Patient-reported outcome (PRO) research has shown that PROs must play a role in the future of health care delivery as the system transitions from volume-based care to value-based care. Building trust among stakeholders and integrating various interests can facilitate implementation of PROs into everyday practice.

Patient-reported outcome measures (PROMs) are instruments that consist of multiple-item scales or single-item measures that are designed to collect patient-reported outcomes (PROs). Research that we have conducted suggests that practicing physicians have limited familiarity with PROMs. Because of the limited knowledge and frequent misconceptions of health care providers regarding patient-centered medicine and PROs, a review of the fundamentals is needed to provide context and a deeper understanding of PROMs.

In a seminal report published in 2002 by the Institute of Medicine (IOM) titled “Crossing the Quality Chasm,” authors outlined 6 specific aims that a health care system must fulfill to deliver quality health care. One of these attributes was titled “Patient-Centered,” and it was suggested that the system of care should revolve around the patient, respect patient preferences, and put the patient in control. PROs became the expression of this attribute and came to be defined by the US Food and Drug Administration as “any report of the patient’s health condition that comes directly from the patient, without interpretation of the patient’s response by a clinician or anyone else.”

Evidence suggests that patient reporting can improve communication, satisfaction, and symptom management. Regulatory authorities have also expressed interest in seeing PRO data included within product submissions. Guidelines and clinical pathways have been developed to help ensure robust measures are used to improve patient outcomes. Payers are interested in PROs as a part of cost-effectiveness research for making reimbursement decisions and reducing the overall cost of care.

Given the growing focus on patient-centeredness in health care, increasing patient involvement in research is warranted. Patient non-compliance to treatment because of quality-of-life (QOL) issues or functional impairment can lead to waste and increased cost of care. In a recently published randomized, controlled clinical trial in patients undergoing outpatient chemotherapy for advanced solid tumors, patients were asked to report 12 common symptoms to their health care providers. Those patients reported greater improvement in health-related QOL (HRQL) than patients assigned to symptom monitoring at the discretion of clinicians. Further, self-reporting engages patients and may improve experience, efficiency, and outcomes of care.

The increasing tendency to integrate PROs into medical practice marks the start of a new era of clinical research and patient care, which has the potential to address two immediate needs in modern health care: (1) the need for patient-centric medicine; and (2) the need for adequate evaluation criteria to support value-based care. Value-based care is inherently patient-centered, as the patient is the recipient of care even when they are not the purchaser.

PROMS IN PATHWAYS PROGRAMS

Our interest in PROs grew out of our work with collaborative clinical pathways programs between insurers and their specialty physician provider networks. In partnership with one large nonprofit health insurer in the mid-Atlantic region of the United States, the first network-wide, collaborative, cancer clinical pathway was launched in August 2008. Due to high levels of physician participation, compliance, and behavioral change, the adoption of that pathway resulted in a 15% cost-of-care reduction and led to improved patient outcomes, including a 7% reduction in emergency room visits and hospitalizations.

This early pathway success led the sponsoring payer to expand the pathway programming with both a second-generation oncology pathways program—the Oncology Medical Home—as well as a collaborative pathway with the rheumatology physician network.

The second generation oncology medical home was piloted in 2011. This program modified the traditional physician reimbursement model used in the pathway program.
by shifting the source of revenue from drug reimbursement margin to enhanced professional charges for cognitive services (evaluation and management [E&M] codes).11 The medical home removed the financial incentive from drug delivery while dramatically increasing it for patient care. Similarly, the rheumatology pathway launched in late 2010 aligned physician desire for prescribing autonomy with payer desires while dramatically increasing it for patient care. Similarly, the rheumatology pathway program was unique on many levels; not only was it the first payer-sponsored, network-wide rheumatology pathway in the United States, but it was also the first pathway of any kind that incorporated PRO data and the first to require use of a point-of-care decision support tool to collect the PROs and manage physician compliance.

Evidence suggests that patient reporting can improve communication, satisfaction, and symptom management.

The PRO aspect of the rheumatology pathway is indicative of what could be accomplished in oncology and warrants further discussion. Seventy-nine rheumatologists in 35 practices participating in this payer-sponsored, rheumatologist-developed pathways program incorporated use of a point-of-care decision support tool, which required a clinical disease activity index (CDAI) assessment at each physician visit. Components of the CDAI include independent patient-reported swollen joint counts (SJC) and tender joint counts (TJC), patient global assessment (PGA) scores, and physician global assessment (PhGA) scores. The CDAI aggregated score reflects disease and treatment burden with ratings ≤ 2.8 indicating remission, 2.9–10 indicating low disease and treatment burden, 10.1–22 indicating moderate disease and treatment burden, and 22.1–76 indicating high disease and treatment burden. CDAI methodology has been published, and its clinical validity and utility have been independently assessed by the American College of Rheumatology (ACR).13

