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Quality of Life in Palliative Care

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Abstract

Introduction: A main goals of palliative care is to improve the health-related quality of life (QOL) of patients with advanced illnesses. The objective of this narrative review is to provide an updated synopsis on the use of QOL questionnaires in the palliative care setting.

Areas covers: Focusing on the palliative cares setting, we will define QOL, discuss how QOL instruments can be used clinically and in research, review approaches to validate these questionnaires, and how they can be used in utility analyses.

Expert opinion/commentary: Several QOL questionnaires, such as EORTC-QLQ-C30, McGill QOL questionnaire and EQ-5D have been validated in the palliative care setting. However, significant gaps impede their application, including lack of determination of their responsiveness to change and minimal clinically important differences, the need to conduct more psychometric validation on QOL questionnaires among patients at various stages of disease trajectory, and the paucity of studies examining utility and cost-effectiveness. Further research is needed to address these knowledge gaps so QOL questionnaires can be better used to inform clinical practice and research.

Keywords

palliative care; patient outcome assessment; quality of life; reproducibility of results; validity of results

1. What is quality of life?

Health related quality of life (QOL) is not the absence of disease or suffering but is largely a response to a series of life events that influence quality and quantity of life (1). QOL can also be defined as a subjective evaluation of life as good or satisfactory overall. Individuals may have a disease yet not be “ill” or experience a reduction in perceived QOL. Similarly, there are individuals without disease who complains of being “ill” and have poor QOL (2–

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Declaration of interest

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4). Individuals with the same disease stage or severity may have vastly different QOL. Group changes in QOL related to disease, therefore, may not reflect individual responses to disease (5–7). This is an important issue when interpreting group related QOL outcomes.

QOL is one of the important outcome measures in clinical trials and the most important determining treatment utility (cost effectiveness). QOL is the principal outcome to palliative care interventions (8–12).

2. What does QOL mean to patients?

Even though innumerable QOL questionnaires has been developed in palliative care, there is not a single questionnaire that fits all purposes and individuals. Patient perspectives when queried about QOL include the following perspectives: Fulfillment of personal goals, good control of physical symptoms, emotional well-being, the ability to lead a normal life and maintain a sense of self, sociability (role within the family and society), existential and transcendent fulfillment, finding meaning in life, adaptability or resiliency, changing values or recalibration of goals with the disease trajectory (13).

In this sense, the World Health Organization definition as “an individual’s perception of their position in life in the context of culture (family and society) and value system in which they live and in relation to their goals, expectations, standards and concerns” is more fitting. “Those who report the very poorest QOL will be least likely to have met their own ‘...goals, expectations, standards and concerns’”(14).This fits well into the concept of “Calman’s gap” (15). This concept views QOL as a ratio or gap between expectation and realization. A narrow gap defines good QOL where patient expectations match reality and poor QOL where patient expectations exceed reality. Collusion and therapeutic misperceptions are a means of falsely maintaining QOL by narrowing the gap. Presenting an overly optimistic future recovery and survival is also another way of falsely narrowing the gap. For example, a recent study found that patients who reported an inaccurate understanding of their advanced illness had better QOL(16). The purpose of palliative care in this context is to reduce this gap through facilitation of a response shift in QOL by helping patients recalibrate expectations and shift important domains with disease projection. Therapies which improve a patient’s sense of who they are as a person will also increase QOL. In addition, excellent symptom management and improvement in function through rehabilitation are means of reducing the gap thus improving QOL.

QOL is not static and will change as the disease progresses (17).There may be changes in reflective items. I and there are changes in causative items in questionnaires that influence QOL scores. Fatigue, physical function, and mood often worsen while pain and certain gastrointestinal symptoms are controlled with progressive disease. Fixed item QOL instruments will not reflect this shift in importance as each item is given equal weight when scoring QOL (18). The European Organization for Research and Treatment of Cancer QOL questionnaire (EORTC-QLQ-C30) commonly used in cancer therapeutic trials has been adapted to palliative care (EORTC QLQ-C15-PAL) which better reflects QOL at the end-of-life (EOL) (19). The SEIQOL-DW questionnaire measures changes in QOL domains with disease course and thus adapted for recalibrations and response shifts over time. This QOL

tool can detect the capacity to change priorities over time and resilience of patient resilience. However, the SEIQOL-DW questionnaire index score does not correlate with objective health, functional status, demographic and clinical parameters. The SEIQOL-DW reflects the patient's capacity to value domains other than health in life, despite having health problems The main drawback to using this type of questionnaire is that one cannot quantitatively measure the minimal clinical important difference (MCID) in QOL to gauge therapeutic responses to interventions nor can it be used to estimate utility in cost-effectiveness analyses (20).

So, at the EOL what domains influence the QOL (and death)? In an article which used the Good Death Inventory, physical and psychological comfort, living at the preferred location, maintaining hope and pleasure, having a good relationship with the medical team, having good family relationships, maintaining independence as long as possible, being respected as a person, feeling fulfilled in having achieved life goals were of primary importance (21). Many of these domains are not assessed by commonly used questionnaires such as the EORTC-QLQ-C30 and the EUROL questionnaire EQ-5D which is a barrier to assessing utility at the EOL (8, 22–26). Because patients often develop delirium in the last weeks/days of life, some investigators have relied on caregivers to provide ratings of the patient's QOL (27).A utility measure is needed to measure quality of dying since standard utility measures like the EQ- 5D gauge levels of health and not dying. Further research is needed to develop and validate QOL questionnaires appropriate for patients at different points of their disease trajectory.

