Applications of Item-Response Theory in Health Outcomes Assessment and Pain Measurement

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Abstract

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A key finding of the Institute of Medicine's 2011 report Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research is the need for improved pain assessment. [1] The following chapters that comprise this dissertation aim, in small part, to address this need. Both chapters focus of pain measurement, and as such are located at the intersection of psychology, public health, and statistical methodology. The first is an assessment of the validity and reliability of previously development measures of Pain Interference and Pain Behavior using fixed and random effects linear modeling. The second reports the development of a novel measure of neuropathic pain quality using factor analytic and item-response theory-based statistical approaches to measurement. Concluding remarks highlight contributions of these study findings to pain-related research.

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Dedication

To Maggie and Elizabeth

Introduction

A key finding of the Institute of Medicine's 2011 report *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research* is the need for improved pain assessment. [1] The following two chapters that comprise this dissertation aim, in small part, to address this need and represent part of my research training program at the University of Washington. Both chapters focus of pain measurement, and as such are located at the intersection of psychology, public health, and statistical methodology. The first is an assessment of the validity and reliability of previously development measures of Pain Interference and Pain Behavior using fixed and random effects linear modeling. The second reports the development of a novel measure of neuropathic pain quality using factor analytic and item-response theory-based statistical approaches to measurement. Concluding remarks highlight contributions of these study findings to pain-related research.

Chapter One:

Clinical Validity of PROMIS® Pain Interference and Pain Behavior

INTRODUCTION

Approximately 100 million people in the United States experience chronic pain, and pain costs up to $635 billion dollars annually in treatment and lost productivity.[1] In order to develop effective treatments for pain and to evaluate treatment effectiveness, researchers and clinicians need psychometrically sound and clinically valid instruments for measuring different aspects of pain. One important aspect of pain is pain interference, defined as the degree to which pain interferes with an individual's daily activities.[2] Pain interference is increasingly recognized as an important facet of patients' pain experiences and has been recommended as a core outcome in clinical trials of pain treatments. [3] Pain behavior, defined as behavior that typically indicates to others that an individual is experiencing pain,[2, 4, 5] can include both verbal (e.g., asking for help, sighing, moaning) and non-verbal (e.g., grimacing, resting, guarding) behaviors. Pain behaviors can be protective by eliciting assistance or support after a precipitating event (e.g. trauma, surgery), but when they are maintained beyond rehabilitation and recovery, pain behaviors can contribute to subsequent physical and psychosocial disability,[6] making them useful targets for behavioral interventions.[7, 8]

The NIH-funded Patient Reported Outcomes Measurement Information System (PROMIS®) has developed a family of instruments that can be used to measure different aspects of physical, mental, and social health.[9] More information on the development, validation, and implementation of all PROMIS measures can be found at www.nihpromis.org, and options

regarding fixed-length and customized short forms and CAT administration can be found at www.assessmentcenter.net. PROMIS Pain Interference (PROMIS PI) [10] and Pain Behavior (PROMIS PB) [11] item banks have been developed using modern psychometric methods,[12, 13] and the psychometric properties of these measures have been previously evaluated in a large cross-sectional sample that included both healthy people and people with various chronic conditions, including those discussed in this paper.[10, 11]

The ability of an instrument to detect true change is a critical feature of clinical validity, and this is the case when comparing effectiveness of interventions in clinical trials or when evaluating patients in clinical settings. Another important aspect of the clinical validity of a measure is its ability to distinguish between individuals who have the same disease or condition, but who differ in terms of severity. Furthermore, when instruments are developed for cross-population comparisons—as is the case with the PROMIS instruments—it is important to evaluate whether the scores can detect change in many different settings and in different clinical samples. Similarly, scores should not reflect change when in fact individuals were stable on the outcome of interest. In this study, we evaluated the clinical validity of PROMIS PI and PROMIS PB scores in adults and how these scores functioned over time in various clinical settings. Specifically, we evaluated: A) score responsiveness to change in groups expected to change over time (e.g., after intervention); B) score stability in clinical groups not expected to experience substantial changes in pain; C) ability of scores to discriminate between groups differing in clinical severity; and D) ability of scores to discriminate among groups self-reporting improved, worsened, or stable health status over time.

METHODS

Data for this study were collected in longitudinal validation studies conducted by PROMIS investigators. The five clinical samples represented in this study included individuals with chronic low back pain (BP), cancer, chronic obstructive pulmonary disease (COPD), depression, and rheumatoid arthritis (RA). Detailed descriptions of recruitment, eligibility criteria, and treatments are available,[14] and a brief description of each sample is detailed below by respective study hypothesis.

STUDY AIM A: Evaluate score responsiveness in groups expected to change after intervention

Responsiveness was evaluated in two clinical samples of participants who were receiving treatment for BP or depression. Participants with BP were recruited from the University of Washington Spine Center in Seattle and local recruitment sites. All participants had BP for at least six weeks and received a spinal injection. Participants with depression were recruited from outpatient treatment clinics at Western Psychiatric Institute and Clinic, Pittsburgh, PA and its affiliates and received treatment in the form of antidepressants, psychotherapy, or both. In the BP and depression treatment studies, we expected to see lower average PROMIS PI and -PB scores after treatment for both the back pain and the depression samples, because epidural steroid injection is a treatment for pain, and antidepressants have been reported to reduce pain.[15] Larger reductions were expected for the BP sample, because the primary target of the treatment protocol was pain reduction.

STUDY AIM B: Examine score stability in groups not expected to experience substantial changes in pain

Participants with any type of cancer were recruited from North Shore University Health System in Chicago, IL. In the cancer sample, participants were administered PROMIS measures in an observational study setting with multiple heterogeneous treatment modalities. While follow-up administration of PROMIS measures took place at approximately two months after baseline assessment, participants were enrolled irrespective of treatment status (i.e. before or after starting treatment regimen). Accordingly, some participants were expected to improve and others were expected to deteriorate, and the timing and treatment modalities were too heterogeneous to support clear expectations of mean change for the cancer sample.

Participants with RA were enrolled in a longitudinal study of patient reported outcomes with multiple recruitment sources that included the Aging Medical Information System (ARAMIS) and the Stanford Rheumatoid Arthritis Registry. Administration of PROMIS measures was intended to evaluate longitudinal changes in this clinical population, and even though RA is known to worsen over time, all participants received routine clinical care that at times included intervention. Like the cohort with cancer, some participants with RA were expected to improve while others were expected to deteriorate due to the heterogeneity of clinical characteristics and treatment status. Mean changes in T-scores were not expected to be as large in terms of magnitude in these cohorts with RA and cancer, and these analyses were considered more exploratory in nature, given the observational nature of these studies.

STUDY AIM C: Evaluate score discrimination between groups differing in clinical severity

Discrimination based on clinical severity was evaluated in a sample of participants with a 10 pack/year history of smoking who met the Global Initiative for Chronic Obstructive Lung Disease clinical criteria for COPD. They were recruited from multiple participating institutions including the University of North Carolina, North Shore University Health System, The University of Pittsburgh, and Duke University. Comparisons were planned between participants with stable COPD and those with COPD-related exacerbations. Participants were defined as stable if they had been exacerbation-free for 2 or more months prior to enrollment and remained free of COPD-related exacerbations throughout the study. Participants with COPD-related exacerbations at enrollment who completed the study without subsequent exacerbations were expected to have higher PROMIS PI and -PB T-scores than those with stable COPD, whose scores were expected to decrease as exacerbations resolved.

STUDY AIM D: Evaluate score discrimination between subgroups defined by self-reported change

We examined the ability of PROMIS PI and -PB to discriminate among groups that reported improved, worsened, or stable status in all 5 clinical samples using general health and pain-specific anchors of change. Participants reporting improved global health status or improved pain were expected to have larger negative effects reflected in decreases in PI and PB T-scores,

while the opposite was expected for those reporting worsening health or pain (i.e. positive change scores indicating increased pain).

Measures

Data were collected at multiple research sites and were combined into a single dataset for this analysis with timing of follow-up varying by clinical sample (BP: 3 months, cancer: 2 months, COPD: 3 months, depression: 3 months, RA: 12 months). For a thorough overview of the qualitative and quantitative methodologies employed in developing and testing the PROMIS PI and -PB item banks, see studies by Amtmann et al,[10] and Revicki et al,[11] among others.[12, 16-18] In addition to standard clinical and demographic descriptors, participants also rated single items related to global health and pain, which served as anchors for subgroup comparisons between those who self-reported improvement, worsening, or no change since baseline. Computer adaptive testing (CAT) was used to collect PROMIS PI and -PB in the back pain, COPD, and depression cohorts. PROMIS short forms (Version 1) were used to assess PROMIS PI and -PB in the arthritis and cancer cohorts.

Statistical analyses

Responsiveness of PROMIS PI and -PB was evaluated in each of the clinical samples using linear mixed models. Mixed effects models are appropriate for estimation of longitudinal changes in health status, because the random effects component accounts for the dependency induced by repeated measurements within individuals.[19, 20] Before carrying out the analyses, the risk of bias from problematic missing data was examined in each clinical sample by assessing relationships between baseline measures and attrition. This risk was found to be minimal, and for

all analyses the data were considered missing at random. When data are missing at random, linear mixed models can be particularly useful as data from participants with only one time-point available are included in estimation.[21, 22] Marginal means for baseline and follow-up PROMIS PI and -PB scores were estimated along with change scores, standard errors, and 95% confidence intervals. Standardized response means (ratio of mean change to the standard deviation of that change) were estimated to compare effect sizes between subgroups defined by single item anchors indicating improved, worsened, or stable pain and global health status over time. Data management and preparation was carried out using SAS 9.3 for Windows (Copyright 2002-2010 SAS Institute Inc.), and all statistical analyses were carried out using STATA/IC 12.1 (Copyright 1985-2011 Stata Corp LP).

