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Normative Mobility Values for Lower Limb Prosthesis Users of Varying Age, Etiology, and Amputation Level

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Abstract

Objective: To establish normative values of lower limb amputation mobility across primary etiologies based on age and amputation level.

Design: Cross-sectional observational analysis of outcomes. A total of 11,995 lower limb prosthesis users were included in the analysis. Participants were grouped by etiology into four categories: cancer, congenital, trauma, and diabetes/dysvascular (DV). Mobility was assessed by using the Prosthetic Limb Users Survey of Mobility (PLUS-M).

Results: Mobility across seven age groups for the four etiologies was established for both above-the-knee amputation (AKA) and below-the-knee amputation (BKA). Differences were found between age groups for individuals- AKA: cancer (χ^2 (6) = 40.97, $p < 0.001$), congenital (χ^2 (3) = 9.41, $p = 0.024$), trauma (χ^2 (6) = 18.89, $p = 0.004$), and DV (χ^2 (5) = 39.73, $p < 0.001$; BKA: cancer (χ^2 (6) = 29.77, $p < 0.001$), trauma (χ^2 (6) = 28.22, $p < 0.001$), and DV (χ^2 (6) = 144.66, $p < 0.001$).

Conclusion: The awareness of differences across amputation etiologies extending across the lifespan of ages can assist the goal-setting process as part of prosthetic rehabilitation. Additionally, refined normative values provide the ability to benchmark new and innovative changes in clinical practice.

Keywords: outcomes, amputee, PLUS-M, rehabilitation, goal-setting, MAAT, reference values

Abbreviations:

DV: Diabetic/dysvascular

PLUS-M: Prosthetic Limb Users Survey of Mobility

AKA: Above the knee Amputation

BKA: Below the Knee Amputation

What is known

Normative values provide targets for goal setting. A previous study has established mobility normative values for the Prosthetic Limb Users Survey of Mobility (PLUS-M) using approximately 1100 patients. These mobility values were limited to large age bands (i.e., four groups at 15 year bands) and two etiologies (i.e., trauma and diabetes/dysvascular).

What is new

From a sample of 11, 995 patients, this study provided normative mobility values using the PLUS-M with smaller age bands (i.e., seven groupings at 10 year bands) and an increased number of etiologies (i.e., trauma, diabetes/dysvascular, cancer, and congenital) expanding the PLUS-M developmental work. These refined normative values can further help with goal setting through reduced ambiguity and the ability to demonstrate empathy across more etiologies when setting personalized mobility goals.

Introduction

For lower limb prosthesis users, functional mobility is invaluable given its association with quality of life, satisfaction, and overall well-being.[1-3] Validated mobility measures, such as the Prosthetic Limb Users Survey of Mobility (PLUS-M), provide the ability to assess patients' functional mobility.[4,5] Such measures, when combined with normative values of the patient's peers' performance, may aid in setting expectations and goals.

Normative values are often used to inform clinical decisions through an understanding of patients with similar clinical presentations. Such reference points may also provide lifetime expectations as patients age. For lower limb prosthesis users, amputation level, etiology, and age are important factors when anticipating mobility outcomes.[5-7] The currently published normative values for PLUS-M demonstrate differences in mean and median across these three factors (i.e., age, etiology, and amputation level).[5] These factors have been shown to significantly impact functional mobility.

However, current PLUS-M normative datasets have limitations. In particular, the initial development sample yielded values for individuals with above-the-knee amputation (AKA) and below-the-knee amputation (BKA) within only two etiologies (i.e, traumatic and diabetic/dysvascular (DV)), and across only four age groupings (i.e., less than 35 years, 36-49, 50-64, and greater than or equal to 65 years). Ultimately, the granularity of the available cohorts is limited by the number of individuals within each group. The result is large age bands with only two etiologies.

The limitation of normative values for only two etiologies can limit goal setting for other individuals. For example, goal setting for an individual with limb amputation/difference due to cancer or a congenital limb condition would need to be based on guidance drawn from either DV or traumatic amputation etiology. Studies have generally shown reduced functional mobility in individuals with DV etiology compared to those with traumatic etiology.[8-10] There may not be functional differences between traumatic amputation compared to cancer or congenital etiology. However, the life journey for patients with either cancer or congenital limb deficiency differs substantially from that experienced by patients with either DV or traumatic amputation.

Amputations attributed to cancer and congenital limb deficiency account for only 2.5% of the total population with limb loss/difference.[11] Importantly, previous studies have noted that the care pathway from amputation to prosthesis fitting, as well as total prosthesis use time, differs clinically for cancer and congenital etiologies when compared to DV and trauma-related etiologies.[12,13] This is consistent with the recommendation that patients with cancer or congenital limb amputations/differences should be managed differently than those with DV or traumatic etiology.[13] This fact further underscores the need for refinement of any materials that could be used for goal setting.[13]

Personalized goal-setting may be better facilitated through increased granularity of patient phenotypes for average mobility. Members of the rehabilitation team would have a better understanding of differences in mobility due to etiology, amputation level, and age to formulate improved care plans. Therefore, the purpose of this study was to expand patient demographics to establish normative values for increased age groups and etiologies for individuals with

amputation. This will provide the benefit of improved expectation setting and understanding differences in functional mobility for various patient phenotypes. The goal was to define normative values for age groupings of smaller size, according to the four primary lower limb amputation/difference etiologies (i.e., DV, trauma, cancer, and congenital) and across two amputation levels. These are the four etiologies commonly encountered in clinical practice.[14]

It was hypothesized that older individuals would exhibit reduced mobility within each of the four primary etiologies. Second, it was hypothesized that differences[10] in mobility would be found across etiologies of trauma, cancer, congenital, and DV, with the latter experiencing the lowest mobility. Finally, it was hypothesized that the rate of mobility decline with aging would be greatest for individuals with amputation attributable to DV etiology. In addressing these hypotheses, it will be possible to establish expanded normative values for lower limb prosthesis user mobility.

