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Health-related profiles of people with lower limb loss

Dagmar Amtmann, PhD, Sara J. Morgan, PhD, CPO, Jiseon Kim, PhD, and Brian J. Hafner, PhD

University of Washington, Department of Rehabilitation Medicine, 1959 NE Pacific Street, Box 356490, Seattle, WA 98195

Abstract

Objective—To construct profiles of self-reported health indicators to examine differences and similarities between people with lower limb loss (LLL) and a normative sample (hereafter called the norm), and to compare health indicators between subgroups based on level and etiology of limb loss.

Design—Survey

Setting—General community

Participants—Adults with unilateral lower limb loss (n=1091) participated in this study. Eligibility criteria included LLL resulting from trauma or dysvascular complications and regular use of a prosthesis.

Interventions—Not applicable

Main Outcome Measures—Patient-Reported Outcomes Measurement Information System 29-item profile (PROMIS-29) version 1.0 measures physical function, pain interference, fatigue, sleep disturbance, anxiety, depression and satisfaction with participation in social roles. The norms are based on 5,239 individuals representative of the U.S. general population in gender, age, race, ethnicity and education.

Results—People with LLL reported statistically significantly worse physical function, pain interference and satisfaction with participation in social roles and significantly less fatigue than the

Corresponding Author: Brian J. Hafner, University of Washington, Rehabilitation Medicine, Box 356490, Seattle, WA 98195, Phone: 206-685-4048, Fax: 206-685-3244, bhafner@u.washington.edu.

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norm. People with transfemoral (i.e., above-knee) amputation significantly differed from people with transtibial (i.e., below-knee) amputation on physical function. Similarly, people with amputation due to trauma and dysvascular etiology significantly differed on physical function and satisfaction with social roles after adjusting for relevant clinical characteristics.

Conclusions—People with LLL generally report worse physical function, pain interference and satisfaction with social roles when compared to norm. People with dysvascular amputation reported worse physical function and satisfaction with social roles than people with traumatic amputation. Health indicator profiles are an efficient way of providing clinically meaningful information about numerous aspects of self-reported health in people with LLL.

Keywords

artificial limb; limb prosthesis; outcome assessment (health care); quality of life; rehabilitation

Loss of a limb has a profound impact on health indicators, including physical, mental, and emotional health. Associations between lower limb loss (LLL) and impaired functional mobility, an aspect of physical health, have been well documented.^{1–8} Limited mobility often persists in the months and years following limb amputation.^{2–4,9} LLL is also associated with other physical and mental health problems, such as pain (e.g., phantom limb,^{10,11} residuum,^{10,11} and back pain^{12,13}) and depression.¹⁰ Health indicators in people with LLL also differ by factors such as level of amputation and etiology.^{5,10,14}

Worse health outcomes are often associated with poor rehabilitation results in people with LLL.¹⁰ For example, people with LLL who experience depression also more commonly report less use of a prosthetic limb, higher perceived vulnerability, and lower self-rated overall health.¹⁰ Conversely, greater participation in social experiences is positively associated with mobility outcomes, such as walking distance.³ Assessment of health indicators in clinics is important as monitoring and addressing physical, mental and social function may improve rehabilitation outcomes in people with LLL.¹ Despite the recognized importance of physical, mental, and social issues related to the rehabilitation of people with LLL,¹⁵ health providers typically focus rehabilitation efforts on patients' physical health and may not adequately assess psychosocial functioning.¹⁶ This tendency to focus on physical recovery may be reinforced by challenges related to availability of brief and psychometrically-sound health assessment instruments that are easy for clinicians to administer, score, and interpret.^{17,18} New measurement tools developed with funding from the National Institutes of Health (NIH), such as Patient-Reported Outcomes Measurement Information System (PROMIS) instruments, allow for efficient assessment of multiple self-reported health indicators.¹⁹ Because PROMIS instruments are brief and the scores are on the same metric, they lend themselves to construction of profiles that include aspects of physical, mental and social health.¹⁹ Well established instruments, such as SF-36, also could be used to examine profiles of health indicators and the studies using such instruments have described worse health indicators in people with LLL compared to those without LLL.^{20,21} However, some domains of SF-36 and related instruments (e.g., SF-12) are different from those included in PROMIS 29. In addition, PROMIS-29 domains can be administered using computer adaptive testing, which increases the precision of the score while minimizing

respondents' burden.²² To date no studies used PROMIS measures to examine health indicators of people with LLL.

This study aimed to examine health indicator profiles in a large sample of people with LLL by comparing scores on physical function, pain interference, anxiety, depression, fatigue, sleep disturbance, and satisfaction with participation in social roles (1) between the overall sample and PROMIS normative sample (the norm) and (2) between subgroups with different levels of limb loss and etiologies of amputation. We hypothesized that (a) individuals with LLL would generally report worse health than the general United States (U.S.) population, especially on physical function, and (b) individuals with higher amputation levels and dysvascular etiology of amputation would report worse health than their peers with lower amputation levels and traumatic etiology of amputation.