RESULTS

The demographic and clinical profile of each cohort has been reported in detail.[14] Pooling across all studies, most participants were non-Hispanic whites (82%), roughly half of all participants across these studies were 60 years old or older (54%), and most participants were female (68%), with the exception of the sample with COPD (42%). The majority of the cohort with stable COPD (n=79) was white (72%), male (56%), and had a Medical Research Council (MRC) Breathlessness Rating of 1 or 2 (56%). The majority of the cohort with COPD-related exacerbations (n=46) was white (73%), male (61%), 50 or more years of age (91%), and had an MRC Breathlessness Rating of 3 or higher (63%). The majority of the BP cohort (n=218) was white (84%), female (56%), 50 or more years of age (62%) with largely moderate to severe back pain (74% ≥8 on 0-10 numeric pain scale). The majority of the depression cohort (n=196) was white (78%), female (74%), 18-49 years of age (52%) and had a Center for Epidemiologic

Studies-Depression score of 22 or greater (73%). The majority of the cancer cohort (n=310) was white (81%), female (61%), 50 or more years of age (76%), and had an Eastern Cooperative Oncology Group Performance Status Rating (ECOG-PSR) of 0 or 1 (77%). The majority of rheumatoid arthritis sample (n=521) was white (88%), female (81%), 50 or more years of age (88%) and had a HAQ Disability Index of 0-1 (57%). From the combined sample of 1370 participants, less than 1% (n=13) did not have sufficient data available to score PROMIS PI and -PB measures.

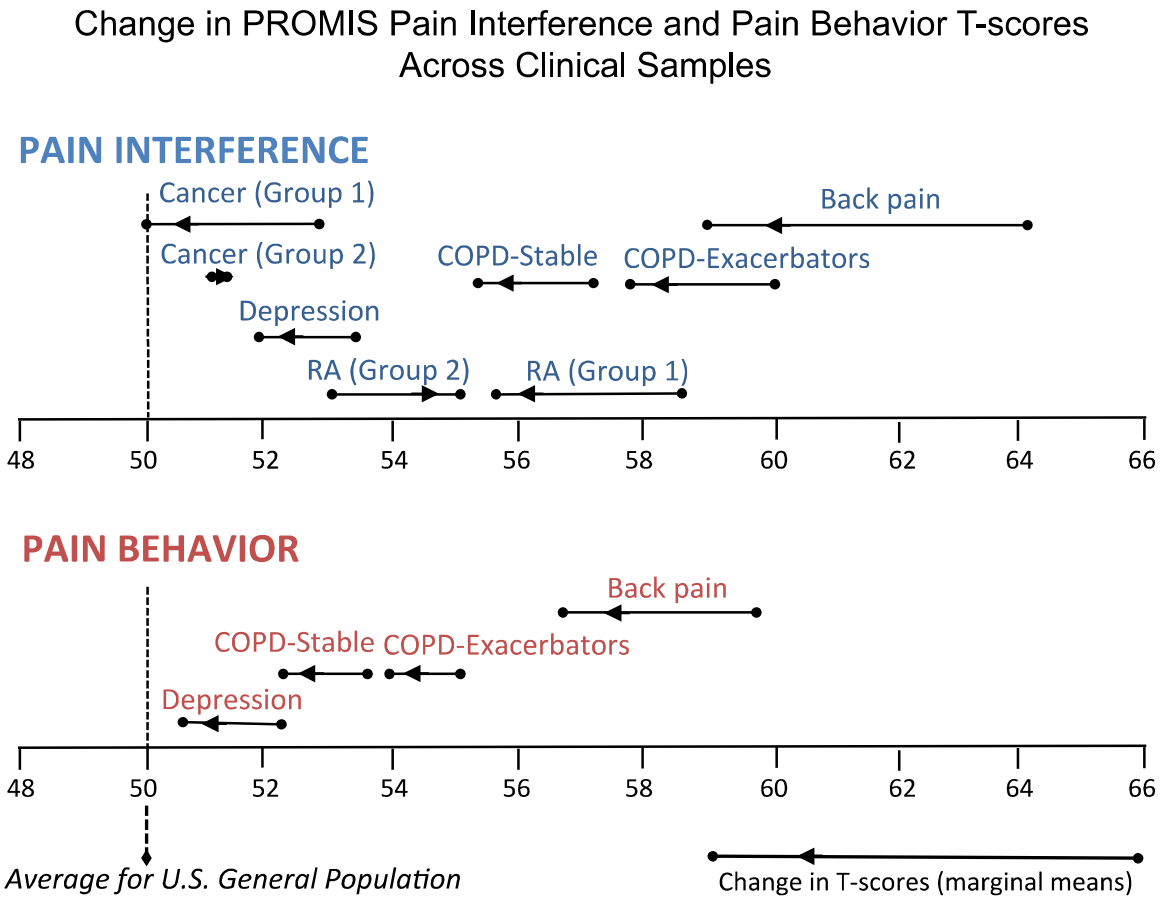
Baseline, follow-up, and change scores from the mixed effects models are presented in Table 1. PROMIS PI and -PB scores are reported on a T-score metric (U.S. general population mean=50, SD=10) that facilitates cross-sample comparisons (Figure 1) with higher scores indicating worse outcomes (i.e., more pain-interference or pain-behavior).

Table 1. Baseline, follow-up, and change in PROMIS Pain Interference and Pain Behavior estimates by clinical sample

	Back Pain		Cancer		COPD-Exacerbation	
	n=218/175	95% CI	n=305/277	95% CI	n=44/44	95% CI
PAIN INTERFERENCE						
Baseline	64.2	(63.2, 65.2)	51.9	(50.8, 52.9)	59.9	(56.6, 63.1)
Follow-up	58.8	(57.6, 59.9)	50.7	(49.6, 51.8)	57.7	(54.4, 61.0)
Change	-5.4**	(-6.6, -4.3)	-1.1*	(-2.1, -0.2)	-2.2	(-5.6, 1.3)
PAIN BEHAVIOR						
Baseline	59.7	(59.1, 60.4)			55.0	(52.0, 58.1)
Follow-up	56.6	(55.8, 57.3)			53.8	(50.8, 56.8)
Change	-3.2**	(-4.0, -2.4)			-1.2	(-4.1, 1.7)

	COPD-Stable		Depression		Rheumatoid Arthritis	
	n=74/70	95% CI	n=196/187	95% CI	n=520/472	95% CI
PAIN INTERFERENCE						
Baseline	57.4	(55.1, 59.7)	53.4	(51.9, 54.9)	55.3	(54.6, 56.0)
Follow-up	55.2	(52.9, 57.5)	51.9	(50.4, 53.4)	55.4	(54.7, 56.2)
Change	-2.2*	(-4.2, -0.1)	-1.5*	(-2.8, -0.2)	0.12	(-0.5, 0.7)
PAIN BEHAVIOR						
Baseline	53.7	(51.5, 55.9)	52.2	(50.7, 53.7)		
Follow-up	52.3	(50.1, 54.5)	50.4	(48.9, 51.9)		
Change	-1.4	(-3.4, 0.5)	-1.8*	(-3.1, -0.5)		

Figure 1. Change in PROMIS Pain Interference and Pain Behavior estimates by clinical sample



*Cancer (group 1, n=51): patients reporting improved global health at follow-up
*Cancer (group 2, n=85): patients reporting worsened global health at follow-up
*RA (group 1, n=60): patients reporting improved global health at follow-up
*RA (group 2, n=92): patients reporting worsened global health at follow-up

STUDY AIM A: Responsiveness in groups expected to change after intervention

The largest changes in PROMIS PI and -PB T-scores were observed for the cohort with BP, which was consistent with expectations in terms of magnitude and direction. Pre-to post-treatment changes in PROMIS PI (Δ=-5.4, 95%CI: -6.6 to -4.3, $p<0.001$) and PROMIS PB (Δ=-3.2, 95%CI: -4.0 to -2.4, $p<0.001$) T-scores were both statistically significant. PROMIS PI and -

PB change estimates were smaller but statistically significant for participants undergoing treatment for depression (Δ=-1.5 [95%CI: -2.8 to -0.2], p=0.027and Δ=-1.8 [95%CI: -3.1 to -0.5], p=0.005, respectively).

STUDY AIM B: Stability in groups not expected to have substantial changes in pain

The smallest estimated change in PROMIS PI T-scores was observed for participants with RA (Δ=0.1), which was not statistically different from zero. Changes in PROMIS PI T-scores for the cohort with cancer were also small but were statistically significant (Δ=-1.1, 95%CI: -2.1 to -0.2, p=0.023). Given that both of these studies were observational in nature (i.e. PRO assessment completed irrespective of changes in treatment status), separate estimates are presented in Figure 1 for participants reporting improved, worsened, or stable health status over time.

STUDY AIM C: Discrimination between groups differing in clinical severity

Although PROMIS PI scores were higher for participants with COPD exacerbations at baseline than for those with stable COPD (mean PROMIS PI T-scores: 59.9 vs. 57.4, respectively), this difference was not statistically significant. Change estimates were in the expected direction for COPD exacerbation (Δ=-2.2) as exacerbation-related symptoms resolved over time, but this difference was not statistically significant. The same trend was observed for PROMIS PB; non-significant differences were in the expected direction but smaller in magnitude (exacerbation vs. stable at baseline [55.0 vs. 53.7], change for exacerbation: [Δ=-1.2]).