Methods

Study design

A retrospective cross-sectional analysis was performed on mobility outcomes completed in the United States between April 2016 and May 2019. The database consisted of adults (i.e., age 18 years and older) with unilateral lower limb amputation with prior experience using a prosthesis.[5] Data were collected from private prosthetic clinics nationwide. Patients were treated at local clinics located in the northeastern, western, southern, and midwestern regions of the United States. As part of the standard of care, clinics involved in populating the database have implemented PLUS-M to assess mobility outcomes. In the event that a patient has multiple

outcomes over time, the highest mobility score was chosen as this was considered to reflect the highest functional mobility level the individual was able to reach at such time with standard of care. The latest mobility outcome was considered, but since prosthesis users are at times faced with transient issues such as open wounds, poor socket fit due to weight loss, and other factors which may limit functional mobility at the time of survey, the authors deemed it necessary to select the highest scores to set normative reference values, as these values may drive peer to peer competition. The highest score represents the greatest potential a patient can attain. Entries contributing to the database were restricted to adults with completed PLUS-M outcomes.[5] This database review was approved by the Western Copernicus Group Institutional Review Board (protocol #20170059) and designated to be exempt from informed consent. This study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (see Supplementary Checklist, Supplementary Digital Content 1, http://links.lww.com/PHM/B435).

Subjects

Adults with unilateral amputation were included in the final sample if the following criteria were met: (1) reported etiology as either cancer, trauma, congenital, or DV, and (2) reported amputation level as either AKA (i.e., transfemoral and knee disarticulation) or BKA (i.e., transtibial and Symes). Patients with missing etiology, amputation level, or who reported other amputation levels (e.g., partial foot) were excluded.

Primary Outcomes Measure

Unlike other non-population-specific mobility instruments, the PLUS-M is specifically designed to assess the self-reported functional mobility of lower-limb prosthesis users, and has several advantages. The PLUS-M short form (v1.2) is a validated outcome instrument.[4] It is sensitive to change over time and easy to implement, but possibly the greatest advantage when initiating in clinical practice is the existing normative data value set. Furthermore, the PLUS-M was proven to have strong psychometric properties such as convergent construct validity and known-groups construct validity. Convergent construct indicates that the PLUS-M is strongly correlated to other mobility instruments demonstrating that the instrument is mostly measuring the domain of mobility. Known-groups validity suggests that this instrument is discriminatory to amputation-related differences among people with lower limb amputation.[4] The version used in the clinic consisted of 12 questions. Each question has five ordinal response categories ranging from "unable to do" to "without any difficulty". Responses from the PLUS-M are summed to a raw score and then transformed into a standardized T-score per the PLUS-M guidelines.[5] A T-Score of 50 (magnitude) represents the population mean for all users. The process of developing cut points for the T-score is beyond the scope of this manuscript, but one can use the 25^{th}, median, and 75^{th} percentile as a guide to determine their current functional mobility relative to the population or sample distribution.

Independent Variables

The two main independent variables used in this study were age and etiology. Participants were stratified into seven age cohorts: ≤ 24, 25-34, 35-44, 45-54, 55-64, 65-74, and ≥ 75, within four categories of etiology (cancer, congenital, trauma, and DV). AKA and BKA

were analyzed separately. Age groupings were chosen to reduce the overall span from 15 years within four groups of [5] to ten years within seven groups while attempting to maintain a minimum of 15 individuals per group.

Statistical Analysis

Descriptive statistics were used to summarize patient demographics across etiology groups. Normative mobility values were described using mean, median, standard deviation, and quartiles for patients with AKA and BKA. Body mass index (BMI) was calculated to account for the missing lower limb.[16,17] Mood's median test and a univariate quantile regression at the 50th percentile were implemented to test for group differences in mobility grouped by age and amputation level (hypothesis 1) for each of the four primary etiologies (i.e., DV, trauma, cancer, and congenital). All post hoc analyses were adjusted using Bonferroni correction for multiple comparisons. An additional quantile regression model was applied to the pooled data for each AKA and BKA to determine differences in mobility by etiology (hypothesis 2) while controlling for age. The quantreg package (version 5.67) was used to calculate the regression coefficient (β) and 95% bootstrap confidence interval (CI) based on the inversion of a rank test described by Koenker.[18] Mood's median test and quantile regression models were utilized for the current study because of their robustness against outliers and non-normally distributed data.[19,20] Lastly, the etiology-related rate of decline in mobility as a function of age (hypothesis 3) was cross-sectionally assessed through separate lines of best-fit applied to the median values for AKA and BKA. This approach of using a regression line to identify the rate of decline for a dependent variable across cross-sectional age groups has been widely reported in the literature.[21-23]

A sensitivity analysis [24] was conducted to evaluate the influence of the excluded groups (i.e., those that did not reach the pre-defined 15 cases-per-group threshold) on the findings of this study. This analysis was completed by performing a robust check using quantile regression analysis to determine whether this inclusion/exclusion would significantly change the results, such as the directionality of the regression coefficients or the confidence intervals.[24] All analyses were performed using R statistical computing software (version 4.0.2).

Results

Of the 15,626 patients with clinical outcomes recorded, 3,631 individuals did not meet the inclusion criteria due to foot and hip amputation, unreported etiology, unreported amputation level, and were excluded from subsequent analysis. A final sample size of 11,995 unilateral prosthesis users was analyzed (figure 1). In the final sample, 62% of the patients reported amputation attributed to DV. Individuals with DV had the highest weight, BMI, and age, followed by those with trauma, cancer, and congenital etiology (table1).

Five subgroups defined by age, etiology, and amputation level did not reach the desired threshold of 15 individuals. Four of these subgroups were of congenital etiology and one was of DV etiology. Consequently, these age groups were omitted from the median test and regression analyses. The sensitivity analysis revealed that the exclusion of groups containing <15 individuals did not significantly influence the magnitude of the estimates or change directionality. Thus, the estimates are robust to exclusion. Descriptive data for these omitted groups were presented for preliminary findings, but were excluded from the final statistical models (Tables 2 and 3).

Age-related differences in mobility for cancer etiology

For individuals with AKA and amputation due to cancer, significant differences in mobility existed between the age groups (χ^2 (6) = 40.97, $p < 0.001$). Post hoc analysis revealed that patients within the 25-34 age group had significantly higher mobility (median = 59.60, interquartile range [IQR] = 56.30 - 63.00) than those in the 35-44 (median = 52.80, IQR = 45.03 - 56.55; p = 0.002), 45-54 (median = 52.35, IQR = 43.45 - 56.30; p = 0.004), 55-64 (median = 49.10, IQR = 40.90 - 55.30; $p < 0.001$), 65-74 (median = 49.8, IQR = 40.75 - 57.58; $p < 0.001$), and ≥ 75 age groups (median = 45.20, IQR = 37.10 - 50.50; $p < 0.001$) (table 2). Similarly, for BKA cancer survivors, the model results showed significant differences in mobility between the groups (χ^2 (6) = 29.77, $p < 0.001$). Pairwise comparison revealed that the mobility for patients in the 25-34 age group (median = 58.4, IQR = 54.40 - 64.50) was significantly higher than those in the 65-74 (median = 50.50, IQR = 41.20 - 54.45; $p < 0.001$), and ≥ 75 (median = 50.15, IQR = 42.70 - 54.40; p = 0.001) age groups (table 3).

