

The Future of Measuring Patient-Reported Outcomes in Rheumatology

Patient-Reported Outcomes Measurement Information System (PROMIS)

DINESH KHANNA,¹ ESWAR KRISHNAN,² ESI MORGAN DEWITT,³ PUJA P. KHANNA,¹ BRENNAN SPIEGEL,⁴ AND RON D. HAYS⁴

INTRODUCTION

The National Institutes of Health Patient-Reported Outcomes Measurement Information System (PROMIS; trademarked by the National Institutes of Health) Roadmap initiative (available at www.nihpromis.org) is a cooperative research program designed to develop, evaluate, and standardize item banks to measure patient-reported outcomes across different medical conditions as well as the US population (1). The goal of PROMIS is to develop reliable and valid item banks using item response theory (IRT) that can be administered in a variety of formats including short forms and computerized adaptive tests (CAT) (1–3). IRT is often referred to as “modern psychometric theory,” in contrast to “classic test theory,” or CTT. The basic idea behind both IRT and CTT is that there is some latent construct, or “trait,” underlying an illness experience. This construct cannot be directly measured, but can be indirectly measured by creating items that are scaled and scored. For example, fatigue, pain, disability, or

even “happiness” are latent constructs, i.e., subjective feelings—we cannot take a picture, snap a radiograph to view them, or run a blood test to check for them. However, we know they exist. People can experience more or less of these constructs; therefore, it is helpful to try to translate that experience into several levels represented by scores. IRT models the associations between items and the latent construct. Specifically, IRT models describe relationships between a respondent’s underlying level on a construct and the probability of particular item responses.

Tests developed with CTT (such as the Health Assessment Questionnaire disability index [HAQ DI] [4], or the Scleroderma Gastrointestinal Tract instrument [5]) require administering all items, even though only some are appropriate for the person’s trait level. Some items are too high for those with low trait levels (e.g., “can you walk 100 yards” to a patient in a wheelchair) or too low for those with high trait levels (e.g., “can you get up from the chair?” to a runner). In contrast, IRT methods make it possible to estimate person trait levels with any subset of items appropriate for the person’s trait levels in an item pool. As such, any set of items from the pool could be administered as a fixed form or, for greatest efficiency, administered as a CAT. CAT is an approach to administering the subset of items in an item bank that are most informative for measuring the health construct in order to achieve a target standard error of measurement. A good item bank will have items that represent a range of content and difficulty, provide high levels of information, and have items that perform equivalently in different subgroups of the target population.

HOW DOES CAT WORK?

Without prior information, the first item administered in a CAT is typically one of medium trait level. For example, “In the past 7 days I was grouchy” with multilevel responses ranging from “never” to “always.” After each response, the person’s trait level and associated standard error are estimated. The next item administered to someone not endorsing the first item is an easier item. If the

Dr. D. Khanna’s work was supported by the NIH (grants U01-AR-057936A and K23-AR-053858-05). Dr. Krishnan’s work was supported by the NIH (grant 2U01-AR-052158). Dr. DeWitt’s work was supported by the NIH (grant U01-AR-057940). Dr. P. Khanna’s work was supported by the NIH (grant U01-AR-057936A) and a Career Bridge Funding Award from the American College of Rheumatology. Dr. Spiegel’s work was supported by the NIH (grants U01-AR-057936A, AR-052177). Dr. Hays’ work was supported by the NIH (grants U01-AR-057936A, P30-AG-021684, and 2P20-MD-000182).

¹Dinesh Khanna, MD, MS, Puja P. Khanna, MD, MPH: University of Michigan School of Medicine, Ann Arbor; ²Eswar Krishnan, MD: Stanford University, Palo Alto, California; ³Esi Morgan DeWitt, MD, MSCE: Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio; ⁴Brennan Spiegel, MD, MSHS, Ron D. Hays, PhD: University of California, Los Angeles.

Address correspondence to Dinesh Khanna, MD, MSc, Associate Professor of Medicine and Director, University of Michigan Scleroderma Program, 24 Frank Lloyd Wright Drive, PO Box 481, Ann Arbor, MI 48106. E-mail: khannad@med.umich.edu.

