The Pain Assessment for Lower Back Impacts (PAL-I): Qualitative Development and Cognitive Evaluation of a New Patient Reported Outcome Measure for the Assessment of Impacts of Low Back Pain

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Introduction

- Low back pain (LBP) is usually defined as pain, muscle tension, or stiffness localized below the costal margin and above the inferior gluteal folds, with or without leg pain (sciatica).
  - Although acute and sub-acute episodes (that last up to 3 months) are the most common presentations of LBP, chronic back pain causes more disability (physical limitations and psychological effects). (Manek 2005)
- Because of the multi-dimensional factors involved in LBP, it is important to assess the patient experience through qualitative interviews in order to better understand LBP related concepts that are relevant to patients and that can be used as an essential endpoint in clinical studies.
  - Ultimately, a well-developed 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 impacts of chronic low back pain (cLBP) through qualitative concept elicitation (CE) and cognitive interviews.

Methods – 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 using semi-structured interview guide with low back pain adult patients recruited from 5 clinical sites across U.S. and one in Germany.
  - 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.
  - Participants in Germany were native speakers of German, and their interviews were conducted in German (simultaneously translated into English)
- Descriptive data included standard demographics , and the painDETECT questionnaire- a screening tool for identifying neuropathic pain, non-neuropathic low back pain patients.

Methods - 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 - Population

- Exclusion Criteria
  - Chronic LBP potentially associated with a specific spinal cause.
  - Any recent low-back surgery or invasive procedures aimed to reduce LBP within the past 1 month.
  - Recent history of clinically significant drug or alcohol abuse or dependence -or- significant psychiatric disorder.
  - Participation in any other investigational device, drug, or biologics product study within the last 30 days.
  - Clinically-significant history of brain injury, stroke, or cancer.
  - Any conditions other than LBP that could confound the assessment or self-evaluation of pain.
  - Opinion of the site investigator or study director, that the subject has any other medical condition 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.

Methods – Concept Elicitation Analyses

- All interviews were audio-recorded and transcribed.
  - Transcripts were cleaned to remove any patient- identifying information prior to analysis
  - The CE interview transcripts 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 patient language
- A Saturation Grid was used to track impacts expressed during the interviews and assess saturation of concept
- Transcripts and interview guide worksheet notations were used to identify impact concepts offered by either spontaneous or probed report during the interview
- Descriptive statistics (count, percent) were summarized to characterize the severity, bother, and spontaneous reports of each expressed impact

Methods – Item Generation

- An item-generation meeting was held by the development team, where concepts identified from published literature, existing instruments, 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 impact concepts to be targeted for PRO measurement.
- During subsequent review by the development team, these targeted concepts were further reduced by removing synonymous or problematic concepts, and a draft version of the questionnaire was prepared for evaluation in cognitive interviews.

Methods – Cognitive Interviews

- Cognitive interviews were conducted with 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.
  - A semi-structured cognitive interview guide was designed to capture the subject's comprehension of items and ability to complete the draft PRO instrument.
  - The draft instrument was completed and evaluated by patients in four separate waves of interviews
  - Following each wave, the development team considered the findings and used the information to modify the draft instrument
- Cognitive interview transcripts were summarized in cognitive report tables for analysis

Results – Demographic/Clinical Characteristics

Characteristic	Concept Elicitation Interviews (n=43)	Cognitive Interviews (n=30)
Age: mean (SD); [range]	48.6 (13.0); [21-73]	43.6 (14.5); [20-77]
Gender: Female (%)	23 (53.5%)	17 (56.7%)
Racial/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%)
Other	3 (7.0%)	1 (3.3%)
Employment outside of home		
Not Employed	14 (32.6%)	5 (16.7%)
Full-time	21 (48.8%)	15 (50.0%)
Part-time	2 (4.7%)	7 (23.3%)
Retired	6 (14.0%)	3 (10.0%)
NRS (0-10) Pain Score: mean (SD); [range]	6.7 (1.3); [4-10]	7.0 (1.4); [4-10]