STUDY AIM D: Discrimination of subgroups based on self-reported change

Table 2 details standardized response means for subgroups defined by self-reported change in pain and global health status. Larger effects were observed when using pain-based anchors and when participants reported improvements in global health status between baseline and follow-up. The largest SRMs for PROMIS PI were observed for those reporting pain reductions in the BP (SRM = -1.09, $p<0.05$) and stable COPD (SRM = -1.14, $p<0.001$) samples. The smallest effects in PROMIS PI were observed for those with RA reporting no changes in pain over time (SRM = 0.00, NS). With respect to PROMIS PB scores, the largest effects were observed for those reporting pain reductions in the BP (SRM = -0.81, $p<0.05$) and COPD (stable: SRM = -0.81, $p<0.05$; exacerbation: SRM = -0.85, $p<0.05$) cohorts, while the smallest effects were observed for those with worsening health status in the depression (SRM = 0.03, NS) and COPD with exacerbations cohorts (SRM = 0.06, NS) along with for those reporting no change in general health in the stable COPD cohort (SRM = -0.02, NS).

Table 2. Standardized response means of PROMIS Pain Interference and Pain Behavior by change in health status and diagnostic subgroups

	Back pain				**Cancer**				**COPD-Exacerbation**			
	Global anchor		Pain anchor		Global anchor		Pain anchor		Global anchor		Pain anchor	
	n	SRM	n	SRM	n	SRM	n	SRM	n	SRM	n	SRM
PAIN INTERFERENCE												
Better	51	-0.94**	112	-1.09*	51	-0.52**	79	-0.43*	7	-0.95*	15	-0.87*
Same	94	-0.58**	32	-0.26	130	-0.19*	109	-0.34*	14	0.49	12	-0.37
Worse	24	-0.47*	27	0.44*	85	0.06	53	0.57*	13	-0.09	14	0.63*
PAIN BEHAVIOR												
Better	51	-0.69**	112	-0.81*					7	-0.85	15	-0.85*
Same	95	-0.59**	32	-0.60*					14	0.39	12	-0.37
Worse	24	-0.52*	28	0.31					13	0.06	14	0.73*

	COPD-Stable				**Depression**				**Rheumatoid Arthritis**			
	Global anchor		Pain anchor		Global anchor		Pain anchor		Global anchor		Pain anchor	
	n	SRM	n	SRM	n	SRM	n	SRM	n	SRM	n	SRM
PAIN INTERFERENCE												
Better	13	-0.70*	21	-1.14**	43	-0.40*	66	-0.73**	60	-0.49*	75	-0.52**
Same	38	-0.15	22	-0.50*	113	-0.15	73	-0.21	297	0.01	215	0.00
Worse	14	0.08	25	0.51*	30	0.06	46	0.67**	92	0.30*	159	0.34**
PAIN BEHAVIOR												
Better	13	-0.70*	21	-0.81*	43	-0.48*	66	-0.65**				
Same	38	-0.02	22	-0.32	113	-0.18	73	-0.17				
Worse	14	-0.08	25	0.47*	30	0.03	46	0.33*				

SRM, Standardized Response Mean; COPD, Chronic Obstructive Pulmonary Disease; *denotes statistical significance at $p < 0.05$; **denotes statistical significance at $p < 0.001$

DISCUSSION

These results provide support for the clinical validity of the PROMIS PI and -PB measures for use in groups of individuals with diverse chronic conditions. In this study, we examined four aspects of clinical validity: responsiveness, stability, discrimination between groups differing in clinical severity, and discrimination among groups defined by self-reported change. We found that PROMIS PI and PROMIS PB T-scores were responsive to change across multiple clinical samples when change was expected, with the largest differences observed for treatments targeting pain, and that scores were relatively stable when no change was anticipated. While we did not find statistically significant differences between PROMIS PI and -PB T-scores when making comparisons in clinical severity of COPD, the differences were in the expected direction. It also should be noted that this cohort was the smallest of all clinical samples and, therefore, had the least statistical power. Both PROMIS PI and PROMIS PB T-scores distinguished among subgroups defined by self-reported change in health status and change in pain over time (i.e., better, worse or the same). Minimal Clinically-Important Differences (MCIDs) often range from 0.3 to 0.5 standard deviation units,[23, 24] and MCID estimates for the PROMIS PI were found to be similar in a cohort of patients with cancer.[25] Of the 40 SRM estimates for patients reporting improved or worsened health status over time, 32 (80%) and 22 (55%) were greater than the 0.3 and 0.5 SD threshold standards, respectively. Moreover, effect sizes across different samples and health conditions were consistent with participants' global and pain-specific impressions of change adding additional support for the clinical validity of these PROMIS measures.

While clinical validity of the PROMIS PI and -PB measures was evaluated in 5 distinct clinical samples in this study, validation in other clinical samples is still warranted. Of particular

interest would be studies in which clinical benchmarks vary by underlying condition and treatment protocol. In such circumstances the addition of clearly defined control groups in intervention trials would further refine estimates of responsiveness and meaningful change. While interpretability of the PROMIS PI and -PB measures is enhanced by the common metric centered on the US general population, further investigation is needed to relate scores to more clinically familiar benchmarks of interest to clinicians involved in treating and studying pain. An expanded evaluation of MCIDs will help interpret the clinical meaning of longitudinal differences in PROMIS PI and -PB T-scores and these analyses are under way.

Measurement of pain interference and pain behavior is a key component of a comprehensive and robust assessment of chronic diseases that include chronic pain as a primary or secondary condition. The clinical validity of PROMIS PI and -PB measures supports their use in pain-related clinical research, including clinical trials and comparative effectiveness research. This study adds further evidence that the PROMIS suite of patient-reported measures are psychometrically robust, valid, and enable efficient, flexible, and comprehensive assessment of chronic pain in addition to many other important aspects of health.

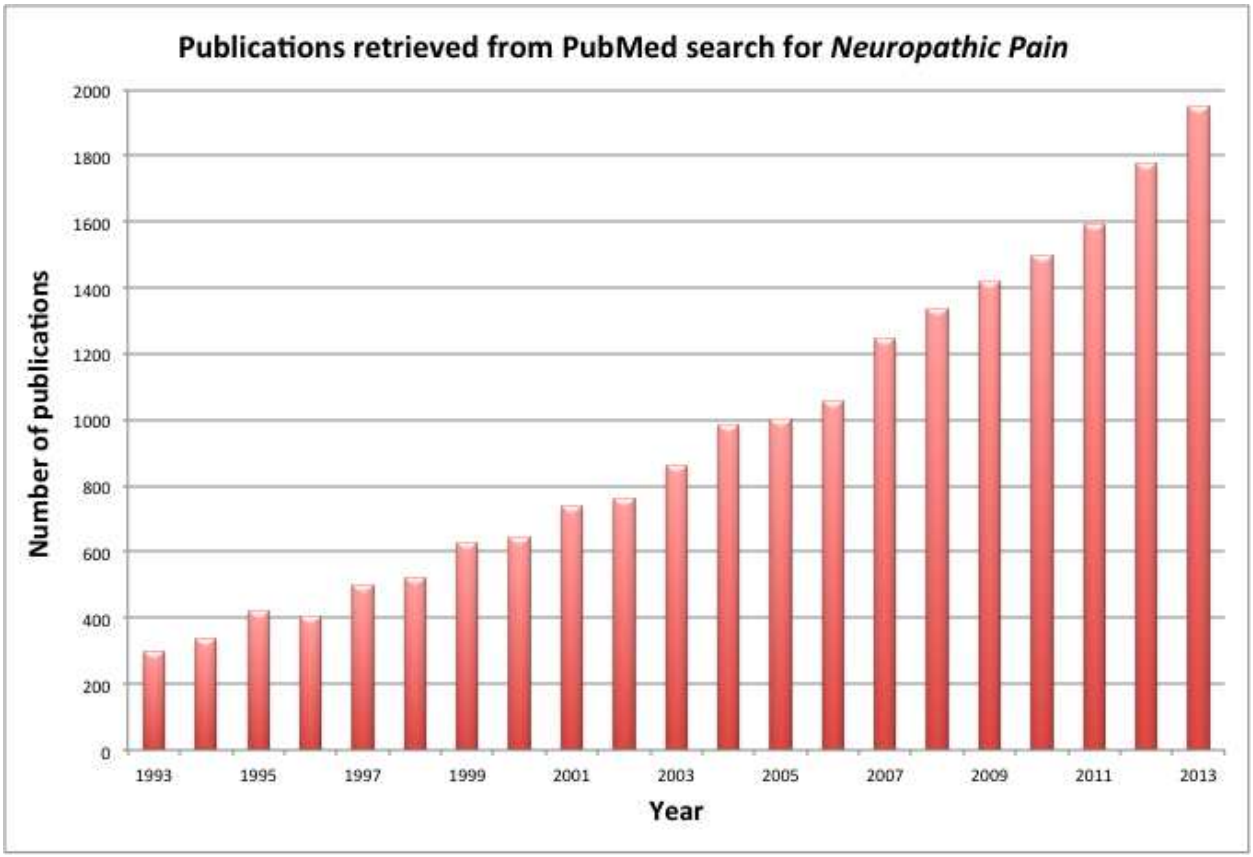
Chapter Two:

Development of a PROMIS® Measure of Neuropathic Pain Quality

INTRODUCTION

Neuropathic pain (NP) is a consequence of many chronic conditions that share a common mechanistic cause: a lesion or disease of the somatosensory nervous system.[26, 27] These conditions include diabetic neuropathy, post-herpetic and trigeminal neuralgias, HIV-related peripheral neuropathy, and treatment-related neuropathies such as phantom-limb pain or cancer-related chemotherapy pain, among others. Estimates of the prevalence of NP varies considerably by condition (e.g. 3% in Carpal Tunnel Syndrome to over 50% in Phantom Limb Pain),[28] and even in the general population, prevalence estimates of pain with neuropathic characteristics range from 7-10%.[29] The costs associated with NP to patients and society are substantial,[27, 30-32] and NP-related research is steadily increasing. A search of *neuropathic pain* in PubMed returns a nearly 10-fold increase in number of citations over the last 20 years alone (Figure 1).[33] While this interest has led to an evolving understanding of NP and the complex processes involved in its generation, treatment of NP continues to largely target symptom palliation with limited efficacy.[34]

