Key Issues in Outcomes Research

Evolving Applications for Patient-Centered Health Status Measures
John A. Spertus, MD, MPH

Abstract—Patient-centered health status measures—assessments of patients’ symptoms, function, and quality of life—have matured substantially over the past 2 decades. Currently, valid, reliable, and sensitive disease-specific measures are available for quantifying the health status of patients with cardiovascular disease. This article briefly reviews the concept of health status measures, with a focus on their interpretation. It then discusses both the rationale and potential applications of health status measures in clinical care. Health status measures are not surrogate measures of outcome but rather highly meaningful outcomes of care. As such, they have important emerging roles as outcomes in clinical trials, as tools for monitoring patients in routine clinical care, as a mechanism for operationalizing and evaluating disease management programs, and as tools for quality assessment/improvement. Over time, it is expected that health status measures will also have an increasingly important role in patient-centered medical decision making. By becoming aware of the evolving roles of health status measures, clinicians can help to accelerate the realization of the Institute of Medicine’s vision for a more transparent, evidence-based, patient-centered healthcare system. (Circulation. 2008;118:2103-2110.)

Key Words: health status ■ outcomes research ■ quality of life ■ review ■ state-of-the-art review

Imagine if you will, that you need to understand how one of your patients with coronary disease or heart failure is doing. You would ask the patient about symptoms, the limitations that the condition imposes on the patient’s ability to function, and how much the symptoms of the disease impair the patient’s quality of life. As you recommend treatment, you would follow that patient’s health status (symptoms, function, and quality of life) to determine whether the treatment was beneficial and whether more or additional therapies were needed. These intuitive, guidelines-endorsed acts are a part of virtually every doctor–patient encounter.1,2 Current methods for quantifying patients’ health status involve either prose descriptions of patients’ activity, symptoms, and quality of life or the use of crude scales such as the Canadian Cardiovascular Society Classification (CCSC)3 for coronary disease and the New York Heart Association (NYHA) for heart failure.4 However, the CCSC and the NYHA, which quantify health status from the physicians’ perspective rather than directly reporting patients’ experiences, are known to have limited reproducibility and sensitivity to important clinical changes.5–8 Furthermore, even these simple quantifications of health status are so infrequently reported in patients’ charts that recent performance measures for high-quality outpatient care explicitly call for documentation of patients’ symptoms and physical activity.9,10

Quantifying patients’ health status is even more difficult when trying to aggregate the experiences of populations of patients. Imagine that you need to understand how most patients treated with one therapy or another have fared (clinical trial outcomes), how all of your patients are doing under your care (routine clinical care), which of your patients need more aggressive treatment (disease management), and how their health status compares with other doctors’ patients (quality assessment). Moreover, at the time that you are explaining treatment options to patients, you may want to describe how the health status of other patients, like them, has been affected by one therapy as opposed to another (shared decision making). These activities—quantifying patient-centered outcomes in clinical trials, systematically monitoring patients over time, disease management of populations of patients, quality assessment/improvement, and shared decision making—are all potential applications of health status measures.

However, as you shift from viewing a single patient at a single point in time to tracking patients serially over time or comparing the health status of patients in different settings and across different providers/assessors, you would recognize the need for a valid, reproducible, and sensitive means for quantifying patients’ health status (their symptoms, function, and quality of life). Formal health status tools are methods of accomplishing this need. They standardize the medical history as it relates to the symptoms, function, and quality of life that patients experience by reproducibly asking patients the same questions in the same way and aggregating the responses into readily interpretable scores. This article briefly outlines the construct and attributes of health status measures and then seeks to demonstrate a range of applications for such

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tools. Future directions for outcomes research and implementation research are highlighted.

**Overview of Health Status Measures**

Health status measures are, most often, self-administered questionnaires that seek to quantify patients’ symptoms, function, and health-related quality of life. In contrast to physicians’ assessment of patients’ symptoms and function (eg, the CCSC and NYHA scales), the current generation of health status measures is completed by patients themselves. The most common framework for conceptualizing health status seeks to independently quantify the ways in which a patient’s disease affects his or her life (Figure 1). Previous articles have described the concept of measuring patients’ health status and their requisite psychometric properties, including validity, reliability, responsiveness, and interpretability (Table). These can either be generic measures that quantify the impact of all of a patient’s medical conditions on his or her health status or disease-specific, focusing on a particular condition of interest. For patients with heart failure, several measures, including the Kansas City Cardiomyopathy Questionnaire (KCCQ), the Minnesota Living with Heart Failure Questionnaire, and the Chronic Heart Failure Questionnaire, have been developed. For coronary artery disease, the most commonly used health status measure is the Seattle Angina Questionnaire.

