-specific tools for tracking mobility among prosthesis users.

Implications

Our findings have several implications that may influence care for individuals with TTA. The prediction models were developed using clinical-based measures and therefore provide a framework for assessing free-living mobility and daily steps for this population. By considering factors such as age, BMI, T2D status, TUG Test performance, and PLUS-M T-scores, practitioners can customize rehabilitation interventions to address a patient's specific needs and clinical profile. This personalized approach allows clinicians to design targeted exercise

programs, prosthetic modifications, and lifestyle interventions aimed at optimizing mobility outcomes.

The inverse relationship between TUG Test performance and daily steps has important clinical implications. According to our findings, longer TUG Test completion times may be associated with decreased daily steps. This suggests that individuals with TTA who take longer to complete the TUG Test may face challenges in maintaining mobility and engaging in daily PA. Difficulties in functional mobility can hinder an individual's ability to move efficiently and negatively impact PA. Consequently, these individuals may experience limitations in work participation, leisure activities, and community engagement. Rehabilitation interventions targeting balance, gait training, and functional mobility can play an essential role in improving TUG Test performance, which may subsequently translate into increased daily steps.

The relationship between the PLUS-M and daily steps also has clinical implications. The PLUS-M T-score provides valuable insight into an individual with TTA's perceived function and prosthesis satisfaction.[16] Findings from the current study imply that this satisfaction may be related to greater daily steps and that individuals who feel more confident with their prosthesis and functional level are more likely to maintain higher levels of mobility. Given this information, identifying factors that contribute to lower PLUS-M T-scores may be important for addressing potential barriers to mobility. By addressing these factors, prosthetists can enhance an individual's comfort and satisfaction with their prosthesis, which may positively influence mobility and daily step count.

Furthermore, the correlation between the PLUS-M and daily steps observed in the current study (r = 0.77) was higher than relationships reported in similar studies between other common PA-specific surveys such as the International Physical Activity Questionnaire (IPAQ) and daily

steps.[220] The strong correlation provides a foundation for setting achievable activity goals. With this information, clinicians can collaborate with individuals with TTA to establish step count goals that align with their PLUS-M T-scores, promoting gradual and realistic progress in rehabilitation. In addition, knowledge of this relationship has clinical relevance because a patient can easily complete the PLUS-M, which can now be used to provide a clinician with more objective information regarding how the T-score may relate to free-living step count. This ultimately enhances the PLUS-M's real-would relevance. As daily step count is a tangible measure of PA, clinicians can now better interpret PLUS-M T-scores in the context of a patient's actual movement patterns, allowing for more meaningful discussions and interventions.

This study also highlights the importance of managing comorbidities among individuals with TTA. In the current study, T2D status was a significant predictor of daily steps in both prediction models. This exemplifies the importance of managing T2D as part of a rehabilitation paradigm. Addressing glycemic control, promoting PA, and providing education regarding the relationship between T2D and PA may improve overall health and mobility outcomes.

Findings from this study also emphasize the significance of carefully selecting a valid tool for assessing free-living steps among individuals with TTA. While the Fitbit Inspire 3 is a cost-effective and readily available accelerometer, our findings indicate that it may not be suitable for accurately estimating steps among individuals with TTA. Clinicians and lower extremity prosthesis users should be privy to the limitations associated with commercially available devices including the Fitbit Inspire 3, which may be designed for the general public rather than lower extremity prosthesis users. While these devices may offer convenience and accessibility, they may not provide valid measurements of daily steps for individuals with TTA.

Given the unique challenges faced by individuals with TTA, specialized instruments for accurately tracking daily steps or modifications to device acceleration signal processing algorithms may be indicated. Research-grade devices can be designed and validated for tracking PA in specific, special populations, and are subjected to rigorous testing and validation procedures.[30,135] Prosthetists should consider utilizing research-grade accelerometers or other specialized tools that have been validated for use in individuals with TTA. These devices can provide more accurate and reliable step count data, enabling practitioners to make informed decisions regarding rehabilitation interventions, prosthetic componentry, and longitudinal rehabilitation progress. Additionally, employing validated tools can contribute to more robust research studies, facilitating advancements in the understanding of mobility outcomes for this population.

Future Directions

There are several directions for future research that may further enhance the understanding of the relationship between daily step count and clinical-based outcome measures among individuals with TTA. Exploring these future directions may strengthen the model's predictive ability on an individual-level and enhance the equation's clinical applicability.

Consideration of Additional Predictors

Further refinements and expansion of the LASSO prediction model are warranted to improve the prediction equation's accuracy and applicability. Consideration of additional variables that were omitted from the current model, such as prosthetic componentry, prosthesis

comfort, and overall prosthesis satisfaction may capture important elements that influence daily steps and represents an area for future research.

