ORIGINAL ARTICLE

Fatigue and Aging With a Disability

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Objective: To compare self-reported fatigue in 4 disability populations with age-matched, U.S. population norms. We assessed fatigue and age in a sample of individuals with spinal cord injury (SCI), postpolio syndrome (PPS), multiple sclerosis (MS), and muscular dystrophy (MD).

Design: This study used survey responses and published age cohort means for fatigue to test the hypothesis that fatigue would be higher in each of 4 clinical samples than the U.S. population norm. We also hypothesized that, for clinical samples, the mean fatigue reported within age cohorts would be higher than the general U.S. population norms for those age ranges derived in the Patient-Reported Outcomes Measurement Information System (PROMIS).

Setting: Survey responses were collected from participants in the Washington state area.

Participants: Participants (N=1836) were persons with MD (n=337), MS (n=580), Post-polio (n=441), and SCI (n=478).

Interventions: Not applicable.

Main Outcome Measure: PROMIS Depression Short Form.

Results: Individuals with disabilities reported higher levels of fatigue than the normative PROMIS population. In the normative population, self-reported fatigue was substantially lower in age cohorts from middle age to retirement age. However, individuals with disabilities did not demonstrate this age cohort effect.

Conclusions: Individuals with disabilities are not only at greater risk to experience fatigue, but this risk, relative to normative values, increases with age. More research is needed to determine the specific negative impact of fatigue symptoms on functioning in individuals with disabilities as they age.

Key Words: Aging; Fatigue; Multiple sclerosis; Muscular dystrophies; Postpoliomyelitis syndrome; Rehabilitation; Spinal cord injures.

CURRENTLY, 12.4% of the United States population is over 65 years of age.[1] By 2030, the percentage is expected to increase to 20.4% making this group the fastest growing age demographic. Consistent with the general "graying" of the U.S. population is the increased prevalence of disabling conditions in later adulthood. In addition, individuals with disabilities are living into later adulthood because of advances in medical knowledge and practice. As individuals with disabilities live longer, they will confront higher levels of many of the same age-related symptoms and conditions associated with aging in general. Moreover, it is possible that they may deal with some of these conditions sooner, or to a greater extent, than individuals who are aging without disabilities. For example, cardiovascular data from individuals with spinal cord injury (SCI) indicate that persons with SCI may age faster than those without SCI.[2,3] The secondary conditions that individuals with disabilities develop as they age can contribute to physical and psychologic dysfunction over and above the effects of the disability itself.

Among the most common secondary symptoms reported by individuals with SCI, multiple sclerosis (MS), muscular dystrophy (MD), and postpolio syndrome (PPS), is fatigue.[4-7] A barrier to understanding the impact of aging on the fatigue of persons living with neuromuscular disorders is the lack of age-specific general population norms. Without such norms, it is difficult to estimate any differential impact of aging with a disability. Several studies have examined fatigue in national population samples by age range,[8-13] but no such study has been performed in the U.S. The effects of chronological age on fatigue in persons with disabilities are not entirely clear. On one hand, the evidence suggests a gradual decrease in fatigue in individuals as they age, in particular from middle age to retirement age, perhaps due to a decrease in responsibilities during this transition period.[14-16] On the other hand, one might expect an increase in fatigue with age—perhaps particularly in the very elderly—due to physical decline. Given the evidence that individuals with disabilities age faster than individuals without disabilities, it is possible that an earlier increase in fatigue with age might be observed in disability samples. However, to our knowledge, age cohort fatigue severity has not been compared across multiple disabilities groups and against age cohort norms in the U.S. general population.