Methods

Study Design

Data for this study were obtained from a cross-sectional, self-reported health survey administered to lower limb prosthesis users in the process of developing an instrument to measure mobility in people with LLL (i.e., the Prosthetic Limb Users Survey of Mobility, PLUS-M, www.plus-m.org). Surveys were administered to study participants by computer, paper, or phone, according to their preferences and included the PROMIS-29 Profile as well as self-reported demographic and clinical characteristics.

Participants

Participants were recruited across the U.S. using flyers posted in 133 private, 4 hospital, and 7 institutional clinics. Magazine advertisements, listserv postings, targeted mailings from a national clinical provider, and postings to journal, clinic, and patient organization websites were also used. All study participants were required to report that they: (1) are 18 years of age or older, (2) have a unilateral amputation below the hip and at or above the ankle resulting from trauma or dysvascular complications, (3) have no other amputations, (4) regularly use a lower limb prosthesis to walk and (5) are able to read, write, and understand English. Amputations at or above the knee were categorized as transfemoral amputations (TFA) and amputations at or above the ankle and below the knee were categorized as transtibial amputations (TTA).

For the purpose of PLUS-M development, recruitment targets were set to include a minimum of 500 people from each of the following sub-groups of people with LLL: (1) those with TTA from either traumatic or dysvascular etiologies, (2) those with TFA from either traumatic or dysvascular etiologies, (3) those with dysvascular LLL at the TTA or TFA level and (4) those with traumatic LLL at the TTA or TFA level. All participants belonged to two of these four subgroups. The subgroups were chosen as they represent the most prevalent etiologies and levels of amputation among people with LLL.^{23,24}

All study procedures were reviewed and approved by University of Washington Institutional Review Board.

Measures

Demographic and Amputation-Specific Measures—Participants were asked to provide basic demographic information including age, gender, race and ethnicity, employment status, veteran status, education and income level. In addition, participants provided information regarding amputation level and etiology, comorbid health conditions, time since amputation (in years), daily prosthesis use (in hours) and average pain intensity.

Health indicators—The PROMIS domain framework organizes the instruments into physical, mental and social health.¹⁹ PROMIS-29 Profile version 1.0 was administered to measure aspects of physical health (physical function, pain interference, fatigue, sleep disturbance), mental health (anxiety, depression) and social health (satisfaction with participation in social roles). The PROMIS item banks, on which the short forms included in PROMIS-29 are based, were developed using rigorous methodology including item response theory (IRT).¹⁹ All PROMIS instruments provide an IRT-based score on the T-metric, with a mean of 50 and a standard deviation of 10. Normative scores for each of the PROMIS-29 health domains are based on samples representative of the U.S. general population in gender, age, race, ethnicity and education.²⁵ A higher score indicates higher levels of the trait that is being measured. For instance, a higher score on depression indicates worse health, while a higher score on physical function indicates better health. With one exception the score of 50 represents the mean of the norm that is representative of the general U.S. population. The sleep disturbance instrument is centered on a population that had a greater percentage of clinical populations than was present in the norm. Thus, the score of 50 on this domains represents a mean of somewhat less healthy population.²⁶

Analyses

Demographic and clinical information for the overall sample and for the sub-groups based on etiology (i.e., trauma and dysvascular complications) and amputation level (i.e., TTA and TFA) were summarized using frequencies, means and standard deviations. Prior to statistical hypothesis testing, score distributions for the variables used in the health profiles were inspected for normality. When distributional assumptions were not supported, both parametric and non-parametric analyses were used and the results compared. Independent, two-tailed *t*-tests and Wilcoxon-Mann-Whitney tests were used for pairwise comparisons to evaluate differences in the amputation level and etiology subgroups. One-sample *t*-tests and one-sample median sign tests were used to compare the PROMIS scores between the normative sample and both the overall sample of people with LLL and subgroups defined by amputation level and etiology. Because of the sample size in this study the reporting of results of the parametric tests, such as *t*-tests, is appropriate as they are robust to violation of normality as the sample size increases.^{27–29} To adjust for relevant demographic and clinical variables we used multiple regression analyses. We fit seven multiple regression models. Eight independent variables were used in each model. The binary variables were used to indicate amputation level (0= transfemoral and 1=transtibial); etiology (0=dysvascular and 1=trauma); and gender (0=male and 1=female). Three binary variables were included to characterize the ethnicity: non-Hispanic black, Hispanic, and other ethnicity (reference group = non-Hispanic white). The years since amputation and age were used as continuous variables.

