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How condition-specific do measures of pain intensity need to be?

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The majority of patient reported outcome (PRO) tools have been developed to assess pain across different pain conditions. These include measures of pain intensity and interference (e.g., the Brief Pain Inventory [5]), pain quality (e.g. the revised Short Form McGill Pain Questionnaire (SF-MPQ-2) [6]), pain distribution (e.g., Michigan Body Map [4]), and pain subtype (e.g., Neuropathic Pain Questionnaire [9]). Regulatory guidance published by the United States Food and Drug Administration (US FDA) in 2009 [13] indicates that PRO measures used in pre-marketing research to support claims in approved medical labeling should be developed using input from the population being studied. In addition, the guidance states that the instrument(s) should be validated in the target population. The suite of NIH Patient Reported Outcomes Measurement Information System (PROMIS) pain measures - pain intensity, interference, quality, and behavior - have been developed in accordance with the FDA guidance for use across chronic conditions; a number of PROMIS pain measures have been validated in back pain [e.g., 11]. The SF-MPQ-2 was also developed with the US FDA guidance in mind as a measure of both neuropathic and non-neuropathic pain.

In this issue, Martin and colleagues [10] present important research detailing the development and initial validation of a new measure of chronic low back pain (cLBP), the Patient Assessment for Low Back Pain - Symptoms (PAL-S). In line with the US FDA guidance, the authors used qualitative research methods to obtain the input of persons with cLBP in the design of the instrument. The study provides evidence that the PAL-S has good test-retest reliability and concurrent validity. Importantly, the development of the measure meets some of the recommendations in the FDA PRO guidance and supports its use in US FDA regulated clinical trials for cLBP. The sensitivity and responsiveness to change of the PAL-S – a crucial psychometric quality in an outcome measure in pain clinical trials – will be examined in the future.

Of note, the US FDA PRO guidance indicates that existing instruments that are not developed according to their guidelines can be used to support labeling claims under certain conditions. Specifically, the guidance states: “An existing instrument can support a labeling claim if it can be shown to reliably measure the claimed concept in the patient population enrolled in the clinical trial” (page 3). Indeed, many recent FDA regulated studies have

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utilized some type of ecological momentary assessment of pain using a single visual analogue scale (VAS) or numerical rating scale (NRS), which have been extensively studied (e.g., [8]). Martin and colleagues [10] indicate in their Introduction that a single scale might not fully capture the range of pain sensations reported in cLBP, suggesting that a new cLBP-specific multi-item scale may be more accurate and sensitive. So which is better? A generic pain scale or a condition specific scale? Ultimately, this is an empirical question that remains to be fully addressed.

Many suggest intuitively that condition-specific measures are superior to generic ones in terms of their content validity and responsiveness to change. However, the literature in pain assessment is mixed on this issue. For example, in a study of low back and leg pain, Walsh and colleagues [14] examined the responsiveness of general- and condition-specific measures to changes in pain symptoms over time. The authors found that the Short Form 36 (SF-36), a general quality of life measure, was as responsive and, in some cases, superior to pain-specific measures in detecting change. In a prospective cohort study of persons with chronic pain, Angst et al. [2] found that the Multidimensional Pain Inventory was the most responsive measure, followed by the SF-36. They suggest both measures may be useful in assessing pain outcomes. Under certain circumstances, a generic measure of pain may have as much utility as a condition-specific measure. For instance, a general measure may be better in pragmatic trials that enroll study participants with multiple comorbid pain conditions (e.g. cLBP *and* arthritis). In such diverse populations a condition-specific outcome measure may not capture non-targeted treatment-effects on other types or sources of pain.

Use of a general pain measure may have other advantages as well. Administration of such a measure across populations enables one to directly compare pain report across diverse patient groups, which may be of interest in some studies. In addition, much research has been done on existing generic pain measures to define changes in the measure that constitute clinically significant improvement. Often, data from these measures are used to establish cutoffs, such as those recommended by the IMMPACT group [7] that reflect a clinically meaningful improvement to a therapy, or that might be used to conduct responder analyses. Research on the PROMIS pain interference scale for back pain research has already established minimally important differences that are clinically significant [1].

As evidenced by the multi-step methods detailed by Martin and colleagues in the development of the PAL-S, creating a new measure according to the FDA guidelines is a resource-intensive endeavor. Therefore, the potential benefits of creating new condition-specific measures relative to validating an existing measure needs to be carefully considered prior to initiating a measurement development project. That being said, any measure used in US FDA regulated research needs to be accepted by the agency as having sufficient reliability and validity in a population to support a labeling claim.