Among the attributes of health status measures listed in the Table, the most challenging is knowing how to interpret health status scores, either cross-sectionally or as changes in scores over time. Understanding how to interpret health status scores is essential to optimally realize the potential of these measures to improve care and is an evolving area of research. Eventually, as health status measures become more commonly used, clinicians will develop an intuitive “feel” for what scores mean, much as they have developed for knowing what a low-density lipoprotein level of 152 mg/dL or an HbA1c of 12.3% means. Toward this end, health status scores can be interpreted by either (1) describing their associations with other clinical metrics with which providers are already familiar or (2) describing the prognostic significance of scores or changes in scores over time. Given that substantial research into the interpretation of the KCCQ (an instrument that I developed and studied) has been conducted, it can be used as an example for the clinical interpretation of health status scores.

**Table. Key Psychometric Properties of a Health Status Instrument**

<table>
<thead>
<tr>
<th>Measurement Property</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Validity</td>
<td>The measure quantifies what it is intended to (face validity), represents all important content of the construct (content validity), and is empirically demonstrated to be associated with the construct it was designed to measure (criterion validity)</td>
</tr>
<tr>
<td>Reliability</td>
<td>Reproducible results are obtained when the measure is repeatedly given to stable patients</td>
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<tr>
<td>Responsiveness</td>
<td>The measure is sensitive to clinical change</td>
</tr>
<tr>
<td>Interpretable</td>
<td>A clinical framework is available to interpret cross-sectional and longitudinal changes in scores</td>
</tr>
<tr>
<td>Translations exist</td>
<td>Linguistically and culturally appropriate translations are available so that multiple patients, from different countries and cultures, can be pooled for analysis</td>
</tr>
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</table>

Both correlational and prognostic frameworks have been provided to facilitate the interpretation of a single KCCQ assessment. The Overall Summary score of the KCCQ summarizes all 3 of the health status domains outlined in Figure 1 and ranges from a score of 0, indicating very frequent symptoms, severe physical and social limitations, and dismal quality of life, to 100, representing no symptoms or limitations and excellent quality of life. For the use of single, cross-sectional KCCQ scores, a strong correlation with the NYHA classification has been repeatedly established (KCCQ Overall Summary scores of >75=NYHA I, 60 to 75=NYHA II, 45 to 60=NYHA III, and scores <45=NYHA IV). KCCQ scores at a single point in time also carry important prognostic significance that can be used to facilitate their interpretation. To simplify the interpretation of KCCQ scores, Soto and colleagues lumped scores into ranges of 25 points in 1516 patients recently discharged from the hospital with a myocardial infarction complicated by heart failure. The unadjusted hazard ratio for the combined end point of cardiovascular death or hospitalization was 1.27, 2.01, and 3.26 for patients with KCCQ scores of 50 to 74, 25 to 49, and <25 compared with those with KCCQ scores >75, a pattern that was maintained after multivariable adjustment. Recent data from the Beta-Blocker Evaluation of Survival Trial (BEST) also support an association between the Minnesota Living with Heart Failure Questionnaire and clinical events.

Correlational and prognostic frameworks for the interpretation of health status scores have also been applied to the interpretation of changes in scores over time. To better understand the interpretation of changes in KCCQ scores, we conducted a prospective, 13-center, 476-patient study in which clinicians, blinded to KCCQ results, made clinical assessments of the change in patients’ heart failure status over a 6-week period. Figure 2 describes the mean change in KCCQ scores associated with clinicians’ assessments of clinical change. Changes in scores of 5, 10, and 20 points represent small, moderate, and large improvements or dete-
tiorations in clinical status. In fact, patients’ KCCQ scores were more discriminative of change in their heart failure status than NYHA classification, 6-minute walk distances, Short Form-12 and EuroQol 5 Dimensions scores, weight, and B-type natriuretic peptide levels.\(^{29}\) Changes in KCCQ scores are also associated with important prognostic implications. In the EPlerenone’s neuroHormonal Efficacy and SUrvival Study (EPHESUS), each 5-point deterioration in the KCCQ Overall Summary score was associated with an 11% increased risk for all-cause mortality and a 12% increased risk for cardiac death and rehospitalization.\(^{30}\) As familiarity with the interpretation of health status scores, such as those being accumulated for the KCCQ, increases, a myriad of clinically important applications can be envisioned.