Figure 1. Number of publications retrieved from PubMed search* of *neuropathic pain* by year



* search conducted 30 April 2014

The clinical manifestation of NP is distinct from other types of chronic pain in that it is often accompanied by positive (e.g., abnormal or unpleasant sensations) and negative (e.g., decreased sensitivity) signs and symptoms that reflect the underlying neural damage.[35, 36] A definitive diagnosis of NP requires identification of the underlying somatosensory dysfunction, but accurate diagnosis can be complicated by varying degrees of neuropathic involvement in pain generation and comorbid nociceptive or idiopathic pain.[35] While a detailed understanding of the mechanisms that lead to NP in some patients but not other comparable patients remains illusive, individuals with chronic NP often describe their pain in ways that are distinct from other painful conditions.[37] Systematic differences in these *pain qualities* present useful diagnostic

information to a clinician or researcher, as they may indicate underlying neurological involvement in pain generation.[35, 38]

A variety of NP measures have been developed that capitalize on these systematic differences in pain qualities. As multiple positive and negative signs and symptoms often accompany neuropathic pain, some of the available NP measures make use of a range of assessment procedures in addition to self-report, including clinical testing (e.g. quantitative sensory testing), interview, or a mixture of these methods with self-report. However, clinical examination is not always possible and self-reported measures are more easily incorporated into epidemiological studies and for screening in clinics and for research studies. Available measures of NP also differ in their intended use and application, as some, like the PainDETECT and the IDpain were developed primarily as screeners for neuropathic pain symptoms.[39, 40] Other measures like the Neuropathic Pain Scale and the Pain Quality Assessment Scale have also been used to document and evaluate the presence of or changes in individual symptoms profiles or sensations in response to treatment.[41-45] A detailed summary of the evidence supporting the precision and utility of self-report measures of NP are presented in Appendix 1. Psychometric evaluations of these and related measures have identified multiple distinct dimensions of the pain experience, including a neuropathic dimension.[46-48] This has lead to the revision of or development of pain measures that conceptualize and describe neuropathic pain as a scale continuum that can reflect magnitude of neuropathic involvement (or certainty of involvement) in self-reported pain.[49, 50] As others have suggested, this conceptualization of neuropathic and nociceptive involvement as a continuum may more closely approximate the shared physiological processes (i.e. ascending and descending neural pathways) involved in neuropathic and nociceptive pain detection and modulation.[51]

For NP and other chronic pain conditions, accurate and comprehensive assessment remains a critical public health challenge.[1] Recently, the multi-center cooperative group collectively referred to as the Patient-Reported Outcome Measurement Information System (PROMIS) was charged with creating a comprehensive battery of valid and precise health status measures appropriate for use in clinical and research settings.[9] As part of the first wave of the PROMIS initiative, multiple health status measures were developed using rigorous qualitative and quantitative statistical approaches to measurement, [2, 52] including measures of Pain Intensity, Pain Interference, and Pain Behavior.[10, 11, 53] The use of item-response theory based statistical models has enabled a high degree of flexibility in administration, as PROMIS measures can be deployed using item banks and computer-adaptive testing (CAT), pen-and-paper based surveys, fixed-length short forms, and customized short forms.[54] More information on the development and validation of the PROMIS suite of measures can be found at www.nihpromis.org and www.assessmentcenter.net.[10, 11, 53] As part of this initiative, extensive data on patient-reported pain qualities have also been collected. In this cross-sectional study, we aimed to evaluate the ability of PROMIS pain quality descriptors to identify distinct pain phenotypes of neuropathic and non-neuropathic origin, and if possible, to develop a scale measure of neuropathic pain quality.

METHODS

Participants

The analytic cohort was comprised of four clinical subgroups representing neuropathic and non-neuropathic pain conditions. The neuropathic pain conditions were diabetic neuropathy

and cancer chemotherapy-induced peripheral neuropathy, and non-neuropathic pain conditions were rheumatoid arthritis and osteoarthritis. Study participants were recruited at multiple sites through a variety of methods including direct in-clinic approaches, mailed letters of invitation to patients identified by clinic physicians, medical records searches, participant registries (National Data Bank for Rheumatic Diseases, http://www.arthritis-research.org/) or targeted advertising within online support and advocacy groups. Clinical recruitment sites included Rehabilitation Institute of Chicago's Center for Pain Management and University of Washington Medical Center's Diabetes Care Centers. Participants completed informed consent and provided authorization to confirm clinical diagnosis with treating physicians. For all groups, inclusion criteria were willingness and ability to provide informed consent, ability to read and speak English, age of at least 18 years, and the ability to see and interact with a computer screen, mouse, and keyboard. The human subjects divisions of participating institutions approved study procedures, and participants were compensated $20 to $30 in cash or gift card according to site-specific institutional review board guidelines.

Subgroup-specific inclusion/exclusion criteria

For the cohort with diabetes, participation required clinically confirmed diabetes and self-reported symptoms of painful peripheral neuropathy that began after onset of diabetes and were present for at least three months prior to starting the study. Comorbid fibromyalgia or rheumatoid arthritis and/or limb amputation were exclusion criteria. For the cohort with chemotherapy-induced peripheral neuropathy, participation required clinical confirmation of

diagnosis and past or current treatment with a chemotherapy agent known to cause peripheral neuropathy. Participation also required self-reported symptoms of peripheral neuropathy that began after administration of chemotherapy that were present for at least three months prior to starting the study. Comorbid fibromyalgia or rheumatoid arthritis and/or stem cell transplant were exclusion criteria. For the cohorts with osteoarthritis and rheumatoid arthritis, participation required clinical confirmation of diagnosis with no additional subgroup-specific exclusion criteria.

Measures

After screening for eligibility, participants were directed to an internet-based survey system, Assessment Center (https://www.assessmentcenter.net), to complete study surveys through computer adaptive testing (CAT) or were provided paper-based short-form (SF) surveys. Surveys included demographic and clinical information and a battery of PROMIS measures assessing Global Physical and Mental Health (SF-version 1.1), Pain Intensity (SF-version 3a), Pain Interference (CAT & SF-version 6b), Pain Behavior (CAT & SF-version 7a), and PROMIS-29 Profile (version 1.0) measures of Physical Function, Fatigue, Anxiety, Depression, Sleep Disturbance, and Satisfaction with Social Roles.

Pain descriptors

During the first wave of the PROMIS initiative, a preliminary set of pain quality descriptors was identified through literature review, and the content of the of pain quality items was revised following focus groups and cognitive debriefing interviews.[12, 52] These pain

quality descriptors were then administered to participants from the US general population and participants with chronic pain recruited from the American Chronic Pain Association. Preliminary analyses supported the hypothesis that the pain quality factors described clinically important sub-domains of pain sensory experience, but the data were not sufficiently unidimensional to proceed with scale calibration. As part of a follow-up study targeting a broader array of pain conditions, participants were administered a revised set of 42 pain quality descriptors with a 5-point Likert response scale. For 40 of the 42 pain quality descriptors, the item-stems were: "In the past 7 days, did your pain feel…" with the remaining 2 items modified slightly to maintain grammatical form when items pertained to shifting locations of pain. Response options for these pain descriptors were: "not at all", "a little bit", "somewhat", "quite a bit", and "very much".

Analysis

The analytic cohort was split into separate development (n=367) and validation (n=368) datasets to enable cross-validation of the dimensional structure of the data. Randomization was carried out within each diagnostic condition to ensure equivalent distributions across datasets. In the developmental dataset, response patterns were examined at the item level to identify items that best distinguished between participants with and without neuropathic pain conditions. Cramer's *V* served as a sample size adjusted measure of effect size representing the strength of relationship between diagnostic category and observed response patterns. Items most strongly associated with diagnostic condition (i.e. items with the highest probabilities of endorsement by those with neuropathic pain) were identified and compared with those identified in the dimensionality assessment.

Exploratory factor analysis (EFA) of the development dataset was carried out, and unidimensionality of the neuropathic descriptors identified in the EFA was then assessed in the holdout sample using Confirmatory Factor Analysis (CFA). Traditional fit indices guided evaluations of model fit (CFI, TLI),[55] and all factor loadings and residual covariances were evaluated in terms of magnitude and statistical significance. Then, IRT-based calibration using Samejima's graded response model for polytomous response formats was carried out using the combined sample to maximize sample size and precision during estimation.[56] Item fit was evaluated with S-X^2 ($p>0.01$), and local dependency was evaluated with standardized LD X^2 indices (<10).[57-59] *T*-scores representing neuropathic pain quality were then derived for all study participants with the mean centered at 50 and the standard deviation set to 10.

Using the development dataset only, sensitivity and specificity analyses were carried out to identify optimal *T* score thresholds that maximized discrimination between participants with neuropathic and non-neuropathic pain conditions. Youden's Index informed threshold selection.[60] Three score thresholds were selected: one to optimize sensitivity, one to optimize specificity, and one representing a balance of both characteristics. Sensitivity and specificity using these thresholds were then validated in the hold-out sample. Reliability and validity of neuropathic pain quality T-scores were then evaluated using ANOVA (known-group comparisons), Chronbach's alpha, item-total correlations, polychoric correlations (internal consistency), and correlations with measures of other health domains (discriminant validity).

