Research White Paper

A Primer for Systematic Reviewers on the Measurement of Functional Status and Health-Related Quality of Life in Older Adults

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Prepared by:
Kaiser Permanente Research Affiliates Evidence-based Practice Center
Center for Health Research
Portland, OR

Investigators:
David H. Feeny, PhD
Elizabeth Eckstrom, MD, MPH
Evelyn P. Whitlock, MD, MPH
Leslie A. Perdue, MPH

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The National Cancer Institute requested and provided funding for this report.

The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review and public comment prior to their release as a final report.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome comments on this evidence report. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.

Carolyn M. Clancy, M.D.
Director
Agency for Healthcare Research and Quality

Jean Slutsky, P.A., M.S.P.H.
Director, Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

Stephanie Chang, M.D., M.P.H.
Director
Evidence-based Practice Program
Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

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Peer Reviewers

<Name>
<Place>
<City>, <ST>

<Name>
<Place>
<City>, <ST>

A Primer for Systematic Reviewers on the Measurement of Functional Status and Health-Related Quality of Life in Older Adults

Structured Abstract

Objectives. Provide a primer for systematic reviewers, clinicians, and researchers on assessing functional status and health-related quality of life (HRQL) in older adults. Evidence-based guidelines are needed to inform best practices. Systematic reviewers are increasingly focusing on interventions that address the problems of older people, who often have functional impairments and multiple morbidities. Key outcomes are function and HRQL.
Methods. The paper provides an overview of the methods for assessing function and HRQL, and evidence on the measurement properties of prominent instruments.
Results. Key measurement properties include construct validity (does the instrument measure what it is supposed to measure?), responsiveness (the ability to detect meaningful change) and interpretation (is the magnitude of change trivial or important?). Special challenges in older adult populations include sparse evidence on the measurement properties; using proxy respondents; a paucity of evidence on the magnitude of change that is patient-important; and threats to detecting patient-important changes due to floor and ceiling effects.
Discussion. Studies of older adults must include measures of HRQL and function. Older adults should be included in randomized controlled clinical trials. HRQL evidence from natural-history cohorts is essential in interpreting results from intervention studies.

Contents

Introduction

A key to improving the health of our aging population is developing evidence-based guidelines that can inform best practices at the patient, health system, and policy levels. The field of systematic review has evolved to include sophisticated meta-analytic techniques and highly structured evidence reviews. However, evidence-based guidelines have focused largely on single diseases and general populations, and have left gaps in recommendations for older, functionally impaired populations with multiple morbidities.[1] Systematic reviewers have primarily considered objective outcomes such as mortality, with less consideration to health-related quality of life (HRQL) and functional outcomes. Yet, these patient reported outcomes could be very useful—both to evaluate the effectiveness of interventions to improve health in older adults, and as a means of defining risk status and identifying important subgroups for analyses.

This paper will identify important issues in using evidence from these measures in systematic reviews, and interpret these issues for clinicians, researchers, and systematic reviewers, using practical clinical scenarios to highlight challenges. In Section II, we briefly describe measurement properties of common instruments used to assess patient-reported outcomes, including the classification of measures, the populations studied, reliability, validity, special considerations for older adults, floor and ceiling effects, and using proxy respondents. Section III focuses on how to interpret functional status and HRQL evidence. Sections IV and V discuss implications for researchers and systematic reviewers; Section VI provides a summary and conclusions. We also include a glossary of key terms and concepts (see Supplementary data, Key Terms and Concepts).

The paper highlights several challenges for systematic reviewers in synthesizing evidence to improve HRQL and reduce functional decline in older adults: 1) randomized trials must include the right patients—those who have enough impairment to make intervention worthwhile, but are not so ill that an intervention can at best marginally improve their situation; 2) current HRQL and functional measures are not always responsive to subtle but important changes; 3) the older population has substantial heterogeneity in disease progression; 4) the natural history of disease in older adults is highly variable. An intervention might slow functional decline, but that can be difficult to demonstrate.

Patient Reported Outcomes, Health-Related Quality of Life, and Function: An Overview of Measurement Properties

In general, we rely on patient-reported outcomes for HRQL and function. This section provides a discussion of the most important considerations when using those measures. Further detail is provided in Appendix A.

Classification of Health-Related Quality of Life Measures

One taxonomy focuses on the types of persons for whom the measure is applicable.[2] Generic measures typically include both physical and mental health, are applicable to virtually any adult population, and can be used to make comparisons across diseases and conditions. Specific measures are applicable to people with a particular disease (breast cancer), condition (frailty), or symptom (pain). Specific measures are often more responsive than generic measures[3,4] but may not capture the effects of comorbidities, do not allow for comparisons across conditions, and thus

have limited usefulness for cost-effectiveness analyses. In addition, there are condition-specific adaptations of generic measures.

Measures can also be classified by their intended purpose.[2,5,6] Evaluative measures capture "within person change" over time. Discriminative measures detect differences among groups (or individuals) at a point in time. Evaluative measures are critical to assessing the effectiveness of interventions and therefore their measurement properties are of interest to systematic reviewers.

How Should Reviewers Approach These Measurement Properties?

In assessing the measurement properties of HRQL instruments there are a number of key questions.[7] How extensive is the evidence on the relevant measurement properties, especially responsiveness and interpretability, of the instruments? How rigorous is that evidence. Is the evidence directly applicable to the issues at hand? Evidence on cross-sectional and longitudinal construct validity and interpretation is central to evaluating the effects of interventions. Construct validity involves the accumulation of evidence and the use of subjective judgments. If a systematic reviewer is confident that the measure is valid and responsive in the setting being reviewed, the reviewer can be more confident in the evidence on the effectiveness of an intervention. If the evidence on validity and responsiveness of the measure in that context is equivocal, interpreting results based on that measure will be challenging.

