THE PAIN ASSESSMENT FOR LOWER BACK SYMPTOMS (PAL-S):

QUALITATIVE DEVELOPMENT AND COGNITIVE EVALUATION OF A NEW PATIENT-REPORTED OUTCOME MEASURE FOR THE ASSESSMENT OF LOW BACK PAIN

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BACKGROUND

- Pain in the lower back affects up to 90% of Americans at some point in their lifetime Up to 50% will have more than one episode. In Germany, the prevalence is higher than 70% [Wenig 2008].
- Chronic Low back pain (cLBP) is second only to the common cold as a cause of lost days at work. It is also one of the most common reasons to visit a doctor's office or a hospital's emergency department, and is the second most common neurologic complaint in the United States, after headache [Manek, 2005].
- Because the severity of cLBP symptoms is directly related to the degree of impairment that patients experience, the patient-reported assessment of symptoms and impacts are essential endpoints for clinical studies.
  - By exploring the patient experience of cLBP through qualitative interviews, it is possible to better understand and document the specific disease-defining concepts that are relevant to the patient as well as to understand the patient's assessment of improvement in his or her condition.
  - Ultimately, a well-developed patient reported outcome (PRO) instrument that has firmly established content validity (based on qualitative data from patients) will be expected to demonstrate greater sensitivity in clinical studies of treatment benefit.

OBJECTIVE

- To develop a patient-reported outcome (PRO) measure to assess the key symptoms of chronic low back pain (cLBP) through qualitative concept elicitation (CE) and cognitive interviews.

METHODS

Study Design

- Qualitative Interviews were conducted with patients with low back pain in the US, the UK and Germany to support content validity and address cross cultural appropriateness of concepts
- Item Generation was conducted using results from literature and instrument reviews, expert clinician input, and results of qualitative interviews with patients having low back pain
- Cognitive interviews were conducted in the US and the UK to refine the draft measure

Study Population

Inclusion Criteria

- For English speaking sites, subjects were eligible if they could read, write, and speak English well enough to understand and complete Informed Consent Form (ICF) and take part in the interview process. Participants in Germany were native speakers of German, and their interviews were conducted in German (simultaneously translated into English).
- Male and female subjects 18 to 80 years of age
- Clinical diagnosis of LBP of non-malignant origin, with pain present for at least 3 months
- Patient reported current LBP score of ≥4 on an 11 point NRS (Numeric Rating Scale) pain scale, and was in otherwise stable general health.

METHODS

Exclusion Criteria

A subject was not eligible for this study if:

- Subject's cLBP was potentially associated with a specific spinal cause, or subject had any recent low-back surgery or had undergone invasive procedures aimed to reduce LBP within the past 1 month.
- Subject had a recent history of clinically significant drug or alcohol abuse/dependence -or- significant psychiatric disorder.
- Subject participated in another investigational device, drug, or biologics product study within the last 30 days.
- Subject had a clinically-significant history of brain injury, stroke, or cancer; or had any conditions other than LBP that could confound the assessment or self-evaluation of pain.
- In the opinion of the site investigator or study director, subject had any other medical condition or disorder that could compromise his/her ability to give written informed consent or interfere with the patient's ability to successfully participate in a face-to-face interview.

Concept Elicitation Interviews

- Appropriate Institutional Review Board (IRB) approval was obtained prior to study initiation.
- Forty-three semi-structured qualitative concept elicitation (CE) interviews were conducted by trained research staff with a representative sample of adult patients with low back pain recruited from 5 clinical sites across different geographical locations in the U.S. and one recruitment site in Germany.
  - –Descriptive data included standard demographics and the painDETECT [Freynhagen et al, 2006] questionnaire was used to identify the presence of a neuropathic pain component.
  - –Research staff used a semi-structured qualitative interview guide, designed to obtain both unprompted and prompted direct patient input about LBP symptoms and how the patients felt these factors affected their ability to function.
  - –Each individual interview lasted approximately 60 minutes and began with open-ended questions and day-reconstruction exercises to elicit spontaneous reports of symptom concepts. Subsequent probing was used to assess condition-related concepts not spontaneously reported by participants.
  - –At the close of the qualitative interviews, patients were asked to rate their most bothersome symptoms and most difficult impacts using a 0-10 numerical rating scale (NRS) with 0 representing no bother and no difficulty at all, and 10 representing the greatest amount of bother and difficulty imaginable.

