Two Companies Following the FDA PRO Guidance Leads to Similar But Different Measures: A Case Study in Psoriasis

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BACKGROUND

- Patient-reported outcomes (PROs) are commonly used during the development of medicines to treat chronic, disabling conditions where the intention is not necessarily to cure but to ameliorate symptoms, facilitate functioning, or improve health-related quality of life.
- A multitude of academic papers, consortia, and conferences address how best to measure the patient experience in clinical trials.[1]
- The Food and Drug Administration's (FDA's) release of the final PRO guidance, *Patient Reported Outcomes: Use in Medical Product Development to Support Labeling Claims in 2009*[2] was a landmark event.
  - The PRO guidance provides recommendations for the development, evaluation, and use of PROs to support potential claims in product labeling.
  - Based on this document, PROs may be used to support treatment benefit claims in FDA-approved product labeling.
  - The claims must be supported by appropriately designed investigations using PROs that have been demonstrated to adequately measure the concept underlying the claim.[3]
- Development of PRO measures relies heavily on the principles outlined in the PRO guidance.
- Due to commercial pressures and drug development timelines, different organizations may be involved in developing PRO measures for the same disease at the same time without the benefit of collaboration in a precompetitive space.

OBJECTIVE

- The objective of this research was to evaluate the similarities and differences between two recently created PRO measures developed by different organizations for the same disease.
- Psoriasis was selected as a case study, because two pharmaceutical companies recently published the following PRO measures to assess the severity of psoriasis-related symptoms:
  - Psoriasis Symptom Diary (PSD)
  - Psoriasis Symptom Inventory (PSI)

METHODS

- Full-length publications related to the development of the PSD and PSI were identified (PubMed) and reviewed.
- The following information regarding the development process and key aspects pertinent to the PRO guidance were extracted from the papers:
  - Patient population
  - Intended context of use
  - Development steps
    - Literature review (yes/no)
    - Qualitative interviews with patients (concept elicitation) (yes/no)
    - Cognitive debriefing interviews (yes/no)
  - Measurement properties established
    - Content validity (yes/no)
    - Reliability (yes/no)
    - Construct validity (yes/no)
    - Ability to detect change (yes/no)
  - Content of final measure
    - Total number of items
    - Item content (e.g., specific symptoms assessed, bothersomeness, impact)
    - Recall period used
    - Response scale and response options
    - Scoring (including direction)
- The authors conducted a qualitative evaluation of the similarities and differences between the measures.

RESULTS

- A total of five publications on the development of the measures were identified (PSD, n = 2; PSI, n = 3).
- Both measures focused on symptoms of moderate to severe psoriasis.
  - Development of both measures was based on literature reviews, patient input, and expert opinion, and had similar psychometric properties.
  - The recall period for both measures is the past 24 hours. However, the measures consist of different numbers of disease-specific symptoms (PSD = 6; PSI = 8).
  - The PSD consists of 16 items (severity of symptoms = 6, skin color = 1, hiding skin = 1, bother of symptoms = 8).
  - The PSI consists of 8 items, all of which measure symptom severity.
  - Additionally, the measures assess symptoms with different response scales; the PSD uses an 11-point numeric rating scale, while the PSI uses a 5-point categorical rating scale. Both measures equate higher scores with greater severity.

Table 1. Overview of Measures

Key Aspects of Guidance	PSD	PSI
Patient population	Patients with moderate to severe psoriasis	Patients with moderate to severe psoriasis
Reported context of use	To support efficacy endpoints in clinical trials of patients with moderate to severe psoriasis	To assess psoriasis symptom severity in patients with moderate to severe psoriasis for use in clinical trials of psoriasis therapeutics
Development steps		
Literature review	✓	✓
Qualitative interviews with patients (concept elicitation)	✓	✓
Cognitive debriefing	✓	✓
Measurement properties		
Content validity	✓	✓
Reliability	✓	✓
Construct validity	✓	✓
Ability to detect change	✓	✓

PSD Sources: Strober et al., 2013[4]; Lebwohl et al., 2014.[5]

PSI Sources: Martin et al., 2013[6]; Bushnell et al., 2013[7]; Revicki et al., 2014.[8]

Table 2. Comparison of Measure Content

Content	PSD	PSI
Total number of items	16	8
Symptom severity		
Itch	✓	✓
Redness	–	✓
Scaling	✓	✓
Burning	✓	✓
Cracking	✓	✓
Stinging	✓	✓
Flaking	–	✓
Pain	✓	✓
Skin color	✓[a]	–
Symptom bother	✓	–
Recall period	Over the past 24 hours	2 versions (24 hours and 7 days)
Response scale	11-point numeric rating scale	5-point categorical rating scale
Response options for severity items	• 0 = no (symptom) • 10 = (symptom) as bad as you can imagine	• 0 = not at all • 1 = mild • 2 = moderate • 3 = severe • 4 = very severe
Scoring	Individual items 0-10, no total score	Items are summed for a total score, ranging from 0 to 32
Score direction	Higher score is worse	Higher score is worse

[a] Skin color is assessed as how noticeable the affected skin color is.