Results

Demographics

A total of 1,091 individuals with LLL completed the PROMIS-29 instrument. Sample demographics and clinical indicators are described in Table 1. The majority of the sample was male (n=768, 71%) and non-Hispanic white (n=871, 80%) with an average age of 55 years. On average, participants were 12 years post-amputation and used their prostheses 12 hours per day. Over a half of the sample had traumatic LLL (n=604, 55%) and almost two-thirds (n=705, 65%) reported LLL at the TTA level. The sample was similar to demographic estimates of people with LLL in the U.S. with respect to gender and age, but less diverse in ethnicity and race.²⁴

The demographic characteristics of the sample differ significantly based on etiology and level of amputation. People with dysvascular LLL were on average 8 years older, had their amputation about 20 years later in life, and their time since amputation was 12 years less compared to people with traumatic LLL.

In addition, more than twice as many people with traumatic LLL were employed and 20% fewer had annual incomes lower than \$25,000 compared to people with dysvascular LLL. Groups based on level of LLL were similar, although people with TFA were about 4 years younger when they had their amputation and were 15% more likely to report no comorbid conditions compared to people with TTA (Table 1).

Comparisons of health domains

The parametric and non-parametric statistical significance statistics were consistent except for 2 comparisons. PROMIS depression score for people with dysvascular etiology compared to the normative sample was found to be statistically significant using non-parametric statistics and the depression score of people with traumatic etiology compared to the normative sample was not significant using non-parametric tests, but was found significant using parametric statistic. For ease of interpretation parametric statistics with Bonferroni adjusted alpha levels³⁰ are provided (Tables 2 and 3).

Comparisons between People with LLL and the Norm

The health profile for the overall sample is shown in Figure 1, and the health profiles by amputation level and etiology are shown in Figure 2. People with LLL reported significantly different scores than the norm in four of the seven health domains assessed. Specifically, mean scores for people with LLL were about 8 points lower for physical function, 2 points lower for fatigue and satisfaction with participation in social roles, and 5 points higher for pain interference than the norm. Our sample did not significantly differ (i.e., differences less than 1 point) from the norm in reported anxiety, depression, or sleep disturbance.

All subgroups (TFA and TTA levels; traumatic and dysvascular amputation etiologies) had physical function scores between 6–12 points lower and pain interference scores 4–6 points higher than the norm. The subgroup with amputation from trauma reported significantly less anxiety, depression, and fatigue than did the norm. However, differences were relatively

small (~1, 2, and 3 points, respectively). Similarly, both subgroups defined by level of amputation reported less fatigue and satisfaction with social roles (between 1 and 2 points) compared to the norm. People with amputation from dysvascular etiology reported lower satisfaction with participation in social roles (difference of about 4 points) than the normative sample. No significant differences were found for sleep disturbance between subgroups with LLL and the normative sample (Table 2).

Comparisons between Subgroups Defined by Amputation Level and Etiology

All amputation subgroups differed significantly in physical function scores. Participants with TTA and traumatic etiologies had higher physical function than participants with TFA and dysvascular etiologies, respectively (etiology: 6 points, level: 2 points). The differences in physical function scores remained statistically significant after controlling for demographic and clinical characteristics. However, the adjusted mean difference increased from 2 to 3 points for level and decreased from 6 to 3 points for etiology (Appendix 1). The direction of the differences were maintained (i.e., people with TTA and traumatic etiologies had higher physical function than their counterparts).

Significant differences were also observed between etiology subgroups in five of the six remaining domains: anxiety, depression, fatigue, pain interference (about 2 points each), and satisfaction with social roles (4 points). For these domains, people with traumatic etiology had better health indicators than people with dysvascular etiology. However, only satisfaction with social roles remained significant after adjusting for demographic and clinical variables, with an adjusted mean difference of 2 points (Appendix 1). No further significant differences were observed between subgroups based on amputation level. In addition, no significant differences were observed between any of the subgroups for sleep disturbance (Table 3).

Discussion

The purpose of this study was to examine health indicators in a large sample of people with LLL by comparing overall and subgroup scores to the norm scores and quantifying differences between subgroups based on etiology and level of amputation. Similar to reports in previous literature,^{24,31} participants with dysvascular LLL were significantly older, had more recent limb loss, and reported a greater number of comorbidities than participants with traumatic LLL. Additionally, people with TFA had significantly longer time since limb loss and were generally healthier than people with TTA, likely because a greater proportion of people in our TTA sample had dysvascular LLL.