LASSO regression aims to reduce bias and improve prediction precision.[184] Including additional variables increases the likelihood of capturing the true relationships between the predictors and daily steps. The inclusion of additional variables may also reduce estimation bias, improving precision. Furthermore, additional variables may account for confounders, which are factors that can introduce bias in the estimated relationships between the predictors and response variable.[221] By identifying relevant confounding variables, LASSO regression can better control for these factors, potentially leading to more accurate predictions.

Advanced Non-linear Modeling Techniques

Exploring non-linear relationships between the predictors and daily steps also represents a direction for future research. In the current study, the decision to employ LASSO regression was made a priori. However, it is acknowledged that this approach assumes a linear relationship between the predictor variables and the response variable.[222] Despite this assumption, the relationship between variables may not always be strictly linear. Nonlinear relationships, interactions between predictors, and complex patterns may persist, which a linear model may not adequately capture. Future research should explore advanced modeling techniques to capture the complexity and non-linearity noted in the relationships between particular predictor variables and daily steps in individuals with TTA. Other machine learning algorithms offer promising alternatives that can handle such complexities and may provide more accurate individual-level predictions in future studies.

One such algorithm is the random forest, which is an ensemble learning method that combines multiple decision trees to make predictions.[223,224] Random forests are more capable of handling nonlinear relationships and interactions, allowing for more flexible data modeling.[223–225] By considering a multitude of decision trees and aggregating their predictions, random forests have the capacity to capture complex patterns and have the potential to provide more robust predictions for daily steps in individuals with TTA.

Support vector machines (SVMs) represent a second machine learning technique that should be explored in future research. SVMs are capable of modeling nonlinear relationships through the use of kernel functions, which transform the original predictor space into a higher-dimensional feature space.[226–229] This transformation enables SVMs to identify optimal decision boundaries, and may be more effective at capturing the intricate relationships between the predictors and daily steps.

In addition to these techniques, deep learning models, such as neural networks, have gained significant attention in recent years due to their ability to "learn" complex patterns and relationships in data.[230–232] Neural networks consist of multiple layers of interconnected nodes that can capture nonlinearity and interactions through their activation functions.[233] These models can automatically "learn" hierarchical representations of the predictors and potentially provide more accurate predictions of daily steps in individuals with TTA.

Comparing and contrasting the performance of different modeling techniques, including LASSO regression, random forests, SVMs, and deep learning models, can help identify the most effective approach for predicting daily step count among individuals with TTA. By evaluating the predictive accuracy, model interpretability, and ability to capture nonlinear and complex relationships, the modeling technique that best suits the data's characteristics and requirements

can be determined. Investigating these methods through future research my improve the accuracy and applicability of prediction models for daily step count estimation in individuals with TTA on an individual level.

Advanced Wearable Technologies

Advancements in wearable technologies and smartphone applications have revolutionized the way PA data are collected and monitored. These technological innovations offer new opportunities to accumulate large amounts of objective, real-time PA information. Therefore, exploring the utility of additional or novel wearable technologies for prediction model building and collecting larger, more robust data represents an area for future research.

Large datasets with many predictors and participants are essential when using advanced statistical techniques like the aforementioned machine learning models. These techniques are more effective and powerful when dealing with abundant data, which may be collected via advanced wearable technologies. Larger and more diverse datasets allow these statistical techniques to identify patterns, relationships, and hidden trends more effectively, leading to better predictions. In scenarios with limited data, it becomes more challenging to derive meaningful and reliable conclusions. By integrating additional wearable devices into future studies, more continuous and high-resolution step count data may be obtained which may improve the effectiveness of prediction models such as those mentioned previously.

In addition to step count, some wearables provide valuable insight into other important aspects of PA. For instance, devices such as the Apple Watch and ActiGraph can capture data on activity intensity, sedentary behavior, activity bouts, and sleep which may enhance the utility of

a prediction equation and offer a more comprehensive appreciation of an individual with TTA's activity profile.[234–237]

Wearables equipped with global positioning system capabilities can capture contextual information related to PA and provide data on the location and context in which PA occurs, such as outdoor walking or indoor exercise.[238–240] These features provide important information regarding environmental factors or specific situations that may influence an individual with TTA's daily step count. By integrating circumstantial data, future research may better delineate the contextual determinants of PA, allowing clinicians to tailor interventions to specific settings or circumstances.

Smartphone application development may also represent an area for future research. Smartphone applications can leverage built-in sensors, such as accelerometers and gyroscopes, to track step count and provide real-time feedback to users. Smartphone-based interventions can deliver personalized activity goals, reminders, and motivational messages to promote engagement and adherence to PA recommendations. Additionally, these applications can integrate social networking features, allowing individuals with TTA to connect with peers, share progress, and receive social support, further enhancing their motivation and engagement in PA.[241] Information obtained from these applications may be used to refine prediction equations, which may improve validity and reliability. These advancements have the potential to improve interventions, promote engagement in PA, and ultimately enhance the understanding of daily step count in individuals with TTA.