Using a similar approach to Mood's median test, the quantile regression coefficient β and the 95% confidence intervals were estimated for cancer survivors with AKA (Table 2) or BKA (Table 3). Patients within the 75 and older cohorts had the lowest quantile regression estimates. When comparing patients within the 75 and older cohort to patients within the ≤ 24 age group for AKA and BKA, the median mobility estimates were β = -12.10 [95 % CI = -16.78, -0.40] and β =-3.90 [95 % CI= -11.51, -0.47], respectively.

Age-related differences in mobility for congenital etiology

Differences in mobility between groups (χ^2 (5) = 9.983, p = 0.125) for individuals with BKA and congenital etiology did not reach statistical significance. Conversely, for individuals with AKA and congenital etiology, differences in mobility between groups were statistically significant (χ^2 (3) = 9.41, p = 0.024). However, post-hoc pairwise comparisons did not reach statistical significance.

Using a similar approach to Mood's median test, the quantile regression coefficient β and the 95% confidence interval were estimated for individuals with congenital AKA or BKA. Since the 65 and older cohorts were not included in the model, patients within the 55-64 age group exhibited lower quantile regression estimates than some of the other groups. When comparing patients within the 55-64 cohort to patients within the 25-34 age group for congenital AKA, the median mobility estimate was β = -2.40 [95 % CI = -11.21, 2.16]. For individuals 65-74 years old with BKA, the median mobility estimate was β =-1.20 [95 % CI = -3.76, 7.45] relative to individuals within the ≤ 24 group.

Age-related differences in mobility for trauma-related etiology

For patients with AKA and traumatic etiology, there was a significant difference in mobility between the age groups (χ^2 (6) = 18.89, p = 0.004). Subsequent post hoc analysis revealed that the mobility for those 25-34 years old (median = 52.00, IQR = 44.50 - 59.60) was significantly greater than the mobility observed among patients in the ≥ 75 age group (median = 45.20, IQR = 37.25 - 53.38; p = 0.005). Likewise, significant differences were observed between the BKA trauma groups (χ^2 (6) = 28.22, p < 0.001). Pairwise comparison revealed that patients in

the age 25-34 group had significantly greater mobility than individuals aged 45 years and older ($p < 0.001$).

Using a similar approach to Mood's median test, the quantile regression coefficient β and the 95% confidence interval were estimated for individuals with trauma AKA or BKA. Patients within the 75 and older cohorts had the lowest quantile regression estimates. When comparing patients within the 75 and older cohort to patients within the ≤ 24 age group for AKA and BKA, the median mobility estimates were β = -6.00 [95 % CI = -12.48, -2.12] and β = -3.10 [95 % CI= -9.10, 2.04], respectively.

Age-related differences in mobility for DV etiology

A significant difference in mobility was observed between the groups (χ^2 (6) = 144.66, $p<0.001$) for individuals with BKA and DV etiology (table 3). Post hoc analysis revealed that the mobility of patients in the ≥ 75 years age group was significantly lower than that in the remaining six age groups ($p < 0.001$). Similar findings were noted for patients with AKA and DV etiology (χ^2 (5) = 39.73, $p < 0.001$).

Using a similar approach to Mood's median test, the quantile regression coefficient β and the 95% confidence interval were estimated for individuals with AKA or BKA due to DV. Patients within the 75 and older cohorts had the lowest quantile regression estimates. When comparing patients within the 75 and older cohort to patients within the 25-34 age group for AKA and ≤ 24 age group for BKA, the median mobility estimates were β = -8.10 [95 % (confidence interval) CI = -14.04, -5.68] and β =-14.20 [95 % CI= -16.61, -7.26], respectively.

Median test of mobility across four primary etiologies for AKA and BKA

For AKA, significant differences existed in mobility between the groups of etiologies (χ^2 (3) = 346.95; $p < 0.001$). Post hoc tests revealed that patients with DV etiology (median = 40.30, IQR = 33.20 - 47.10) had significantly lower mobility than patients with trauma (median = 49.10, IQR = 42.10 - 55.30; $p < 0.001$), cancer (median = 50.50, IQR = 43.30 - 57.30; $p < 0.001$), and congenital etiology (median = 52.00, IQR = 47.10 - 57.30; $p < 0.001$). Using a similar approach, quantile regression applied at the median estimate showed that significant differences in etiologies persisted ($p < 0.001$) for AKA (table 4), while controlling for age.

For BKA, similar results were noted for mobility across the groups (χ^2 (3) = 464.78; $p < 0.001$). Post hoc tests revealed that patients with DV etiology (median = 46.40; IQR = 39.00 - 53.60) had significantly lower mobility than patients with trauma (median = 52.70, IQR = 45.80 - 61.00; $p < 0.001$), cancer (median = 53.6, IQR = 46.40 - 61.00; $p < 0.001$), and congenital etiologies (median = 58.4, IQR = 49.10 - 65.15; $p < 0.001$). Lastly, etiologies remained significant ($p < 0.001$) after adjusting for age using quantile regression for BKA (table 4).

Rate of mobility decline across etiologies

Mobility decreased linearly and curvilinearly across age groups (figures 2A and 2B). The DV group showed the steepest decline in mobility with advancing age in both the AKA and BKA groups.

Discussion

The current study sought to establish normative mobility values for individuals with lower limb difference/amputation due to cancer or congenital etiologies, and expand those available for etiologies associated with trauma and DV. These values may be used to improve individualized goal-setting. Clinicians can help patients set goals based on how well individuals that are similar to them are able to perform when achieving their highest reported mobility, subsequently preventing unrealistic goals as well as encouraging attainable goals. Importantly, normative values for amputation secondary to cancer and congenital limb deficiency were provided in this analysis.