Results – Demographic/Clinical Characteristics

Characteristic	Concept Elicitation Interviews (n=43)	Cognitive Interviews (n=30)
Marital Status		
Married or Living as Married	24 (55.8%)	14 (46.7%)
Living with Partner	5 (11.6%)	5 (16.7%)
Widowed	3 (7.0%)	--
Separated	1 (2.3%)	1 (3.3%)
Divorced	8 (18.6%)	4 (13.3%)
Never Married	2 (4.7%)	6 (20.0%)
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%)

Results – Concept Elicitation Interviews

- A total of 43 interviews were conducted with participating patients
- Analysis of the transcripts resulted in the identification of 2,200 patient expressions about impacts of their LBP
  - Patient expressions were coded and grouped into 71 symptom and impact concepts
- Saturation of concept was achieved within the first 22 coded transcripts
  - A total of 68 concepts (95.8%) were identified in the first group of 11 transcripts
  - The remaining 3 concepts (4.2%) were identified in the second group of 11 transcripts
  - No new concepts emerged during the last two groups of transcripts
- Inter-rater agreement on the assignment of codes between raters was > 97%.

Results – Impact Concepts

- Impacts regarding "Household Activities" were the most predominant patient expressions (N=127)
  - The next most frequently expressed impact concepts were "Work Activities", "Sitting" and "General Daily Activity Limitations"
- Patients also rated their impacts on a scale of 0-10 (0-not difficult at all; 10- Extremely Difficult).
  - Climbing Stairs (9.5)
  - Standing (8.4)
  - Sports (8.4)
  - Work/School/Volunteer Duties (7.9)
  - Leisure Activities (7.9)
  - Sleep Difficulties (7.9)

Results – Item Generation

- During the item-generation process, the development team and external expert panelists reviewed the qualitative data from the CE interviews as the basis for selection of concepts for inclusion in PRO measurement.
  - Tabulated results of the CE interviews were reviewed and all possibly-relevant symptom and impact concepts that could be considered for PRO measurement were identified.
  - The list of selected symptoms and impacts was reduced to identify the target concepts that were to be included in PRO measurement.
- Separate measures were development for symptoms and impacts
  - Details of the process to development the symptom measure presented separately: PMR173 - The Pain Assessment for Lower Back Pain Symptoms (PAL-S): Qualitative Development and Cognitive Evaluation of a New Patient-Reported Outcome Measure for Low Back Pain

Results – Item Generation

- Existing PRO instruments that assess pain-related impacts were evaluated for coverage of the targeted concepts
- Oswestry Disability Index (ODI v.2.0) would provide the best coverage for the targeted concepts, but that some concepts identified as relevant to patients were not adequately covered.
  - The ODI was developed by Fairbank and Davies (Fairbank et al. 1980) to indicate the extent to which a person's functional level is restricted by disability. The authors recommend the use of the version 2.0, which has been used in adult populations with LBP.
  - Modifications were made to some existing items and additional items were developed in order to bolster the content validity of the instruments.
  - Additional items were required to assess impacts related to climbing stairs, restricted body movements (such as bending, turning, twisting, rising from sitting), feeling depressed because of LBP, feeling anxious because of LBP, and the need for assistance to get around due to LBP.

Results – Item Generation

Targeted Impact Concepts

- Personal Care
- Lifting
- Walking
- Sitting
- Standing
- Sleeping
- Sex Life
- Social Life
- Traveling
- Climbing Stairs*
- Body Movement*
- Feeling Depressed*
- Feeling Anxious*
- Needing Assistance to get around*

**Items not adequately addressed in ODI v.2.0*

Results – Cognitive Interviews

- The 15-item draft questionnaire was evaluated in four waves (30 subjects) of cognitive interviews.
- Patient input led to the deletion of two items and modifications to the existing items.
- The resulting 13 item instrument, named the Pain Assessment for Lower Back - Impacts (PAL-I) was found to be comprehensive, understandable, and relevant to patients with LBP for reporting their impact experience.

Pain Assessment for Lower Back - Impact

- The newly created low back pain impact measure is a 13 item instrument, each item using a progression of six different states of no interference to inability to perform the activity being asked about
- The instrument specifies a 7-day retrospective recall period for each of the items.
- Additional validation work is being planned, including a pilot quantitative mixed-methods study to help confirm content validity

Conclusions

- The PAL-I is a 13-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 impacts of LBP that are relevant to patients with the condition.
- Future quantitative studies are underway to confirm the measurement properties of the PAL-I

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