Applications of Health Status

Outcomes in Clinical Trials

The purpose of clinical trials is to systematically test the benefits of one treatment over another. But what benefits are most important? Often, to enhance statistical power, clinical trials use physiological, anatomic, or metabolic outcomes to demonstrate the benefits of therapy. However, Fleming and DeMets\(^{31}\) eloquently articulated the challenge of relying on surrogate measures of patients’ outcomes and demonstrated how the medical profession has frequently been misled by inappropriately assuming that a reduction in an adverse surrogate outcome (eg, premature ventricular contractions after a myocardial infarction) would be associated with a clinically important outcome (eg, reduced risk of sudden cardiac death).\(^{32}\) Even commonly used clinical events, such as target vessel revascularization and hospitalizations, can be argued to be surrogates of costs and the processes of medical care rather than direct measures of patient survival, symptoms, function, and quality of life. To avoid erroneous conclusions based on an inappropriate reliance on surrogate outcomes, some clinical trials focus on the 2 uncontested outcomes that are meaningful to patients, survival and health status.

This distinction between surrogates and clinically meaningful outcomes is particularly important if the results are to be applied to and shared with patients. Patients want to know how proposed treatments will affect their survival, symptoms, function, and quality of life,\(^{33,34}\) particularly because some patients would be willing to exchange a longer life for a life with better health status.\(^{35,36}\) Further underscoring the importance of health status, Lewis and colleagues\(^{37}\) found that more than half of patients with severe heart failure would be willing to exchange the duration of their survival for an improved health status. In fact, a substantial proportion of their heart failure population would have been willing to decrease their expected survival by >50% to achieve optimal quality of life.

To better understand how a new treatment affects patients’ health status, clinical trials are now being designed to explicitly measure patients’ health status at the time of enrollment and during follow-up.\(^{34,38}\) Not only does the inclusion of health status support explicit quantification of patient-centered benefits from treatment, but it also supports the application of clinical trial results into practice. By enabling clinicians to compare their patients’ health status scores with those of patients enrolled in the clinical trial, greater insight into the applicability of a trial’s results to their individual patients can be gained. Despite the importance of health status to patients and the fact that they are clinically meaningful as opposed to many surrogate outcomes, it is rare that health status measures serve as the primary end point in cardiovascular clinical trials.\(^{39,40}\)

To further support the use of health status measures in clinical trials, outcomes researchers and clinical researchers should consider new opportunities to apply and interpret health status measures in clinical trials so that such trials can be more efficiently designed and their results can be more efficiently applied into practice. First, health status measures can be used to identify potentially eligible candidates for clinical trials. For example, several ongoing studies in the Veterans Affairs Health System are identifying patients with health status scores below a certain threshold (eg, Seattle Angina Questionnaire scores \(\leq 60\), indicating patients with weekly or daily angina) so that the most symptomatic individuals can be identified (John Rumsfeld, MD, PhD, personal communication, 2007). Second, health status measures can be used to improve the interpretation and application of a study’s results. For example, knowing the threshold of change that is clinically significant can allow the relative proportions of patients who improve significantly to be compared.\(^{32,41}\) These numbers can then allow calculation of the number of patients needed to be treated for 1 patient to significantly benefit in terms of health status. Finally, it is likely that the health status benefits of a clinical intervention are not evenly distributed across the entire population tested. Although the use of subgroup analyses in standard clinical trials is common, such analyses to identify those patients with the greatest opportunity to benefit in terms of their health status are rare. In the future, it is expected that system-level interventions targeting the most symptomatic patients, more explicit estimates of number-needed-to-treat for health status benefits from treatment, and risk stratification of health status benefits will become more common components of study design and analysis.

An important opportunity to stimulate the evolution of health status assessments in clinical trials is for the Food and Drug Administration to more clearly embrace the importance of health status outcomes. Although the Division of Cardiac Devices has been open to the inclusion of health status measures in clinical trials, having held multiple conferences with researchers, industry, and the Heart Failure Society of
America and having created summary position papers, the Office of Drug Evaluation has been less proactive. Although the Division of Drug Marketing, Advertising, and Communications has been engaging the medical community since at least 1999 in discussions of patient-reported outcomes, a Draft Guidance Document was not published until February 2006, and no final guidance has yet been issued. To advance the field, the Food and Drug Administration needs to work collaboratively with researchers to establish the needed attributes of potential measures, to create a repository of “approved” instruments, to outline suggestions for the timing, analysis, and interpretation of such measures, and to begin supporting the efforts of investigators and industry to document the patient-centered benefits and comparative effectiveness of novel treatments.