As hypothesized, older individuals with BKA or AKA reported reduced mobility across the four primary etiologies. As expected, the oldest age group had the lowest mobility across amputation level and etiology. The age-related decline in mobility for the traumatic and DV groups is consistent with the findings of previous studies.[5,6] In particular, PLUS-M developers reported lower mobility values across amputation levels for older prosthesis users with traumatic and DV etiologies. The PLUS-M developmental sample found median mobility scores of prosthesis users over 64 years with AKA and BKA due to DV were 42.8 and 44.6, respectively. In the current study, the median mobility scores for the 65-74 (i.e., 40.30) and ≥ 75 (i.e., 37.70) age bands for persons with DV and AKA were lower than the PLUS-M developmental cumulative mobility scores for individuals over 64 years old. However, the mobility scores of persons 65-74 with BKA were higher (i.e. 65-74 group median = 45.80) than the PLUS-M aggregated score. This parsing out of the 65 and older group may suggest that having smaller age

bands, as reported in this analysis, provides improved ability for goal setting based on patient peers with increased similarity providing more relative peer-to-peer comparison.

The age-related decline in mobility for BKA was statistically significant for cancer, trauma, and DV, but not for congenital limb deficiency. However, the qualitative analysis of the linear trend across age groups reflects a consistent gradual decline with age. Subsequently, the statistical analysis may have been underpowered for the congenital amputation group, recognizing that three of the age groupings were omitted from the statistical model. The overall greater functional mobility reported among those with congenital limb deficiency is consistent with a previous study that demonstrated that patients with congenital limb deficiency tended to have improved physical function and psychosocial outcomes in adulthood.[12] The study suggested that improved mobility outcomes for individuals with congenital lower limb difference/amputation may be attributed to patients' perception of limb differences. In particular, lower limb prosthesis users with congenital limb deficiencies are accustomed to their deficiency from birth. Therefore, they often do not perceive amputation as a disability or traumatic event, which may aid in willingness to participate in activities during childhood, subsequently driving motor development and ultimately leading to improved mobility in adulthood. It is not clear if long term living with amputation would have a similar effect, although it would be challenging to understand if such an effect can overcome the decline in mobility with the aging process. This should be further explored.

It was also hypothesized that there would be differences in mobility among the four etiologies with the DV group demonstrating the lowest mobility. As expected, the DV etiology

had the lowest median mobility scores across amputation levels and was significantly different from trauma, cancer, and congenital disease. Montesinos-Magraner et al. reported significant differences in mobility (i.e., locomotor capability index) among the four primary amputation etiologies, which is consistent with our findings.[12]

A recent classification analysis with amputation attributed to cancer, congenital, and trauma collapsed into a singular non-DV group when determining the functional ambulatory status among lower limb prosthesis users.[10] The present study showed no statistical differences between the amputations attributed to cancer and trauma. A significant difference was found between amputation attributed to congenital versus cancer and congenital versus trauma. This finding supports larger-scale studies that collapse etiologies attributed to cancer and trauma into a single non-diabetes/vascular disease etiology to achieve increased statistical power. Nevertheless, for personalized goal setting and the ability to demonstrate empathy as a care provider, the separation of these etiologies is important.

It is well reported that those with amputation secondary to DV have reduced mobility compared with non-DV etiology [6]. For example, Davies et al. demonstrated that nonvascular amputees had increased mobility compared to vascular etiology.[6] Therefore, it is not surprising that individuals with DV have a greater decline in mobility with age. It is interesting to note that the best-fit line for mobility versus age among individuals with DV and BKA had a linear fit, while the best-fit line for individuals with DV and AKA showed a logarithmic decline. In contrast to the steep drop in mobility for DV, the traumatic etiology had a gentle decline from age 18 to 54, which then flattened from age 55 and onwards for both amputation levels. The

weakest fit lines were noted in the congenital and trauma populations, although only the congenital above-the-knee group dropped slightly to what should be considered a medium effect, while all others are considered a large effect size.[25,26] These findings are valuable and insightful because mobility seems to decline at different rates across amputation levels for cancer, congenital, and trauma compared to DV. This observation allows for targeted rehabilitation for those that require differing levels of intervention and care to increase and/or maintain mobility, allowing for improved resource allocation. Understanding the magnitude in the differences among the four etiologies may aid in the allocation of targeted interventions, and allows for a more nuanced discussion at the patient-clinician level for goal setting during the rehabilitation process. Individuals with amputation can struggle to understand realistic goal setting, which is also dependent on the underlying cause of amputation. For example, having more foresight that individuals with DV are likely to perform poorer than individuals with amputation associated cancer or congenital limb difference, may aid in the shared decision-making process by patient and clinician to provide intervention or set mobility goals to improve function.

The normative values in the current analysis may also aid future intervention studies. In particular, with an understanding of the general decline in mobility due to aging, longitudinal studies may have the ability to benchmark intervention performance in "bending the curve" or reducing the rate of decline in mobility associated with age. Thus, an intervention that slows the decline in mobility with age could be considered an effective treatment. Additionally, future work should advance this effort through increased granularity, with greater specificity surrounding age, amputation level and/or residual limb length, and specifics regarding the primary categories of amputation etiology (e.g. type of trauma or type of cancer).

Study Limitations

This study had some limitations. The generalizability of this study's findings may not extend to individuals with bilateral amputations. Future studies should consider age-related declines in mobility in individuals with bilateral amputation. However, this study represents a wide variety of lower limb patients that are diverse, which can increase generalizability among those with unilateral lower limb amputation. Normative values are useful for clinicians and patients with unilateral lower limb amputation and should be considered as a part of evidence-based practice. Another limitation to this study is that there were a small number of age subgroups that did not consist of more than 15 individuals per group. Setting normative reference values with these smaller age groups may not provide an accurate representation of the group's functional mobility. Future studies are needed to further establish accurate reference values for these subgroups.