Reviewing Measures of Health-Related Quality of Life: Special Considerations for Older Adults Populations

Most measures of HRQL were not designed specifically for use in older adult populations. Further, many measures of HRQL were validated in populations whose mean age was 64-86, but age ranges vary by instrument.[8,9] Extensive evidence on the reliability and validity of an instrument does not necessarily imply that there is abundant evidence supporting its use among older adults, especially those at the upper extremes of the age ranges.

To illustrate this we briefly review measurement properties for several widely used generic measures of HRQL: the Short-Form 36 (SF-36) and its preference-based version, the Short-Form 6D (SF- 6D or Six Dimensions), EuroQol-5D (EQ-5D), the Health Utilities Index Mark 3 (HUI3), and the Quality of Well-Being Scale (QWB). The SF-36 includes eight domains: physical functioning (PF), role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health.[10,11] The EQ-5D includes a five attribute health-status classification system: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression, with three levels per attribute: no problem, some problem, or extreme problem.[12] The HUI3 system includes eight attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain and discomfort, with five or six levels per attribute, from severely impaired ("so unhappy that life is not worthwhile") to no problem or normal ("happy and interested in life").[13] The original version of the Quality of Well Being Scale (QWB) included three attributes (mobility, physical activity, and social activity) and a problem/symptom complex.[14] The more recent QWB-SA (self-administered) retains the same structure but includes fewer levels within each attribute and fewer problems/symptoms.[15]

How well do these measures work in older adults? In a prospective cohort study of patients aged 75+ years, Brazier and colleagues examined test-retest reliability in patients who self-identified as stable: patients who indicated that their health had not changed. Correlations for domains of the SF-36 ranged from 0.28 to 0.70; the correlation for EQ-5D scores was 0.67.[16] In a

paper based on one of the original Medical Outcome Study (MOS) surveys (n = 3,445), one of the major studies upon which the SF-36 is based, McHorney and colleagues reported lower completion rates by item for those aged ≥ 75 years than for the 65-74 group, who in turn had lower completion rates than persons <65. However, estimates of internal consistency reliability (Cronbach's alpha) did not vary by age, education, poverty status, diagnosis, or disease severity.[17]

A study of patients aged 65+ years who identified themselves as stable reported intraclass correlation coefficients (ICCs) for SF-36 domains ranging from 0.65 to 0.87. Andresen and colleagues also showed evidence of cross-sectional construct validity for the SF-36 in that domain scores were lower for those who were older and for those with more severe comorbidities.[18]

Naglie and colleagues reported test-retest reliability estimates for patients with mild (mini-mental state examination [MMSE] scores 19-26) or moderate (MMSE 10-18) cognitive impairment, and proxy family caregivers for three generic preference-based measures, EQ-5D, HUI3, and the QWB. Follow-up assessments were done approximately two weeks after the initial assessment. Comparing initial and re-test responses by patients, the ICCs for the entire cohort of were 0.79, 0.47, and 0.70 respectively; for those with mild cognitive impairment the ICCs were 0.70, 0.75, and 0.81; for moderate impairment 0.83, 0.25, and 0.59. Comparing initial and re-test proxy responses, the ICCs were 0.71, 0.81, and 0.70. The results for HUI3 and the QWB were sensible; test-retest reliability for those with mild cognitive impairment was reasonable but persons with moderate cognitive impairment were not reliable respondents.[19]

Two generalizations emerge from these examples, first, the severely cognitively impaired are, in general, not capable of providing reliable and valid responses. If such persons are included in a study and alternative assessments by proxy respondents are not obtained, there will be reliability bias. Second, if the highly cognitively impaired are excluded, reliability in samples of older adults appear to be of the same order of magnitude as in general adult samples.

Floor and Ceiling Effects

If the range of function covered by a measure is less than the range experienced by the patients, especially frail older adults, the measure may lack responsiveness. The SF-36 (and therefore SF-6D) has well known floor effects that have been recognized in a wide variety of clinical settings and samples.[20-34] In a prospective cohort study comparing utility scores before and after elective total hip arthroplasty a gain of 0.10 was registered by SF-6D and a gain of 0.23 by HUI3.[22] In a natural history cohort of 124 patients recruited shortly after a stroke and followed for 6 months, the gain in overall HRQL observed in the 98 survivors (18 lost to follow-up) was 0.24 according to the EQ-5D[12] and 0.25 according to the HUI3,[13] but only 0.13 according to SF-6D.[35] Floor effects attenuated the ability of SF-36 and SF-6D to capture gains when many patients had moderate or severe burdens at baseline. The magnitude of improvement experienced by patients was underestimated because some patients were "worse off" than the measure could capture before the intervention; this underestimation could seriously bias estimates of the magnitude of change associated with interventions and cost-effectiveness estimates of those interventions.

Similarly, ceiling effects can threaten responsiveness. The absence of levels for mild problems in the EQ-5D probably accounts for the ceiling effects associated with the instrument in population health survey and clinical applications. In a review of generic preference-based measures used in studies of patients with rheumatoid arthritis, ceiling effects associated with EQ-

5D attenuated its responsiveness.[19,36-38] Similarly, a lack of responsiveness of EQ-5D has been reported in clinical studies of urinary incontinence in females[39] and treatments for leg ulcers.[40]

Proxy Respondents

Cognitive impairment or physical disability may attenuate older adults' ability to respond, and this situation may be temporary or chronic. One approach to this problem is to rely on a proxy respondent—a family member or caregiver who is familiar with the subject's current status. Agreement between self and proxy report then becomes an important issue; the "proxy as an agent" (if "X" could respond, what would she/he say) must be distinguished from the "proxy as an informed observer" (which of the following best describes the current condition of "X"). Most investigations of agreement have adopted the informed-observer approach.