Routine Clinical Care
As already noted, the hallmark of an outpatient visit is to establish the limitations imposed by cardiovascular disease on a patient’s health status. Although novel technologies have been introduced to create greater objectivity in the acquisition of information obtained from the cardiac physical examination (eg, echocardiography), similar strategies have not been routinely accepted in elevating the reproducibility of the patient’s history. Although some may argue that the CCSC and NYHA scales are examples of creating a standardized history for the acquisition of patients’ health status, these represent physicians’ assessments of their patients’ health status rather than being directly acquired from patients themselves. In fact, it has already been established that the NYHA classification is not as accurate in quantifying patients’ function as a standardized patient-reported measure.

Thus, the routine collection of health status measures in longitudinal care may represent an important potential advance in clinical care.

Drawing on the Institute of Medicine’s challenge to create a more patient-centered healthcare system, Rumsfeld has previously described the opportunities for formal health status measures to be routinely used in clinical care. One advantage of routinely collecting health status measures is that it offers clinicians an ongoing assessment of “how patients are doing” with respect to the current management of their cardiovascular disease. For example, patients with high scores on the Seattle Angina Questionnaire are those without angina or significant functional or quality of life limitations and are unlikely to benefit from additional titration of their antianginal medications or from coronary revascularization. In contrast, those with low scores may benefit substantially from additional treatment. Reproducibly capturing patients’ health status in routine clinical care can allow a rapid distillation of their clinical status, indicate whether their health status is improving, stable, or deteriorating, and highlight the need for additional treatment.

A second advantage of the routine use of health status assessment is the ability to risk-stratify patients’ risk for mortality. As described above for the KCCQ or as previously demonstrated for the Seattle Angina Questionnaire, health status assessments are prognostic of mortality and hospitalizations. Risk stratification, which is performed so that the most intense therapy can be offered to those at the greatest risk for death, is a cornerstone of modern cardiovascular care. Although physiological, anatomic, and biochemical markers can all risk-stratify patients, the expense or risks of these tests preclude their routine, repeated use over time. However, a simple questionnaire can be readily completed and interpreted, at no risk and minimal cost, and can provide important prognostic information through which patients’ care can be optimized.

Finally, the reproducibility of health status measures means that they can be an important component to providing care. It is difficult for clinicians to accurately remember how a patient was doing at a previous visit 3, 6, or 12 months ago. Similarly, when different physicians evaluate the same patient at different points in time, it is difficult to know what one’s colleague means when he or she calls the patient’s heart failure “stable.” By explicitly quantifying the symptoms and function of patients in the medical record, more consistent assessments over time and better coordination of care among providers may be achieved. In recognition of this, performance measures for high-quality care in coronary disease and heart failure explicitly include the documentation of patients’ symptoms and function (http://www.qualityforum.org).

Critical barriers to the routine clinical use of health status measures remain, however. These include developing mechanisms to integrate their collection in the process of routine clinical care, facilitating their scoring and interpretation at the time of a patient visit, and testing the association of transparent assessments of patients’ health status on subsequent medical decision making and its impact on patients’ long-term health status and survival. A promising initial step is the creation of the Improving Continuous Cardiac Care program, an outpatient data collection effort designed to collect American College of Cardiology/American Heart Association performance measures in routine clinical care (www.improvingcardiaccare.org). This project will provide the infrastructure for collecting health status data for patients with coronary disease and heart failure and may provide the opportunity to address some of the current gaps in knowledge related to the use of health status data in clinical care.

Disease Management Programs
Congruent with the advantages of health status measures in managing individual patients, health status measures also have a potential role in the management of populations of patients. Managing populations of patients is often referred to as disease management. Disease management programs are “multidisciplinary efforts to improve the quality and cost-effectiveness of care for selected patients suffering from chronic conditions.” Yet the current practice of physician reimbursement does not provide incentives for clinicians to routinely offer such programs to all patients. Thus, a need exists to identify, from among a population of patients, those most likely to benefit from such a program. Health status measures offer an important opportunity to quantify the status of patients’ cardiovascular disease so that those who are most impaired may be readily identified for enrollment into a disease management program. In the original cohort used to test the psychometric properties of the KCCQ (n=129),
scores of <50 on both the KCCQ Overall Summary and Self-Efficacy scales were associated with a significantly higher risk of mortality and rehospitalization in the development cohort of this instrument. These patients with scores <50 on the Self-Efficacy scale had a 64% rate of dying or being rehospitalized within 1 year compared with a 33% rate for those with a Self-Efficacy score of ≥50 and an Overall Summary score of <50 and a 13% event rate in those whose scores were ≥50 on both domains. If the disease management program were first offered to those with Self-Efficacy scores <50, followed by those with Overall Summary scores of <50 and then to the remainder of patients, those with the worst predicted outcomes could be the first to be offered an expensive but potentially beneficial program, whereas those with better self-efficacy and health status would be offered the program only to the extent that sufficient resources were available. Because of the small and selected nature of this population, such thresholds are merely speculative. However, further research to validate and refine the use of health status measures to identify patients most likely to benefit from disease management and to test the efficacy of such programs in high-risk patients may improve their use and cost-effectiveness.