Data management, descriptive statistics, correlational analyses, and ROC analyses were carried using Stata/IC 12.1 (Copyright 1985-2011, StataCorp LP). Dimensionality assessment was conducted using Mplus 6.12 (Copyright 1998-2011, Muthen & Muthen), and IRT

calibration was carried with IRTPRO 2.1 (Copyright 2011, Scientific Software International, Inc).

RESULTS

Participants

A total of 735 participants with pain related to CN (n=134), DN (n=181), OA (n=106), and RA (n=314) comprised the analytic cohort (Table 1). Mean age (sd) was 58.2 (12.6), with the younger CN subgroup averaging 52.5 (13.4) years of age, and the older OA subgroup averaging 64.5 (9.6) years. The majority of participants were white (88.8%), female (71.9%), and half (49.8%) had earned a college or advanced degree. Participants with OA and RA reported painful symptoms for nearly 20 years (mean = 19.4, SD=12.2) and had an average of 18.4 years (SD=12.0) since diagnosis. Participants with CN experienced symptoms of neuropathy for an average of 2.2 years (SD=2), while those with DN experienced symptoms of neuropathy for nearly 10 years (mean = 9.8, sd = 9.2). Substantial deficits in physical and mental health were observed across all subgroups, with the largest departures from the general population mean observed for physical function (mean T-score of 39.5) and pain intensity (mean T-score of 59.2).

Table 1. Demographic and clinical profile of study participants

	Neuropathic Pain				Non-Neuropathic Pain				All Pain Conditions	
	Cancer		Diabetes		Osteoarthritis		Rheumatoid Arthritis		All Diagnoses	
	n=134	%	n=181	%	n=106	%	n=314	%	n=735	%
Female	94	70.2	73	40.3	93	87.7	268	85.6	528	71.9
Missing					1	-			1	-
Race/Ethnicity										
White	99	73.9	149	82.8	100	94.3	300	96.8	648	88.8
Black	28	20.9	10	5.6	3	2.8	3	1.0	44	6.0
Asian	5	3.7	2	1.1	1	0.9	1	0.3	9	1.2
Multiple/Other	2	1.6	19	10.6	2	1.9	6	2.0	29	4.0
Missing			1	-			4	-	5	-
Education										
Some high school	5	3.7	10	5.6	1	0.9	2	0.6	18	2.4
High school / GED	27	20.2	20	11.2	10	9.4	51	16.3	108	14.8
Some college, technical degree, AA	33	24.6	79	44.4	32	30.2	97	31.0	241	33.0
College degree (BA/BS)	43	32.1	31	17.4	32	30.2	94	30.0	200	27.4
Advanced degree (MA,PhD,MD)	26	19.4	38	21.4	31	29.3	69	22.0	164	22.4
Missing			3	-			1	-	4	-
	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
Age in years	52.5	13.4	58.8	13.1	64.5	9.6	58.2	11.9	58.2	12.6
Years since diagnosis			20.4	13.8	18.0	11.4	18.6	12.2		

Years with symptoms of neuropathy	2.2	2.2	9.8	9.2						
Years with symptoms of arthritis					19.2	12.5	19.5	12.1		
PROMIS-Global										
Physical Health	41.5	10.1	40.2	8.1	41.3	7.8	41.3	8.5	41.1	8.6
Mental Health	45.4	10.9	44.5	9.3	47.0	8.6	46.7	9.1	45.9	9.5
PROMIS-29 Profile										
Physical Function	39.7	7.9	39.9	8.4	37.4	6.4	39.8	7.5	39.5	7.7
Fatigue	56.6	10.3	55.5	9.3	55.6	9.3	56.1	10.2	56.0	9.9
Pain Intensity	50.3	10.4	50.2	7.4	53.0	6.9	51.2	6.4	51.0	7.6
Pain Interference	57.9	10.1	58.2	9.1	60.5	7.7	59.8	7.9	59.2	8.7
Pain Behavior	56.4	8.2	57.0	6.5	58.2	4.3	57.5	4.9	57.3	6.0
Sleep Disturbance	53.7	9.3	54.6	8.2	52.9	9.5	52.8	8.6	53.4	8.8
Depression	54.6	12.1	52.9	9.8	49.9	8.7	50.4	9.3	51.7	10.0
Anxiety	56.1	12.0	52.7	9.6	50.7	9.3	50.0	8.9	51.9	10.0
Satisfaction with Social Roles	44.1	9.6	42.5	8.2	42.8	9.1	43.8	9.3	43.4	9.1

Item selection, scaling, and scoring

Of the 42 pain quality descriptors evaluated, 5 (12%) were more likely to be endorsed by participants with neuropathic pain with moderate to large effect sizes (Cramer's *V*: 031 - 0.57). In exploratory factor analysis of the developmental dataset, these same five items loaded together on a unique factor for all factor solutions between 2 and 7; beyond 7 factors, eigenvalues were consistently below 1.0. Confirmatory factor analysis in the validation dataset indicated that the 5-item unidimensional model fit the data well (CFI = 0.98 / TLI = 0.96), and all factor loadings were statistically significant and greater than 0.75. Inspection of residual correlations found that 9 of 10 residuals were lower than 0.10 with the largest residual at 0.13 further supporting unidimensionality of the data.

During IRT-based scale calibration, the sample estimated mean difficulty was set to a mean of 0 and standard deviation of 1. All five items demonstrated adequate fit [all $p>0.01$, S-X^2) and were free from problematic local dependency (all LD-X^2 indices <10). Discrimination parameters (**α**) ranged from 1.98 from 4.05, and difficulty parameters (**β**) ranged from -0.37 to 2.09 (Table 2).

Table 2. Discrimination and difficulty parameters of 5 indicator items of neuropathic pain quality

	a	b_1	b_2	b_3	b_4
In the past 7 days, did your pain feel …					
Numb	1.98	-0.27	0.30	0.95	1.73
Tingly	3.09	-0.37	0.24	0.83	1.58
like pins and needles	4.05	-0.31	0.19	0.70	1.22
Stinging	2.13	0.09	0.63	1.28	1.97
electrical	2.02	0.48	0.95	1.48	2.09

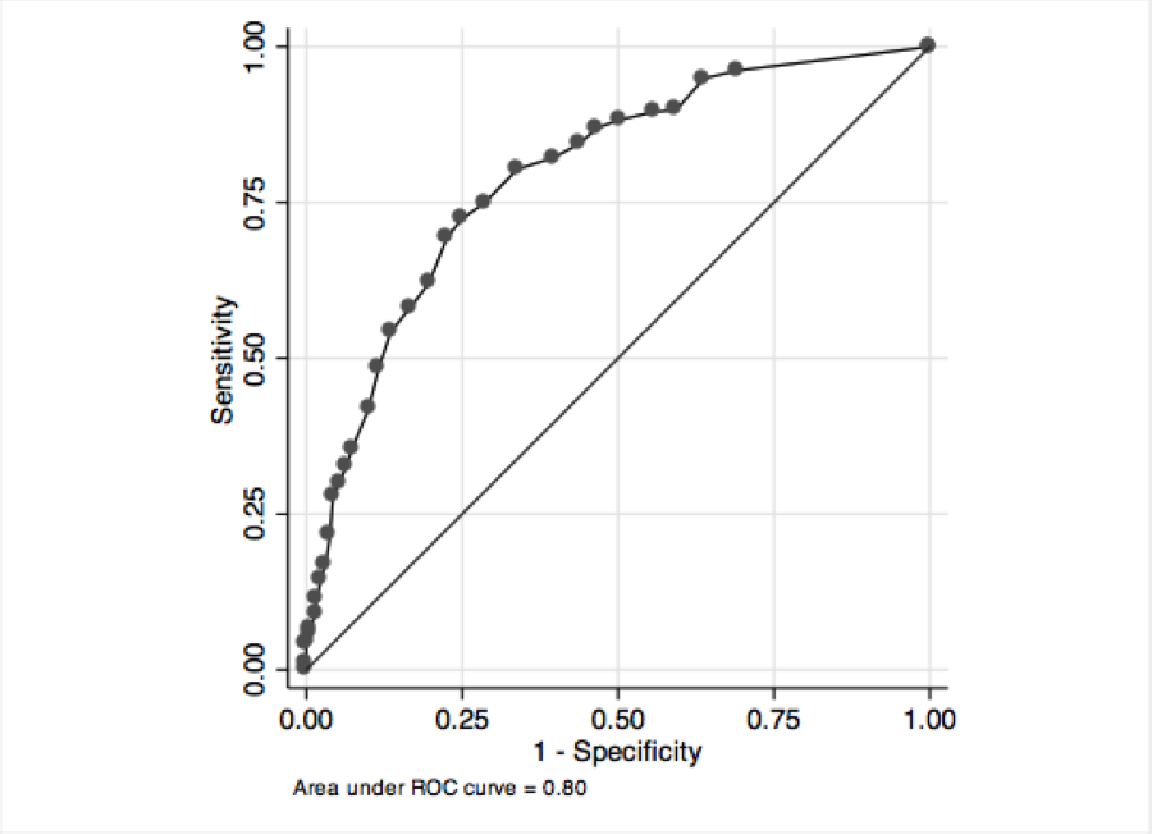
T-scores representing neuropathic pain quality were re-centered to a mean of 50 and standard deviation of 10 with a simple transformation, as follows: T-score = θ*10 + 50. Individual participant T-scores were calculated to evaluate score sensitivity in discriminating between neuropathic and non-neuropathic pain conditions (Table 3).