Magaziner and colleagues examined agreement between self- and proxy-report in a prospective cohort of patients aged ≥ 65 years (n = 361) being followed after hip fracture.[41] Both sets of respondents independently completed questionnaires on ADLs, IADLs, mental status, and depressive symptoms. Proxies tended to rate patients as more disabled than the patients rated themselves. Agreement was higher when the proxy and subject lived together; agreement was also higher when the proxy was a sibling or spouse as compared to offspring and non-relative. Even mild cognitive impairment in the patient was associated with less agreement. Agreement was often lower on less observable aspects of physical and mental health.

Clearly, in studies that gathered responses from both patients and their proxies, the responses were not interchangeable. The degree of agreement was affected by the observability of that aspect of health status, the degree of familiarity of the proxy with the current condition of the patient, and in some cases, the burden being experienced by the proxy caregiver.[42] The extent to which agreement varies with respect to these factors varies across studies. However, in general, these factors are associated with quantitatively important differences in the degree of agreement. Nonetheless, the results indicate a reasonable amount of agreement. Furthermore, evidence suggests that more reliable and valid information is available from proxy respondents who have frequent contact with patients who are becoming incapable of responding than is available from the patient directly. Whether differences in source of measure, patient versus proxy, impacts results in a systematic review could be evaluated through meta-regression or other techniques.

Interpretation of Measures of Functional Status and Health-Related Quality of Life

Minimum Important Difference

How to interpret the results of an intervention to prevent functional decline or improve HRQL is a key issue. Is the magnitude of change important? A statistically significant effect may not always translate to an important change from baseline. Thus, one must also consider the clinically important difference (CID), or minimum important difference (MID), defined as:

"The smallest difference in score in the outcome of interest that informed patients or informed proxies perceive as important, either beneficial or harmful, and that would lead the patient or clinician to consider a change in management."[43] Guyatt and colleagues suggest the use of the term "patient-important" rather than "clinically important" to focus on the "preeminence of the patient's values and preferences."[44,45]

MIDs are estimated using anchor-based or distribution-based approaches.[46-51] In the anchor-based approach, the change in HRQL score is related to a well-established meaningful measure.

The anchor itself must be an independent measure and be readily interpretable—for example, the categories of the New York Heart Association functional classification system or ability to climb a flight of stairs. There must be an appreciable correlation when measured at the same time in the same person between the anchor and the target measure.[50] In contrast, the distribution-based approach is based on statistical criteria. It compares the magnitude of change compared to some measure of the variability of scores such as effect size (ES).

Similar to evidence on construct validity, evidence on the usefulness of MIDs accumulates and evolves over time. If a guideline on the MID for an instrument generates results that are congruent with clinical evidence and evidence from other measures, confidence in the usefulness of that MID increases over time. There is mixed evidence on the extent to which MIDs are context free.

Ware and Keller, using SF-36 data from the Medical Outcomes Study, provided examples of the usefulness of anchor-based approaches.[52] The PF scale ranges from 0 to 100. Thirty-two percent of respondents with a score of 40 can walk one block without limitations; at a score of 50, 49.7% are able to walk a block. A change in PF score of 10 is clearly important. Yet a change of 10 in PF from 80 to 90 implies that 98.8% of respondents instead of 98.4% of respondents will be able to walk a block. Given that the standard deviation (SD) for the PF scale is 23.3,[11] a change of 10 is equivalent to an ES of 0.43, moderate in the scheme proposed by Cohen.[53] In this example, the anchor-based interpretation is meaningful while the distribution-based interpretation (ES) has the potential to be misleading.

However, a number of studies report results in which anchor-based and distribution-based approaches provide similar estimates of the threshold for a patient-important difference.[51] If a systematic reviewer cannot find evidence in support of an anchor-based criterion for a measure, one default option is to use 1.0 standard error of measurement or 0.5 SD.

Absolute or Relative Change?

An advantage of ES and standardized response mean (SRM) is that they can be used to make comparisons across studies and among measures. However, within a study the stimulus (intervention) is the same so one can compare the absolute magnitude of change among measures that use a common scale such as the conventional scale for preference-based (utility) measures in which 0.00 = dead and perfect health = 1.00. In general, clinicians and systematic reviewers are more interested in the absolute magnitude of change than in the relative magnitude of change expressed in SD units (ES or SRM).

One level of interpretation is to consider if the mean magnitude of change observed in a RCT is patient- or clinically important. More relevant is the proportion of patients achieving no, small, moderate, or large change.[50] As Guyatt and colleagues note, mean change can be misleading if, for instance, there is heterogeneity in treatment effect such that an important minority of patients improved moderately while the majority experienced no change.[54] The proportion that benefit can then be used to calculate the number needed to treat, the inverse of the absolute risk reduction, which has intuitive appeal to clinicians. Johnston and colleagues discuss an algorithm that allows systematic reviewers to make comparisons across studies using MIDs.[55] A related approach focuses on individual-level data and the classification of patients as responders if the change that individual experienced is greater than or equal to a threshold—in a sense, a criterion for a patient-important difference defined at the individual level.[56,57]

