

SPONTANEOUS AND PROBED DISEASE-DEFINING CONCEPTS IDENTIFIED THROUGH CONCEPT ELICITATION INTERVIEWS IN LOW BACK PAIN

Kelly P. McCarrier¹, Steven I. Blum², Mona L. Martin¹, Hiltrud Liedgens³, Manjari Quintanar-Solares¹, Abhilasha Ramasamy², Charles Argoff⁴, Rainer Freyhagen⁵, Donald L. Patrick⁶, Mark Wallace⁷.



¹Health Research Associates, Mountlake Terrace, WA, USA; ²Forest Research Institute, Jersey City, NJ, USA; ³Grunenthal GmbH, Aachen, Germany; ⁴Albany Medical College, Albany, NY, USA; ⁵Benedictus Krankenhaus Tutzing and Technische Universität München Germany; ⁶University of Washington, Seattle, WA, USA; ⁷UCSD, San Diego, CA, USA.

ISPOR EU Congress
Berlin, Germany
Nov 3-7, 2012

Health Research Associates, Inc.

INTRODUCTION

- 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%.^{1,2}
- Because the severity of chronic low back pain (LBP) 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 LBP 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 identify symptoms and impacts associated with chronic low back pain that patients report spontaneously and in response to probes during qualitative concept elicitation interviews.

METHODS

Concept Elicitation Interviews

- Appropriate Institutional Review Board (IRB) approval was obtained prior to study initiation.
- Forty-three qualitative concept elicitation (CE) interviews were conducted for cross-sectional assessment in a 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.
 - Information from the concept elicitation interviews served to support the selection and development of appropriate PRO concepts for use in assessment of LBP-related outcomes in clinical trials.
- Each individual interview was conducted by a trained researcher and lasted approximately 60 minutes.
 - Descriptive data collected at enrollment included standard demographic and clinical variables.
 - Research staff used a semi-structured qualitative interview guide, designed to obtain both unprompted and prompted direct patient input about LBP symptoms and their impacts and how the patients felt these factors affected their ability to function.
 - Open-ended questions and day-reconstruction exercises were used to elicit spontaneous reports of symptom/impact concepts. Subsequent probing was used to assess condition-related concepts not spontaneously reported by participants.
 - Interviewers used worksheets to track and notate spontaneous and probed concepts.

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.

Exclusion Criteria

- Subjects were not eligible for this study if:
- Subject's chronic LBP was potentially associated with a specific spinal cause.
 - 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 or 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.
 - Subject 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 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.

Analyses

- All interviews were audio-recorded and transcribed. Transcripts were cleaned to remove any patient-identifying information prior to analysis.
- Transcripts and interview guide worksheet notations were used to identify symptom and impact concepts offered by either spontaneous or probed report during the interview.
 - Concepts described by patients in their own words during day reconstruction exercises and open-ended questions were categorized as spontaneous mentions. Symptoms and impacts expressed by patients in response to probes by the interviewer about condition-related concepts were categorized as probed mentions.
- Descriptive statistics (count, percent) were summarized to identify concepts most often reported spontaneously versus those more often mentioned in response to probing by the interviewer.

Table 1: Characteristics of Interview Participants

		TOTAL (N=43)
Age (Years):	Mean (SD)	48.6 (13.0)
	Median	48.0
	Range	21-73
Gender:	Male	20 (46.5%)
	Female	23 (53.5%)
Marital status:	Married or Living as Married	24 (55.8%)
	Living with Partner	5 (11.6%)
	Widowed	3 (7.0%)
	Separated	1 (2.3%)
	Divorced	8 (18.6%)
	Never Married	2 (4.7%)
	Missing	5 (11.6%)
Highest Level of Education:	Less than High School	3 (7.0%)
	High School	13 (30.2%)
	Some College	13 (30.2%)
	Bachelor's Degree	5 (11.6%)
	Graduate or Professional School	4 (9.3%)
	Missing	5 (11.6%)
Employment outside home:	Not Employed Outside Home	4 (9.3%)
	Full-time	21 (48.8%)
	Part-time	2 (4.7%)
	Retired	6 (14.0%)
	Not Employed	10 (23.3%)
Racial and Ethnic group:	White/Caucasian (Non-Hispanic)	32 (74.4%)
	White/Caucasian (Hispanic)	2 (4.7%)
	Hispanic/Latino	1 (2.3%)
	Black/African American	4 (9.3%)
	Asian	2 (4.7%)
	American Indian (Hispanic)	1 (2.3%)
	Other: Mixed Race	2 (4.7%)
Pain Intensity: (NRS=0-10)	Mean (SD)	6.7 (1.3)
	Median	7.0
	Range	4-10

RESULTS

- A total of 43 interviews were conducted with participating patients (mean age: 48.6 \pm 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 symptom expressions and 2,220 impact expressions
- Patient expressions were coded and grouped into 71 symptom and impact concepts (Tables 2 and 3)
 - Saturation of concept was achieved within the first 22 coded transcripts
 - Inter-rater agreement on the assignment of codes between raters was > 97%.