In the past two years, we have presented multiple PRO-related findings from this unique program at international meetings. Recording PROs in real-time concurrent with clinician-reported outcomes represents the most direct and accurate comparative assessments of disease and treatment impact. Concurrent collection of PROs has been considered all but impossible; yet our data suggests otherwise. Our findings show that 3185 patients considered active (defined as having ≥ 2 physician visits over the study period) contributed PRO information over the course of 13,723 visits to the clinic.14 At least one CDAI component was documented in 90% of visits, and PGA and PhGA scores were both documented in 66% of visits. SJC and TJC were least likely to be documented. Almost all patients (99%) not in remission with CDAI scores ≥ 2.8 had all 4 CDAI components documented.14

Further, we not only successfully collected PROs but also were able to show their potential impact. One such analysis sought to compare PGA and PhGA scores to determine patient-physician discordance for rates of disease and treatment impact on perceived well-being. A total of 3406 patients, 77% of whom were women, had 9769 physician visits during the study period where both PGA and PhGA were captured. The linear correlation between the PGA and PhGA scores and the significant difference in mean scores (3.26 vs 2.51 for PGA and PhGA, respectively) indicated that physicians underestimated disease severity and treatment-related adverse events and their impact on patient perceived well-being.15

We designed the pathway to incorporate PROMs as a critical component for measuring pathway effectiveness. The capture of CDAI scores concurrent with pathway adoption and compliance would allow for correlation of patient experience with changes in treatment pattern and site of care. A steering committee of 12 physicians created the pathway with the following unique elements: (1) obligatory use of a real-time decision-support and data-capture tool; (2) use of disease-modifying anti-rheumatic drugs (DMARD) as first-line treatments for at least 12 weeks before use of biologic agents; and (3) requirement that dose, schedule, and adjustments for biologic agents follow package-label prescribing guidelines.

Would such a pathway reduce cost, and, if so, what would be the impact on the patient? PROM analysis provided stakeholders with the answer. Pathway compliance resulted in a 9% increase in the percent of patients on DMARD therapy. Concurrent CDAI assessment revealed no decrease in the percentage of patients categorizing their burden as in remission or low, and costs were reduced without a negative impact on patient burden or satisfaction.16

PROS AND MEDICATION THERAPY MANAGEMENT
Our PRO research has extended beyond clinical pathways and into specialty pharmacy. Managing high-cost and highly toxic orphan and ultra-orphan drugs of precision medicine presents medication therapy management (MTM) problems for payers and their pharmacy benefit management and specialty pharmacy vendors, who increasingly leverage volume to lower cost. The rapid expansion of this drug class, fragmentation between pharmacy and medical benefit, and increasing use of pathways-based disease management highlight the need for a solution to these problems. PROs may
be the most direct and accurate assessment of disease and treatment impact on medication compliance and adherence.

We conducted a 1-month pilot study of a novel PRO-based MTM solution in conjunction with a regional mid-Atlantic insurer. Patient risk stratification by diagnosis (oncologic and rheumatologic) and drug resulted in a scripted phone call triage performed by a pharmacy technician. All patients were contacted at initial fill of a specialty pharmacy prescription and periodically thereafter based on their risk profile. Patient queries were designed to identify barriers to medication possession. A total of 956 phone calls by pharmacy technicians were required to initially reach all 239 patients. The PRO algorithm identified 68 patients (28%) experiencing problems that either restricted possession or limited adherence to the prescribed drug. These issues were categorized as financial, clinical, QOL, self-administration, or literacy. Remediation resulted in a positive outcome for 65 patients (95%) who were then able to initiate or continue their prescribed treatment. As a result, a medication possession ratio (MPR) of 97% was achieved, an outcome that compares favorably to published results.

**BARRIERS TO GREATER PRO MEASUREMENT**

Our PRO experience and research has reinforced our belief that PROs and PROMs must play a role in the future of health care delivery as the system transitions from volume-based care to value-based care. Our observations are consistent with an increasing body of evidence demonstrating the unique contribution of PROs to the value assessments of patients, providers and payers. It is critical that the clinician understand that PROs are not merely a review of systems by another name. It is equally critical that physicians realize the scientific rigor by which PROMs are validated.

We conducted market research to assess physician knowledge and perceptions about PROMs. Medical oncologists representing diverse geography and practice type participated in a live meeting in April 2016. Our findings, which have not yet been published, revealed that, despite many of these physicians having extensive experience with clinical research, none were actively collecting PRO data nor had experience in PRO-based research. The physicians were also generally not familiar with PROMs. There was confusion among some of the physicians as for whom PROMs were utilized and by whom and how they were created and validated. Throughout the discussion, physicians were most concerned with the potential burden the PRO collection process and logistics would place on practice staff and patients themselves. However, all of the participating physicians agreed that PRO studies could provide valuable data that would assist with providing more effective and cost-appropriate care to patients. More specifically, they were interested in the potential of PROs to demonstrate improvement in quality of care, which they believed critical to Oncology Care Model success.