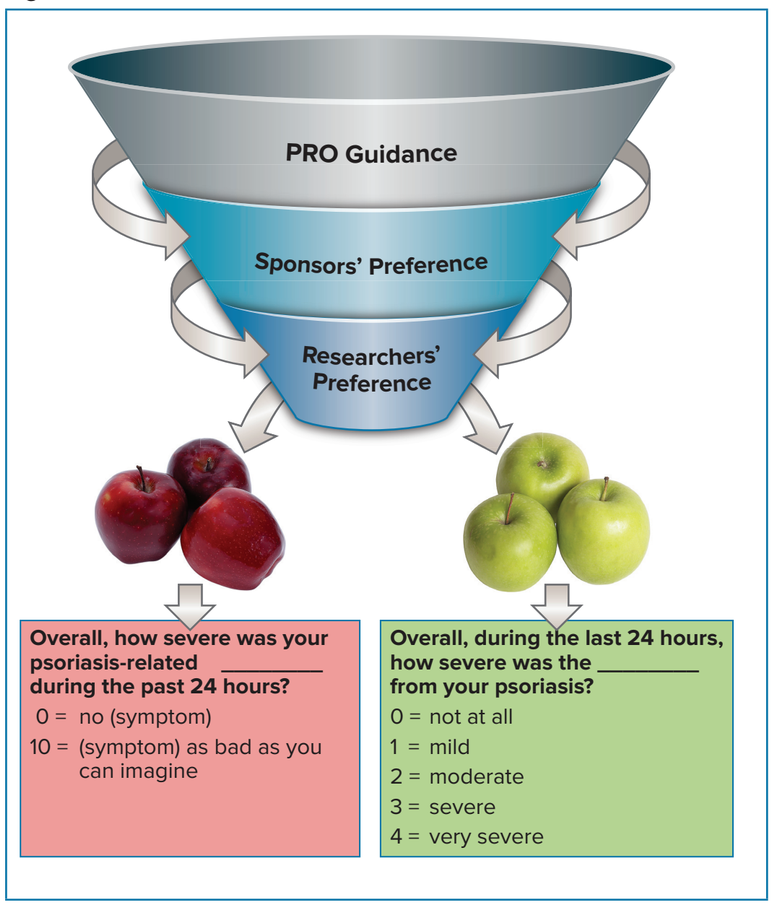
PSD Sources: Strober et al., 2013[4]; Lebwohl et al., 2014.[5]

PSI Sources: Martin et al., 2013[6]; Bushnell et al., 2013[7]; Revicki et al., 2014.[8]

DISCUSSION

- Our intent was not to evaluate or determine whether one measure better assessed psoriasis-related symptoms, but rather to analyze the scientific process used and whether similarities and differences exist in the final questionnaires when different organizations approach the same topic following the same general road map.
- Both organizations followed the process as outlined in the FDA's PRO guidance[2] to develop their symptom diary:
  - Performed literature reviews, and designed and implemented qualitative studies for concept elicitation.
  - Used data from their literature review and qualitative work to generate preliminary items
  - Conducted cognitive interviews
  - Fielded preliminary versions of their diary in a trial to obtain psychometric data
  - Refined the measure and included in phase 3 trials
- While the overall process and content was similar, the specifics of the measures contain nuanced differences, such as the following:
  - Response scale: 0-10 versus 0-4 rating scale
  - Item structure: recall period after versus before mentioning the symptom
- The differences possibly are due to preferences and philosophies of the sponsors and researchers involved (Figure 1).

Figure 1. One Process But Two Measures



LIMITATION

- Only one detailed case study was performed.

CONCLUSION

- This example demonstrates that PRO measures developed to assess the same concept and aligned with the FDA's PRO guidance[2] may be similar but ultimately, not identical. The differences are possibly due to preferences and philosophies of the sponsors and researchers involved.

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