Table 3. Sensitivity and specificity of T-score thresholds in predicting neuropathic pain conditions

Dataset	T-score Threshold (≥)	Sensitivity	Specificity	Correctly Classified
Development	43	0.90	0.38	0.60
	50	0.76	0.73	0.74
	57	0.40	0.90	0.69
Validation	43	0.93	0.42	0.64
	50	0.77	0.67	0.71
	57	0.44	0.90	0.70
Combined	43	0.92	0.40	0.62
	50	0.77	0.70	0.73
	57	0.42	0.90	0.70

T-score thresholds of 43 and 57 were identified using the developmental dataset that optimized sensitivity (0.90) and specificity (0.90), respectively. Sensitivity (0.93) and specificity (0.90) were confirmed in the validation dataset using these same thresholds. A threshold of 50 was selected as a cut-point that maximized sensitivity and specificity (0.77 and 0.70, respectively in the combined sample). Receiver operator characteristic analyses indicated that the area under the curve was 0.80 suggesting good discriminatory ability of T-scores (Figure 2). However, Youden's indices associated with each score were consistently below the 0.8 threshold recommended for diagnostic testing.

Figure 2. Receiver Operator Characteristic (ROC) curve for T-scores



Validity and Reliability

Evidence of construct validity was supported by known groups comparisons. A 10-point mean difference ($F=251.74$, $p<0.0001$) in T-scores was observed between participants with neuropathic and non-neuropathic pain conditions (Table 4). Moreover, correlations with measures of other health-related domains were negligible in magnitude, suggesting adequate discriminant validity (Table 5). The largest correlations with neuropathic pain quality scores were observed for measures of pain intensity, pain interference, anxiety, and depression (r = 0.09 to 0.20).

Table 4. Neuropathic pain quality T-score comparisons by diagnostic subgroup

	T-score	SD	n	F*	p
Overall	50.00	9.22	735	251.74	< 0.0001
Neuropathic pain	55.38	8.11	315		
Cancer	55.50	8.33	134		
Diabetes	55.29	7.97	181		
Non-neuropathic pain	45.96	7.85	420		
Osteoarthritis	46.93	8.77	106		
Rheumatoid Arthritis	45.64	7.50	314		

*F test represents two-group comparison (neuropathic vs non-neuropathic pain)

Table 5. Correlations between Neuropathic Pain Quality T-scores and other health domains

	Neuropathic Pain Quality	
PROMIS Pain Measures		
Pain Interference	-0.109	*
Pain Behavior	-0.076	*
Pain Intensity	-0.093	*
PROMIS Global		
Physical Health	-0.028	
Mental Health	-0.102	*
PROMIS-29 Profile (1.0)		
Physical Function	0.043	
Anxiety	0.196	*
Depression	0.164	*
Fatigue	-0.002	
Sleep Disturbance	0.076	*
Satisfaction with Social Roles	-0.018	

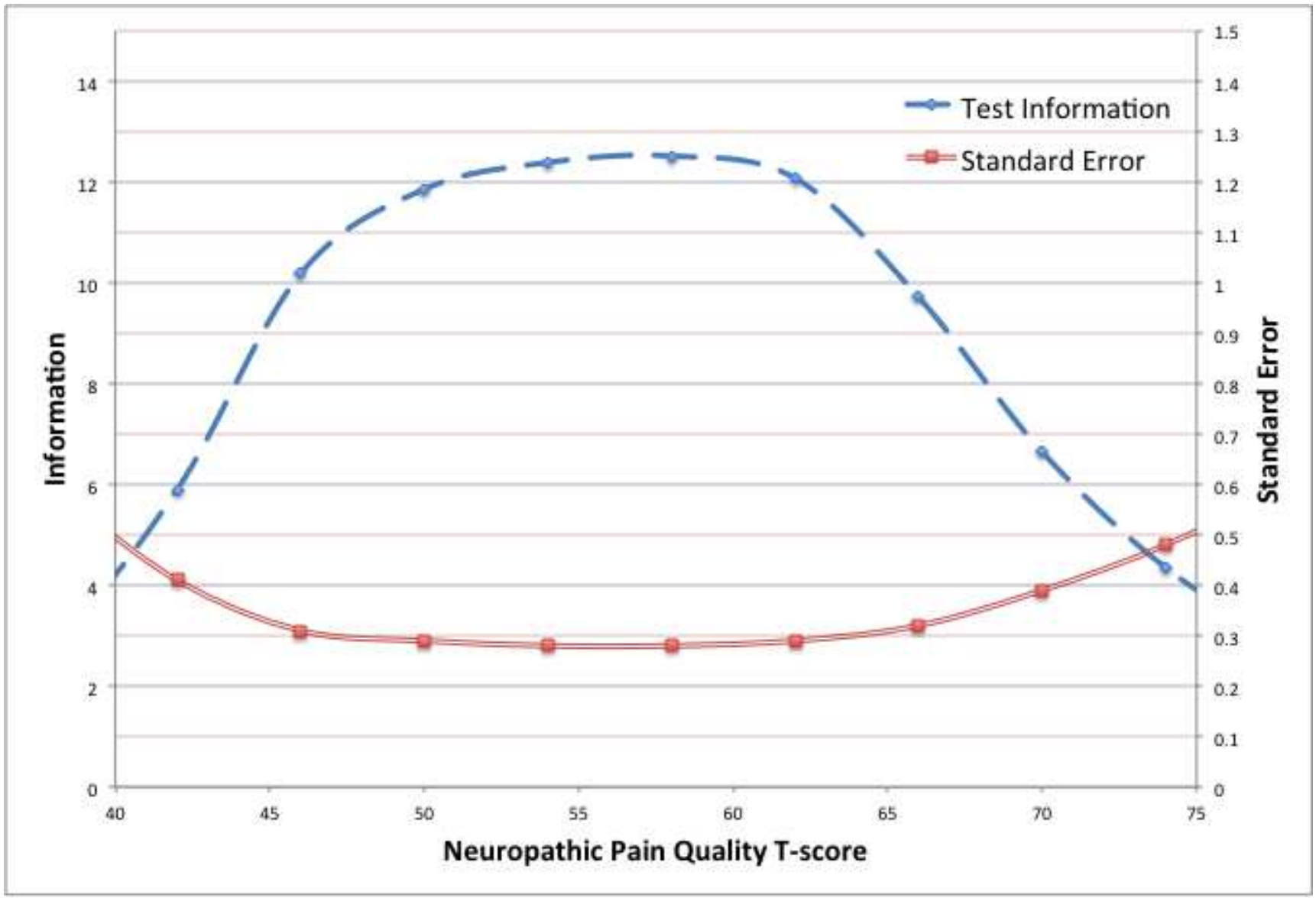
- indicates statistical significance with $\alpha = 0.05$

High internal consistency was also indicated by results from the factor analysis and multiple indices of interdependence (Chronbach's alpha = 0.87, item-total correlations corrected for overlap [0.62-0.79], polychoric correlations [0.50 - 0.79]). An expanded evaluation of reliability from the IRT-calibration indicated that item information was maximized (>10) for T-scores between 45 to 65 (Figure 3). A sum score to T-score crosswalk table is presented in Table 6 to facilitate scoring from raw response options.

Table 6. Sum score to T score crosswalk table

Sum score	T score		Sum score	T score
5	37		16	58
6	43		17	59
7	45		18	61
8	47		19	62
9	49		20	63
10	50		21	65
11	52		22	66
12	53		23	68
13	54		24	70
14	56		25	74
15	57			

Figure 3. Reliability of T-scores



DISCUSSION

In this study, we aimed to assess the ability of PROMIS pain quality descriptors to discriminate between individuals with neuropathic and non-neuropathic pain conditions and to develop a scale measure of neuropathic pain quality. We adopted a multi-staged approach to item-identification and scale development, converging on a unique set of pain quality descriptors. The resulting 5-item measure appears to be valid, reliable, and effective at identifying patients with neuropathic involvement in pain generation.

With respect to the performance of T-scores as a descriptive scale measure, we found reliability to be higher than most estimates reported in the literature for currently available self-report measures of NP (see Appendix 1). The level of precision achieved with this brief 5-item measure likely reflects the advantages of a multistage psychometric approach to modeling that included functional evaluations of individual items, factor analytic models, and IRT-based scale calibration. Nevertheless this increased reliability did not necessarily lead to increased diagnostic utility, as our estimates of sensitivity and specificity were comparable to those previously reported (see Appendix 1). While it is unclear how much diagnostic information can be gleaned from pain quality descriptors, it is possible that at a certain point, additional gains in reliability may no longer translate into increased diagnostic utility. For this and other reasons, it is important to emphasize that a self-report measure of NP cannot replace clinical judgment with respect to the clinical diagnosis of NP. Nevertheless, assessment of neuropathic pain quality may provide information that is useful and diagnostically relevant when attempting to locate underlying sources of pain generation in a clinical setting.

With respect to validity of this scale measure, we found negligible correlations between pain intensity and interference and neuropathic pain quality, which supports the hypothesis and methods adopted to measure neuropathic pain quality as a distinct construct. While statistically significant, the direction and magnitude of these correlations may simply reflect lower average pain intensity and interference estimates reported by participants with NP in our analytic cohort. It is important to note, however, that the highest correlations from convergent and discriminant validity analyses were observed between neuropathic pain quality and mood. It is possible that these correlations may also reflect average differences in depression and anxiety observed in our sample, but evidence detailing the efficacy of anti-depressants and mood stabilizers in the treatment of NP suggest a more complex relationship and potentially shared neurological mechanisms.[15, 51]

Limitations & Future Research

In this study, response patterns of participants from four distinct patient populations were evaluated, and it is possible that participants from populations with other chronic neuropathic and nociceptive pain conditions may describe their pain in systematically different ways. However, more similarities than differences in pain quality descriptors have been reported among individuals with many different NP conditions, suggesting that the clinical expression of NP is likely “trans-etiological”[46] Pain quality descriptors identified in this study were also similar to those from other previously developed measures of NP (e.g., tingling, numbness, pins and needles, electric, among others.),[38, 61] despite the heterogeneity of NP populations utilized

during instrument development. Nevertheless, limitations in the diagnostic resolution that pain quality descriptors provide have led others to suggest that differences in reported neuropathic pain qualities may more accurately reflect different mechanisms involved in NP (as opposed to etiology).[62] It remains to be seen whether treatments targeting individual NP mechanisms defined by pain quality descriptors will translate into more personalized and effective pain relief, but this remains a promising area of future research.