It is known that unbalanced group sizes may impact the power of the study. Of note, conducting a post hoc power analysis for a retrospective study is debatable in the literature[27,28] and some studies advise against the value of its use retrospectively.[29] A power analysis was not conducted for this study due to the retrospective nature and the large sample size (n=402) [30] entered in the model with the fewest individuals. However, 95% confidence intervals were presented to estimate the uncertainty around the effect of the estimate, which is commonly noted as more appropriate for retrospective studies rather than power analyses.[29]

Prior studies have indicated that having unequal group sizes may result in a reduction in power, but in most non-experimental studies having heterogeneous group sizes is not

uncommon. This is often a limitation with retrospective cross-sectional study designs. The strategy to address unbalance group sizes was to maintain a 15 person threshold per group and perform a subsequent sensitivity analysis to determine the impact of this inclusion/exclusion on the regression estimates. In addition, to remove patients from an analysis to achieve homogeneity in a group's sample size is not recommended by some studies. Therefore, the authors followed the guidance from prior work which recommended, that when measuring group differences, the analysis should have a reasonable sample size of 30 observations per cell to achieve 80% power but no fewer than seven observations per cell.[30]

Another limitation is that the amount of time an individual had used a prosthesis was not incorporated, which may have affected the outcomes. Additionally, these data were based on patient-reported outcomes, which may be influenced by recall bias or imprecision. For example, an individual's self-reported mobility may be higher than mobility measured in a different manner, which could influence the relationship between mobility and etiology or age, as assessed in this study. This is mitigated by the use of the PLUS-M instrument, which is highly validated for mobility, and several other studies have used patient-reported outcome measures with robustness.[4,10,31]

Another limitation of this study is its retrospective nature and potential prescription bias for patients. For example, a recent study demonstrated that among a sample of 881 individuals with DV etiology that were eligible for advanced prosthetic technology, only 137 received that technology.[32] This finding indicates a potential prescription bias, which may further contribute to reduced mobility outcomes among individuals with lower limb amputation beyond age and

etiology. As a result, the extent to which mobility differences are attributed to physiological differences versus a potential prescription bias, whereby non-dysvascular or younger patients have increased access to newer technologies with increased benefits. This prescription bias is facilitated by the current K-level classification system, which provides access to technologies such as microprocessor knees and energy-storage-and-return feet only to individuals that are healthier and have a higher classification. Future work is needed to understand the potential mobility that could be reached for individuals with amputation due to various etiologies while accounting for potential prescription bias.

Conclusion

In summary, the normative values established in this study can be used by clinicians and rehabilitation professionals to set personalized mobility goals for patients with similar age, etiology, and amputation levels. More resources should be provided to patients with DV to ensure that mobility is maintained according to the normative values provided in this study. Prosthetists evaluating patients with mobility scores far below the reported group medians should consider a more comprehensive evaluation that includes additional interventions aimed at maximizing mobility. Finally, the normative values in the current analysis provide a potential platform for gauging future intervention success in the presence of age-and etiology-related challenges.

References

1. Norvell DC, Turner AP, Williams RM, Hakimi KN, Czerniecki JM. Defining successful mobility after lower extremity amputation for complications of peripheral vascular disease and diabetes. *Journal of vascular surgery*. 2011;54(2):412-419.
2. Pell JP, Donnan PT, Fowkes FG, Ruckley CV. Quality of life following lower limb amputation for peripheral arterial disease. *Eur J Vasc Surg*. 1993;7(4):448-451.
3. Wurdeman SR, Stevens PM, Campbell JH. Mobility analysis of AmpuTees (MAAT 1): Quality of life and satisfaction are strongly related to mobility for patients with a lower limb prosthesis. *Prosthet Orthot Int*. 2018;42(5):498-503.
4. Hafner BJ, Gaunaurd IA, Morgan SJ, Amtmann D, Salem R, Gailey RS. Construct validity of the prosthetic limb users survey of mobility (PLUS-M) in adults with lower limb amputation. *Arch Phys Med Rehab*. 2017;98(2):277-285.
5. UWCORR. Prosthetic limb user survey. Prosthetic Limb Users Survey Web site. www.plus-m.org. Updated 2013. Accessed Dec, 2016.
6. Davies B, Datta D. Mobility outcome following unilateral lower limb amputation. *Prosthet Orthot Int*. 2003;27(3):186-190.
7. Seker A, Kara A, Camur S, Malkoc M, Sonmez MM, Mahirogullari M. Comparison of mortality rates and functional results after transtibial and transfemoral amputations due to diabetes in elderly patients-a retrospective study. *International Journal of Surgery*. 2016;33:78-82.
8. Deathe AB, Miller WC. The L test of functional mobility: Measurement properties of a modified version of the timed "up & go" test designed for people with lower-limb amputations. *Phys Ther*. 2005;85(7):626-635.

9. Wong CK, Chen CC, Benoy SA, Rahal RT, Blackwell WM. Role of balance ability and confidence in prosthetic use for mobility of people with lower-limb loss. *Journal of Rehabilitation Research & Development*. 2014;51(9).

10. Wurdeman SR, Stevens PM, Campbell JH. Mobility analysis of amputees (MAAT 4): Classification tree analysis for probability of lower limb prosthesis user functional potential. *Disabil Rehabil Assist Technol*. 2019:Epub ahead of print.

11. Varma P, Stineman MG, Dillingham TR. Epidemiology of limb loss. *Phys Med Rehabil Clin N Am*. 2014;25(1):1-8. doi: 10.1016/j.pmr.2013.09.001 [doi].

12. Montesinos-Magraner L, Issa-Benítez D, Meléndez-Plumed M, González-Viejo M, Castellano-Tejedor C. Physical and psychosocial functions of adults with lower limb congenital deficiencies and amputations in childhood. *Rehabilitation research and practice*. 2016;2016.

13. Raichle KA, Hanley MA, Molton I, et al. Prosthesis use in persons with lower- and upper-limb amputation. *J Rehabil Res Dev*. 2008;45(7):961-972. doi: 10.1682/jrrd.2007.09.0151 [doi].

14. Sabzi Sarvestani A, Taheri Azam A. Amputation: A ten-year survey. *Trauma Mon*. 2013;18(3):126-129. doi: 10.5812/traumamon.11693 [doi].

15. STROBE statement. [internet] version 4 as published in oct/nov 2007. https://www.strobe-statement.org/index.php?id=available-checklists. Accessed 25/06, 2020.

16. Tzamaloukas AH, Patron A, Malhotra D. Body mass index in amputees. *JPEN J Parenter Enteral Nutr*. 1994;18(4):355-358. doi: 10.1177/014860719401800414 [doi].

17. Tzamaloukas AH, Leger A, Hill J, Murata GH. Body mass index in patients with amputations on peritoneal dialysis: Error of uncorrected estimates and proposed correction. *Adv Perit Dial*. 2000;16:138-142.