Conclusions

Mobility plays an important role in the independence and overall quality of life for individuals with TTA. Therefore, restoring mobility is a primary focus in rehabilitation after TTA. While clinical-based outcome measures are commonly used to evaluate mobility and assess the effectiveness of prosthetic rehabilitation programs, their applicability is often limited to controlled environments. The emergence of wearable technologies has provided a valuable tool for assessing free-living mobility, allowing for a more comprehensive understanding of the complexity of an individual with TTA's ambulatory profile. Machine learning prediction models may provide a framework for assessing free-living mobility and daily steps. These techniques permit personalized rehabilitation interventions based on an individual's clinical presentation and clinical-based outcome measure performance. These advancements have the potential to improve interventions, promote engagement in PA, and contribute to a better understanding of mobility outcomes for this individuals with TTA.

Appendix

Table of Contents

Syracuse University

INSTITUTIONAL REVIEW BOARD
MEMORANDUM

TO: Tiago Barreira
DATE: December 12, 2022
SUBJECT: Expedited Protocol Review - Approval of Human Participants
IRB #: 22-356
TITLE: *Development and Cross Validation of a Prediction Equation for Estimating Step Count in Individuals with Transtibial Amputation*

The above referenced protocol was reviewed by the Syracuse University Institutional Review Board for the Protection of Human Subjects (IRB) and has been given **expedited approval.** The protocol has been determined to be of no more than minimal risk and has been evaluated for the following:

1. the rights and welfare of the individual(s) under investigation;
2. appropriate methods to secure informed consent; and
3. risks and potential benefits of the investigation.

This protocol is approved as of **December 12, 2022.** An Expedited Status Report will be requested annually, until you request your study be closed.

It is important to note that federal regulations require that each participant indicate their willingness to participate through the informed consent process and be provided with a copy of the consent form. Regulations require that you keep a copy of this document for a minimum of three years after your study is closed.

Your consent form has been date stamped with the approval date. If at any time during the course of your research, a revised consent document is submitted to the IRB via an amendment, it will be stamped with the date the amendment is approved.

Formal amendment requests are required for any changes to the initially approved protocol. It is important to note that changes cannot be initiated **prior** to IRB review and approval; except when such changes are essential to eliminate apparent immediate harm to the participants. In this instance, changes must be reported to the IRB within five days. All protocol changes must be submitted on an amendment request form available on the IRB web site at: Amendment-Request-Form.doc.

Any unanticipated problems involving risks to subjects or others must be reported to the IRB within 10 working days of occurrence on the Report of Unanticipated Problems form located on the IRB website at: Report-of-Unanticipated-Problems.doc.

Thank you for your cooperation in our shared efforts to assure that the rights and welfare of people participating in research are protected.

Katherine McDonald
IRB Chair

DEPT: Exercise Science, 100 F Women's Building, Syracuse, NY 13244 **STUDENT:** Kyle Leister

Office of Research Integrity and Protections
214 Lyman Hall, 100 College Place
Syracuse, NY 13244

T: 315.443.3013
orip@syr.edu

Written Informed Consent

Principal Investigator: Tiago Barreira, PhD
Telephone: 315-443-5588
Email: tvbarrei@syr.edu
IRB Protocol #: 22-356

Protocol Title: Development and cross-validation of a prediction equation for estimating step count in individuals with transtibial amputation

Introduction of the Principal Investigator/Key Research Personnel:
My name is Kyle Leister, and I am a doctoral candidate at Syracuse University and a Certified Orthotist/Prosthetist. I am inviting you to participate in a research study that I will be conducting as part of my dissertation. This study will be conducted in collaboration with Drs. Tiago Barreira, Joon Young Kim, Sara Burke, and Victor Duenas, all of whom are researchers at Syracuse University. Ms. Morgan Ellis will also serve as a research assistant in this study. Involvement in this study is voluntary, so you may choose to participate or not. Your decision will not impact your prosthetic treatment plan in any way. This sheet will explain the study. Please feel free to ask questions about the research. Follow up questions can be asked via email (krleiste@syr.edu) or telephone (412-726-7950).

Introduction:
The purpose of this form is to provide you with information about participation in a research study and offer you the opportunity to decide whether you wish to participate. You can take as much time as you wish to decide and can ask any questions you may have now, during, or after the research is complete. Your participation is voluntary and will not impact the care that you receive at Hanger Clinic.

What is the purpose for this research study?