Submitted for publication May 30, 2011; accepted in revised form August 4, 2011.

person endorses the first item, the next item administered is a harder item. CAT is terminated when the standard error falls below an acceptable value. This provides an estimate of one's score with the minimal number of questions and no loss of measurement precision. In addition, scores from different studies using different items can be compared using a common scale. IRT models estimate the underlying scale score (θ) from the items. All items are calibrated on the same metric and independently and collectively provide an estimate of θ . Hence, it is possible to estimate the score using any subset of items and to estimate the standard error of the estimated score. This allows assessment of health outcomes across patients with differing medical conditions (such as comparing scores of someone with arthritis to someone with heart disease) at various degrees of physical and other impairments, both at the lowest and highest ends of trait levels.

PROMIS IN RHEUMATOLOGY

The Life Story of PROMIS Tools

Since the beginning of PROMIS in 2004, much progress has been made in developing measures of self-reported health within a domain hierarchy (Figure 1). Physical functioning, fatigue, pain, emotional distress, and social health were the core domains of interest. While all these domains are relevant to rheumatic diseases, the physical health domain encompassed most of the traditionally important outcomes in rheumatology, such as physical function, pain, and fatigue.

In PROMIS, the term physical function was preferred over the term disability and represented the ability to perform activities of daily living including instrumental activities (e.g., shopping) (6). The PROMIS physical function item bank containing 124 new items was developed from 1,865 available items culled from 160 English language questionnaires. In addition to administering the item bank using CAT, PROMIS has developed several static short forms including: 1) a 20-item PROMIS HAQ, which corresponds to the HAQ DI, 2) a PROMIS 10-item static, or short form with items selected as the "best" from the physical function items, and 3) a PROMIS 20-item static form also selected from the "best" PROMIS items. PROMIS HAQ differs from the HAQ DI by deleting the 1-week time frame and increasing the response option set from the original 4 choices to 5 by adding "with a little difficulty." Measurement properties of different PROMIS item banks (PROMIS HAQ, PROMIS 10-item short form, PROMIS 20-item short form, and 10-item PROMIS CAT) were compared to the HAQ DI and physical functioning 10-item scale (PF-10) of the Short Form 36 in 378 patients with rheumatoid arthritis, osteoarthritis, and normal aging cohorts (7). PF-10 provided the least content information followed by HAQ DI, which was better for patients with physical disability (SD less than or equal to -1) but performed poorly for the average population (Figure 2).

PROMIS items (10 or 20 items) performed better than PF-10 and HAQ DI. The PROMIS CAT outperformed all the static items (Figure 2). The CAT maintained acceptable performance in populations whose physical function is

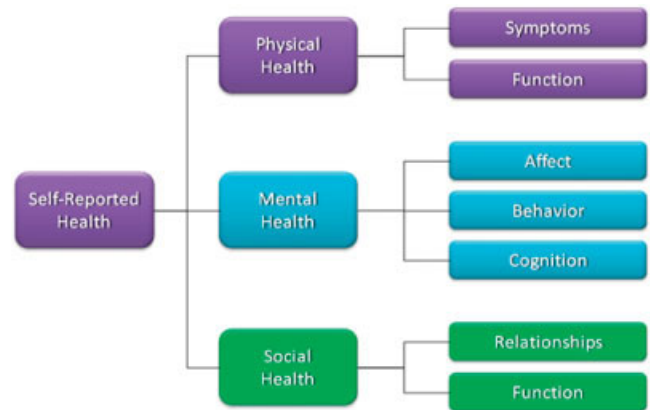


Figure 1. Patient-Reported Outcomes Measurement Information System (PROMIS) domain hierarchy. Color figure can be viewed in the online issue, which is available at [http://onlinelibrary.wiley.com/journal/10.1002/\(ISSN\)1529-0131](http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)1529-0131).

1.5 SDs better than the population norm. This has implications for our patients because as better treatments become available for rheumatic diseases we are likely to observe healthier cohorts of patients with arthritis. Thus, accurate assessment of those in the positive health range of physical functioning becomes increasingly important.

What PROMIS Means for Rheumatology

Physical function, global health assessment, and fatigue are important constructs in rheumatic diseases, in both adults and pediatrics. The availability of PROMIS tools will also catalyze research on the less well-studied impact of rheumatic diseases in all health domains. In the next sections, we discuss the advantages of PROMIS, its current use in rheumatology, and the future of PROMIS in rheumatology.