Consistent with our hypotheses, participants with LLL reported worse health indicators compared to the norm that represents the U.S. general population on several health domains with the biggest differences observed on physical function. Our finding that etiology was associated with more health indicators than amputation level contrasts with findings from a review that concluded that higher levels of amputation were associated with increased anxiety, social discomfort, and depression while etiology had weak or no associations with these outcomes.¹⁰

Physical Function

Pronounced differences in physical function were observed between people with LLL and the norm, and indicate that people with LLL have considerably lower self-reported physical function than the general U.S. population. Participants with LLL, in general, had physical function scores that were more than a half standard deviation (i.e., 8 points) lower than the average score for the norm. This difference in scores exceeds established minimally important differences (MIDs) estimated for physical function in people with cancer (MID: 4–6 points)³² and rheumatoid arthritis (MID: 2),³³ suggesting that this difference is clinically meaningful. Such differences in self-reported physical function between people with and without LLL are consistent with previous findings.^{1–3} Additionally, participants with TTA and traumatic etiologies had higher physical function scores than participants with TFA and dysvascular etiologies.

Pain Interference and Fatigue

Overall and subgroup scores for participants with LLL were significantly worse than the norm for pain interference, indicating that people with LLL have greater pain that interferes with participation in life activities than the general population. Differences between group scores were approximately 5 points, which are within the established MID of 4–6 points.³² Previous studies have found greater experiences of pain in people with LLL compared to people without LLL,^{1,2,34,35} and one study found that more than 90% of 255 participants with LLL reported chronic experiences with pain.¹¹ Additionally, participants with dysvascular etiology had significantly greater pain interference than people with traumatic etiology. However, neither the level of amputation or etiology were statistically significantly associated with pain interference after controlling for demographic and clinical characteristics.

Participants with LLL in our study reported less fatigue than the norm. In addition, subgroups based on level and etiology of amputation had lower fatigue scores than the norm, with the exception of the subgroup with dysvascular amputation etiology. The overall finding that fatigue is lower in people with LLL than people without LLL is contrary to results of previous research.^{1,36} It is possible that lower fatigue in people with LLL may be due to lower physical activity, however, differences reported in our study were generally small (i.e., between 1–3 points) and are unlikely to be clinically meaningful.

Social Health, Anxiety, Depression, and Sleep Disturbance

People with dysvascular LLL reported satisfaction with social roles over 4 points lower than both the norm and people with traumatic LLL. Although MID has not been estimated for this measure, an alternative and commonly used option is to use 0.5 of a standard deviation as a clinically meaningful difference,³⁷ which is 5 points for PROMIS instruments. Thus, these scores approximate a clinically meaningful difference in social role satisfaction between people with dysvascular LLL and the general population and support findings from previous research.¹⁴ Traumatic etiology was significantly associated with satisfaction with social roles after controlling for demographic and clinical characteristics, however the difference may no longer be clinically significant. The overall sample did not significantly differ from the U.S. general population in anxiety, depression, or sleep disturbance.

Overall, our results suggest that limb loss is associated with generally worse health when compared to a normative sample: physical function, satisfaction with social roles and pain interference were most negatively affected. Level of amputation is associated with worse physical function and etiology of amputation is associated with both physical function and satisfaction with social roles. However in the regression models, time since amputation was the best predictor for most health indicators in people with LLL with greater time since amputation associated with better health outcomes.

Study Limitations

The sampling strategy for this study was selected for the primary purpose of PLUS-M instrument development. As a result, the sample is not representative of the population of persons with LLL in the U.S. For example, the majority of the sample had amputation secondary to trauma whereas, in the U.S., the majority of people with LLL have amputation secondary to dysvascular etiology.^{24,38} Because people with LLL from dysvascular etiology reported worse health than people with LLL from traumatic causes in this study, it is likely that the profiles based on these data present better health and higher function than a profile based on a more representative sample. Therefore, it is possible that differences between the norms and scores of people with LLL are underestimated in this study. In addition, only English speakers were included in the study due to the limited funds. Thus the results cannot be generalized to the people with LLL with limited English proficiency.

In addition, MIDs, which assist in determining the clinical meaningfulness of statistically significant mean differences, have not been established for PROMIS instruments in people with LLL. The MIDs used to interpret data presented in this manuscript were based on those established in people with cancer³² and arthritis.³³ Thus, these MID estimates should be used with caution as they may not accurately describe MIDs for people with LLL. Further, to our knowledge, there are no established MIDs in any population for PROMIS measures of satisfaction with social roles and sleep disturbance.

Finally, pain in people with LLL often presents in ways unique to this population. People with LLL commonly experience phantom and residual limb pain,¹⁰ which cannot be assessed with a general measure of health such as PROMIS-29. The lack of specific pain measurement limits discussion on differences in pain type between subgroups of people with LLL, however, it allows for comparisons to normative sample.

Conclusions

Health indicator profiles provide clinically meaningful information and can be used to efficiently examine numerous aspects of self-reported health in people with LLL. Results suggest that people with LLL generally report worse physical function, satisfaction with social roles, and pain interference when compared to the general population. Additionally, people with dysvascular amputation report worse physical function and satisfaction with social roles than people with traumatic amputation. The large number of participants with LLL in this study is rare in the limb loss literature and strengthens these conclusions.