Recently, the opportunity to compare outcomes across different age cohorts has been greatly enhanced by the Patient Reported Outcomes Measurement Information System (PROMIS).[17,18] PROMIS is an initiative funded by the National Institutes of Health, whose objective is to develop measures of key symptoms and outcomes applicable to a range of chronic conditions. Among the outcome measures developed by PROMIS is a measure of fatigue impact, defined as "an overwhelming, debilitating, and sustained sense of exhaustion that decreases one's ability to carry out daily activities, including the ability to work effectively and to function at

List of Abbreviations

MD	muscular dystrophy
MS	multiple sclerosis
PPS	postpolio syndrome
PROMIS	Patient Reported Outcome Measurement Information System
SCI	spinal cord injury

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one's usual level in family or social roles."[19 (p 1318)] A very large sample (>20,000) was used in the initial collection of responses to the PROMIS items (Wave I testing). Mean scores for 6 age ranges have been published (ie, 18–34y, 35–44y, 45–54y, 55–64y, 65–74y, and ≥75y).[20]

The purpose of this study was to compare self-reported fatigue experience and impact in multiple disability populations with age-matched, U.S. population norms. Using a community-based survey approach, we assessed fatigue and age (among other variables) in a sample of individuals with SCI, PPS, MS, and MD. We hypothesized that fatigue would be higher in each of our 4 clinical samples compared to the U.S. population norm. Second, we hypothesized that for clinical samples, the mean fatigue reported within age cohorts (18–34y, 35–44y, 45–54y, 55–64y, 65–74y, and ≥75y) would be higher than the PROMIS general U.S. population norms for those age ranges.

METHODS

Participants

Participants were recruited for an ongoing longitudinal study examining the role of secondary conditions in aging with a disability, specifically with MS, MD, PPS, or SCI. Recruitment strategies included advertisements in organization newsletters and websites (eg, Muscular Dystrophy Foundation), and inviting persons in the university's registry of persons with disabilities and other condition-specific registries (eg, SCI Model Systems). In addition, we contacted participants from prior studies who had agreed to be contacted about future studies. To be eligible, participants had to have a self-reported diagnosis of MS, MD, PPS, or SCI; be able to read and write English; and provide written consent. The Institutional Review Board at the University of Washington, Seattle reviewed and approved study procedures.

Measures

Demographic and disability-related descriptive variables. All participants were asked to provide basic demographic information (age, race/ethnicity, sex, marital status, income, and questions about work history).

Fatigue. Fatigue was measured using the PROMIS 7-item fatigue short form (Appendix 1). The PROMIS Fatigue item bank and the short forms derived from it have been found to have strong psychometric properties.[21] For example, in the PROMIS Wave I data collection, more than 95% of the sample were measured with reliability greater than 0.9 (based on item response theory information calculations). All psychometric information of the PROMIS measures is publicly available at Assessment Center (http://www.assessmentcenter.net/ac1). A unique characteristic of the scores of all PROMIS measures, including the PRO-Fatigue SF, is that scores are reported on a T score metric that is anchored to mean levels of each outcome in a healthy U.S. general population.[22] The T score metric has a mean of 50 and an SD of 10. Higher scores indicate higher fatigue. The use of this metric improves the interpretability of scores. For example, on the PROMIS 7-item fatigue short form, if a person scores a 70 (or the sample mean is 70) this indicates a level of fatigue that is 2 SDs above the mean of the PROMIS healthy normative U.S. sample.

Additional measures. Participants also completed measures of other secondary symptoms (eg, pain, physical function, mobility, depression, and sleep and wake function) and health conditions (eg, falls, recent relapse, skin problems, and urinary tract infection). Time since diagnosis/injury was obtained by self-report. In the current paper, only the descriptive information and analyses related to the age and fatigue variables are presented, as these are the focus of this paper.

Analyses

Descriptive analyses. We first computed means and SDs of the demographic and disability-related variables. To describe the relationship between fatigue and chronological age in our clinical populations, we used regression analyses to estimate the linear and curvilinear relationships in each clinical sample separately. The regression analyses were used to distinguish 2 potential associations between aging and fatigue: fatigue that increases steadily across the life span and fatigue that increases in earlier ages and decreases in later ages.

