Generic patient-reported outcome measures (PROMs) for cancer have outlived their utility. More relevant and accurate PROMs are required in order to demonstrate the true value of oncology interventions to patients.

Patient-reported outcome measures (PROMs) cover a wide range of different outcomes including perceived clinical severity, disease burden, satisfaction with treatment, quality of life, and utility. Each of these outcomes requires a different type of PROM. Patient-reported outcomes (PROs) have been defined as “a report coming directly from patients about how they feel or function in relation to a health condition and its therapy without interpretation by healthcare professionals or anyone else.” Unfortunately, this definition is rather restrictive as it focuses on only one type of outcome—health-related quality of life (HRQL).

It should be noted that PROs should not be confused with patient-centric outcomes. Whereas “patient-reported” indicates that the information is provided by the patient, “patient-centric” implies that the information collected is of specific concern to the patient. In fact, most PROMs do not collect patient-centric data.

Too often, PROMs are selected and used without a clear justification,2,3 and few PROMs are of adequate psychometric quality to produce publishable data. To demonstrate the true value of oncology interventions to patients, more relevant and accurate PROMs are required.

**PROMS COMMONLY USED IN ONCOLOGY**

Unlike in other medical specialties, the only PROMs used in oncology assess HRQL. In the 1980s,4 two generic cancer outcome measures, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)5 and the Functional Assessment of Chronic Illness Therapy, Functional Assessment of Cancer Therapy – General (FACT FACT-G), were developed.6 These PROMs were produced independently by physicians to collect information of relevance to physicians; consequently, they focus on HRQL outcomes. Both are generic oncology measures with rather crude add-ons intended to be specific to different cancers or symptoms. Additionally, the EORTC QLQ-C30 and FACT FACT-G measure vastly different sets of outcomes and cannot be used interchangeably.7

Available evidence suggests that the EORTC QLQ-C30 is a relatively poor measure of HRQL.8-10 It fails to meet most of the criteria generally recommended for selecting instruments for use in clinical trials. The lack of adequate patient involvement during the development of the instrument is reflected in poor response rates in practice.11 There is no evidence that the measure has been able to show differences in efficacy between alternative active interventions. This is due to its inadequate psychometric properties.

The FACIT FACT-G also predominantly measures HRQL, although a few items do go beyond and assess patients’ emotional response to their illness. Still, there is limited evidence of its dimensionality or psychometric qualities, as the published data relate to early versions of the measure.5 In fact, for some modules there appear to be no published data to support their quality.

Despite these shortcomings, a recent review of PROMs used in oncology12 found that the EORTC QLQ-C30 (used mainly in Europe) and the FACIT FACT-G (preferred in North America) remain the most commonly used PROMs in this field. Yet, since these were first developed, the ability to measure PROs has advanced considerably in terms of theoretical underpinnings, instrument development methodologies, and statistical modelling.

Where other measures have been used in cancer studies, they are also generic HRQL PROMs, developed for use in other diseases or individual symptom scales that are not specific to a particular cancer.13 Disease-specific measurement is a fundamental requirement of good PROMs—without this specificity, important issues will be missed and irrelevant questions asked. Given that there are almost 200 different forms of cancer,14 the absence of high-quality, holistic PROMs specific to individual cancers is striking.

**THE NEED FOR NEW PROMS IN ONCOLOGY**

A recent review of the use of PROMs in trials of the 16
Box 1. Requirements for Oncology Patient-Reported Outcome Measures

1) Must have a coherent outcome measurement model guiding the selection of items for the measure. The model should cover all aspects of patients’ lives and not just those directly influenced by health services.

2) Should be disease-specific so that the content is carefully tailored to the experiences of respondents.

3) Must be independent of the nature of the intervention(s), allowing different combinations of clinical and non-clinical treatments to be evaluated.

4) Must be patient-centric. This can only be done by conducting unstructured, qualitative interviews with patients with the aim of determining the factors that most affect patients’ lives. The measurement model adopted must also be taken into account. Wherever possible, specific words used by the interviewed patients should be incorporated into the measure.