Advantages of PROMIS over traditional instruments. PROMIS employs a uniform qualitative process with detailed systematic review, focus groups, cognitive interviews, and translatability for each item bank. PROMIS has devoted substantive resources to ensuring that outcome measures are understood and usable by diverse populations. Items are written at a grade school level and tested for comprehensibility among low-literacy populations. All items are reviewed and modified as needed for their translatability. To enhance inclusiveness, PROMIS informatics assessment tools are rendered accessible to populations with sensory limitations and others requiring assistive technology. Lastly, PROMIS measures are grounded in a life course perspective, as it is the group's ultimate goal to produce single metrics for the same domain across the full lifespan (i.e., PROMIS is linking measures developed for children with those developed for adults).

PROMIS instruments have been found to have better precision than existing measures; a quality that may lead to reduction in sample size in clinical studies (6). The severity of patient-reported outcomes in rheumatic diseases can be compared head-to-head with other chronic conditions such as heart failure. It is possible to "customize" the set of items by selecting a set of items that is matched to the severity level of the target population.

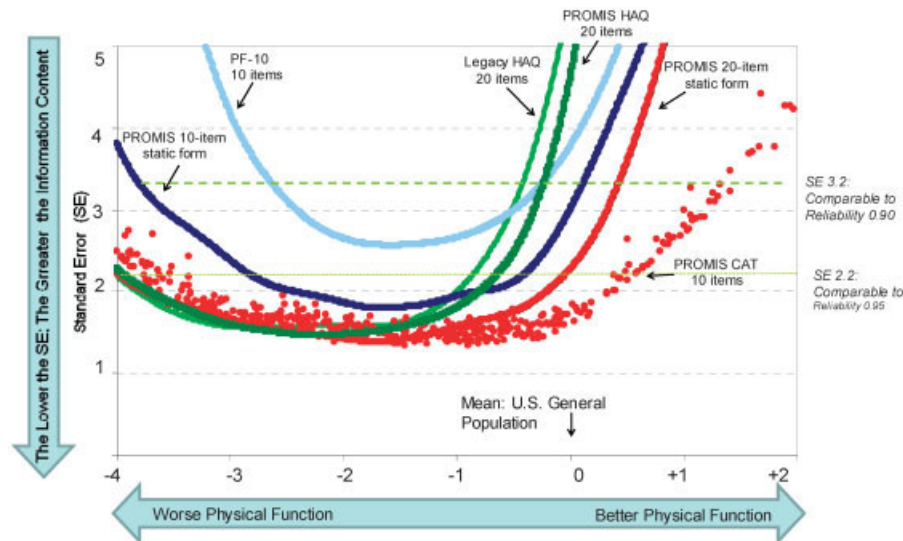


Figure 2. Comparison of information content of 6 physical function instruments: Health Assessment Questionnaire disability index (HAQ DI), Patient-Reported Outcomes Measurement Information System (PROMIS) HAQ, PROMIS 10-item short form, PROMIS 20-item short form, physical functioning 10-item score (PF-10; from Short Form 36), and 10-item PROMIS computer (CAT). Instruments with greater information content have SE curves that are lower and have a greater SD range at a reliability >0.95 . More items are better than fewer, item response theory (IRT)-based (PROMIS) is better than non-IRT-based items, and CAT is better than static. Adapted with permission from ref. 7.

PROMIS items are currently available at no cost, enabling freer exchange of information and data, stimulating outcomes research.

Utilization of CAT to administer PROMIS items does require a computer, and that may limit its applicability in a busy clinical practice. Although a person may receive different set of items from an item pool at each visit, users can track which items were administered in the CAT and track theta scores over time.

Current PROMIS item banks and their validation in rheumatology. *PROMIS item banks for adult patients.* PROMIS item banks developed for adults (including anger, anxiety, abilities and general concern, depression, fatigue, pain behavior, pain interference, physical function, positive and negative psychosocial impact of illness, sleep disturbance, sleep impairment, satisfaction with participation in discretionary social activities) are available at www.nihpromis.org. Additional short forms have been developed for constructs such as global health, global satisfaction with sex life, etc. All these item banks measure important constructs that are applicable to patients with arthritis and other rheumatologic conditions. As an example, the feasibility of 11 PROMIS item banks was recently assessed in a single-center, observational study in patients with systemic sclerosis (8). The average number of items completed for each CAT-administered item bank ranged from 5 to 8 (69 CAT items per patient), and the average time to complete each CAT-administered item bank ranged from 48 seconds to 1.9 minutes per patient (average time 11.9 minutes/per patient for 11 banks). The time to complete the item banks was not significantly different in patients with physical disabilities (such as hand contractures and digital ulcers).