Hypothesis tests. To test the hypothesis that mean fatigue reported in each of the 4 clinical populations would exceed the norm for the general U.S. population, we used a series of 4 one-sample t tests to test mean PROMIS 7-item fatigue short form scores against a test value of 50, the U.S. population mean, not adjusted for age ($\alpha=0.05$, 1-tailed test). To account for multiple comparisons, we used a Bonferonni correction, yielding a corrected alpha value of 0.0125 (0.05/4).

To test our hypothesis that reported fatigue would be higher across age cohorts than the general U.S. population, we used a series of 1-sample t tests to test mean PROMIS 7-item fatigue short form scores against the published U.S. population age cohort means.[20] For example, the PROMIS mean for the 18 to 34 year old age range was 50.3. When comparing our 18 to 34 year old age cohorts, we conducted the 1-sample t test using the test value of 50.3. An overall alpha value of 0.05 (1-tail) was used. We corrected for multiple comparisons within each clinical sample using a Bonferonni correction (0.05/6 age cohorts=0.00625). For the PPS scores insufficient data were available for persons who were less than 45 years of age in our sample (n=1). We conducted only 4 t tests for this sample; therefore, the corrected alpha value for the PPS age cohort comparisons was 0.0125 (0.05/4).

RESULTS

Descriptive Analyses

A total of 2041 surveys were mailed to potential participants and 1877 were returned; 15 of these were excluded (eg, no consent, returned survey after completion of study). Of the retained 1862 surveys, 1836 included responses to the fatigue items (participants were allowed to skip individual items as well as entire scales). Therefore, the overall participation rate for the current study was 90% (1836/2041). Table 1 reports the means and SDs of the demographic and disability-related variables. The regression analyses examined the linear and curvilinear relationship between fatigue and chronological age. These resulted in very modest R values. Specifically, the respective r values for linear and quadratic relationships were 0.05 and 0.06 (MD), 0.11 and 0.14 (MS), 0.02 and 0.06 (PPS), and 0.09 and 0.13 (SCI). Recall that the null in the statistical test for correlations is that the relationship is no greater than what would have occurred by chance. In only 3 of the 8 tested relationships were the associations greater than would have been expected by chance.

Table 1: Sample Demographics

Characteristics	MD (n=337)		MS (n=580)		PPS (n=441)		SCI (n=478)	
	n*	%	n*	%	n*	%	n*	%
Sex*								
Men	141	41.8	102	17.6	110	24.9	315	65.9
Women	196	58.2	477	82.2	331	75.1	163	34.1
Ethnicity*								
Black	1	0.3	16	2.8	6	1.4	40	8.4
Asian	3	0.9	2	0.3	4	0.9	10	2.1
White	328	97.3	554	95.5	421	95.5	417	87.2
Hispanic/Chicano	3	0.9	8	1.4	7	1.6	7	1.5
Native American	6	1.8	7	1.2	8	1.8	14	2.9
Pacific Islander	0	0	0	0	0	0	2	0.4
Other	5	1.5	4	0.7	5	1.1	4	0.8
Education*								
<High school	5	1.5	5	0.9	5	1.1	15	3.1
High school or General Educational Development	51	15.1	56	9.6	40	9.1	78	16.3
Some College, vocational, technical	88	26.1	197	34.0	122	27.7	164	34.3
College degree	95	28.2	190	32.7	125	28.3	144	30.1
Advanced degree	98	29.1	131	22.6	149	33.8	77	16.1
Diagnosis* (years since)								
1–5y	76	22.6	92	15.9	49	11.1	71	14.9
6–10y	79	23.4	126	21.7	64	14.5	135	28.2
11–20y	91	27.0	203	35.0	143	32.4	118	24.7
>21y	81	24.0	153	26.4	121	27.4	143	29.9
Age								
Mean (range)	53.3 (20–89)		54.5 (21–84)		67.2 (41–94)		49.9 (21–88)	

*Numbers may not add to total because of missing data.