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Abbreviations

IRT	item response theory
LLL	lower limb loss
MID	minimal important difference
PLUS-M	Prosthetic Limb Users Survey of Mobility
PROMIS	Patient-Reported Outcomes Measurement Information System
TFA	transfemoral amputation
TTA	transtibial amputation
U.S.	United States

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Fig. 1.

PROMIS Profile-29 scores for the overall sample of people with LLL (N=1091). The bars represent the mean score in each domain. Scores above 50 indicate that the sample of people with LLL had more of the measured construct (e.g., anxiety, sleep disturbance) and scores below 50 indicate that the sample of people with LLL had less of the measured construct. 50 represents the mean of the large samples representative of the US general population, except for sleep disturbance where 50 represents a mean of a large sample that includes a slightly higher proportion of less healthy people than the general population.

Fig. 2. PROMIS Profile-29 scores for subgroups based on etiology and level of amputation. Bars represent the mean score in each domain. Scores above 50 indicate that the sample of people with LLL had more of the measured construct (e.g., anxiety, sleep disturbance) and scores below 50 indicate that the sample of people with LLL had less of the measured construct.

Sample characteristics[‡]

Table 1

	Amputation Etiology				Amputation Level	
	Overall n=1091	Trauma n=604	Dysvascular n=487	Transtibial n=705	Transfemoral n=386	
	Mean (SD) or % (N)	Mean (SD) or % (N)	Mean (SD) or % (N)	Mean (SD) or % (N)	Mean (SD) or % (N)	
Demographic characteristics						
Age at survey (years)	55.0 (13.4)	51.1 (13.8)	59.8 (11.2)***	55.4 (13.0)	54.2 (14.2)	
Gender (%)						
Male	70.6 (768)	70.1 (421)	71.3 (347)	70.9 (499)	70.1 (269)	
Female	29.4 (320)	30.0 (180)	28.8 (140)	29.1 (205)	30.0 (115)	
Race/Ethnicity						
Non-Hispanic White	80.4 (871)	81.7 (490)	78.7 (381)**	81.3 (570)	78.6 (301)	
Non-Hispanic Black	9.1 (99)	6.7 (40)	12.2 (59)	8.1 (57)	11.0 (42)	
Hispanic	6.3 (68)	6.7 (40)	5.8 (28)	6.3 (44)	6.3 (24)	
Other	4.2 (46)	5.0 (30)	3.3 (16)	4.3 (30)	4.2 (16)	
Military status						
Active Military/Veteran	20.2 (218)	18.1 (108)	22.8 (110)	19.8 (138)	21.0 (80)	
Socioeconomic characteristics						
Employment Status						
Employed	31.7 (345)	44.4 (267)	16.1 (78)***	31.6 (222)	32.0 (123)	
Retired	25.1 (273)	18.3 (110)	33.5 (163)	24.9 (175)	25.5 (98)	
On Disability	32.1 (349)	23.0 (138)	43.4 (211)	32.7 (230)	31.0 (119)	
Other	11.0 (120)	14.3 (86)	7.0 (34)	10.8 (76)	11.5 (44)	
Individual Income						
< \$25,000	48.5 (516)	40.0 (235)	58.9 (281)***	48.9 (337)	47.6 (179)	
\$25,000 – \$39,999	20.0 (213)	18.4 (108)	22.0 (105)	20.6 (142)	18.9 (71)	
\$40,000 – \$54,999	10.3 (110)	12.4 (73)	7.8 (37)	9.3 (64)	12.2 (46)	
\$55,000 – \$69,999	7.1 (76)	9.5 (56)	4.2 (20)	7.0 (48)	7.5 (28)	
70,000	14.1 (150)	19.7 (116)	7.1 (34)	14.2 (98)	13.8 (52)	