PROMIS item banks for pediatric patients. PROMIS version 1.0 item banks and short forms developed for children include anger, anxiety, asthma impact, depressive symptoms, fatigue, pain interference, physical function (separate banks for upper extremity and mobility), and peer relationships and are available at www.nihpromis.org. The PROMIS Cooperative Network is currently in the process of evaluating the pediatric version 1.0 item banks in multiple pediatric chronic conditions including juvenile idiopathic arthritis (JIA) and chronic musculoskeletal pain, widespread or regional. Importantly, the process includes a qualitative component including semistructured interviews with children. Longitudinal validation in these pediatric conditions, among others, is underway.

New PROMIS item banks under development. The PROMIS Cooperative Network has increased the focus and energy on development of pediatric item banks with 4 of 12 of the PROMIS II sites (project period 2009–2012) dedicated to work in pediatrics. This includes development of new pediatric item banks to assess pain behavior, pain quality, physical activity, subjective well-being, experience of stress and others, all of which are important in patients with chronic arthritis. Current efforts are also focused on linking adult and pediatric item banks measuring the same construct to allow measurement from childhood through adolescence then transition to adulthood on the same metric. The PROMIS Cooperative Network is also developing new item banks pertinent to chronic diseases. These include development of gastrointestinal symptoms items, self-efficacy for self-management of chronic illness, and others.

Future of PROMIS in rheumatology. The PROMIS mission is to use measurement science to create a state-of-the-art assessment system for self-reported health to advance

patient-reported outcome measurement in clinical research and day-to-day practice. Similar to other patient-reported outcomes, this will facilitate the incorporation of the patient's voice into clinical trials and clinical practice. The American College of Rheumatology has endorsed the assessment of functional status in patients with rheumatoid arthritis at least every 12 months. For patients with JIA, it is recommended that functional status and health-related quality of life be assessed at 6 month intervals (9). This exacts new requirements of patient-reported outcome measures, including exceptional ease of use, rapidity of administration, interpretability, and a clear benefit of using the data in patient-provider interactions and care management. Rheumatology is a specialty that is well versed in the use of measures of disability, pain, and other aspects of health-related quality of life. PROMIS offers an opportunity to accelerate uptake and expand the use of patient-reported outcomes from research advocates to all clinicians.

Using PROMIS in Clinical Practice

Being able to administer a choice of fatigue, pain interference, physical function, or depression measures, among many other options, in the waiting room on a Tablet, laptop, personal computer, and potentially a Smart Phone and have instant scoring, calibration to population norms, and be ready to share with the patient at point of care is compelling.

As an example, Figures 3 and 4 show results from a 50-year-old patient with early diffuse systemic sclerosis. This patient was administered CAT item banks for physical function and depression that took approximately 2

Computerized Adaptive Test (CAT) Report

Date: 01-Nov-10
Your age: 50
Your gender: Male
Computerized Adaptive Tests: Depression, Physical Function

Your score on the Depression CAT is 70. The average score is 50.
 Your score indicates that your level of Depression is higher (worse) than:

- 98 percent of people in the general population
- 96 percent of people age 45-54
- 98 percent of males

Your score on the Physical Function CAT is 33. The average score is 50.
 Your score indicates that your level of Physical Function is higher (better) than:

- 6 percent of people in the general population
- 9 percent of people age 45-54
- 5 percent of males

Figure 3. Computer generated Patient-Reported Outcomes Measurement Information System (PROMIS) report of a 50-year-old man with recently diagnosed systemic sclerosis. The report provides the patient's scores for depression and physical function scales and compares it to the US general population.

Your scores for the CATs you completed are shown below.

The diamond \blacklozenge is placed where we think your score lies. This diamond is placed on your T-Score, which is a standardized score that is based on an average score of 50, based on responses to the same questions in the United States general population. The T-score also has a standard deviation of 10 points, so a score of 40 or 60 represents a score that is one standard deviation away from the average score of the general US population.

The Standard Error (SE) is a statistical measure of variance and represents the possible range of your score. The lines on either side of the diamond in your profile report show the possible range of your actual score around this estimated score. It is very likely that your score is in the range of these lines.