Hypothesis Tests

Study hypothesis 1: mean fatigue scores in the clinical samples exceed the norm for the general U.S. population. The results of the *t* tests comparing the PROMIS fatigue scores for the clinical samples as a whole with the U.S. population mean (50) are presented in table 2. As can be seen, hypothesis 1 was supported. The fatigue scores for each clinical sample were significantly ($P<.001$) higher than the U.S. norms, ranging from 0.24 SD units higher (for the SCI sample) to 0.87 SD units higher (for the PPS sample).

Study hypothesis 2: mean fatigue scores in each age cohort of the clinical samples exceed the U.S. norms for each age cohort. Figure 1 presents the comparisons between age cohort means within each clinical sample to the PROMIS age-specific norms for fatigue, with statistically significant differences indicated by an asterisk. Summaries of the *t* test results are reported below. Tables presenting detailed results for every comparison are available from the authors.

MD age cohort means were significantly higher than the general population means. Average differences ranged from 2.91 to 11.19 points; that is MD means were 0.29 to 1.12 SD units higher than those of the general population across the age cohorts. Moreover, the pattern of fatigue in the various age cohorts indicated a peak in the 45 to 54 year old age cohort that mirrors a similar peak in the general population. What is notable about the comparisons is that, whereas in the general population, fatigue drops off substantially in later age cohorts, in the MD sample this drop off is not nearly so pronounced.

In the MS sample, fatigue was higher than any other clinical group except PPS. All age cohort comparisons with the general population were statistically significant (0.69 to 1.02 SD units higher than those of the general population). The highest fatigue reported in the MS sample was for those in the 35 to 44 year old age cohort, with lower fatigue in older cohorts except for those 75 years and older. However, the means for the 75 years and older cohort were based on a small sample size (n=15) and may not generalize to other samples.

The PPS sample had few persons in the age cohorts younger than age 55. For the older PPS age cohorts, the reported mean fatigue levels were the highest observed among our samples.

Table 2: Comparison Between PROMIS General Population Mean of 50 and Mean Fatigue Scores for Persons With MD, MS, PPS, and SCI

Diagnosis	Mean ± SD	n	*t*	*df*	Probability (1-tailed)	Mean Difference	95% Confidence Interval of the Difference
MD	56.1±8.2	337	13.8	336	<0.001*	6.1	5.3–7.0
MS	58.1±8.2	580	23.7	579	<0.001*	8.1	7.5–8.8
PPS	58.7±7.2	441	25.3	440	<0.001*	8.7	8.0–9.3
SCI	52.4±7.7	478	6.9	477	<0.001*	2.4	1.7–3.1

*Indicates probabilities below the corrected α value of 0.013.