- After amputation, walking impacts the way you complete daily activities. Activity trackers can provide information about your ability to walk in your home. This information may be used to understand the relationship between how we measure walking ability in the clinic and how much you actually walk each day.
- Because mobility is important, better understanding of how your performance on a clinical test may translate into how much you walk each day is needed. This relationship may provide your prosthetist with more information regarding how well your treatment plan is working. The purpose of this study is to make an equation to estimate how your performance on clinic tests may be related to the number of steps you take each day.
- A second purpose of this study is to determine the accuracy of the FitBit tracker for measuring daily step count among prosthesis users. Findings from this aim may be

important because the FitBit is easier to get than trackers made for research. Because of this, the FitBit may be a better option for people who are interested in monitoring daily step count.

What will I be asked to do?

- After completing the consent form, screening questionnaire, and three mental health questionnaires, you will be asked to complete two walking tests and one self-reported questionnaire about your walking. The screening questionnaire, mental health questionnaires, walking questionnaire, and walking tests should each take 10 minutes to complete. During this section you will be asked questions about your prosthesis, cause of amputation, and overall physical and mental health. These questions will be used to help build our step prediction equation. All information will be deidentified and coded. Next, you will be provided with two different activity trackers that you will be asked to wear for 7 days. This portion of the protocol should take approximately 10 minutes to complete. The entire protocol will take approximately 60 minutes to complete. All tasks are described below:
- **The Prosthetic Limb Users Survey of Mobility:** You will be asked to complete the PLUS-M 12 Item Short Form. The PLUS-M is a survey for measuring the mobility of adults with lower limb amputation who have experience using a lower limb prosthesis**.**
- **Timed Up and Go Test:** You will be asked to complete the TUG Test. To complete the TUG test, you will be asked to sit with your back against a chair and arms resting on the chair's arms. You will then be asked upon hearing the word "go," to stand, and walk at a normal, comfortable pace to a line on the floor three meters away, turn around, return to the chair, and sit down again. You will be asked to complete this task two times.
- **L Test of Functional Mobility:** You will be asked to complete the L Test. To complete the L Test, you will be asked to will start in a seated position with your back against a chair and arms resting on the chair's arms. Upon hearing the word "go," you will be asked to stand, walk to a line three meters away, turn 90 degrees, and walk to a second line located seven meters away. You will then need to turn 180 degrees, return to the chair, and sit down again. You will be asked to complete this task two times.
- **activPAL and FitBit Wearables:** You will be provided with two wearable activity trackers. The activPAL tracker will be attached to your thigh with special, medical tape. The FitBit will be worn on your non-dominant wrist. You will be asked to wear the devices at all times for 7 days, only removing when in contact with water. Written and verbal instructions will be provided to you. After 7 days, you will be asked to mail the trackers back in a self-addressed stamped envelope which will be provided to you.

Information about your daily step count, survey responses, and your performance on the walking tests will be available to you upon request. Information about the research results will also be available once the study is completed.

What are the possible risks of participation in this research study?

Participation involves the same risks as those that you man experience when leisurely walking in your home with or without a prosthesis. Taking part in this study may involve

the following physical risks: loss of balance while completing two walking tests, increased heart rate, and physical exertion. Additional risks during the walking test may include shortness of breath and the possibility of falling. The likelihood of these risks should not be increased by participation in this study. While wearing the Fitbit and activPAL on the wrist and thigh, some skin discomfort may occur. If this happens you should remove the devices and try to wear it again on another time/day. Mr. Leister is CPR trained and will monitor your progress during the functional mobility test. Additionally, a Mr. Leister is a certified/licensed prosthetist will be available to monitor your prosthesis during walking trials.

What are the possible benefits of participation in this research study?
There will be no direct benefits to society at large in this study. However, information from this study may be used to improve clinical care. The results of this study may inform thousands of FitBit users about its accuracy to measure step count and may provide clinicians with a tool for estimating step count outside of the clinical setting.

How will my privacy be protected?
To maintain confidentiality, all electronic medical records and data collected will be maintained using an encrypted laptop and maintained on encrypted- and password-protected hard drives. Data obtained during this study will be coded. The code will be tied to a specific identifier which will be kept in a locked filing cabinet at the Syracuse University Kinesmetrics Laboratory. The data will be coded as it is collected. All data collection documents will contain only code numbers and will not have names or identifiers. The key to the code and consent forms will be stored in a locked filing cabinet in a locked office at Syracuse University (Kinesmetrics Laboratory) under the care of Mr. Leister. Only Mr. Kyle Leister, Dr. Tiago Barreira, and Dr. Joon Young Kim, Dr. Sara Burke, Dr. Victor Duenas, and Ms. Morgan Ellis will have access to these documents/files.