The larger PROMIS pain quality project also includes data from participants with fibromyalgia, and considerable deliberation regarding the status of fibromyalgia as a NP or non-NP pain condition preceded analysis. The extent of neuropathic involvement in fibromyalgia related pain remains unclear,[63, 64] and given our intent to develop a scale measure of NP that discriminates well between individuals with and without NP, it seemed prudent to limit this analysis to participants with more clearly defined neuropathic and non-neuropathic pain conditions. Future investigations into the pain qualities reported by participants with fibromyalgia and mixed or idiopathic pain conditions may further elucidate the underlying pathophysiological mechanisms involved.

Patient-reported pain, like other symptoms, likely represents the aggregate expression of complex biological, cognitive, and contextual processes. Moreover, the experience of pain is multi-faceted, and clinical experts have acknowledged the need for more comprehensive pain assessment in clinical research.[3, 65] Valid and reliable measures that are sensitive to systematic differences in pain qualities will likely provide a more informative profile of patient experiences in clinical settings. They may also take

on a larger role in advancing our understanding of the mechanisms underlying pain generation and palliation. It is our hope that more robust instrumentation will serve both of these ends and accelerate the arrival of more effective and personalized clinical treatments of NP.

Appendix 1. Summary of evidence documenting psychometric and diagnostic properties of self-report measures of neuropathic pain*

First Author	Year	Language	n (neuropathic)	n (non-neuropathic)	Chron-bach alpha	Internal structure	Factors	ROC-AUC	SN	SP	Test-retest
Measures developed for discrimination											
Neuropathic Pain Questionnaire (12-items)											
Krause [66]	2003	English	149	233	0.95	PCA/EFA	6		66.6	74.4	
Hallstrom [67]	2011	Swedish	28	12				0.78	50.0	100.0	k = 0.89
Li [68]	2012	Chinese	36	23				0.82	52.9	91.4	
Backonja [69] (3 items)	2003	English	110	168					64.5	78.6	
Self-report Leeds Assessment of Neuropathic Symptoms and Signs (7 items)											
Bennett [70]	2005	English	100	100	0.76				74.0	76.0	
Weingarten [71]	2007	English	69	117					57.0	69.0	
Koc [72]	2010	Turkish	137	107	0.74				72.0	77.0	r = 0.97
painDETECT (9 items)											
Freynhagen [39]	2006	German	228	164	0.83	PCA	2	0.91	0.84, 0.85	0.84, 0.80	
Hallstrom [67]	2011	Swedish	28	12				0.71	0.68	0.83	k = 0.59
De Andres [73]	2012	Spanish	71	71	0.86	EFA	2	0.88	0.81	0.81	ICC = 0.93

Idpain (6 items)											
Portenoy [40]	2006	English	190	502		PCA/EFA		0.73, 0.69			ICC = 0.74
Galvez [74]	2008	Spanish	145	138	0.66	FA	1	0.89	0.81	0.84	r = 0.98
Kitisomprayoonkul[75]	2011	Thai	24	49	0.32			0.89	0.83	0.80	
Chan [76]	2011	Chinese	60	32				0.78	0.81	0.65	ICC = 0.72
Li [68]	2012	Chinese	36	23				0.95	0.87	0.90	
Padua [77]	2013	Italian	255	137					0.78	0.74	
Measures developed for description											
Short-Form McGill Pain Questionnaire 2 (6 items in NP subscale)											
Dworkin [48]	2009	English	575	533	0.78	EFA	3				
Lovejoy [78]	2012	English	19	167	0.85	CFA	4				
Adelmanesh [79]	2012	Persian	74	184	0.81	EFA	4				
Neuropathic Pain Symptom Inventory (12 items)											
Bouhassira [80]	2004	French	176			PCA/EFA	5				ICC = 0.89
Padua [81]	2009	Italian	255	137		CFA	5				
deAndrade [82]	2011	Portuguese	94				5				ICC = 0.77
Sommer [83]	2011	German	68	169	0.75	Cluster analysis	6		0.80	0.82	ICC = 0.89
Villoria [84]	2011	Spanish	548		0.80, 0.90	PCA	5				ICC = 0.68

ROC-AUC: Receiver Operator Characteristic - Area under Curve; SN: Sensitivity; SP: Specificity; SF: Short-Form; PCA: Principal Component Analysis; EFA: Exploratory Factor Analysis; CFA: Confirmatory Factor Analysis; FA: Factor Analysis; ICC: Intraclass Correlation Coefficient
*Relevant articles were identified using a validated PubMed search algorithm designed to identify articles reporting psychometric properties and key words, “pain” and (“neuropathy” or “neuropathic” or “neuropathies”) on 21 April 2013.[85] Similar searches were carried out in Scopus and PsycINFO, PsycArticles, PsycExtras (EBSCO-ASC) to ensure comprehensiveness of the search. Only self-report measures (i.e. requiring no clinical examination or interviews) that produce *scores* representing NP were included.

Conclusion

While advances in physiological testing and electrophysiological imaging have greatly enhanced our understanding of the mechanisms involved in pain generation and modulation, to date these advances have yet to yield a biometric or physiological outcome quantifying perceived pain that is superior to that of self-report.[86, 87] As such, self-reported pain measures will likely to continue to occupy a key role in medical and epidemiological research of chronic pain. The projects outlined in this dissertation highlight how advanced statistical methodologies have enabled valid and reliable assessment through self-report. Moreover, scores from these measures reflect health status from the patient perspective, which has become a national priority in public health research.[88] It is my hope that the development and validation of these self-report measures of chronic pain will serve to advance our understanding of the physiological and psychosocial factors that affect individuals living with chronic pain and bring relief to this growing and largely underserved community.

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2014-2015 Co-Investigator, Small Grant Award, Orthotic and Prosthetic Education and Research Foundation. Enhancing quality, utility, and interpretability of self-report outcome measures for prosthetic applications: psychometric evaluation of reliability, mode-of-administration equivalence, measurement error, and detectable change, Principal Investigator: Brian Hafner, PhD, $24,994.

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CONFERENCES & SYMPOSIA
Oral Presentations at Refereed National & International Conferences

Accepted / Presented

Hafner BJ, **Askew RL**, Abrahamson DC, Fiedler G. Reliability, stability, and detectable change of outcome measures for persons with transfemoral amputation. Proceedings of the American Academy of Orthotists & Prosthetists (AAOP) 40th Annual Meeting and Scientific Symposium, Chicago, IL, February 26-March 1, 2014

Chung H, Kim J, **Askew RL**, Cook KF, Amtmann D. Assessing measurement invariance of three depression measures between neurologic and community samples. Quality of Life Research, 22(Suppl. 1), 72. Paper presentation at the 2013 annual conference of International Society for Quality of Life Research, Miami, FL.

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Johnson KL, Amtmann D, Kim J, Chung H, Bamer A, **Askew RL.** Longitudinal trajectories of sleep problems in people with multiple sclerosis. Oral presentation at the 121st Annual meeting of the American Psychological Association (July 31 – August 4, 2013) Honolulu, Hawaii

Amtmann D, **Askew RL**, Bamer A, Johnson KL, Cook K. Longitudinal trajectories of pain behaviors in people with chronic pain. Oral presentation at the 121st Annual meeting of the American Psychological Association (July 31 – August 4, 2013) Honolulu, Hawaii

Amtmann D, Abrahamson DC, Morgan SJ, Salem R, **Askew RL**, and Hafner BJ. The development of the PLUS-M, a new measure of mobility for prosthetic limb users. Oral presentation at International Society for Prosthetics and Orthotics (ISPO) World Congress, Hyderabad, India, February 4-7, 2013.

Amtmann D, **Askew RL**, Abrahamson DC, Morgan SJ, and Hafner BJ. Empirical support for distinct mobility groups of prosthetic users. Oral presentation at the International Society for Prosthetics and Orthotics (ISPO) World Congress, Hyderabad, India, February 4-7, 2013.

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International Society for Quality of Life Research (ISOQOL), Budapest, Hungary, 24-27 October 2012.

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Askew RL, Amtmann D, Weir V, Johnson KL. Identifying unmet needs of individuals with MS: A latent class analysis. Oral presentation at the 140th Annual Meeting of the American Public Health Association (APHA), San Francisco, CA. 27 - 31 October 2012. (#259541)

Askew RL, Amtmann D, Kim J, Chung H, Johnson KL. Effects of pain on depression are mediated by fatigue, anxiety, and sleep in MS. Oral presentation at the 140th Annual Meeting of the American Public Health Association (APHA), San Francisco, CA. 27 - 31 October 2012. (#259491)

Askew RL, Xing Y, Ross MI, Lee JE, Gershenwald JE, Cormier JN. Mapping FACT-Melanoma quality of life scores to EQ-5D patient preference weights. Oral presentation at the 16th annual scientific meeting of the International Society for Quality of Life Research, New Orleans, LA, USA. 28-31 Nov 2009

Xing Y, Chang GJ, Hu C, **Askew RL**, Ross MI, Gershenwald JE, Lee JE, Mansfield PF, Lucci A, Cormier JN. Conditional survival estimates provide better prognostic information for melanoma survivors: results from the SEER dataset 1988-2000. Oral presentation at the 4th Annual Academic Surgical Congress, Fort Myers, FL, US. 4-6 Feb 2009. (ID: QS334)

ABSTRACTS (POSTERS)
Published from Refereed National & International Conferences

Kim J, Chung H, Amtmann D, **Askew RL**, Park R, Wu S, Cook KF (2013). Validation of CESD-20 and PHQ-9 Crosswalks to PROMIS Depression in Multiple Sclerosis. Quality of Life Research, 22(Suppl 1), 63. Poster presented at the 2013 annual conference of International Society for Quality of Life Research, Miami, FL. (New Investigator Award)

Amtmann D, Bamer A, **Askew RL**, Brockway JA, Yorkston K, Johnson KL. Predictors of self-efficacy in a large sample of individuals with disabilities. Poster presented at the 121st Annual meeting of the American Psychological Association (July 31 – August 4, 2013) Honolulu, Hawaii

Simpson S, **Askew RL**, Harrast M. Caffeine Use in the Seattle Marathon. Poster presented at the 2013 Annual meeting of the American Medical Society for Sports Medicine, San Diego, California.