5) Should provide an index of outcomes rather than a profile in order to support the interpretation of results. The index should indicate the overall combined impact of both illness and interventions. It is not valid to add together different types of outcomes (for example, different symptoms or types of functioning), although this is common practice.

6) Should produce a one-dimensional scale, such that all items in the scale measure the same construct and these measurements can be added together to arrive at a total score. To achieve this, the scale needs to fit an Item Response Theory model, preferably the Rasch model. Scores on the measure that form an ordinal scale allow for parametric statistical techniques to be applied to the data. This also reduces sample size requirements for clinical studies.

7) Must include scales that are reliable, valid, and able to detect real change where it occurs. Fundamental requirements for these qualities to be achieved are: a coherent measurement model; highly specific content; and fit to the Rasch model.

8) Must include scales that are easy to administer and complete using simple language and avoiding complex response formats such as visual analog scales and multi-choice response formats.

most commonly used regulatory-approved treatments for advanced or metastatic breast cancer highlighted the lack of effective outcome measurement. The review identified 1727 publications that included PROMs. Of these, more than 1700 were judged to be unsuitable for review, as they did not summarize treatment benefits and/or toxicity of a selected treatment using a PROM. Most studies failed to report the results of the PRO analyses. None of the assessments in the reviewed studies compared different interventions, only reporting change from baseline in treated groups. Consequently, there is no PRO evidence available comparing the effectiveness of the regulatory-approved treatments for metastatic breast cancer.

Other groups have reported similarly disappointing results in oncology. King et al found that evidence on the effectiveness of PROMs in patient management of brain cancer was inconsistent, although they did believe that such data did aid patient–physician communication.

A fundamental problem with PRO measurement in oncology is an overreliance on HRQL measures. Patrick and Erikson define HRQL as “the value assigned to duration of life as modified by the impairments, functional states, perceptions and social opportunities that are influenced by disease, injury, treatment or policy.” This means that HRQL measures take no account of other influences on the quality of the lives of patients, such as personality, financial resources, education, or the availability of family members for support.

Another major shortcoming of HRQL PROMs is that they assess a range of symptoms and functional impairments resulting from disease, generating a profile of these outcomes. This makes interpreting changes in HRQL difficult, as some outcomes may improve while others deteriorate. According to the European Medicines Agency, a single domain, such as pain or fatigue, is not considered to be a HRQL outcome and cannot be the basis for a claim of HRQL improvement, even though it is patient-reported.

Instrument developers often try to overcome this problem by adding together scores from the different outcomes. Unfortunately, there is no scientific justification for doing so, and the “total” scores are largely meaningless.

HRQL PROMs have prospered because they have been preferred by the pharmaceutical industry, which traditionally sought to show the benefit of their products to clinicians and to the US Food and Drug Administration whose primary concerns are clinical efficacy and safety rather than patient value. European health authorities are now requiring evidence of patient benefit in addition to safety and efficacy, exemplified in comments made by European Medicines Agency executive director, Guido Rasi, who explained the shift by saying, “As patients live with their condition on a day-to-day basis, their views on the therapeutic effect of a medicine and its impact on their quality of life… may differ from those of other stakeholders.”

There is a clear need for new PROMs for oncology that are modern, disease-specific, of high quality, and capable of determining the impact of interventions from the patients’ perspective. The characteristics necessary for such PROMs are provided in Box 1.

Only one non-HRQL measurement model has been widely operationalized in health research. This needs model, which relates outcomes to needs fulfilment, grew out of qualitative research conducted to determine how disease and its treatment affects the lives of patients. Symptoms such as pain and fatigue, as well as functions including...
employment, hobbies, and socialization, are important insofar as they influence the fulfillment of basic human needs. Subsequent analyses demonstrated that these needs can be combined into a coherent unidimensional scale capable of determining the impact of both clinical and non-clinical interventions. In contrast to HRQL PROMs, needs-based measures are patient-centric, disease-specific, and based on a coherent outcome measurement model. The development of such measures for use in oncology could help to determine the true, holistic impact of cancer and the value of its treatment for patients.