18. Koenker R, Portnoy S, Ng PT, Zeileis A, Grosjean P, Ripley BD. Package 'quantreg'. *Reference manual available at R-CRAN: https://cran.rproject.org/web/packages/ quantreg/quantreg.pdf*. 2018.

19. Mishra P, Pandey CM, Singh U, Keshri A, Sabaretnam M. Selection of appropriate statistical methods for data analysis. *Ann Card Anaesth*. 2019;22(3):297-301. doi: 10.4103/aca.ACA_248_18 [doi].

20. Yu K, Lu Z, Stander J. Quantile regression: Applications and current research areas. *Journal of the Royal Statistical Society: Series D (The Statistician)*. 2003;52(3):331-350.

21. Anton MM, Spirduso WW, Tanaka H. Age-related declines in anaerobic muscular performance: Weightlifting and powerlifting. *Med Sci Sports Exerc*. 2004;36(1):143-147. doi: 10.1249/01.MSS.0000106283.34742.BE [doi].

22. Kallman DA, Plato CC, Tobin JD. The role of muscle loss in the age-related decline of grip strength: Cross-sectional and longitudinal perspectives. *J Gerontol*. 1990;45(3):M82-M88.

23. Schimpl M, Moore C, Lederer C, et al. Association between walking speed and age in healthy, free-living individuals using mobile accelerometry—a cross-sectional study. *PloS one*. 2011;6(8):e23299.

24. Konstantopoulos S, Li W, Miller S, van der Ploeg A. Using quantile regression to estimate intervention effects beyond the mean. *Educational and psychological measurement*. 2019;79(5):883-910.

25. Cohen J. A power primer. *Psychol Bull*. 1992;112(1):155-159.

26. Cohen J. *Statistical power analysis for the behavioral sciences.* 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988:567.

27. Levine M, Ensom MH. Post hoc power analysis: An idea whose time has passed? *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*. 2001;21(4):405-409.

28. Zhang Y, Hedo R, Rivera A, Rull R, Richardson S, Tu XM. Post hoc power analysis: Is it an informative and meaningful analysis? *Gen Psychiatr*. 2019;32(4):e100069-2019. doi: 10.1136/gpsych-2019-100069 [doi].

29. Noordzij M, Tripepi G, Dekker FW, Zoccali C, Tanck MW, Jager KJ. Sample size calculations: Basic principles and common pitfalls. *Nephrology dialysis transplantation*. 2010;25(5):1388-1393.

30. VanVoorhis CW, Morgan BL. Understanding power and rules of thumb for determining sample sizes. *Tutorials in quantitative methods for psychology*. 2007;3(2):43-50.

31. Hafner BJ, Morgan SJ, Abrahamson DC, Amtmann D. Characterizing mobility from the prosthetic limb user's perspective: Use of focus groups to guide development of the prosthetic limb users survey of mobility. *Prosthet Orthot Int*. 2016;40(5):582-590.

32. Wurdeman SR, Miller TA, Stevens PM, Campbell JH. Microprocessor knee technology reduces odds of incurring an injurious fall for individuals with diabetic/dysvascular amputation. *JPO*. 2020;32(2S):64-69.

Figure Captions:

Figure 1: A database containing adults with unilateral amputation was reviewed. Patients with confirmed cancer, congenital, traumatic or diabetic/dysvascular (DV) etiology were identified and included in the final sample.

Figure 2: The optimal best fit line across age group medians was plotted for cancer, congenital, trauma and diabetic/dysvascular (DV) etiologies for both individuals with above-the-knee (figure 2A) and below-the-knee amputation (figure 2B). DV shows greatest decline with age.