Observational Data

Sometimes a reviewer must rely on observational data on the effects of an intervention. It may therefore be useful to compare the trajectory observed in the study to trajectories observed in natural history cohort studies of older adults. Evidence from such cohort studies might also be useful for interpreting results from controlled clinical trials.[58] When serving a high-risk population, slowing the rate of decline in functional status or HRQL may be a realistic goal and the maintenance of stability (as opposed to improvement) may be a marker of success.[59] Evidence from a natural history cohort can serve as a useful comparator for the results of an intervention tested in an observational study. Such evidence provides an answer to a counterfactual question: what would have happened in the absence of an intervention? Two examples:

The Statistics Canada longitudinal National Population Health Survey (NPHS) (http://www.ncbi.nlm.nih.gov/pubmed/19388366?dopt=Citation) displayed 10-year trends in overall HRQL for a cohort of respondents 40 years and older living in the community at baseline in 1994/95. The rate of decline in HRQL (measured by HUI3) accelerated in respondents aged in their mid-70s. The rate of decline is higher when those who were institutionalized and those who died during the follow-up period were included in the analyses.[60] Data from the NPHS could serve as a benchmark for comparisons.

Another example of a longitudinal natural history cohort is the Beaver Dam study (http://www.ncbi.nlm.nih.gov/pubmed?term=1923372). Begun in 1987-1988 in Beaver Dam, Wisconsin, a cohort of 4,926 respondents aged 43-84 years was enrolled.[61-63] Respondents have been followed since, most recently surveyed at 15 years of follow-up (from 2003 to 2005).[64] HRQL instruments used in the Beaver Dam study included the SF-36, the QWB,[65] and the time-trade off,[66] a direct preference-elicitation technique in which respondents place value on their current state of health by determining the number of years in their current state they would be willing to give up to enjoy a shorter period in perfect health. The Beaver Dam study provides a rich source of natural history data, and although participants reported a wide range of income levels, its mainly white population (99%) may not generalize to the entire U.S.

Implications for Researchers

Assessing Health-Related Quality of Life

As Feinstein suggested, "assessments of health status are important because improvements in symptoms, other clinical problems, and functional capacity are usually the main goals of patients in seeking clinical care."[67] Similarly, Osoba and King argue that "the ultimate goal of health care is to restore or preserve functioning and well-being related to health, that is health-related quality of life."[68] These ideas are underscored in the Public Comment Draft Report of the Patient-Centered Outcomes Research Institute (PCORI) Methodology Committee presented on July 23, 2012 (http://www.pcori.org/2012/methodology-report/).

Studies investigating ways to improve or maintain functional status in older adults need to include the assessment of HRQL. But using which measures? Generic measures provide the basis for broad comparisons, the ability to reflect comorbidities, and the ability to detect side effects and other consequences. More targeted measures often focus on the most salient domains and are often more responsive than generic measures.

One criterion in guiding the choice of and mix of type of measures should be the availability of evidence on the reliability, construct validity, and responsiveness of the measure in the context

in which it will be applied. Sometimes there is a tension between choosing measures with well documented measurement properties in that application and choosing widely-used measures that permit comparison to other studies.

There is a risk of "premature" standardization.[69] For instance, if a widely-used generic measure is chosen to enhance the ability to make comparisons to other studies, but that generic measure has inferior measurement properties relative to some other generic measures in the relevant area of application—say substantial floor effects, then neither internal validity nor external generalizability are well served. Measures need to be chosen on the basis of relevance and their track record in the context of the study at hand. Further, as the examples presented in the paper illustrate, in general scores and change scores among generic measures are not interchangeable.

Studies of older adults must attend to these multiple challenges. Inclusion and exclusions criteria need to match the level of vulnerability of study participants appropriate for an intervention. Interventions need to be systematized and reproducible. Control and intervention groups must reflect the variability of health trajectories in older people (no easy task, as this is infrequently known at the start of a trial). Multiple inter-related outcomes need to be considered. Measures need to be appropriate for the baseline population to avoid floor and ceiling effects; and researchers need to agree on a small number of measures that are appropriate for older populations. MIDs should be determined beforehand in a study.

Systematically adding measures of HRQL and functional status to studies of older adults and the routine use of these measures in chronic care management would importantly add to the evidence available.[45,70,71] In particular, routine collection would provide evidence on persons seldom included in clinical trials, such as patients with multiple chronic conditions, concomitant medications, and older adults.[72,73] The use of measures of symptom or function from the Patient Reported Outcomes Measurement Information System (PROMIS) would enhance the ability to make focused comparisons across populations and studies (http://www.nihpromis.org/).[74-76] The usefulness of adding HRQL assessments to studies and registries would be enhanced by adherence to reporting standards for HRQL evidence.[77-80]

Implications for Systematic Reviewers

Systematic reviewers should review the methods of the empirical studies assessing HRQL and functional status in light of the normative study design criteria outlined above in Section IV. But what if not all the criteria are met? For instance, if the existing evidence is based solely or almost exclusively on the basis of condition-specific measures of HRQL, the risk of a false negative result on the effectiveness of the intervention may be lower (specific measures are often more responsive) but the risk of a false positive result (concluding that the net benefits of the intervention are positive) may be higher because of the attenuated ability to detect side effects, effects that might offset some or even all of the treatment effects. Further, the ability to make broad comparisons will be attenuated because no generic measure was used in the underlying studies. Alternatively, if the underlying research is based mainly on results from generic measures, the risk of a false negative may be higher (generic measures are often less responsive than specific ones) while the risk of a false positive may be lower due to the ability to detect important side effects and the ability to make broad comparisons will be enhanced. Of course, if the generic measure was not carefully selected, floor and/or ceiling effects may attenuate the advantages of generic measures.