In conclusion, Martin and colleagues [10] present a well-designed and executed mixed-methods study to develop and validate a new measure of pain specifically for use in cLBP clinical trials. The preliminary results are promising. Yet, crucial measurement characteristics, such as minimally important difference and sensitivity and responsiveness to

change need to be examined in order to fully understand the utility of the PAL-S in cLBP clinical trials. Comparison of the PAL-S to well-established measures, such as the SF-MPQ-2 which contains many items that overlap with those of the PAL-s, is warranted. Though pain intensity is an undeniably important outcome in cLBP clinical trials, it is essential that researchers also consider assessing other patient-centered outcomes such as pain interference and functional ability [3,12].

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References

1. Amtmann D, Kim J, Chung H, Askew RL, Park R, Cook KF. Minimally important differences for Patient Reported Outcomes Measurement Information System pain interference for individuals with back pain. *J Pain Res.* 2016; 9:251–255. [PubMed: 27175093]
2. Angst F, Verra ML, Lehmann S, Aeschlimann A. Responsiveness of five condition-specific and generic outcome assessment instruments for chronic pain. *BMC Med Res Methodol.* 2008; 8:26. [PubMed: 18439285]
3. Ballantyne JC, Sullivan MD. Intensity of chronic pain—The wrong metric? *N Engl J Med.* 2015; 373:2098–2099. [PubMed: 26605926]
4. Brummett CM, Bakshi RR, Goesling J, Leung D, Moser SE, Zollars JW, Williams DA, Clauw DJ, Hassett AL. Preliminary validation of the Michigan Body Map. *Pain.* 2016; 157:1205–1212. [PubMed: 26835782]
5. Cleeland CS, Ryan KM. Pain assessment: Global use of the Brief Pain Inventory. *Annals, Academy of Medicine, Singapore.* 1994; 23:129–138.
6. Dworkin RH, Turk DC, Revicki DA, Harding G, Coyne KS, Peirce-Sandner S, Bhagwat D, Everton D, Burke LB, Cowan P, Farrar JT, Hertz S, Max MB, Rappaport BA, Melzack R. Development and initial validation of an expanded and revised version of the Short-form McGill Pain Questionnaire (SF-MPQ-2). *Pain.* 2009; 144:35–42. [PubMed: 19356853]
7. Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, Haythornthwaite JA, Jensen MP, Kerns RD, Ader DN, Brandenburg N, Burke LB, Cella D, Chandler J, Cowan P, Dimitrova R, Dionne R, Hertz S, Jadad AR, Katz NP, Kehlet H, Kramer LD, Manning DC, McCormick C, McDermott MP, McQuay HJ, Patel S, Porter L, Quessy S, Rappaport BA, Rauschkolb C, Revicki DA, Rothman M, Schmader KE, Stacey BR, Stauffer JW, von Stein T, White RE, Witter J, Zavisic S. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *Journal of Pain.* 2008; 9:105–121. [PubMed: 18055266]
8. Geisser ME, Palmer RH, Gendreau RM, Wang Y, Clauw DJ. A pooled analysis of two randomized, double-blind, placebo-controlled trials of milnacipran monotherapy in the treatment of fibromyalgia. *Pain Prac.* 2011; 11:120–131.
9. Krause SJ, Backonja MM. Development of a neuropathic pain questionnaire. *Clin J Pain.* 2003; 19:306–314. [PubMed: 12966256]
10. Martin ML, Blum SI, Liedgens H, Bushnell DM, McCarrier KP, Hatley NV, Ramasamy A, Freynhagen R, Wallace M, Argoff C, Eerdeken M, Kok M, Patrick DL. Mixed-methods development of a new patient-reported outcome instrument for chronic low back pain: part 1 - the Patient Assessment for Low Back Pain - Symptoms (PAL-S). *PAIN.* 2018:XXX–XXX.
11. Papuga MO, Mesfin A, Molinari R, Rubery PT. Correlation of PROMIS physical function and pain CAT instruments with Oswestry Disability Index and Neck Disability Index in spine patients. *Spine.* 2016; 41:1153–1159. [PubMed: 26909832]
12. Sullivan MD, Ballantyne JC. Must we reduce pain intensity to treat chronic pain? *Pain.* 2016; 157:65–69. [PubMed: 26307855]

13. United States Food and Drug Administration. Guidance for Industry. Patient-reported outcome measures: Use in medical product development to support labeling claims. 2009. Available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282>. Accessed: February 16, 2018.
14. Walsh TL, Hanscom B, Lurie JD, Weinstein JN. Is a condition-specific instrument for patients with low back pain/leg symptoms really necessary? *Spine*. 2003; 28:607–615. [PubMed: 12642770]

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