Analyses

- All interviews were audio-recorded and transcribed. Transcripts were cleaned to remove any patient-identifying information prior to analysis, were coded and analyzed by trained qualitative coders using Atlas.ti, and were summarized by like-content using an iterative coding framework.
  - –Coded concepts were grouped by similarity of content and analyzed to identify the most relevant expressions and most common language used by patients.
- A Saturation Grid was used to track symptoms expressed during the interviews and assess saturation of concept.
- Transcripts and interview guide worksheet notations were used to identify symptom concepts offered by either spontaneous or probed report, and to capture patient ratings of severity and bothersomeness for expressed symptoms.
  - –Descriptive statistics (count, percent) were summarized to characterize the severity, bother, and spontaneous reports of expressed symptoms.

Item Generation

- An item-generation meeting was held by the development team, where concepts identified from published literature and existing instruments, clinical expert panel input, and the qualitative data from the CE interviews were reviewed as the basis for selection of concepts for inclusion in PRO measurement.
- This initial evaluation process resulted in the selection of candidate symptom concepts to be targeted for PRO measurement.
  - –Data from this study has also been used to develop a separate companion PRO instrument (PAL-I, detailed in Ramasamy, et al, 2013) designed to assess symptom impact and functional impairment in cLBP.
- During subsequent review by the development team, these targeted symptom concepts were further reduced by removing synonymous or problematic concepts. A draft version of the questionnaire was prepared for evaluation in cognitive interviews. This draft questionnaire was developed through the evaluation of existing PRO instruments, the identification and modification of candidate items and the drafting of novel items.

Cognitive Interviews

- Cognitive interviews were conducted using a separate sample of adults with cLBP (recruited through the same process as used for the CE interviews) in order to evaluate concept relevance, understandability, and structure of the draft items, and to facilitate further instrument refinement.
- The draft instrument was completed and evaluated by patients in four separate waves of cognitive interviews (targeting five patients per wave)
  - –Following each wave, the development team considered the findings and used the information to modify the draft instrument
- A semi-structured cognitive interview guide was designed to capture the subject's comprehension of items and ability to complete the draft PRO instrument.
  - –Updated versions of the interview guide were created for each of the three interview waves
- Cognitive interview transcripts were summarized in cognitive report tables for analysis.

RESULTS

Concept Elicitation

- A total of 43 interviews were conducted with participating patients (mean age: 48.6±13.0, 53.5% female) representing a broad range of demographic characteristics (Table 1).
- Among the CE interview participants, the mean (SD) pain NRS score was 6.7(1.3).
- Analysis of the transcripts resulted in 1,342 different patient-reported expressions about their low back pain symptoms.
- The coded symptom expressions were grouped into 27 different symptom concepts
  - –Saturation of concept was achieved for LBP symptoms within the first 11 coded transcripts, as no newly-appearing concepts emerged in subsequent transcripts.
  - –Inter-rater agreement on the assignment of codes between raters was > 97%.

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RESULTS

Table 1: Participant Demographic and Clinical Characteristics

Participant Characteristic			Concept Elicitation Total N=43 (100%)	Cognitive Interviews Total N=30 (100%)
Age (Years):	-	Mean (SD)	48.6 (13.0)	43.6 (14.5)
	-	Range	21-73	20-77
Sex:	-	Female	23 (53.5%)	17 (56.7%)
Highest Level of Education Completed:	-	Less than High School	3 (7.0%)	---
	-	High School	13 (30.2%)	6 (20.0%)
	-	Some College	13 (30.2%)	13 (43.3%)
	-	Bachelor's Degree	5 (11.6%)	3 (10.0%)
	-	Graduate or Professional School	4 (9.3%)	7 (23.3%)
	-	Missing	5 (11.6%)	1 (3.3%)
Employment outside home:	-	Not Employed Outside Home	4 (9.3%)	1 (4.0%)
	-	Full-time	21 (48.8%)	15 (50.0%)
	-	Part-time	2 (4.7%)	7 (23.3%)
	-	Retired	6 (14.0%)	3 (10.0%)
	-	Not Employed	10 (23.3%)	4 (13.3%)
Racial and Ethnic group:	-	White (Non-Hispanic)	32 (74.4%)	20 (66.7%)
	-	White (Hispanic)	2 (4.7%)	--
	-	Hispanic/Latino	1 (2.3%)	1 (3.3%)
	-	Black/African American	4 (9.3%)	5 (16.7%)
	-	Asian	2 (4.7%)	3 (10.0%)
	-	American Indian (Hispanic)	1 (2.3%)	--
	-	Other: Mixed Race	2 (4.7%)	1 (3.3%)
Pain Intensity: (NRS=0-10)	-	Mean (SD)	6.7 (1.3)	7.0 (1.4)
	-	Median	7.0	7.0
	-	Range	4-10	4-10