If a natural history cohort study that matches the characteristics (or which has a subset of participants who match) of the one being studied in the systematic review is available and that

study included suitable measures of HRQL and functional status, then evidence from the observational study can help interpret the results of the intervention study being reviewed. If the match is less than perfect, the systematic reviewer will have to compromise.

Appendix B Table 1 provides a brief summary of the relevant measurement properties for a number of widely-used generic measures and a few of the disease-specific measures chosen to illustrate the issues covered in this paper. This is intended to be illustrative, rather than a comprehensive review. Measures based on each of the three major paradigms of HRQL are included in the Appendix B Table 1, the psychometric paradigm (SF-36), the clinimetric paradigm (Chronic Respiratory Questionnaire), and the preference-based/economics/decision science paradigm (HUI3).

Summary and Conclusions

As the field of geriatrics embraces these and other recommendations to strengthen the evidence base for evaluating interventions that can prevent functional decline in older adults, systematic reviewers will be able to apply a more rigorous set of criteria that will allow for stronger evidence to guide patient care. Systematic reviewers can employ our framework to ensure that all the challenges inherent in interpreting the literature for this growing population are considered.

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Tables

Table 1. Brief definitions of important measurement properties

Term	Definition
Reliability	A reliable measure is consistent and reproducible[56]
Internal Consistency	The extent to which items are measuring the same concept.[81]
Intra- and Inter-Observer Reliability	The extent of agreement across assessments or among individuals.[82]
Validity	The measure accurately reflects the concept it is intended to measure.[81]
Content Validity	The extent to which the measure covers the full range of meanings included in the concept.[81]
Criterion Validity	The extent of agreement between the measure and a gold standard measure of the same concept.[56]
Construct Validity	Evidence that the relationships among items and domains conform to a priori hypotheses and that logical relationships exist between the measure and characteristics of patients and patient groups.[56]
Convergent Validity	Convergent validity refers to evidence of a moderate or strong relationship between measures of the same concept or construct.[82]
Discriminant Validity	Discriminant validity refers to evidence of the lack of relationship between measures of a different concept or construct.[5,81]
Cross-Sectional Construct Validity	Evidence of construct validity based on comparisons at a point in time.
Responsiveness (Longitudinal Construct Validity).	The ability of a measure to capture meaningful change when it occurs.[81]
Interpretation	The ability to attach meaning to the scores provided by a measure.[83]

Table Note: The brief definitions provided are not meant to be definitive; each of the concepts is expanded upon in the text. The sources from which the definitions are paraphrased are cited.

Appendix A. Glossary of Key Terms and Concepts

Health-Related Quality of Life. There are a wide variety of definitions of HRQL. Some focus on the domains of health status that comprise HRQL, usually including physical health, mental health, social and role function, and pain and discomfort. Patrick and Erickson provide a useful definition (1993, p 22):[84] "Health-related quality of life is 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."

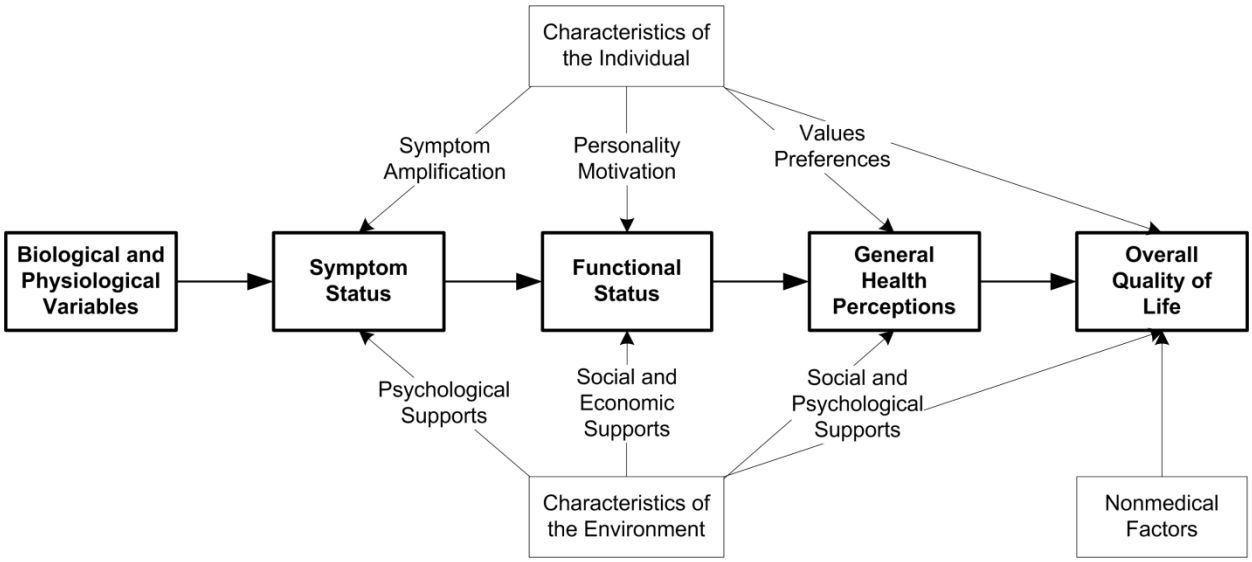
Functional Status: Starfield: "The capacity to engage in activities of daily living and social activities."[85]

Frailty: Fried's definition is the presence of at least three of five factors: 1) unintentional weight loss (10 pounds or more in a year), 2) general feeling of exhaustion, 3) weakness (as measured by grip strength), 4) slow walking speed, and 5) low levels of physical activity.[86] Frailty is a risk factor for further decline in functional status and mortality, and can be associated with a wide variety of chronic conditions.