THE EVOLVING ROLE OF PROMS IN ONCOLOGY
Health care systems around the world are changing. There are too many demands for services and too few resources to fund them. Three major developments can be identified that attempt to address this problem: the development of care pathways, outcomes-based reimbursement (OBR), and big data analytics.

According to Gebhardt and colleagues, "clinical pathways are an efficient means of ensuring that the best, most evidence-based treatment is being used for patients." They later state that it is important to establish patient-centric metrics such as the success of an intervention, survival rates, and treatment toxicity; notably, these are not patient-reported outcomes. In their review of the development and implementation of two pathways introduced at the UPMC Cancer Center (Pittsburgh, PA), they failed to show any evidence of improvement in patient value. Qualitative research conducted to evaluate the state of care pathways in US health care settings found that PROs were not included as key data sources for care pathway development or as commonly used evaluation metrics for such pathways. Furthermore, 62% of key stakeholders cited failure to demonstrate patient outcomes as a barrier to pathway expansion. These studies suggest that evaluation of clinical pathways focuses primarily on standardizing practices and creating savings for providers and payers rather than on whether they produce benefit to patients.

The move from fee-for-service to an OBR model also requires the ability to measure patient value by means of PROMs. Yet again, it seems that patient outcomes are not being used in such models. As Gupta et al argue, "The current metrics used for value-based reimbursement...are surrogate measures that do not measure value directly." Patients need to consider both clinical and non-clinical interventions when designing programs to maximize potential outcomes. Non-clinical interventions such as social care, education programs, wearable technology, health apps, exercise regimes, and lifestyle changes, all have a role to play in improving patient value, especially when combined with effective clinical treatment. By definition, HRQL outcomes are unable to determine the impact of such interventions.

Big data analytic studies also need holistic unidimensional PROMs that are independent of the nature of the intervention. Rumsfeld and colleagues conclude, "If big data analytics are shown to improve quality of care and patient outcomes...big data will fulfill its potential as an important component of a learning health-care system." Cichosz et al also emphasize that predictive models based on big data “must demonstrate impact, namely, their use must generate better patient outcomes.” Surprisingly, a quick review of the big data in health literature highlights the fact that little attention has been paid to the inclusion of PROMs. Indeed, outcomes are rarely defined in discussions of big data analytics.

PROMs that are relevant for patients and payers...are essential for implementing and evaluating modern approaches to health service provision.

These major developments all require the availability of disease-specific PROMs that go beyond the assessment of HRQL outcomes. While the HRQL PROMs used in oncology provide information of value to the clinician, they do not necessarily indicate what is of primary concern to the patient. HRQL outcomes are also of limited value to clinical pathway development and evaluation, OBR, and big data analytics, as they do not assess non-clinical interventions.

PROMs that are relevant for patients and payers, and that better exemplify patient value, are essential for implementing and evaluating modern approaches to health service provision. Complementary measures of HRQL can have value for clinicians. However, it is questionable whether the dated, generic HRQL measures such as the QLQ-C30 and the FACT-G provide an adequate quality of measurement.

CONCLUSION
PRO measurement in oncology lags compared with other clinical specialties. Innovative approaches to health care delivery, evaluation, and reimbursement are welcomed, but they rarely consider patient outcomes in a meaningful manner. Too often, emphasis is placed on motivating physicians, easing commissioning, and reducing costs, irrespective of the effects these changes have on the patient. There is a clear need for the development of high-quality, disease-specific PROMs that assess the true concerns of patients and that evaluate the impact of both clinical and non-clinical interventions on a variety of outcomes. Only then will it be possible to demonstrate the true impact of oncological and other interventions on the lives of patients.
References


COUNTERPOINT

Incorporating Routine Patient-Reported Outcomes Assessment Into Cancer Care: Building Momentum

Edward Stepanski, PhD

While the collection and reporting of patient-reported outcome data in oncology trials and care settings has yet to reach its full potential, it has made some progress in recent years.