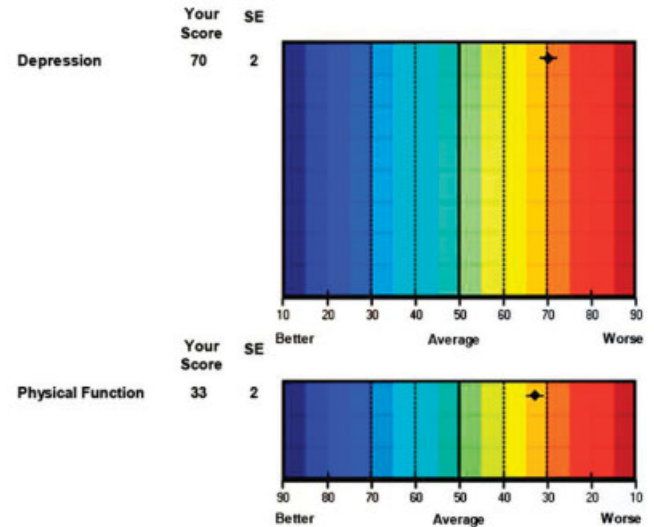


Figure 4. Computer-generated Patient-Reported Outcomes Measurement Information System (PROMIS) graph of a 50-year-old man with recently diagnosed systemic sclerosis. The report depicts the patient's score for depression and physical function scales and compares it to the US general population. Color figure can be viewed in the online issue, which is available at [http://onlinelibrary.wiley.com/journal/10.1002/\(ISSN\)1529-0131](http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)1529-0131).

minutes to complete. The profile provides his current physical function (1.7 SDs below US general population) and depression status (2 SDs below US population). This information (presented in the form of a PROMIS report in Figure 3 and a graph as shown in Figure 4) can be used for clinical care. This patient was referred for psychological counseling to help him adjust to his newly diagnosed systemic sclerosis and also prescribed physical therapy. The item banks can be administered at each clinic visit to assess change in symptoms from baseline visit. Current work is ongoing to assess the feasibility of incorporating PROMIS item banks in routine clinical practice.

In conclusion, PROMIS has developed items banks that are relevant to rheumatology, can be "customized" to a patient or a practice, and are currently freely available. The item banks provide tremendous flexibility for creation of fixed length short forms or CAT administration. This quick assessment can generate a patient report to monitor health over time.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published.

REFERENCES

1. Cella D, Yount S, Rothrock N, Gershon R, Cook K, Reeve B, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years. *Med Care* 2007;45 Suppl 1:S3–11.
2. Reeve BB, Hays RD, Bjorner JB, Cook KF, Crane PK, Teresi JA, et al. Psychometric evaluation and calibration of health-related quality of life item banks: plans for the Patient-Reported Outcomes Measurement Information System (PROMIS). *Med Care* 2007;45 Suppl 1:S22–31.
3. Hays RD, Liu H, Spritzer K, Cella D. Item response theory analyses of physical functioning items in the medical outcomes study. *Med Care* 2007;45 Suppl 1:S32–8.
4. Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. *Arthritis Rheum* 1980;23:137–45.
5. Khanna D, Hays RD, Maranian P, Seibold JR, Impens A, Mayes MD, et al. Reliability and validity of the University of California, Los Angeles Scleroderma Clinical Trial Consortium Gastrointestinal Tract Instrument. *Arthritis Rheum* 2009;61:1257–63.
6. Fries JF, Krishnan E, Bruce B. Items, instruments, crosswalks, and PROMIS. *J Rheumatol* 2009;36:1093–5.
7. Fries JF, Cella D, Rose M, Krishnan E, Bruce B. Progress in assessing physical function in arthritis: PROMIS short forms and computerized adaptive testing. *J Rheumatol* 2009;36:2061–6.
8. Khanna D, Maranian P, Rothrock N, Cella D, Gershon R, Khanna PP, et al. Feasibility and evaluation of the construct validity of PROMIS and “Legacy” instruments in an academic scleroderma clinic. *Value Health*. In press.
9. Lovell DJ, Passo MH, Beukelman T, Bowyer SL, Gottlieb BS, Henrickson M, et al. Measuring process of arthritis care: a proposed set of quality measures for the process of care in juvenile idiopathic arthritis. *Arthritis Care Res (Hoboken)* 2011;63:10–6.