Health Status: A person's current state of health. Typically that includes functional status, morbidity, physiologic outcomes, and some notion of well-being.[84]

Conceptual Framework. An intervention is grounded in some conceptual framework about how the intervention would work and what dimensions of health status it would impact. The systematic reviewer must examine the conceptual framework of the original work to determine if the study included measurement instruments capable of capturing the intended effects. Wilson and Cleary[87] provide a useful framework that can guide the choice of measures and the interpretation and presentation of results (Figure 1).

Figure 1



Reliability. A reliable measure is consistent and reproducible. *Internal consistency* is the extent to which items intended to assess health or functional status in a particular domain are

correlated with each other and not correlated with items intended to measure other domains. Internal consistency is often measured with Cronbach's alpha. Scores > 0.70 are usually considered to have acceptable internal consistency for group comparisons.[46] See Table 1, *Intra- and Inter-Observer Reliability*. This form of reliability examines the agreement between two raters—for instance, self and proxy assessment. The intra-class correlation coefficient (ICC) (continuous response scale) or kappa statistic (categorical responses) is used to assess the extent of agreement; kappas and ICCs > 0.70 are generally regarded as acceptable.[46]

Test-Retest Reliability. Test-retest reliability examines the agreement among scores in stable persons at two points in time. The interval between testing is generally one to two weeks—long enough that the person is unlikely to recall their previous response and short enough that it is unlikely the condition of the person has changed. Again, ICCs > 0.70 are regarded as acceptable for group comparisons. A good measure provides stable scores for stable persons.

Validity:

Content Validity. Content validity is the "extent to which the items are sensible and reflect the intended domain of interest."[5] Does the content of the measure make sense? Are the items included relevant to the domain of interest? Do the items cover the full range relevant to that domain? Are the items comprehensible to respondents? There is no formal statistical test to evaluate content validity. In practice, content validity is evaluated using a structured set of criteria, including those listed above.[88-90]

Criterion Validity. Criterion validity is the extent to which a measure agrees with a gold standard measure (the criterion). Predictive validity relies on criterion validity (for instance, in the question, "Does baseline self-rated health predict admission to a nursing home or mortality?"; mortality or nursing home admission is regarded as the criterion). In applications other than the assessment of predictive validity, the field of HRQL lacks gold standards and thus relies on the evaluation of construct validity.

Construct Validity. Construct validity is a measure's ability to perform as expected. It involves specifying *a priori* hypotheses about how the measure should perform based on an underlying model or conceptual framework, testing those hypotheses, and accumulating evidence over time and across settings. *Cross-sectional construct validity* involves making comparisons at a point in time. In *convergent validity* we expect a high correlation between two different measures of the same concept or measures of highly related domains such as mobility and self-care, or anxiety and depression. In *discriminant validity* we expect little or no correlation between measures of domains that are unrelated, such as vision and pain. Another strategy for assessing construct validity is *known-groups comparisons*. We would expect the scores for a measure of mobility to be systematically related to known groups based on the categories in the New York Heart Association functional classification system.[91]

Responsiveness (Longitudinal Construct Validity). Longitudinal construct validity measures within-person change over time. Does the measure capture meaningful change when it occurs? Change scores for those known to have changed (by some other criterion) should exceed change scores for those known not to have changed. For those who have changed, change scores should be systematically related to the degree of change. Measures for which there is substantial evidence of responsiveness in the relevant area enhance the confidence of the reviewer in the validity of the estimates of change.

Responsiveness is often assessed using effect size (ES, the magnitude of the change divided by the standard deviation of baseline scores), the standardized response mean (SRM, the magnitude of change divided by the standard deviation of change scores) or other related

measures that are ratios of signal to noise.[92] Cohen provides a scheme to interpret the magnitude of ES: small (0.20); moderate (0.50); or large (≥ 0.80) change[53]. A related measure, the standard error of measurement (SEM), is also frequently used. SEM is computed as the standard deviation at baseline times the square root of one minus test-retest reliability.[93]

The Distinction Between Predictive Validity and Responsiveness. Predictive validity refers to the ability of a baseline score to predict subsequent events. For instance, in both population health survey and clinical studies, self-rated health (SRH) (excellent, very good, good, fair, or poor), has been shown to predict mortality, admission to nursing homes, and other major health outcomes.[94-103] As there are only five options, the responsiveness of SRH is limited. However, predictive validity does not necessarily imply that a measure will be able to detect within-person change over time.

Appendix B. Measurement Properties

Table 1. Brief review of evidence on measurement properties for generic measures and selected disease-specific measures frequently used to assess health status and health-related quality of life in the older adults