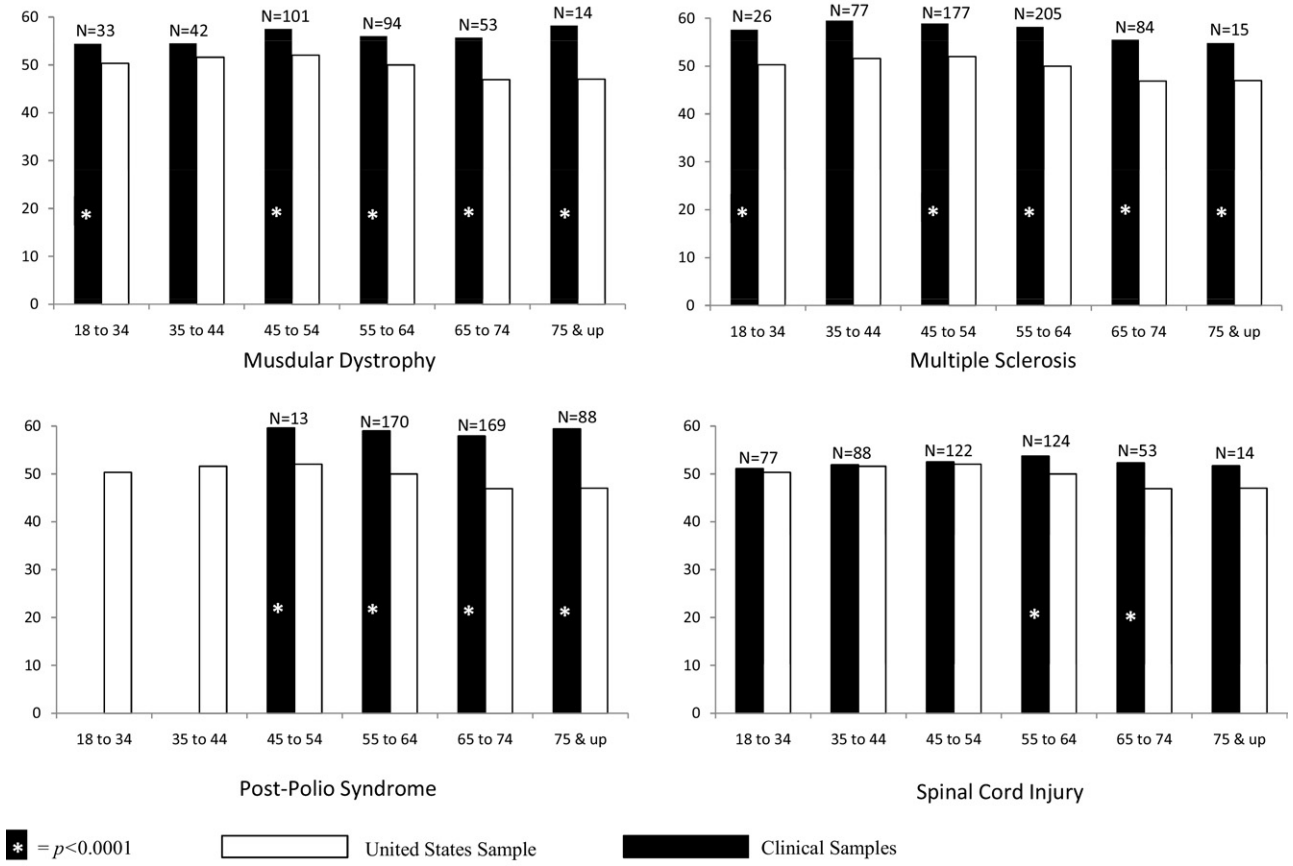

Fig 1. Comparison of age-specific mean fatigue scores by clinical group to PROMIS general population age-range norms. Statistically significant differences are indicated by an asterisk.

Differences in means between PPS and the general population were all statistically significant, and ranged from 0.76 to 1.24 SD units higher than those from the general population.

In contrast to the results for MD and for the general population, for SCI the peak reported fatigue was in the 55 to 64 year old age cohort. The results for the SCI age cohorts younger than 55 years were very similar to those for the general population. Fatigue severity was significantly higher for age cohorts 55 to 64, 65 to 74, and 75 and up, with differences around half an SD.

DISCUSSION

Fatigue and its measurement is a topic that has gained considerable interest in both geriatric and disability research. This is not surprising when one considers the potential impact of this symptom. In middle-aged and older adults with medical disabilities, self-reported fatigue is associated with worse physical function,[23-26] is equally or more impairing than problems such as pain and gait instability,[23,27] and is an independent predictor of mortality.[28] There is also evidence that fatigue is particularly impactful in neurodegenerative conditions such as MS, MD, and PPS.[4,29,30]

The present study described rates of fatigue reported by individuals with physical disabilities in different age cohorts. One of the unique strengths of this study was the availability of a large national survey of fatigue impact (provided through the NIH-funded PROMIS project), allowing for direct comparisons with weighted U.S. norms.