Askew RL, Amtmann D, Kim J, Chung H, Johnson KL. The relationship between pain and depression in MS. International Journal of Multiple Sclerosis Care. May 2012. 14 (S2), 21. DOI: 10.7224/1537-2073-14.S2.1. Poster presented at the 4th Cooperative Meeting of the Consortium of Multiple Sclerosis Centers (CMSC) and the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS), San Diego, CA, US. 30 May-02 June, 2012. (#CG21)

Askew RL, Amtmann D, Weir V, Johnson KL. Exploring unmet needs in MS: Who needs what? International Journal of Multiple Sclerosis Care. May 2012. 14 (S2), 21. DOI: 10.7224/1537-2073-14.S2.1. Poster presented at the 4th Cooperative Meeting of the Consortium of Multiple Sclerosis Centers (CMSC) and the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS), San Diego, CA, US. 30 May-02 June, 2012. (#RH25)

Kim J, Amtmann D, Cook K, Johnson KL, Bamer AM, Chung H, **Askew RL**. Psychometric properties of three depression scales in people with multiple sclerosis. International Journal of MS Care. May 2012. 14 (S2), 85. DOI: 10.7224/1537-2073-14.S2.1 Poster presented at the 4th Cooperative Meeting of the Consortium of Multiple Sclerosis Centers (CMSC) and the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS), San Diego, CA, US. 30 May-02 June, 2012.

Saraiya DS, You YN, **Askew RL**, Vu TM, Lynch PM, Rodriguez-Bigas M. The importance of tumor studies in the initial evaluation for Lynch syndrome: a comparison of MMR positive and negative patients. Hereditary Cancer in Clinical Practice. 10 March 2011. 9(S1): 34. doi:10.1186/1897-4287-9-S1-P34. Poster presentation at the 14th Annual Meeting of the Collaborative Group of the Americas on Inherited Colorectal Cancer (CGA-ICC), Dallas, TX. 12-13 Oct, 2010.

Cormier JN, Shih YCT, Xu Y, Pan IW, **Askew RL**, Ross MI, Gershenwald JE, Lee JE, Royal R, Xing Y. The impact of physician specialty on quality of melanoma care. Journal of Clinical Oncology. 20 May 2010. 28(15s). Poster presentation at the 2010 Annual Meeting of the American Society of Clinical Oncology, Chicago, IL. 4-8 Jun 2010. (#8563)

Xing Y, Bronstein Y, Ross MI, **Askew RL**, Lee JE, Gershenwald JE, Royal R, Cormier JN. Diagnostic imaging modalities for the surveillance of melanoma patients: A meta-analysis. Journal of Clinical Oncology. 20 May 2010. 28(15s). Poster presentation at the 2010 Annual Meeting of the American Society of Clinical Oncology, Chicago, IL. 4-8 Jun 2010. (#8581)

Goel N, **Askew RL**, Xing Y, Ross MI, Gershenwald JE, Lee JE, Mansfield PF, Lucci A, Royal RE, Cormier JN. Standards for lymph node ratio in dissections for melanoma patients: can they be achieved? Annals of Surgical Oncology. February 2010. 17(S1): S1-139. Poster presentation at the 63rd Annual Cancer Symposium of the Society of Surgical Oncology. St. Louis, MO. 3-7 Mar, 2010. (P255)

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2010). DOI: 10.1186/1897-4287-8-S1-P20. Poster presentation at the 13th Annual Meeting of the Collaborative Group of the Americas on Inherited Colorectal Cancer. Honolulu, HI. 16-17 Oct, 2009: #29.

Contreras CM, Badgwell BD, **Askew RL**, Feig BW, Cormier JN. Radiographic and clinical factors associated with improved outcomes in cancer patients with bowel obstruction. Journal of Clinical Oncology, 20 May 2009. 27(15S). Presentation for the 45th Annual Meeting of the American Society of Clinical Oncology. Orlando, FL, US. 29 May – 2 June 2009. # e20564

Bowles T, Xing Y, Hu C, Mungovan KS, **Askew RL**, Chang GJ, Gershenwald JE, Lee JE, Mansfield PF, Ross MI, Cormier JN. Conditional survival estimates improve over 5 years for patients with node-positive melanoma. Annals of Surgical Oncology. February 2009. 16(Suppl 1): 31–123. (ID: P228) DOI: 10.1245/s10434-008-0291-6. Poster presentation at the 62nd Annual Cancer Symposium of the Society of Surgical Oncology, Phoenix, AZ, US. 4-8 March 2009.

Chang SB, **Askew RL**, Xing Y, Mungovan KS, Gershenwald JE, Lee JE, Lucci A, Mansfield PF, Ross MI, Cormier, JN. Prospective analysis of postoperative morbidity following inguino-femoral lymph node dissection (ILND) in patients with node positive melanoma. Annals of Surgical Oncology. Febrruary 2009. 16(Suppl 1): 31–123 (ID: P236) DOI 10.1245/s10434-008-0291-6. Poster presentation at the 62nd Annual Cancer Symposium of the Society of Surgical Oncology, Phoenix, AZ, US. 4-8 March 2009.

Cormier JN, Xing Y, Zaniletti I, **Askew RL**, Stewart BR, Armer JM. Prospective cohort study assessing limb volume change (LVC) and quality of life in breast cancer survivors. Journal of Clinical Oncology, 20 May 2008. 26(15S). Poster presentation at the 44th Annual Meeting of the American Society of Clinical Oncology. Chicago, IL, US. 30 May – 3 June 2008. #9561

Blazer DG, Lazar A, Xing Y, **Askew RL**, Lev DC, Feig BW, Pisters PW, Pollock RE, Hunt KK, Cormier JN. Improved outcomes in patients with lymph node-only stage IV disease in molecularly confirmed (EWSR-1) clear cell sarcoma: Results from a large single-institution experience and SEER database analysis. Journal of Clinical Oncology, 20 May 2008. 26(15S). Poster presentation at the 44th Annual Meeting of the American Society of Clinical Oncology. Chicago, IL, US. 30 May – 3 June 2008. #10571.

Unpublished Conference Abstracts

Badgwell BD, Contreras C, **Askew RL**, Krouse R, Feig B, Cormier JN. Radiographic and clinical factors associated with improved outcomes in cancer patients with bowel obstruction. Presentation at the 6th Annual Academic Surgical Congress, Huntington Beach, CA, US. 1-3 Feb 2011. (ID:22.5)

Smalky KA, Saez H, **Askew RL**, Kallen M, Tinter R, Cormier JN. Cancer-related lymphedema: An educational intervention for genitourinary and gynecologic oncology outpatient nurses. Poster presentation at the International Symposium for the Multinational Association of Supportive Care in Cancer / International Society of Oral Oncology. Rome, Italy. 25-27 June 2009: #19-233

Askew RL, Tong PL, Tomas LC, Mungovan KS, Ross MI, Lee JE, Gershenwald JE, Mansfield PF, Lucci A, Cormier JN. Post-surgical limb volume changes associated with increased symptom reporting and changes in quality of life for patients with melanoma undergoing lymph node surgery. Poster presentation at Medical Issues in Cancer Survivors, University of Texas M.D. Anderson Cancer Center, Houston, TX, US. 6–7 Feb 2009.

Cormier JN, Xing Y, Zaniletti I, **Askew RL**, Stewart BR, Armer JM. Minimal limb volume change has a significant impact on breast cancer survivors. Poster presentation at the 8th National Lymphedema Network International Conference, San Diego, CA, US. 27-31 Aug 2008. (ID: 950069)

McKinley G, Kneuper S, Pruitt S, Wuelling S, **Askew RL**. Do cancer screening hotlines promote informed decision making for prostate cancer screening? Poster presentation at the 31st Annual Meeting of the American Society of Preventive Oncology. Houston, TX, US. 2-4 March 2007.

EDITORIAL & REVIEW ACTIVITIES

Journal reviewer

Quality of Life Research (2012 – Present)

TEACHING

University of Washington, Seattle

Academic Courses

PSY315: Understanding Statistics in Psychology, Spring 2011, Instructor: Laura Little, PhD; University of Washington, Seattle, WA. Teaching Assistant: responsibilities include leading two lecture lab/sections per week, grading, supplementary tutorials, and exam reviews

PSY209: Fundamentals of Psychological Research, Winter 2011, Instructor: Michael Passer, PhD; University of Washington, Seattle, WA. Teaching Assistant: responsibilities include leading two lecture lab/sections per week, grading, supplementary tutorials, and exam reviews

PSY101: Introduction to Psychology, Autumn 2010, Instructor: Michael Passer, PhD; University of Washington, Seattle, WA. Teaching Assistant: Responsibilities include grading, leading supplementary tutorials, and exam reviews

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