Patient-reported outcomes (PROs) are defined as “any report of the status of a patient’s health condition that comes directly from the patient’s response, without interpretation of the patient’s response by a clinician or any

Affiliations: Vector Oncology, Memphis, TN

Disclosures: Dr Stepanski is an employee of Vector Oncology.
one else.” Uses of PRO data in health care range from the “micro” to the “macro.” At the micro level, PROs collected from individual patients can help providers make more informed patient-level treatment decisions, such as changing dosing for antidepressant medications based on depression severity score. At the macro level, aggregated PRO data collected from a large group of patients as part of a clinical trial may inform clinical guidelines or be used to guide health policy decisions, such as how pain ratings aggregated across large samples identify the need for improved pain management strategies.

Initiatives calling for increased inclusion of PROs as endpoints in oncology clinical trials, and as a standard assessment in the practice of clinical medicine, go back many years. However, while the collection and reporting of PRO data in oncology trials and care settings has made some progress in recent years, it has yet to reach its full potential. The primary focus in oncology treatment research and clinical care is tumor burden, with symptom burden receiving less attention. A renewed emphasis on the importance of PROs in oncology is steadily increasing, largely in response to trends in health care reimbursement. Migration from a fee-for-service system to a patient-centric, value-based system requires that patient assessments be included in determining when treatments are successful. Additionally, there have been compelling studies presented this year that demonstrate how systematic symptom monitoring as part of routine clinical care results in markedly improved outcomes.

PROS AND VALUE-BASED HEALTH CARE

The term “value-based care” covers a wide swath of ground but generally refers to a cost–benefit ratio, in which “benefit” includes a variety of treatment outcomes, and “cost” refers to the toxic and monetary consequences of treatment. Approaches to measuring treatment benefit vary significantly but usually cite the importance of the patient experience as an expected element in any value calculation. The health care field is still in an early “consensus-building phase,” with calls to standardize treatment outcomes measurement, routinely including PROs.

An example of the current status of attempts to drive this process in oncology can be found in the American Society of Clinical Oncology (ASCO) Value Framework, an algorithm that calculates standard metrics and allows treatment options to be compared using a value-based perspective. Measures of clinical benefit, toxicity, and cost are included in this algorithm to deliver normalized metrics for treatment regimens being considered by patients and providers.

Toxicity assessments would ideally include PROs, but these need to be reported at higher rates in pivotal trials to warrant inclusion in the standard algorithm. Additionally, patient needs, goals, and preferences must be assessed to optimize treatment decisions.

After the Value Framework was published in 2015, ASCO invited feedback from a broad set of stakeholders within the cancer care community. In response to this feedback, ASCO has just published an updated version of their value framework that addresses many of the concerns and comments of the community. The revised model acknowledges that “a substantial number of respondents commented on the lack of inclusion of PROs in the value framework.”

A renewed emphasis on the importance of PROs in oncology is increasing, largely in response to trends in health care reimbursement.

Yet, there is already an editorial response to the revised framework calling for even more ambitious measurement of PROs to reevaluate treatment utilities for patients over the course of treatment. These authors make the case that the net health benefit is dynamic across the course of treatment and that it changes as patients experience toxicity, financial barriers, or other factors that might affect the value of their treatment. These valid points highlight the complexity of designing a value-based approach to measuring treatment outcomes, as well as the need to include the patient experience as part of a coherent solution.