Organizations that may inspect and copy your information include the IRB and other representatives of this organization, as well as collaborating institutions and federal agencies that oversee human subject research. We may publish the results of this research. However, we will keep your name and other identifying information confidential. The information collected may be used for future research or distributed to another investigator for future research studies without additional consent from you.

Because this research will be conducted in a laboratory or clinical setting, there are limitations to the protection of your privacy and the confidentiality of the data collected. All data collection will occur in a private room within your clinic or at the Kinesmetrics Laboratory. Data obtained from this study will not be transferred to other institutions and will remain on a single laptop and encrypted hard drive.

Will I receive compensation for participation?
If you complete the entire experimental protocol (approximately 45 minutes in clinic, followed by 7 days of activity tracker usage in your home), you will be awarded a $75.00 gift card. The gift card will be awarded to you after you send the FitBit and activPAL back to us in the provided self-addressed stamped envelope. If you are unable to

complete the entire protocol, you will be awarded a $10.00 gift card. Gift cards will be sent to your home address in the mail.

What are my rights as a research participant?

- Your participation is voluntary.
- You may skip and/or refuse to answer any question for any reason.
- You are free to withdraw from this research study at any time without penalty.
- Your participation will not influence your treatment at Hanger Clinic.

Who may I contact with questions now, during, or after the research is complete?

- For questions, concerns or more information regarding this research you may contact Kyle Leister at krleiste@syr.edu, or at 412-726-7950. You may also contact Dr. Tiago Barreira at tvbarrei@syr.edu, or at 315-443-5588.
- If you have questions or concerns about your rights as a research participant, you may contact the Syracuse University Institutional Review Board at (315) 443-3013.

All of my questions have been answered, I am between the ages of 30 and 80, and by signing this consent form, I agree to participate in this research study. I have received a copy of this form for my personal records.

---------- **Date:** _____

Printed Name of the Participant

_____

Signature of the Participant

---------- **Date:** _____

Printed Name of the Researcher

_____

Signature of the Researcher

Participant Data Sheet

Date: ____/_____/_____

Age: _____

Sex: M F

Ethnicity:

	American Indian or Alaskan Native		Hispanic or Latino
	Asian		Native Hawaiian or Pacific Islander
	Black or African American		White

Zip Code: _____

Height: _____ inches

Mass: _____ pounds

BMI: _____

Amputation Date: _____

Cause of Amputation:

	Vascular Disease/Diabetes		Cancer/Tumor
	Injury/Trauma		Congenital/Birth
	Infection (Without Diabetes)		Other

Age of Current Prosthesis: _____

Years of Prosthesis Utilization: _____

Comorbidity Information

Type 2 Diabetes Status: _____

Date Diagnosed: _____

Treatment Modality: _____

Other Comorbidities: _____

Functional Mobility Test Scores

	TUG TEST	L TEST OF FUNCTIONAL MOBILITY
Trial 1		
Trial 2		
Trial 3		
Average		

PROM Score

PLUS-M 12 Item Short Form	
T-Score	

Activity Tracker Values

DAYS	FITBIT STEPS	ACTIVPAL STEPS
Monday		
Tuesday		
Wednesday		
Thursday		
Friday		
Saturday		
Sunday		
Average		

Prosthetic Limb Users Survey of Mobility (PLUS-M™) Version 1.0

12-item Short Form

PLUS™
Mobility Short Forms v1.0

Name: _____ **Date:** _____

Instructions: We want to know how well you can move around using your prosthetic leg. Please respond to all questions as if you were wearing the prosthesis you would normally use to perform the task.

If you choose not to do an activity because it is not safe for you to do, please choose "unable to do." If you normally use a device that helps you walk or balance (e.g., a cane, crutch, or walker) while performing the task, please answer the questions as though you were using that device. Do not answer questions as if you are sitting in a wheelchair or receiving support from another person.

Please mark one box per row.

Question	Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
1. Are you able to walk a short distance in your home?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
2. Are you able to step up and down curbs?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
3. Are you able to walk across a parking lot?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
4. Are you able to walk over gravel surfaces?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
5. Are you able to move a chair from one room to another?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
6. Are you able to walk while carrying a shopping basket in one hand?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
7. Are you able to keep walking when people bump into you?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
8. Are you able to walk on an unlit street or sidewalk?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
9. Are you able to keep up with others when walking?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
10. Are you able to walk across a slippery floor?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
11. Are you able to walk down a steep gravel driveway?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)
12. Are you able to hike about 2 miles on uneven surfaces, including hills?	☐ (5)	☐ (4)	☐ (3)	☐ (2)	☐ (1)

PLUS™
Mobility Short Forms v1.0

Scoring the PLUS-M™ 12-Item Short Form

PLUS-M™ short forms are scored with a T-score. To find the T-score, sum scores for all responses on the short form. This is the raw score. Do not use the raw score for any purpose other than to look up the T-score using the conversion table below. If any questions on the short form are unanswered, refer to the PLUS-M™ Short Form Users Guide for instructions on scoring *incomplete* short forms.