Figure 1

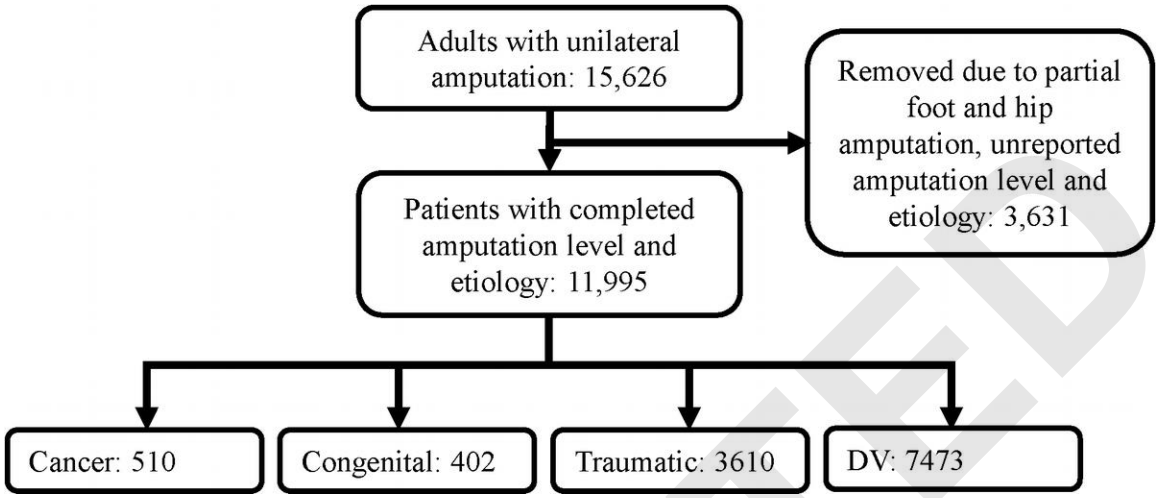

Figure 2

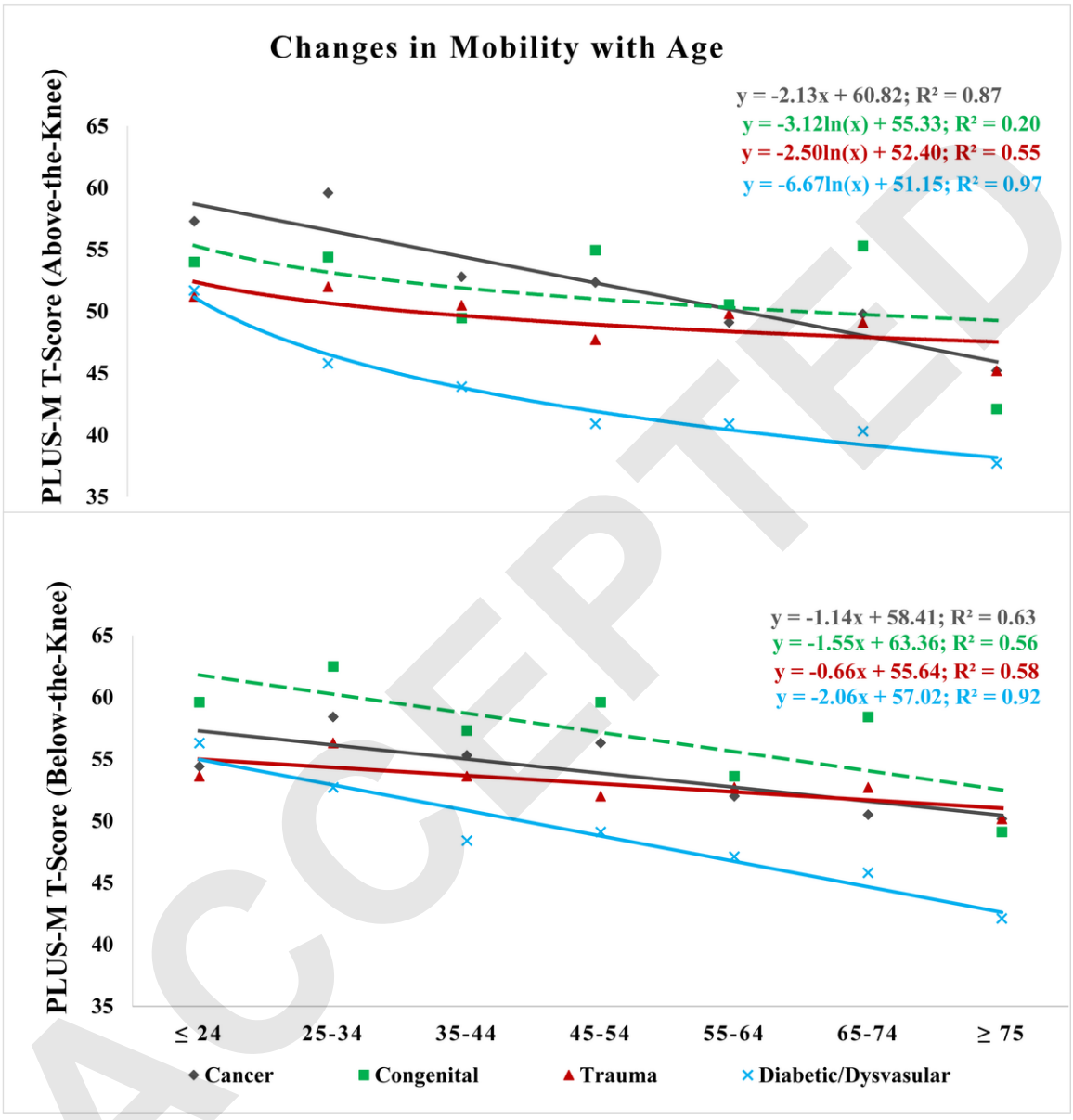

Table 1. Patient Demographics by Etiologies

	Cancer (N= 510)	Congenital (N= 402)	Trauma (N= 3610)	Diabetes/ Dysvascular (N=7473)
Variables	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**	**Median (IQR)**
Age at evaluation (years)	53.8 (36.0-66.4)	42.5 (31.0-56.1)	55.0 (43.0-65.0)	62.0 (54.0-70.3)
Height (m)	1.73 (1.65-1.78)	1.70 (1.63-1.78)	1.75 (1.70-1.83)	1.75 (1.68-1.83)
Weight (kg)	79.4 (66.8-90.7)	79.4 (67.1-92.5)	86.2 (74.8-101.6)	88.9 (74.8-104.8)
Body Mass Index (Kg/m2)	29.2 (25.2-33.0)	29.3 (25.5-34.2)	30.2 (26.6-34.7)	30.9 (26.8-35.8)
	N (%)	**N (%)**	**N (%)**	**N (%)**
Gender				
Male	293 (57.5)	212 (52.7)	2892 (80.1)	5405 (72.3)
Female	217 (42.5)	190 (47.3)	718 (19.9)	2068 (28.7)
Amputation Level				
Above-Knee	259 (50.8)	122 (30.3)	1051 (29.1)	1485 (19.9)
Below-Knee	251 (49.2)	280 (69.7)	2559 (70.9)	5988 (80.1)

Table 2: Normative Values for Mobility among Above the Knee Prosthesis Users

				Percentiles					95% CI for Median	
Mobility	**n**	**Mean**	**SD**	**25th**	**50th (Median)**	**75th**	**Mood's Median Test (P<0.05)**	**β**	**Lower Bound**	**Upper Bound**
All	2917	44.79	11.22	37.70	45.20	52.70	__	__	__	__
Cancer										
≤ 24	17	52.61	10.35	45.80	57.30	61.00	ns	*		
25-34	34	59.64	7.76	56.30	59.60	63.00	ns	2.30	-0.78	13.47
35-44	38	49.85	11.01	45.03	52.80	56.55	b	-3.70	-8.29	6.29
45-54	32	50.35	8.82	43.45	52.35	56.30	b	-4.60	-9.20	6.85
55-64	57	48.49	8.92	40.90	49.10	55.30	b	-8.20	-13.13	3.09
65-74	42	48.97	10.22	40.75	49.80	57.58	b	-7.50	-11.59	2.54
≥ 75	39	43.99	9.90	37.10	45.20	50.50	b	-12.10	-16.78	-0.40
Congenital										
≤ 24	12	54.00	6.89	52.18	54.00	56.30	__	__	__	__
25-34	34	54.40	11.21	48.40	54.40	65.15	ns	*		
35-44	26	49.45	6.82	45.78	49.45	52.00	ns	-4.60	-11.33	-0.52
45-54	16	54.95	8.11	49.98	54.95	59.60	ns	-0.80	-7.72	4.89
55-64	18	50.55	9.72	45.03	50.55	56.55	ns	-2.40	-11.21	2.16
65-74	13	55.30	10.57	47.75	55.30	60.45	__	__	__	__
≥ 75	3	42.10	4.37	37.10	42.10	__	__	__	__	__
Trauma										
≤ 24	21	51.01	8.69	44.55	51.20	57.30	ns	*		
25-34	107	51.96	10.47	44.50	52.00	59.60	ns	0.80	-5.75	5.13
35-44	151	50.36	10.56	42.70	50.50	57.30	ns	-0.70	-6.53	3.64
45-54	221	48.87	9.37	42.10	47.70	55.30	ns	-3.50	-9.94	-0.56
55-64	267	48.77	9.50	42.70	49.80	55.30	ns	-1.40	-7.59	2.97
65-74	192	48.01	10.12	42.10	49.10	54.40	ns	-2.10	-7.61	1.51
≥75	92	44.40	10.88	37.25	45.20	53.38	b	-6.00	-12.48	-2.12
Diabetic/Dysvascular										
≤ 24	12	49.67	11.03	41.65	51.70	56.80	__	__	__	__
25-34	23	47.95	9.17	43.90	45.80	53.60	ns	*		
35-44	63	43.81	10.96	36.40	43.90	52.70	ns	-1.90	-7.54	1.21
45-54	177	41.79	11.36	34.10	40.90	48.05	b	-4.90	-12.53	-1.75
55-64	481	40.58	10.07	33.65	40.90	47.10	b	-4.90	-10.38	-1.59
65-74	454	40.15	10.11	33.20	40.30	47.70	b	-5.50	-10.97	-2.85
≥ 75	275	37.36	9.51	30.00	37.70	43.90	b,d,e,f	-8.10	-14.04	-5.68