	Amputation Etiology				Amputation Level	
	Overall n=1091	Trauma n=604	Dysvascular n=487	Transfemoral n=705	Transfemoral n=386	
	Mean (SD) or % (N)	Mean (SD) or % (N)	Mean (SD) or % (N)	Mean (SD) or % (N)	Mean (SD) or % (N)	
Education						
HS graduate or less	29.4 (319)	25.8 (155)	33.7 (164)**	29.3 (206)	29.5 (113)	
Some college/tech school	38.3 (416)	37.0 (222)	39.9 (194)	40.0 (281)	35.3 (135)	
College graduate	20.3 (220)	23.0 (138)	16.9 (82)	19.8 (139)	21.2 (81)	
Advanced degree	12.1 (131)	14.2 (85)	9.5 (46)	11.0 (77)	14.1 (54)	
Amputation Characteristics						
Amputation Level						
Transfemoral	31.7 (346)	39.2 (237)	22.4 (109)***	--	--	
Knee Disarticulation	3.7 (40)	4.8 (29)	2.3 (11)	--	--	
Transfemoral	63.5 (693)	54.5 (329)	74.7 (364)	--	--	
Ankle Disarticulation	1.1 (12)	1.5 (9)	0.6 (3)	--	--	
Amputation Etiology						
Trauma	55.4 (604)	--	--	47.9 (338)	68.9 (266)***	
Dysvascular	44.6 (487)	--	--	52.1 (367)	31.1 (120)	
Age at amputation (years)	43.1 (17.6)	33.8 (15.6)	54.7 (12.4)***	44.5 (17.0)	40.6 (18.5)***	
Years since amputation	11.8 (14.0)	17.2 (16.2)	5.1 (5.5)***	10.8 (12.9)	13.6 (15.6)**	
Daily prosthesis use (hours)	12.4 (4.1)	13.4 (3.6)	11.3 (4.4)***	12.9 (3.9)	11.6 (4.4)***	
Health Characteristics						
Comorbid Health Conditions						
Asthma	8.9 (96)	9.7 (58)	7.9 (38)	9.1 (64)	8.3 (32)	
Arthritis	25.6 (276)	22.2 (132)	29.9 (144)**	26.4 (184)	24.2 (92)	
Cancer	4.3 (47)	3.0 (18)	6.0 (29)*	4.1 (29)	4.7 (18)	
Diabetes	35.6 (388)	6.3 (38)	71.9 (350)***	45.7 (322)	17.1 (66)***	
Digestive problems	5.7 (62)	4.1 (25)	7.6 (37)*	5.8 (41)	5.4 (21)	
Heart trouble	16.4 (178)	4.2 (25)	31.5 (153)***	18.2 (128)	13.0 (50)*	
HIV or AIDS	0.6 (7)	0.5 (3)	0.8 (4)	0.7 (5)	0.5 (2)	

	Amputation Etiology			Amputation Level	
	Overall n=1091	Trauma n=604	Dysvascular n=487	Transfemoral n=386	Transfemoral n=705
	Mean (SD) or % (N)	Mean (SD) or % (N)	Mean (SD) or % (N)	Mean (SD) or % (N)	Mean (SD) or % (N)
Kidney disease	7.8 (85)	0.7 (4)	16.6 (81) ***	3.1 (12) ***	
Liver Problems	1.6 (17)	1.0 (6)	2.3 (11)	2.3 (9)	
Stroke	2.7 (29)	0.8 (5)	4.9 (24) ***	2.3 (9)	
Number of Comorbid Conditions					
0	37.0 (404)	59.8 (361)	8.8 (43) ***	31.6 (223)	46.9 (181) ***
1	34.1 (372)	30.6 (185)	38.4 (187)	33.9 (239)	34.5 (133)
2	16.8 (183)	7.6 (46)	28.1 (137)	19.0 (134)	12.7 (49)
3	12.1 (132)	2.0 (12)	24.6 (120)	15.5 (109)	6.0 (23)
Average pain intensity	3.4 (2.4)	3.2 (2.4)	3.6 (2.4) *	3.4 (2.4)	3.2 (2.3)

[#] Numbers may not add to total because of missing data and percentages may total more than 100% due to rounding.

Dysvascular mean/distribution significantly different from trauma mean/distribution or TFA mean/distribution significantly different from TTA mean/distribution at:

* = $p < 0.05$;