PLUS-M™ 12-item Short Form (v1.0) T-score Conversion Table

Raw Score	T-score	SE	Percentile
12	21.8	4.4	0.2%
13	25.2	3.4	0.7%
14	27.2	3.1	1.1%
15	28.7	2.9	1.6%
16	30.0	2.7	2.3%
17	31.2	2.5	3.0%
18	32.2	2.3	3.8%
19	33.2	2.2	4.6%
20	34.1	2.1	5.5%
21	34.9	2.1	6.5%
22	35.6	2.0	7.6%
23	36.4	2.0	8.6%
24	37.1	1.9	9.8%
25	37.7	1.9	11.0%
26	38.4	1.9	12.3%
27	39.0	1.9	13.6%
28	39.7	1.9	15.1%
29	40.3	1.9	16.6%
30	40.9	1.9	18.1%
31	41.5	1.9	19.8%
32	42.1	1.9	21.5%
33	42.7	1.9	23.3%
34	43.3	1.9	25.2%
35	43.9	1.9	27.2%
36	44.5	1.9	29.3%

Raw Score	T-score	SE	Percentile
37	45.2	1.9	31.5%
38	45.8	1.9	33.7%
39	46.4	1.9	36.1%
40	47.1	1.9	38.5%
41	47.7	1.9	41.1%
42	48.4	1.9	43.7%
43	49.1	2.0	46.4%
44	49.8	2.0	49.1%
45	50.5	2.0	51.9%
46	51.2	2.0	54.8%
47	52.0	2.1	57.8%
48	52.7	2.1	60.8%
49	53.6	2.1	63.9%
50	54.4	2.2	67.0%
51	55.3	2.3	70.2%
52	56.3	2.4	73.4%
53	57.3	2.5	76.7%
54	58.4	2.6	79.9%
55	59.6	2.8	83.2%
56	61.0	2.9	86.4%
57	62.5	3.1	89.5%
58	64.5	3.3	92.6%
59	67.1	3.8	95.6%
60	71.4	4.9	98.4%

Record the PLUS-M™ T-score here.

↓↓↓↓

PLUS-M™ T-score

For T-scores with standard error (SE) greater than 3.0, use of the PLUS-M™ CAT (www.plus-m.org) is recommended to obtain better measurement precision. Percentile indicates the percent of the PLUS-M™ development sample that reported lower mobility than is reflected by the corresponding T-Score. For more information on interpretation of PLUS-M™ T-scores, please refer to the PLUS-M™ Short Form Users Guide.

Syracuse University

Hanger CLINIC

VOLUNTEERS NEEDED FOR A MOBILITY STUDY

Research Purpose: To develop an equation to predict daily step count based on your performance on three clinical tests and measurements from two activity trackers.

Participation involves a survey, two mobility tests, and wearing two step trackers for 7 days. The research will occur at your local Hanger Clinic location.

Time Commitment:

● Screening: 10 min ● PLUS-M Survey: 10 min ● Mobility Tests: 10 min ● Activity Tracker Fitting: 10 min

- **Total Time Commitment: 1 clinic visit (45 minutes) + 7 days of step tracker usage in your home.**

You may qualify if you:

- Utilize a below knee prosthesis
- Have at least three months experience using a prosthesis

You may receive a gift card worth up to $75.00 as payment for full participation. Payment will be pro-rated for partial participation.

For information or to schedule a time to participate, please contact us at
(412) 726-7950 or **krleiste@syr.edu**

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- Assistant Professor of Rehabilitation Science.

Teacher Assistant, Syracuse University, Syracuse, NY, January 2021 – May 2023
- Classes Taught: EXE-385 Motor Behavior Across the Lifespan; Lab.

Research Assistant, Syracuse University, Syracuse, NY, January 2021 – May 2023
- Assist Dr. Tiago Barreira in various research objectives including study design, statistical analyses, and manuscript composition.

Certified Orthotist/Prosthetist, Hanger Clinic, Syracuse, NY, October 2020 – June 2023
- Provide high quality O&P intervention for patients with a myriad of acute and chronic pathologies on a part time (24+ hours per week) basis.

Certified Orthotist/Prosthetist, Hanger Clinic, Houston, TX, Sept. 2016 – Oct. 2020
- Provide high quality O&P intervention for patients with a myriad of acute and chronic pathologies on a full time (40+ hours per week) basis.