a, significantly different vs ≤ 24; b, significantly different vs 25-34; c, significantly different vs 35-44, d, significantly different vs 45-54; e, significantly different vs 55-64; f; significantly different vs 65-74; g, significantly different vs ≥ 75; ns, non-significant differences between groups, Age groups with less than 15 individuals were not included in model. * Indicate reference category for quantile regression model

Table 3: Normative Values for Mobility among Below the Knee Prosthesis Users

				Percentiles					95% CI for Median	
Mobility	**n**	**Mean**	**SD**	**25th**	**50th (Median) 75th**		**Mood's Median Test (P<0.05)**	**β**	**Lower Bound**	**Upper Bound**
All	9078	48.87	11.3	41.5	49.1	56.3	_	_	_	_
Cancer										
≤ 24	21	55.88	10.35	48.05	54.40	65.50	ns	*		
25-34	39	59.03	9.56	54.40	58.40	64.50	ns	4.00	0.49	9.44
35-44	39	54.31	10.64	47.10	55.30	61.00	ns	0.90	-5.74	4.65
45-54	38	55.05	9.55	49.45	56.30	63.00	ns	1.90	-4.14	5.17
55-64	47	52.33	9.65	45.20	52.00	59.60	ns	-2.40	-6.55	2.92
65-74	45	48.35	10.18	41.20	50.50	54.45	b	-3.90	-9.34	0.50
≥ 75	22	49.00	10.45	42.70	50.15	54.40	b	-3.90	-11.51	-0.47
Congenital										
≤ 24	23	57.70	9.68	49.80	59.60	67.10	ns	*		
25-34	64	60.60	10.03	53.80	62.50	71.40	ns	2.90	-1.25	11.59
35-44	61	56.70	10.34	49.45	57.30	63.50	ns	-2.30	-7.22	7.86
45-54	50	59.60	9.56	51.45	59.60	71.40	ns	0.00	-3.39	7.48
55-64	45	51.60	12.30	41.50	53.60	62.50	ns	-6.00	-12.91	1.37
65-74	24	58.00	10.58	51.80	58.40	66.45	ns	-1.20	-3.76	7.45
≥ 75	13	49.70	9.81	43.00	49.10	56.50	_	_	_	_
Trauma										
≤ 24	63	54.28	10.22	47.70	53.60	61.00	ns	*		
25-34	243	56.34	9.78	50.50	56.30	62.50	ns	2.70	-2.48	8.02
35-44	412	54.08	10.84	45.80	53.60	62.50	ns	0.00	-6.39	6.87
45-54	533	53.12	10.59	45.80	52.00	61.00	b	-1.60	-7.21	4.71
55-64	635	52.47	10.89	44.50	52.70	61.00	b	-0.90	-6.57	4.62
65-74	463	52.99	10.44	46.40	52.70	59.60	b	-0.90	-6.45	5.60
≥ 75	210	50.18	12.17	41.95	50.15	59.60	b	-3.10	-9.10	2.04
Diabetic/Dysvascular										
≤ 24	16	54.97	6.78	48.93	56.30	60.65	ns	*		
25-34	103	51.37	9.29	45.20	52.70	57.30	ns	-3.60	-7.22	2.33
35-44	381	48.04	10.51	42.10	48.40	55.30	ns	-7.90	-10.27	-1.63
45-54	1123	48.45	10.30	42.10	49.10	55.30	ns	-7.20	-9.62	-0.84
55-64	2004	46.91	10.70	40.30	47.10	54.40	b,d	-9.2	-11.63	-2.82
65-74	1594	45.68	10.79	38.40	45.80	52.70	a,b,d	-10.50	-12.93	-4.12
≥ 75	767	42.23	10.46	35.60	42.10	49.80	a,b,c,d,e,f	-14.20	-16.61	-7.26

a, significantly different vs ≤ 24; b, significantly different vs 25-34; c, significantly different vs 35-44, d, significantly different vs 45-54; e, significantly different vs 55-64; f; significantly different vs 65-74; g, significantly different vs ≥ 75; ns, non-significant differences between groups. * Indicate reference category for quantile regression model

Table 4: Quantile Regression Model at the 50th Percentile for Functional Mobility

		95% CI		
	Estimate	Lower Bound	Upper Bound	p
AKA				
Diabetes	*			
Cancer	9.54	8.14	10.51	< 0.001
Congenital	8.44	7.06	9.27	< 0.001
Trauma	7.36	6.49	8.43	< 0.001
Age	-0.13	-0.17	-0.11	< 0.001
BKA				
Diabetes	*			
Cancer	6.06	4.37	6.84	< 0.001
Congenital	8.79	7.48	10.17	< 0.001
Trauma	5.32	4.73	6.00	< 0.001
Age	-0.14	-0.17	-0.11	< 0.001

AKA: above-the-knee amputation and BKA: below-the-knee amputation