** = $p < 0.01$;

*** = $p < 0.001$.

Table 2

Pairwise comparisons to PROMIS norms for HRQOL indicators and symptoms

Domain	Group	M	SD	Comparison value	95% CI of the difference	t	df
Physical function	overall	41.85	8.34	50.00	-8.64, -7.65	-32.23**	1087
	Transfemoral	40.54	7.56	50.00	-10.22, -8.70	-24.54**	383
	Transtibial	42.57	8.66	50.00	-8.07, -6.79	-22.78**	703
	Dysvascular	38.52	7.48	50.00	-12.15, -10.81	-33.81**	484
	Trauma	44.53	8.03	50.00	-6.11, -4.83	-16.73**	602
Anxiety	overall	49.41	9.49	50.00	-1.16, -0.03	-2.07	1089
	Transfemoral	49.76	9.60	50.00	-1.20, 0.73	-0.48	385
	Transtibial	49.21	9.42	50.00	-1.49, -0.09	-2.23	703
	Dysvascular	50.37	9.59	50.00	-0.49, 1.22	0.84	485
	Trauma	48.63	9.34	50.00	-2.11, -0.62	-3.60**	603
Depression	overall	49.29	9.31	50.00	-1.26, -0.15	-2.50	1089
	Transfemoral	49.42	9.33	50.00	-1.52, 0.35	-1.23	385
	Transtibial	49.23	9.31	50.00	-1.46, -0.08	-2.20	703
	Dysvascular	50.47	9.69	50.00	-0.40, 1.33	1.07	485
	Trauma	48.35	8.90	50.00	-2.36, -0.94	-4.55**	603
Fatigue	overall	48.47	9.37	50.00	-2.09, -0.98	-5.39**	1086
	Transfemoral	47.85	9.00	50.00	-3.05, -1.25	-4.68**	384
	Transtibial	48.80	9.56	50.00	-1.90, -0.49	-3.32**	701
	Dysvascular	49.64	8.87	50.00	-1.15, 0.44	-0.88	483
	Trauma	47.52	9.66	50.00	-3.25, -1.71	-6.30**	602
Sleep disturbance	overall	49.39	9.05	50.00	-1.15, -0.07	-2.22	1087
	Transfemoral	49.28	9.10	50.00	-1.64, 0.19	-1.55	383
	Transtibial	49.45	9.02	50.00	-1.21, 0.12	-1.61	703
	Dysvascular	49.75	9.49	50.00	-1.10, 0.60	-0.58	484
	Trauma	49.10	8.67	50.00	-1.59, -0.20	-2.54	602
Satisfaction with social roles		47.95	9.92	50.00	-2.64, -1.46	-6.81**	1089

Domain	Group	M	SD	Comparison value	95% CI of the difference	t	df
Pain interference	Transfemoral	48.09	9.33	50.00	-2.84, -0.98	-4.02**	385
	Transtibial	47.88	10.23	50.00	-2.88, -1.36	-5.50**	703
	Dysvascular	45.58	9.30	50.00	-5.25, -3.59	-10.48**	485
	Trauma	49.86	9.99	50.00	-0.93, 0.66	-0.33	603
	overall	54.83	8.91	50.00	4.30, 5.36	17.87**	1087
	Transfemoral	54.08	8.79	50.00	3.20, 4.96	9.10**	384
	Transtibial	55.24	8.96	50.00	4.58, 5.90	15.50**	702
	Dysvascular	55.74	8.76	50.00	4.95, 6.52	14.41**	483
	Trauma	54.10	8.98	50.00	3.38, 4.82	11.22**	603

Notes: We used bonferroni adjusted alpha levels of 0.01 (0.05/5) for five pairwise comparisons for each measure

** = $p < 0.01$.

Table 3
Pairwise comparisons between subgroups based on amputation level and etiology for HRQOL indicators and symptoms

Domain	Amputation Level						Amputation Etiology						t	df			
	Transfemoral			Transtibial			Dysvascular			Trauma							
	M	SD	n	M	SD	n	M	SD	n	M	SD	n					
Physical function	40.54	7.56	384	42.57	8.66	704	38.52	7.48	485	44.53	8.03	603	-3.86**	1086	-12.66**	1086	
Anxiety	49.76	9.60	386	49.21	9.42	704	50.37	9.59	486	48.63	9.34	604	0.92	1088	0.60, 2.87	3.01**	1088
Depression	49.42	9.33	386	49.23	9.31	704	50.47	9.69	486	48.35	8.90	604	0.32	1088	1.01, 3.23	3.75**	1088
Fatigue	47.85	9.00	385	48.80	9.56	702	49.64	8.87	484	47.52	9.66	603	-1.60	1085	1.01, 3.24	3.73**	1085
Sleep disturbance	49.28	9.10	384	49.45	9.02	704	49.75	9.49	485	49.10	8.67	603	-0.31	1086	-0.44, 1.73	1.17	1086
Satisfaction with social roles	48.09	9.33	386	47.88	10.23	704	45.58	9.30	486	49.86	9.99	604	0.34	1088	-5.44, -3.13	-7.26**	1088
Pain interference	54.08	8.79	385	55.24	8.96	703	55.74	8.76	484	54.10	8.98	604	-2.06	1086	0.57, 2.70	3.02**	1086

Notes: we used bonferroni adjusted alpha levels of 0.025 (0.05/2) for two pairwise comparisons for each measure

* = $p < 0.025$;

** = $p < 0.01$.

Appendix 1

Summary of the multiple regression analyses with the PROMIS-29 T-scores as dependent variables and demographic and clinical characteristics as independent variables