Prosthetic Resident, Hanger Clinic, Houston, TX, January 2018 – January 2019
- Completed year-long residency requirements to sit for American Board of Certification Prosthetics Exam.

Orthotic Resident, Hanger Clinic, Houston, TX, May 2015 – May 2016
- Completed year-long residency requirements to sit for American Board of Certification Orthotics Exam.

Research Assistant, Northwestern University Human Movement Science Department, Chicago, IL, December 2014 – May 2015
- Assist in experimental design, data collection, manuscript writing, and subject recruitment under the guidance of Keith Gordon, PhD.

PROFESSIONAL SERVICES:
- Peer Reviewer, Rehabilitation and Assistive Technologies Engineering
- Peer Reviewer, Prosthetics & Orthotics International
- Peer Reviewer, Journal of Prosthetics and Orthotics
- Peer Reviewer, Journal of Applied Biomechanics
- Peer Reviewer, Gait and Posture
- Guest Lecturer, AMPOWER Community Group, Virtual Symposium, 2021
- Guest Lecturer, Texas Women's University, Houston, TX, 2018
- Guest Lecturer, St. Joseph's Hospital, Houston, TX, 2017
- Guest Lecturer, Baylor College of Medicine, Houston, TX, 2017 – 2019
- Guest Lecturer, Physical Therapy Program, College of Health Care Professions, 2016 – 2019

MEMBERSHIPS:
- American Academy of Sports Medicine, 2021 – Current
- International Organization for Health, Sports, and Kinesiology, 2021 – Current
- American Academy of Orthotists and Prosthetists, 2013 – Current
- American Orthotic and Prosthetic Association, 2013 – Current
- Association of Children's Prosthetics and Orthotics Clinics, 2015 – Current

HONORS/AWARDS:
- International Organization for Health, Sports, and Kinesiology. Graduate Student Excellent Oral Presentation Award, 2021
- AbbVie Immunology. Scholarship, 2021

- Hanger Clinic Education Fair. Resident Research Award, 2019
- University of Houston. Graduate Tuition Fellowship, 2016 – 2019

PEER REVIEWED PUBLICATIONS:

1. **Leister KR,** Heffernan K, Miller T, Barreira TV. (May 2023). Physical activity and mental health during the COVID-19 pandemic among individuals with amputation. *Public Library of Science - ONE.* 18(5): e0283762.

2. **Leister KR**, Cilhoroz B, Rosenberg J, Brown E, Kim JY. (May 2022). Metabolic Syndrome: Operational definitions and aerobic and resistance training benefits on physical and metabolic health in children and adolescents. *Diabetes & Metabolic Syndrome: Clinical Research and Review*, 16(6).

3. **Leister KR,** Garay J, Barreira TV. (April 2022). Validity of a Novel Algorithm to Detect Bed, Wake, and Sleep Times in Adults. *Journal for the Measurement of Physical Behaviour*, 5(2), 76-84.

4. Cilhoroz B, Zaleski A, Taylor B, Fernandez A, Santos L, **Leister KR**, Thompson PD, Pescatello, LS. (August 2021). The relationship between post-exercise hypotension and heart rate variability before and after training. *Medicine & Science in Sports & Exercise*, 53(8S), 87.

5. **Leister KR**, Wurdeman SR. (April 2021). A walking bout among individuals with type 2 diabetes reveals altered foot thermodynamics associated with unilateral transtibial amputation. *Prosthetics Orthotics International*, 45(2), 178-183.

6. **Leister, KR**. (May 2018). Efficacy of lower extremity dynamic stretching orthoses for contracture management. *American Academy of Orthotist and Prosthetist Critically Appraised Topics Library.*

ABSTRACTS/PRESENTATIONS

1. **Leister KR**. (May 2023). The relationship between disability and sleep in a nationally represented sample. *The American Academy of Sports Medicine Annual Meeting*. Denver, CO. (poster)

2. **Leister KR**. (March 2022). COVID-19's impact on physical activity and mental health among individuals with amputation. *American Academy of Orthotist and Prosthetist Annual Scientific Meeting*. Atlanta, GA. (podium)

3. **Leister KR**. (June 2021). Validating a novel algorithm to detect sleep and wake times in adults. *The American College of Sports Medicine Annual Meeting.* Virtual Platform. (virtual poster)

4. Cilhoroz B, Zaleski A, Taylor B, Fernandez A, Santos L, **Leister KR**, Thompson PD, Pescatello LS. (June 2021). The relationship between post-exercise hypotension and heart

rate variability before and after training. *The American College of Sports Medicine Annual Meeting.* Virtual Platform. (virtual poster)

5. **Leister, KR**. (May 2021). Metabolic Syndrome: exercise benefits on physical and metabolic health in adults versus youth. *International Organization of Health, Sports, and Kinesiology*. Virtual Platform. 2021. (virtual podium)

6. **Leister KR**, Alimusaj M, Kaluf B. (March 2020). Clinicians interested in clinical research. *American Academy of Orthotist and Prosthetist Annual Scientific Meeting*. Chicago, IL. (panel)

7. **Leister KR.** (February 2020). Efficacy of lower extremity dynamic stretching orthoses for contracture management. *Hanger Clinic Live Directed Case Models Symposium.* Nashville, TN. (podium).