Through market research, we have also been able to identify some of the major threats to widespread PRO measurement, the greatest of which being the misconception that PROs and HRQOL can be used interchangeably. A recent study identified a core set of the most useful PROs, including overall general QOL, general health, physical ability, satisfaction with caregivers, satisfaction with services and care organization, coping, defecation, appetite, ability to do usual activities, medication use, fatigue, negative and positive feelings, fear of recurrence, and social relationships. Even though this list was developed for a specific condition (pancreatic cancer), it illustrates that a variety of PROs can be used effectively in clinical and research practice to inform treatment decisions and value-based care. The PROs most commonly collected for both of these goals can be divided roughly into four categories:

- **Measuring the “immeasurable.”** This requires clinicians to assess symptoms that cannot be measured without asking the patient directly, such as fatigue, pain, QOL, distress, or appetite.

- **Adherence.** This includes patients’ level of adherence to treatment plans, any intentional or unintentional barriers to adherence, and their motivation to follow a prescribed regimen.

- **Satisfaction.** This involves treatment satisfaction, health-care provider and practice satisfaction, and doctor-patient communication satisfaction. The subcategories of satisfaction may be use, trust, efficiency, and effectiveness of treatment.

- **Needs assessment.** This involves assessing patients’ unmet needs and preferences and includes looking at treatment preferences such as side effects versus symptoms trade-offs or willingness to pay versus willingness to risk, in order to improve quality of life. A sub-category of needs assessment frequently used by drug development companies is trial optimization PROs. Trial optimization PROs assess patients’ specific needs to inform clinical trial design in order to make it as patient-friendly and non-intrusive as possible, with the goal of enhancing recruitment and retention without sacrificing research standards.

To optimize PROs, both practically and functionally, appropriate PROMs need to be developed and validated. PROM development and validation is an iterative process, which can be both rigorous and strenuous. To summarize, it follows five essential steps: (1) conceptual framing; (2) concept elicitation; (3) cognitive debriefing; (4) generation of preliminary survey items; and (5) psychometric evaluation. Additionally, it is essential to keep in mind that validated instruments should only be used within the population for which they were validated.

Many PROMs, including a well-known generic Short Form Health Survey (SF-36) that measures quality of life, or a Treatment Satisfaction Questionnaire for Medication (TSQM), are appropriate to use with a broad patient
population. The disease-specific PROMs, however, demonstrate higher sensitivity and responsiveness in the populations for which they were designed. For example, since the publication of the first Functional Assessment of Cancer Therapy – General (FACT-G) in 1993, more than 50 tumor-specific functional assessment instruments have been developed and validated. To name just a few, such cancer-specific instruments include Functional Assessment of Cancer Therapy – Breast, for breast cancer; Functional Assessment of Cancer Therapy – Lung, for lung cancer; and Functional Assessment of Cancer Therapy – Head and Neck, for head and neck cancer. Over the past decade, the Patient Reported Outcome Measurement Information System (PROMIS) Health Organization developed an item bank for measuring PROs for a wide variety of diseases and conditions, with the goal of creating new generic and disease-specific measures. However, it is also important that physicians and the industry recognize the value PROs have for improving outcomes and the potential barriers that currently exist to their implementation. A recent study found that the main barriers for assessing PROs in pediatric oncology practice included time, insufficient staff, logistics, and financial resources, sentiments that were echoed by physicians in our market research group. Between 2010 and 2014, only 3 of 40 (7.5%) oncology drugs received PRO-related labeling.

Another important barrier to PRO implementation is disagreement and tension among different stakeholders. Clinicians are concerned that payers might misuse and misinterpret the data, whereas performance-measure developers do not completely trust the quality of data collected in clinicians’ offices. The collecting of PROs facilitates doctor-patient communication, increases providers’ awareness of patient symptoms and needs, and informs and guides patient-centric treatment decision-making. The use of PROs in clinical practice enhances detection of HRQOL problems and satisfaction with care among oncology patients. In parallel with the use of PROs in treatment process, the use of PRO performance measures (PRO-PM) for assessment and evaluation has been emerging. The PROs aggregated across patients may be used to assess the quality of health care practices and providers. Regulators and policymakers use information collected via PRO-PM to evaluate and compare the quality of health care practices and providers, to incentivize decisions, and encourage quality improvement. Consumers and patients may use PRO-PM to make an informed choice of health care provider or center. Despite these benefits, PROs remain misunderstood and underutilized. Efforts should be made to build trust among different stakeholders and to integrate and incorporate various interests in order to facilitate successful implementation of PROs into everyday clinical, industry, and regulatory practice.

References