PRO COLLECTION IN ROUTINE CLINICAL CARE

The utility of routine inclusion of PRO data in oncology care requires empirical assessment. Basch et al published a pivotal paper this year demonstrating improved outcomes across multiple domains when PRO data were systematically collected and presented to the provider team. This randomized controlled trial was methodologically rigorous and deserves careful attention. A sample of 766 patients with advanced solid tumors was randomized to receive either usual care or routine PRO assessment. The PRO instrument evaluated 12 common symptoms of cancer or cancer treatment. Stratification for “computer-experienced” versus “computer-inexperienced” was included, with the computer-experienced cohort reporting symptoms from their homes using the internet between clinic visits. Both groups provided symptom reports during clinic visits. These data were presented to the health care team for review at the time of the patient’s visit. When symptom data were collected remotely, alerts were sent to nursing staff when scores increased by 2 or more points or exceeded an absolute threshold of grade 3 or higher. Nurses then triaged patients according to usual clinic practice, which consisted of telephone counseling about symptom management. Patients in the PRO cohort experienced significant benefits across a
variety of endpoints, including a higher quality of life, decreased emergency room visits, decreased hospitalization rates, and increased 1-year survival. Patients in the PRO cohort received active chemotherapy treatment for an average of 2 months longer (6.3 vs 8.2 months, $P = .002$), presumably because it was possible to better manage toxicity when symptoms were routinely evaluated. Given that hospitalization is an important driver of cost in cancer care, techniques that reduce that cost while also improving outcomes are key to achieving success in a value-based care model.

**Patient ratings [of symptoms of drug toxicity] provide unique input to clinical decision-making that can translate to more time on therapy and better outcomes.**

Research to define the mechanisms underlying these improvements in outcomes with PRO assessment is still needed. One obvious hypothesis is that PRO data provide a novel source of information that makes it easier for the care team to manage toxicity, allowing for a more complete delivery of planned therapy. The additional 2 months of chemotherapy in the PRO cohort supports the interpretation that patients in this group were less likely to experience early treatment discontinuation. Although health care providers have historically evaluated symptoms of drug toxicity as part of the clinical encounter, studies have shown that clinician ratings of these symptoms significantly underestimate severity when compared to patient ratings.\(^8,9\) Patient ratings provide unique input to clinical decision-making that can translate to more time on therapy and better outcomes.

An additional finding of particular interest in the Basch et al study\(^7\) is that the subgroup of computer-inexperienced patients had larger effect sizes across all endpoints compared with the entire cohort.\(^7\) These patients only completed PRO assessments during their time in the clinic because they did not have access to the internet at home. This subgroup was older, mostly male, had less education, and higher likelihood of minority status compared to the overall sample (all at $P < .001$).\(^7\) One interpretation of the large effect size of routine PRO assessment in this subgroup is that these patients were less likely to volunteer clinically relevant information. Therefore, the PRO symptom assessment closed an important gap in the health care team’s knowledge of the patient’s symptom burden, facilitating better treatment decisions. This interpretation requires empirical verification, however. The effect seen in this subgroup also shows that remote monitoring is not required, as automated in-clinic PRO assessment delivered significant benefit.

Another recent study reports the results of using a web-based application to assess 12 common symptoms associated with treatment for lung cancer.\(^10\) Patients were randomized to an experimental condition or usual care. In the experimental group, symptom data were analyzed in concert with other clinical data, and alerts were sent to the oncologist if the automated algorithm identified patterns suggesting the patient would benefit from unscheduled medical intervention. One-year survival was significantly improved in the experimental condition compared with the group that received usual care (75% vs 49%; $P = .0025$).\(^10\) Furthermore, at time of relapse, 77% of the experimental group had good performance status, allowing them to receive a new treatment, versus 33% of patients in the usual care group with good performance status ($P < .001$).\(^10\) One proviso is that these data are only in abstract form, and a fuller report of the findings is needed.

**CONCLUSION**

In summary, there is growing evidence that routine assessment of the patient experience with validated scales leads to better treatment outcomes in cancer care. Improved outcomes that are achieved while also containing costs will be required as part of value-based care models. Inclusion of PRO measures when developing treatment plans is required to create the evidence needed for more value-based care strategies.

**References**


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 status of a 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-centered 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.
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 HRQL 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 level, 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.

CONCLUSION
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 PROMs in clinical practice enhances detection of HRQL 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