8. **Leister KR**. (September 2019). Diabetic amputee foot temperature discrepancies. *American Orthotic and Prosthetic Association National Assembly*. San Diego, CA. (podium)

9. **Leister KR**, Wurdeman S, DiBello S, Childers L. (March 2019). So, you're considering a PhD? *American Academy of Orthotist and Prosthetist Annual Scientific Meeting.* Orlando, FL. (panel)

10. **Leister KR**. (March 2019). Why do diabetic amputees succumb to contralateral amputation? An investigation of foot temperature differences. *American Academy of Orthotist and Prosthetist Annual Scientific Meeting*. Orlando, FL. (podium)

11. **Leister KR**. (February 2019). A walking bout among individuals with type 2 diabetes reveals altered foot thermodynamics associated with unilateral transtibial amputation. *Hanger Clinic Education Fair*. Las Vegas, NV. (podium)

12. **Leister KR**. (February 2019). A walking bout among individuals with type 2 diabetes reveals altered foot thermodynamics associated with unilateral transtibial amputation. *Hanger Clinic Education Fair*. Las Vegas, NV. (poster)

13. **Leister, KR**. (October 2017). Foot temperature differences in transtibial amputees and non-amputated type II diabetics. *University of Houston Health and Human Performance Research Symposium*. Houston, TX. (podium)

14. **Leister, KR.** (March 2017). Compliance monitoring in adolescent idiopathic scoliosis: a synthesis of the literature. *Association of Children's Prosthetic and Orthotics Clinic Annual Meeting.* Houston, TX. (podium)

15. **Leister, KR**. (March 2017). The effect of cleat placement on force generation in a cyclist with a transtibial amputation. *American Academy of Orthotists and Prosthetists 2017 Annual Scientific Meetin*g. Chicago, IL. 2017. (podium)

16. **Leister, KR**. (October 2016). The effect of cleat placement on force generation in a cyclist with a transtibial amputation. *University of Houston Health and Human Performance Research Symposium*. Houston, TX. (podium)

17. **Leister, KR**. (April 2016). CLOVES Syndrome: A presentation of two cases. *Association of Children's Prosthetic-Orthotic Annual Meeting*. Denver, CO. (podium)

RECENT AWARDS/FUNDING

Title: Dissertation Summer Fellowship
Agency: Syracuse University
Funding Type: Research Fellowship
Role: Doctoral Candidate
Funding Period: 5/15/2023 – 8/31/2023
Deadline: 8/31/2022 (Funded - $4,500.00)

Title: "The relationship between disability and sleep in a nationally represented sample"
Agency: Syracuse University Graduate Student Organization
Funding Type: Professional, Academic, and Creative Work Grant
Role: Principal Investigator
Deadline: 6/2/2023 (Funded – $500.00)

Title: "Development and cross validation of a prediction equation for estimating step count in individuals with transtibial amputation"
Agency: The Bernard D. and Louise C. Rostker IVMF Dissertation Research Fund
Funding Type: Dissertation Fellowship
Role: Principal Investigator
Funding Period: 10/17/2022 – 10/17/2023
Deadline: TBD (Funded – $17,150.00)

Title: Pre-Dissertation Summer Fellowship
Agency: Syracuse University
Funding Type: Research Fellowship
Role: Doctoral Student
Funding Period: 5/15/2022 – 8/31/2022
Deadline: 8/31/2022 (Funded - $4,000.00)

Title: "Physical activity and mental health during the COVID-19 pandemic among individuals with amputation"
Agency: Syracuse Graduate Student Organization
Funding Type: Travel Grant
Role: Principal Investigator
Deadline: 3/5/2022 (Funded - $500.00)

Title: "Validating a novel algorithm to detect sleep and wake times in adults"
Agency: Syracuse University School of Education Council

Funding Type: Travel Grant
Role: Principal Investigator
Deadline: 6/5/2021 (Funded - $500.00)

Title: "Foot temperature differences between individuals with type II diabetes and transtibial amputation and individuals with type II diabetes without amputation"
Agency: The Orthotic and Prosthetic Education Research Foundation (OPERF)
Funding Type: Research Fellowship
Role: Principal Investigator
Project period: 5/1/2018 - 4/30/2019
Deadline: 4/30/2019 (Funded - $5,000.00)