Dependent variable	Independent variable	Unstandardized coefficient (B)	SE B	Standardized coefficient (β)	p	R ²	Adjusted R ²
Physical function	(Intercept)	45.72	1.25	-	<.0001	0.26	0.26
	Amputation transtibial ^a	3.29	0.47	0.19	<.0001		
	Traumatic etiology ^b	3.34	0.56	0.20	<.0001		
	Female gender	-2.11	0.48	-0.12	<.0001		
	Non-Hispanic black ^c	-1.52	0.78	-0.05	0.05		
	Hispanic ^c	-2.79	0.92	-0.08	0.00		
	Other ethnicity ^c	-3.10	1.11	-0.07	0.01		
	Years since amputation	0.16	0.02	0.27	<.0001		
	Age	-0.16	0.02	-0.25	<.0001		
Anxiety	(Intercept)	53.16	1.60	-	<.0001	0.06	0.06
	Amputation transtibial ^a	-0.90	0.60	-0.05	0.13		
	Traumatic etiology ^b	-0.87	0.72	-0.05	0.22		
	Female gender	2.33	0.62	0.11	0.00		
	Non-Hispanic black ^c	1.52	0.99	0.05	0.13		
	Hispanic ^c	1.19	1.18	0.03	0.31		
	Other ethnicity ^c	2.57	1.40	0.05	0.07		
	Years since amputation	-0.11	0.02	-0.16	<.0001		
	Age	-0.04	0.02	-0.06	0.07		
Depression	(Intercept)	53.90	1.57	-	<.0001	0.06	0.06
	Amputation transtibial ^a	-0.67	0.59	-0.03	0.26		
	Traumatic etiology ^b	-1.46	0.70	-0.08	0.04		
	Female gender	1.65	0.61	0.08	0.01		
	Non-Hispanic black ^c	0.31	0.97	0.01	0.75		
	Hispanic ^c	1.07	1.16	0.03	0.35		

Dependent variable	Independent variable	Unstandardized coefficient (B)	SE B	Standardized coefficient (β)	p	R ²	Adjusted R ²
Fatigue	Other ethnicity ^c	3.90	1.38	0.08	0.00		
	Years since amputation	-0.10	0.02	-0.16	<.0001		
	Age	-0.05	0.02	-0.08	0.03		
	(Intercept)	50.89	1.58	-	<.0001	0.06	0.06
	Amputation transibial ^a	0.35	0.59	0.02	0.55		
	Traumatic etiology ^b	-1.01	0.71	-0.05	0.15		
	Female gender	2.23	0.61	0.11	0.00		
	NonHispanic black ^c	-1.34	0.98	-0.04	0.17		
	Hispanic ^c	-1.01	1.17	-0.03	0.39		
	Other ethnicity ^c	2.48	1.39	0.05	0.07		
Sleep disturbance	Years since amputation	-0.12	0.02	-0.17	<.0001		
	Age	-0.02	0.02	-0.03	0.34		
	(Intercept)	55.16	1.55	-	<.0001	0.04	0.03
	Amputation transibial ^a	0.01	0.58	0.00	0.99		
	Traumatic etiology ^b	-0.83	0.69	-0.05	0.23		
	Female gender	1.17	0.60	0.06	0.05		
	Non-Hispanic black ^c	-0.43	0.96	-0.01	0.65		
	Hispanic ^c	-0.68	1.14	-0.02	0.55		
	Other ethnicity ^c	2.84	1.35	0.06	0.04		
	Years since amputation	-0.05	0.02	-0.08	0.02		
Satisfaction with social role	Age	-0.09	0.02	-0.14	<.0001		
	(Intercept)	48.99	1.65	-	<.0001	0.09	0.08
	Amputation transibial ^a	0.75	0.62	0.04	0.23		
	Traumatic etiology ^b	2.33	0.74	0.12	0.00		
	Female gender	-0.47	0.64	-0.02	0.46		
	Non-Hispanic black ^c	0.89	1.03	0.03	0.39		
	Hispanic ^c	-2.79	1.22	-0.07	0.02		

Dependent variable	Independent variable	Unstandardized coefficient (B)	SE B	Standardized coefficient (β)	p	R ²	Adjusted R ²
Pain interference	Other ethnicity ^c	-3.20	1.45	-0.07	0.03	0.06	0.05
	Years since amputation	0.14	0.02	0.19	<.0001		
	Age	-0.07	0.03	-0.10	0.00		
Pain interference	(Intercept)	56.52	1.51	-	<.0001	0.06	0.05
	Amputation transistibial ^a	0.89	0.57	0.05	0.12		
	Traumatic etiology ^b	-0.66	0.68	-0.04	0.33		
	Female gender	1.74	0.58	0.09	0.00		
	Non-Hispanic black ^c	1.27	0.94	0.04	0.18		
	Hispanic ^c	2.33	1.11	0.06	0.04		
	Other ethnicity ^c	3.13	1.32	0.07	0.02		
	Years since amputation	-0.09	0.02	-0.15	<.0001		
	Age	-0.03	0.02	-0.05	0.18		

Note:

^aReference group: Amputation transfemoral;

^bReference group: Dysvascular etiology;

^cReference group: non-Hispanic white.