- Determined by number of patient expressions, the most predominant symptom-related concepts (greater than 6.6% of all patient expressions) were "Unspecified Pain", "Hurt", "Numbness" and "Ache".
- Numbness (reported spontaneously by 51.2 % of participants) was the symptom most often offered spontaneously by patients, followed by Burning (39.5%), and Pain that was Shooting (37.2%), Stabbing (37.2%), and Sharp (37.2%) [see also McCarrier et al, 2012].
- The most bothersome were "Excruciating Pain", "Sharp Pain", "Unspecified Pain" and "Shooting Pain" [see also Ramasamy et al, 2012].
- The symptoms that patients rated as most severe were "Unspecified Pain", "Sharp Pain", "Shooting Pain", "Heaviness" and "Tightness". Patients also described that the most difficult symptoms to be "Sharp Pain", "Throbbing Pain" and "Spasms".
- Severity was identified by patients as the most relevant attribute to assess pain symptoms.

Item Generation

- During an item-generation meeting, the development team (composed of clinical and outcomes research scientists from the study sponsors' teams, HRA scientists, and external expert panelists) met to review qualitative CE data and other evidence.
  - –Predominance of symptom mentions, whether such mentions were spontaneous or probed, and the relative severity and bother of the symptoms/impacts provided a context for evaluating individual concepts
- The evaluation process resulted in the selection of 22 specific symptom concepts to be targeted for PRO measurement.
- Group consensus noted that the Pain Quality Assessment Scale-Revised (PQAS-R; Jensen et al, 2010) provided reasonable coverage for many of these targeted concepts, but that some concepts identified as relevant to patients were not adequately covered by this instrument, and that the wording of some existing items might be problematic for patients.
  - –Modifications were made to existing items and new items were developed to create a draft version of the new symptom instrument for evaluation in cognitive interviews.

Cognitive Interviews

- A total of 30 subjects participated in four waves of Cognitive Interviews. The subjects were an average of 43.6 years old, were 56.7% female, 66.7% white (non-Hispanic), and had an average pain intensity (NRS) score of 7.0 at enrollment (Table 1).
- During the first wave of cognitive interviews, the 22-item draft questionnaire was evaluated.
- Patient input led to the deletion of nine items and substantial modifications to the existing items. Subsequent modifications were evaluated in the additional three waves of interviews.
- Cognitive interview data provided evidence from patients that the instrument was found to be comprehensive, relevant to their LBP experience, comprehendible, and easy to complete.

Pain Assessment for Lower Back Symptoms (PAL-S)

- The newly-created instrument, the Pain Assessment for Lower Back Symptoms is a 14-item instrument that measures each concept at its most intense using an 11-point (0-10) numeric rating scale (Table 2).
- The instrument specifies a 7-day retrospective recall period for each of the items.
- The instrument uses a primary descriptor in bold text and a parenthetical description containing patient-generated synonyms to help further specify the quality or pain sensation.

Table 2: Concepts Assessed in PAL-S Items

PAL-S Item
1. Please rate **how bad your worst back pain** was over the past 7 days.
2. Please rate your worst **sharp** (stabbing) back pain over the past 7 days.
3. Please rate your worst **prickling** (pins and needles) back pain over the past 7 days.
4. Please rate your most **sensitive** (as if sunburned or raw to touch) back pain over the past 7 days.
5. Please rate your worst **tender** (like a bruise) back pain over the past 7 days.
6. Please rate your worst **radiating** (spreading) back pain over the past 7 days.
7. Please rate your worst **shocking** (jolting) back pain over the past 7 days.
8. Please rate your worst **shooting** back pain over the past 7 days.
9. Please rate your worst **burning** back pain over the past 7 days.
10. Please rate your worst **cramping** (squeezing) back pain over the past 7 days.
11. Please rate your worst **muscle spasms** in your back over the past 7 days.
12. Please rate your worst **throbbing** (pounding) back pain over the past 7 days.
13. Please rate your worst **aching** (sore, nagging) back pain over the past 7 days.
14. Please rate the worst **stiffness** (tight, less flexible) in your back over the past 7 days.

CONCLUSION

- The PAL-S is a 14-item PRO measure intended for use as an endpoint in LBP clinical trials to support medical product labeling. It was developed in accordance with the FDAs PRO Guidance and best practices.
- Qualitative interviews have provided evidence for content validity.
- Cognitive interviews provided evidence that the instructions, items and response options are comprehensible, easy to complete and address key symptom sensations of LBP that are relevant to patients with the condition.
- Future quantitative studies are underway to confirm the measurement properties of the PAL-S.

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