As hypothesized, individuals with disabilities reported significantly greater levels of fatigue than reported in the general U.S. population. This was true regardless of age or disability type. These data are consistent with those from other studies reporting significant prevalence and impact of fatigue in MS,[4] SCI,[6] PPS,[7] and MD.[30] In persons with disabilities, movement and performance of activities of daily living are more energy consuming, and this may cause greater fatigue. It is worth noting that the causes of fatigue probably vary somewhat by disability type. Generally speaking, MS, PPS, and MD are more likely to cause fatigue through a combination of central neurologic processes (eg, activity-dependent conduction block in MS[31]; the effects of sleep disorders such as central apnea and periodic limb movements[32,33]; and through the increased physical effort associated with movement after deconditioning, especially in MD[34]). In SCI (and depending on the level of injury), fatigue can be a side effect of medications used to manage spasticity or pain,[35-38] and can also result from obstructive sleep apnea problems commonly seen in this population.[39]

The relationship between chronological age and fatigue impact is complicated. Although counterintuitive, the trend from the larger literature is one of decreasing fatigue with increasing age from middle-age onwards. This effect has been replicated in studies reporting lower levels of fatigue in individuals over age 60[14-16] as compared to their younger peers.

This pattern is consistent with the life-span developmental model of aging,[40] in that certain periods of adulthood are

associated with greater physical and psychosocial demands than others. For example, middle-age is often a period of career peak and maximum workload, the launching of young-adult children toward independence, increased financial strain as one prepares for retirement, and other challenges. In contrast, the period after retirement (ie, the young-old period) is associated with a significant decrease in daily hassles and stress and an increase in well-being.[41,42] It follows that fatigue would be greatest during middle-age, a period of greatest net demand on resources. It should be noted, however, that in developing nations, fatigue may not have the same age-cohort pattern.

Our data indicate that, for individuals with physical disabilities, the pattern of fatigue over time is not the same as that seen in the general U.S. population. In our MS and SCI samples with disabilities, as in the general U.S. population, there was a peak in reported fatigue; this peak was in a younger cohort in MS (34–44y) and in an older cohort in SCI (56–64y). Another notable difference between the U.S. population and the clinical samples was the levels of fatigue in age cohorts older than the peak fatigue cohort. In the general U.S. population, fatigue mean scores were 0.20 SDs (55–64y), 0.51 SDs (65–74y), and 0.50 SDs (≥75y) below the peak fatigue score mean of 52.0 (45–64y). In contrast, in the disability samples, mean fatigue scores did not become lower in the older age cohorts (relative to the cohort where the highest mean peak fatigue scores were observed). Essentially, the retirement bonus conferred on most individuals as they age is attenuated in those with disability; they do not experience the same degree of relief from fatigue in the young-old period; there appears to be an age- and disability-related fatigue gap. This gap might be explained by disease progression or the development of secondary symptoms that may be accelerating in midlife and contributing to more fatigue. Also, individuals with disability may have less control over their decision to retire, a factor that is associated with poorer adjustment and well-being in general.[43]

Finally, in the normative population, there is very little change in fatigue levels for most adults moving from young (65y) to middle (≥75y) old age. In contrast, in the disability samples, we see a slight but consistent increase toward greater fatigue at this point in the lifespan. Again, this increase in fatigue could reflect ongoing physical decline associated with disease progression.

It is also worth noting that the pattern of fatigue in SCI age cohorts was different than for the other 3 disability groups we studied. Cross-sectional data on these individuals would suggest levels of fatigue that are closer to the U.S. population as a whole in the younger age cohorts, but higher in older cohorts. This difference may be associated with the unique features of SCI. SCI typically results from an acute event and loss of function rather than from an ongoing neurodegenerative process. Also, SCI typically does not involve changes in brain structures that regulate fatigue (such as in MS[31]).