TABLE 2: Symptom Probed vs. Spontaneous List

SYMPTOMS	TOTAL (N=43)		
	Spontaneous N (%)	Probed N (%)	Not Affected N (%)
Numbness	22 (51.2%)	9 (20.9%)	12 (27.9%)
Burning	17 (39.5%)	6 (14.0%)	20 (46.5%)
Stabbing Pain	16 (37.2%)	11 (25.6%)	16 (37.2%)
Sharp Pain	16 (37.2%)	13 (30.2%)	14 (32.6%)
Shooting Pain	16 (37.2%)	9 (20.9%)	18 (41.9%)
Tingling	14 (32.6%)	14 (32.6%)	15 (34.9%)
Stiffness	11 (25.6%)	24 (55.8%)	8 (18.6%)
Throbbing Pain	10 (23.3%)	12 (27.9%)	21 (48.8%)
Pressure	7 (16.3%)	17 (39.5%)	19 (44.2%)
Cramping	4 (9.3%)	14 (32.6%)	25 (58.1%)
Excruciating Pain	4 (9.3%)	18 (41.9%)	21 (48.8%)
Electric Shocks	4 (9.3%)	12 (27.9%)	27 (62.8%)
Squeezing	4 (9.3%)	12 (27.9%)	27 (62.8%)
Pins and Needles	4 (9.3%)	13 (30.2%)	26 (60.5%)
Heaviness	4 (9.3%)	4 (9.3%)	35 (81.4%)
Hot	4 (9.3%)	10 (23.3%)	29 (67.4%)
Pulsating Pain	2 (9.3%)	9 (20.9%)	32 (74.4%)
Prickling	2 (4.7%)	4 (9.3%)	37 (86.0%)
Piercing Pain	1 (2.3%)	8 (18.6%)	34 (79.1%)
Jolt	1 (2.3%)	10 (23.3%)	32 (74.4%)
Drilling Pain	1 (2.3%)	1 (2.3%)	41 (95.3%)
Cutting Pain	---	4 (9.3%)	39 (90.7%)
Itchiness	---	1 (2.3%)	42 (97.7%)
Deadness	---	7 (16.3%)	36 (83.7%)
Stinging	---	9 (20.9%)	34 (79.1%)

- The LBP-related symptoms (Table 2) most often reported spontaneously among interview participants included: Numbness (51.2% of participants), Burning (39.5%), and Pain that was Shooting (37.2%), Stabbing (37.2%), and Sharp (37.2%).
 - The symptoms reported most often in response to probes included Stiffness (55.8% of participants), Excruciating Pain (41.9%), Pressure (39.5%), Cramping (32.6%), and Tingling (32.6%).
- The impact concepts (Table 3) most often reported spontaneously included interference with: Walking (65.1%), Sitting (62.8%), Exercise (58.1%), Leisure Activities (58.1%), Sleeping (55.8%), Housework (53.5%), and Emotional Impacts (48.8%).
 - Impacts reported most often in response to probes included low Energy because of pain (67.4%), Productivity (65.1%), Financial Impact (46.5%), Driving (39.5%), and Work (39.5%).

TABLE 3: Impact Probed vs. Spontaneous List

IMPACTS	TOTAL (N=43)		
	Spontaneous N (%)	Probed N (%)	Not Affected N (%)
Walking	28 (65.1%)	10 (23.3%)	5 (11.6%)
Sitting	27 (62.8%)	11 (25.6%)	5 (11.6%)
Exercise	25 (58.1%)	12 (27.9%)	6 (14.0%)
Leisure Activities	25 (58.1%)	8 (18.6%)	10 (23.3%)
Sleeping at Night	24 (55.8%)	12 (27.9%)	7 (16.3%)
Housework	23 (53.5%)	12 (27.9%)	8 (18.6%)
Emotional Impacts	21 (48.8%)	13 (30.2%)	9 (20.9%)
Work	17 (39.5%)	17 (39.5%)	9 (20.9%)
Driving	15 (34.9%)	17 (39.5%)	11 (25.6%)
General Mobility	14 (32.6%)	10 (23.3%)	19 (44.2%)
Social Activities	13 (30.2%)	12 (27.9%)	18 (41.9%)
Relationships	9 (20.9%)	16 (37.2%)	18 (41.9%)
Team Sports	7 (16.3%)	9 (20.9%)	27 (62.8%)
Personal Care	5 (11.6%)	12 (27.9%)	26 (60.5%)
Level of Independence	5 (11.6%)	11 (25.6%)	27 (62.8%)
Energy, Physical Stamina	4 (9.3%)	29 (67.4%)	10 (23.3%)
Overall Productivity	3 (7.0%)	28 (65.1%)	12 (27.9%)
Financial Impact	1 (2.3%)	20 (46.5%)	22 (51.2%)

CONCLUSION

- Symptoms and functional impacts associated with chronic low back pain were identified through qualitative concept elicitation interviews.
- Strength of these findings is suggested by achievement of saturation of concept.
- Relevant patient-identified concepts should be considered in the development of patient-reported outcome instruments.
 - Concepts reported spontaneously provide good support for relevance to the patient experience.
 - Concepts identified primarily through probing may be less prominent features of the LBP experience, potentially due to patients' accommodation to their condition.
- Overall, the strongest concepts for inclusion in PRO instruments will be those symptom and impact concepts with high levels of both spontaneous and probed responses, followed by those with high levels of spontaneous support and low levels of probed mentions. Concepts appearing only in response to probes are potentially weaker candidates for inclusion in PRO instruments.

References

1. Manek NJ, MacGregor AJ. (2005) Epidemiology of back disorders: prevalence, risk factors, and prognosis. *Curr Opin Rheumatol* 17:134-4.

2. Wenig CM, Schmidt CO, Kohlmann T, Schweikert B. (2008) Costs of back pain in Germany. *Eur J Pain Jun* 2;13(3):280-6.

This study was sponsored by Forest Research Institute and Grunenthal GmbH. Charles Argoff, MD, Rainer Freyhagen, MD, Donald Patrick, PhD, and Mark Wallace, MD, are paid consultants to Forest and Grunenthal. Forest, Grunenthal and Health Research Associates were involved in the study design and analysis. All authors were involved in the interpretation of data and decision to submit this abstract to ISPOR-EU. Funding for poster development was provided by Forest and Grunenthal to Health Research Associates.