	SF-36	Barthel ADL	Lawton IADL	HUI3	CRQ
Content Validity	Built upon previous measures. Represents health concepts most frequently included in health surveys and additional concepts strongly supported by empirical evidence[10]	Developed to determine the amount of nursing care hospital patients undergoing rehabilitation would need[104]	No information on how items were selected[105]	Theoretical and empirical evidence have guided the creation of HUI3; selection of attributes was guided by the importance the general population placed on each attribute[106]	The items were generated from a literature review, consultations with health professionals, and interviews with patients about concerns/problems most important to them[107]
Internal Consistency	Moderate to high levels for all domains, Cronbach's alpha ranging from 0.49 (Social Functioning) to 0.96 (Physical Functioning)[8] Eight factor solutions supporting each of the domains were supported by factor analysis as well as two factor solutions for the 2 component scores (physical and mental health)[8]	Factor analysis indicated that the instrument was unidimensional for stroke patients, but multidimensional for geriatric and hip-fracture patients[108] Rasch analysis indicated that using a total score was not appropriate for older adults in the acute care setting[109] Cronbach's alpha of 0.84 upon admission and 0.85 upon discharge for stroke inpatients receiving rehabilitation[110] Internal consistency coefficients of 0.87 (admission) to 0.92 (discharge)[104]	Acceptable internal consistency (Cronbach's alpha > 0.7)[105] Two subscales found with factor analysis with Cronbach alpha of 0.91 and 0.78[105]	Little overlap among attributes, ranging from 0.02 (vision and speech correlations) to 0.35 (emotion and cognition correlations)[111]	Cronbach's alpha ranges from 0.76 (Mastery) to 0.90 (Emotional function) and 0.93 total[112] Cronbach's alpha ranges from 0.51 (Dyspnea) to 0.88 (Mastery)[113]
Inter-Observer Reliability *In general*					

	SF-36	Barthel ADL	Lawton IADL	HUI3	CRQ
Inter-Observer Reliability *In older adults*		Fair-moderate agreement for individual items, high percentage of agreement for the total score[114] Acceptable agreement for the total score between a doctor interview of a close relative and occupational therapist; kappa values ranged from 0.42 to 0.92[115] Self-report was the least reliable compared to physiotherapist testing and nurse assessment or testing and; agreement was also lowest for items on transfers, feeding, dressing, grooming, and toileting[104] Physician's score from interview tended to be higher than nurses' scores from observations among short-stay patients; only 4 individual items had a kappa coefficient above 0.40[116] For stroke patients, weighted kappa statistics ranged from 0.53 to 0.94 for individual items and the ICC was 0.94 for the total score[117]		Among caregivers and stroke patients, caregivers with pain overestimated patient pain and depressed caregivers underestimated patient pain[118] ICC>0.7 for patient-proxy responses at 1, 3, and 6 months post-stroke. ICC=0.59 at baseline[119] Overall score had ICC=0.70 for patient-proxy responses at baseline and ICC=0.86 at 6 months[120]	
Test-Retest Reliability *In general*	Generally good test-retest (ICC ranging from 0.57 to 0.80, except	For patients retested after 3 weeks, scores for 35 of 41 patients were		Kappa values for attributes ranged from 0.14 to 0.73. ICC for	High test-retest reliability for Fatiguq, Emotion and Master

	SF-36	Barthel ADL	Lawton IADL	HUI3	CRQ
	Mental health at 0.28) among stroke patients[121]	within 10 points of the original score[104]		overall scores was 0.73[122] 8 of 10 individual questions and 6 of the 8 attributes had moderate or better kappa coefficients[123] ICC of 0.87 for MS subjects[124] Test-retest for rheumatoid arthritis patients, ICC: 0.81 (0.66-0.90)[125] Good test-retest for breast hypertrophy patients, ICC=0.84[126] Test-retest among epilepsy patients, 0.87 +/- 0.3 (95%)[127] ICC of 0.77 from a population survey[128]	(Spearman-Brown reliability coefficient ≥0.9), lower test-retest for Dyspnea (0.73)[129] No trends towards improvement or deterioration in stable COPD patients who were administered the test 6 times at 2-week intervals[107] High degree of test-retest reliability among Dyspnea, Emotional function, and Mastery[130]
Test-Retest Reliability *In older adults*	Low to high levels for all domains, ranging from 0.24 (Social Functioning) to 0.87 (General Health Perceptions). Most domains have high levels of reliability, except Social Functioning and Role Limitations – Emotional[8]	No studies of test-retest in general older adult population[114] Among stroke patients, agreement was >75% for individual items[131]		Acceptable test-retest reliability for hip fracture patients[132] Test-retest reliability intra-class correlation coefficient for mild cognitive impairment 0.75 (0.32-0.92); moderate impairment, 0.25 (0.00-0.74)[19]	
Cross-sectional Construct Validity *In general*	Discriminating between individuals with chronic medical illness and psychiatric, varying severity of medical			Demonstrated validity with childhood cancer, adult oncology, population health survey[111], colorectal	

	SF-36	Barthel ADL	Lawton IADL	HUI3	CRQ
	conditions, osteoarthritis, epilepsy, depressive symptoms, panic disorder, total hip replacement, migraine, missing work due to illness, and varicose vein surgery[123]			cancer, stroke, arthritis[122], neurological disability[124], and MS[133]	
Cross-sectional Construct Validity *In older adults*	Items correlate more highly with the proposed domain than with other domains[8]	Rank correlation coefficient with SF-36 in stroke patients ranged from 0.22 for Role Limitations – Emotional and 0.81 for Physical Functioning subscales[134] Rank correlation coefficient with the Nottingham health profile for stroke patients ranged from -0.19 for Sleep and -0.84 for Physical Mobility subscales[134] Scores correlated with Berg balance scale and Fugl-Meyer motor assessment at stroke recovery stages[117]	4 IADL items (telephone, medications, finances, and transportation) were associated with cognitive impairment in older community-dwelling adults[135] Was not helpful in identifying dementia in a clinic-based population[136] Indeterminate construct validity[105]	Demonstrated validity among groups with hearing loss[137], Alzheimer's disease[138], chronic conditions[139], socioeconomic status[140,141], type 2 diabetes[142], coronary heart disease[143], Parkinson disease[144], socioeconomic status	
Longitudinal Construct Validity (Responsiveness) *In general*	SF-36 scales and summary scores have been linked to utilization of health care services, progression of depression, loss of job within 1 year, and 5-year survival. Physical functioning, Role-physical, and Bodily pain are responsive to knee and			Responsive to treatments of osteoarthritis of the knee and elective total hip arthroplasty for osteoarthritis[111]	Responsive to changes after respiratory rehabilitation (Guyatt 1987, de Torres 2002), changes 10 days post acute COPD exacerbation (Aaron 2002), improvements and deteriorations in how patients felt[145] Dyspnea section was responsive to changes