In addition to identifying patients at greatest risk for enrollment into a disease management program, health status measures can be used to quantify the patient-centered benefits of a program to the population that it serves. Analogous to the benefits of including health status measures in clinical trials, disease management programs often need to substantiate their benefits so that their funding can be supported. By measuring the health status of patients before and after enrollment into a disease management program, the benefits of the program can be explicitly quantified. For example, 3 of 5 randomized controlled trials of disease management demonstrated improved scores in the Minnesota Living with Heart Failure questionnaire. Using health status tools to quantify the benefits of a disease management program as implemented in a given practice can be invaluable in justifying that program to administrative and referring physicians alike. In addition, comparing the results of different strategies of disease management can permit a scientific exploration of those elements most needed to optimize the care of patients.

Quality Assessment and Efficiency
As already noted, the process of explicitly documenting the health status of patients with coronary disease and heart failure is currently endorsed as a performance measure of quality. However, beyond the process of documentation, the use of the formal health status assessments as outcomes can permit comparisons between different practices. By examining the processes of care in practices that maintain a better risk-adjusted health status in their patients, it would be possible to identify treatment strategies that could be more broadly disseminated to improve patient care. As an example, if it is discovered that patients in your practice have a greater burden of heart failure or anginal symptoms than other practices, examining your use of medications, devices, revascularization, or disease management programs in comparison to your peers may identify important opportunities to improve care. Moreover, the use of health status outcomes is congruent with an emerging focus on comparing other outcomes, such as mortality, in quality assessment. National benchmarks for symptom management and quality of life outcomes are currently lacking but represent an important research opportunity for the outcomes community.

Shared Decision Making
Decision aids are tools to assist patients in making deliberate decisions about treatment options that best optimize their chance for attaining their desired healthcare goals. To provide patients with evidence-based, individualized estimates of outcomes relative to alternative treatments, prediction models of relevant clinical outcomes are needed. Risk prediction and identification of the determinants of survival in cardiovascular disease have long been areas of intense research. Numerous prediction models exist for estimating survival after an acute coronary syndrome among patients with heart failure, and after coronary revascularization. Although the incremental prognostic value of patients’ health status can be used to improve the precision of mortality prediction models in heart failure or coronary disease, as an important outcome to patients, in and of itself, an urgent need exists to define the predictors of health status outcomes among cardiac patients.

Preliminary efforts, for example, have shown that for a given amount of symptoms and function, older patients have a better quality of life than younger patients, although any further decrement in function is associated with even greater reductions in quality of life among the elderly compared with the young. Similarly, depression and other psychosocial traits, gender, marital status, education and socioeconomic status, medical comorbidities, and smoking have all been associated with differences in cardiovascular patients’ quality of life. Yet the distillation of these variables into prediction models of health status outcomes after common clinical scenarios (eg, acute myocardial infarction or heart failure hospitalization) or clinical treatments (eg, coronary revascularization [percutaneously or surgically] versus medical therapy or the use of a biventricular pacemaker versus medical therapy in heart failure) has not been developed. This is a particularly fertile and important area of outcomes research.

Once prediction models are available, the final phase of implementation is to use these models in helping patients to select a treatment option based on their own goals and values. Although the technology for rendering individualized risk predictions of health status outcomes at the time of medical decision making currently exists, the paucity of available models precludes its routine use. Thus, critical next steps are to define the clinical scenarios in which therapeutic choices might influence health status outcomes, create risk-prediction models for these outcomes with a focus on actionable domains that physicians can target, create a resource so that these models can be shared throughout the research community, expand the incorporation of these models into novel decision aids, deploy these decision aids in clinical practice, and test their impact on medical decision making and outcomes. As the outcomes research community overcomes
these obstacles, the opportunity for patients to play the pivotal role envisioned by the Institute of Medicine will be close at hand.44

**Conclusion**

The field of health status measurement has matured rapidly over the past decade. As a window into the status of patients with cardiovascular disease with respect to their symptoms, function, and quality of life, the era for these metrics to be used as outcomes in clinical trials, tools for patient management, selection criteria for disease management programs, methods for quality assessment/monitoring, and tools for allowing patients to share in their medical decision making is dawning. A continued commitment by the outcomes research community will provide the necessary research to enable the potential of patient-centered outcomes to be realized.

**Disclosures**

Dr Spertus owns the copyrights to the KCCQ and the Seattle Angina Questionnaire.

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