Study Limitations

This study has a number of limitations that should be considered when interpreting the findings. One key distinction that is often made in the fatigue literature is the difference between fatigue and fatigability.[44] Whereas fatigue represents a global state of mental and physical energy depletion, fatigability refers to the change in the feeling of tiredness as a function of the duration, intensity, or frequency of activity. Fatigability therefore takes into account activity levels, and defines how tired an individual gets in relation to defined activities.[45] Fatigability is generally measured as the difference between 2 fatigue levels, for example, immediately after and a few hours after a period of intense activity. The distinction is not merely semantic. Fatigability has demonstrated stronger associations with objective biomechanical factors such as body mass index and lower-extremity strength than fatigue, which is more closely tied to self-reports of outcomes such as pain and vitality.[44] There are also biological factors in aging that may contribute to greater fatigability, but not necessarily to greater fatigue.[45] In the present study, we assessed only fatigue and not fatigability. Given the possibility that fatigability may show a different trajectory than fatigue across the lifespan and have greater impact on actual functioning, future studies should incorporate this important measurement concept.

Another limitation comes in our use of cross-sectional data, which weakens our ability to make causal inferences regarding the effects of age on fatigue. Future studies should investigate fatigue trajectories by following individuals across time. Also, although our use of the PROMIS measure of fatigue impact made for simple and direct comparison to national norms, the precision of our estimates in our clinical populations was limited by sample size in each age cohort. For example, fewer than 50 individuals with SCI, MD, or MS reported being over the age of 75. Findings based on these small samples may lack stability and require replication. Finally, our sample was geographically limited and may not represent individuals with disabilities as a whole. Additional research using other samples of individuals with MD, MS, PPS, and SCI is needed to determine the generalizability of our findings.

CONCLUSIONS

Despite the study's limitations, the analyses presented are the first to directly compare levels of fatigue to a large national sample of the general U.S. population. We found, as hypothesized, that individuals with disabilities reported higher levels of fatigue than the normative population. Also, whereas in the general population reported fatigue was substantially lower in older age cohorts relative to middle age, the clinical samples that we studied did not appear to benefit as much from this age cohort effect. This means that individuals with disabilities are not only at greater risk than individuals without disabilities to experience fatigue, but that this risk for increased fatigue, relative to normative values, increases with age. More research is needed to determine the specific negative impact of fatigue symptoms on functioning in individuals with disabilities as they age, and to identify, develop, and test the efficacy of different treatments that might buffer or eliminate any negative effects found. Potential treatments that might be studied include pharmacologic interventions,[46] nonpharmacologic approaches such as activity and energy conservation management,[47] and cognitive behavioral therapy. By contributing to reductions in the severity and negative impact of fatigue in persons with disabilities, such research could enhance the overall quality of life of individuals aging with a disability.[48]

APPENDIX 1: PROMIS FATIGUE SHORT FORM AND SCORING KEY

Please respond to each question by marking one box per row.

In the past 7 days…

	Never	Rarely	Sometimes	Often	Always
How often did you feel tired?.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
How often did you experience extreme exhaustion?.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
How often did you run out of energy?.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
How often did your fatigue limit you at work (include work at home)?.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
How often were you too tired to think clearly?.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
How often were you too tired to take a bath or shower?.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
How often did you have enough energy to exercise strenuously?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

Scoring instructions: Sum across all items to obtain the raw score. In the table below, identify the T score associated with the raw score.

Raw Score	T score	Raw Score	T score	Raw Score	T score
7	29.4	17	52.2	27	66.3
8	33.4	18	53.7	28	67.8
9	36.9	19	55.1	29	69.4
10	39.6	20	56.4	30	71.1
11	41.9	21	57.8	31	72.9
12	43.9	22	59.2	32	74.8
13	45.8	23	60.6	33	77.1
14	47.6	24	62.0	34	79.8
15	49.2	25	63.4	35	83.2
16	50.8	26	64.8		

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