	SF-36	Barthel ADL	Lawton IADL	HUI3	CRQ
	hip replacement and heart valve surgery. Mental health, Role-emotional, and Social functioning are responsive to recovery from depression[11]				after treatment for patients with chronic airflow limitation[146]
Longitudinal Construct Validity (Responsiveness) *In older adults*	Hypothetical improvement in health states was associated with small to large effect sizes in community-dwelling older women[8]	Admission scores predicted mortality, length of hospital stay and subsequent progress among stroke patients[104] It was difficult for the index to obtain a change score for those at the upper or lower score ranges for older adults in the acute care setting; the index does not have appropriate scale width to monitor changes[109] Responsive to change from 1 to 3 months in recovering stroke patients[147] Responsive to change in patients undergoing inpatient neurorehabilitation[148] Responsive to changes over time in stroke patients[117]	Indeterminate responsiveness[105]	Measured significant improvement after hearing aid fitting[137]	
Evidence of Floor Effects *In general*	No floor effects for the Physical and Mental component summary scores observed in the general U.S. population. About 10% were			No floor effects on the subscales for MS subjects[124]	No floor effects[145]

	SF-36	Barthel ADL	Lawton IADL	HUI3	CRQ
	observed to have the lowest scores in role-emotional and role-physical[149] Floor effects for people aged over 45 years who had a stroke for physical functioning (18%), role physical (54%), vitality (10%), social functioning (17%), and role emotional (35%)[150]				
Evidence of Floor Effects *In older adults*	Developers suggested that older adults may have more floor effects because they may have more sickness than the general population. Floor effects in excess of 20% were reported for Role Limitations Emotional and Physical by 12 studies[8]	Minimal floor effects for the total score for multiple sclerosis, stroke, and spinal cord injury patients upon admission to a neurorehabilitation unit. Seven of ten individual items had floor effects[151] Floor and ceiling effects may lead to underestimating problems in a third of stroke patients[152]			
Evidence of Ceiling Effects *In general*	No ceiling effects for the Physical and Mental component summary scores observed in the general U.S. population. 40% in physical functioning, 71% in role-physical, 32% in bodily pain, 52% in social functioning, and 71% in role emotional were observed to have the highest scores[149] Ceiling effects for people			Ceiling effects were present in only 3% of MS subjects for the overall utility and each of the subscales[124] May be problematic for population screening and long-term follow-up studies[122]	No ceiling effects[145]

	SF-36	Barthel ADL	Lawton IADL	HUI3	CRQ
	aged over 45 years who had a stroke for role physical (16%), bodily pain (25%), social functioning (18%), role emotional (51%), and mental health (12%)[150]				
Evidence of Ceiling Effects *In older adults*	Ceiling effects in excess of 20% for Role Limitations Emotional and Physical and Social Functioning (includes 16 studies)[8]	Minimal ceiling effects for patients upon admission to a neurorehabilitation unit for multiple sclerosis, stroke, and spinal cord injury. Ceiling effects were present at discharge. Nine of ten individual items had ceiling effects upon admission and ceiling effects increased at discharge[151] Unacceptable ceiling effects for older adults in the acute care setting[109] Ceiling effects among patients recovering from a stroke or transient ischemic attack[153] Various studies have shown that the index has ceiling effects among stroke patients[154]	20% of dementia patients obtained the highest score[105] In clinic patients, most achieved a high IADL score[136]		
Interpretation	The smallest amount that the SF-36 score can change if patients move up or down one response level varies from 5-12.5, although the clinically important differences are higher	A change of 1.85 in the total score can be considered the minimally important difference for stroke patients[156] The Barthel index ranges from 0-20 or 0-100, but it		Changes of 0.03 in overall scores are important and in some situations, 0.01 may be meaningful. Within attributes, changes of 0.05 are meaningful[106]	Mean clinically important difference of 0.5[158]

	SF-36	Barthel ADL	Lawton IADL	HUI3	CRQ
	for asthma, COPD, and heart disease patients[155] The SF-36 ranges from 0-100, but it is not an interval scale. For example, a change of 10 points means something different when going from 40 to 50 versus 85 to 95[52]	is not an interval scale. Equal changes in scores for individual items do not correspond to equal changes in functioning[157]			
Comments		BI has considerable imprecision (95% CI of ±4 points; 20 point scale)[114] Group level indicators of responsiveness (e.g. effect sizes, standardized mean differences) are potentially misleading for the BI[159] Designed for use with long-term hospital patients with neuromuscular or musculoskeletal disorders; only suitable for the institutionalized populations for which it was designed[157] BI has been extensively studied in stroke populations, but less studied in the general older adult population.			Normal distribution[112]

Table Note: This table is intended to be illustrative, rather than a comprehensive review.

Abbreviations: ADL = activities of daily living; BI = Barthel Index; CI = confidence interval; COPD = chronic obstructive pulmonary disease; CRQ = chronic respiratory questionnaire; HUI = Health Utilities Index; IADL = instrumental activities of daily living; ICC = intraclass correlation; SF = short form; U.S. = United States.