3. Why measure QOL?

QOL questionnaires may be used for non-research purposes, to survey important domains to identify areas of distress for the purposes of beginning a conversation on what is important to the patient. The Missoula-VITAS QOL Index is validated and is an excellent tool to use for this purpose (28–30).

Quality of life questionnaires often are a primary or secondary outcome in many palliative care interventional trials. These questionnaires should ideally not only be validated and reliable, but also be sensitive and responsive to changes in QOL over time (clinimetrically sound). Specifically for this purpose, the MCID needs to be established for the population for which the questionnaire is being used (31).

QOL questionnaires are also used to help manage service delivery and monitor quality. The EORTC-QLQ- C15 PAL, the Palliative Care Outcome Scale (POS) and the Support Team Assessment Schedule (STAS) have been used to audit palliative care for quality outcomes (32, 33). As healthcare becomes more value-based, QOL questionnaires will be increasingly used to inform policy makers about cost effectiveness (utility) of various interventions. Utility represented by quality adjusted life years saved (QALY) is an unique challenge to palliative care (34), which will be discussed in a later section. Certain QOL questionnaires (EQ-5D and SF-36) are utility tools which can discrimination levels of health (35–38).

4. Reliability, Validity, Responsiveness: Are there unique problems in palliative care?

The validity of a QOL questionnaire is assessed in multiple ways. Face validity involves reviewing the questions to see if items make intuitive sense. Content validity assesses the degree to which the domains of interest are represented fully in the questionnaire. Construct validity is the measure of correspondence to what is expected by comparison to either another validated questionnaire or to objective measure (e.g. performance score). This "external" validation may be convergent (predicting an outcome) or divergent (discriminating between different distinct groups). QOL may not change with the course of disease. It is also important to recognize that the validity of a questionnaire is highly dependent on the disease state. Static questions that may be appropriate for one disease state may be irrelevant later in the disease course and may be left blank by perplexed patients (e.g. appetite and food consumption when a patient is dependent on PEG tube for feeding at the EOL) (39). It is this important to recognize the appropriate population for which the questionnaire has been validated. An important challenge to QOL assessments in palliative care is the highly diverse patient population with different diagnoses, disease states/ prognosis, and languages. It is thus particularly important to validate questionnaires for specific populations. Unfortunately, in palliative care there has been a relative lack of adequately powered studies to validate many existing QOL questionnaires. Most remain under developed.

Reliability refers to the degree to which a questionnaire is free from random error, and includes both internal consistency and reproducibility (i.e. test-retest reliability, inter-rater reliability). Internal consistency measures how well items within a domain or subscale correspond with each other. This is determined most often by Cronbach alpha or factor analysis (40). A high degree of reliability (Cronbach alpha >0.7) facilitates power calculations using a questionnaire's MCID (41). Internal consistency requires an adequate number of individuals completing the instrument which is estimated to be at least 100 and adequate categories per item, usually 7 or more (40). Items within domains are either reflective or causative (causative items directly influence QOL such as pain or nausea). Causative items can cluster making factor analysis a poor fit for measuring internal consistency. Reliability also involves repeatability which needs to be measured when QOL is stable. Test and retest reliability generally requires at least 50 patients to be reliable (40, 42–44). The difficulty with palliative care patients is that QOL is less likely to be stable. Repeatability is assessed too soon (within days), there is likely to be recall bias. The appropriate interval to determine reliability in palliative care is not established (40). Interrater reliability becomes important if there are multiple assessors. An intraclass correlation coefficient (Kappa) is the proportion of agreement corrected for chance which can be used if there are multiple assessors. Kappa is scaled from −1 to +1. The negative value indicates poorer agreement than chance, zero represents chance agreement and positive better than chance agreement. The intraclass correlation coefficient can only be used for binary or nominal scale ratings (45).

Responsiveness measures instrument sensitivity to change over time which have clinical or patient centered importance (46). This requires measuring random measurement error or variability and corresponding changes in mean scores pre-and post-intervention that an individual, group experiences or between group differences. There are 2 approaches to measuring sensitivity; a distributional and anchor based approach, which will be discussed further (6, 47–53). Finally, in the last weeks and days of life, delirium is common which can affect how QOL can be assessed. Surrogate substitution will add another element of variability since there is not a perfect correspondence between patient surrogate assessment of QOL.

5. Why is it important to measure meaningful changes in QOL? What are the methods?

Clinicians have difficulty in interpreting QOL and QOL scores. What magnitude of change is clinically significance? This is particularly true for palliative care where the primary outcome is QOL. QOL should be measured regularly either at every clinical visit or consistently over time to detect patient's improvement, stability or deterioration with palliative interventions over time. Unfortunately,QOL is not routinely measured, is poorly collected in clinical trials and usually a secondary or tertiary outcome (54).

Responsiveness can be estimated by repeating QOL questionnaires over time in observational studies, in single arm interventional studies or randomized trials. Minimal important differences are estimated by various statistical methods: the paired T test, Cohen effect size, standardized response mean and responsiveness (31, 51, 52, 54). The basic statistical principle is the pre-and posttest mean (assuming normality) is divided by intra or intergroup random error or variability. For the Cohen, standard mean difference, for example, is the difference between the group mean pre- and post-intervention divided by the standard deviation of the group baseline values. A minimal important different (MID) in effect size is often designated as a standardized mean different (SMD) of 0.2 (although not universally embraced as some would use 0.5), moderately important differences are 0.5 and large differences 0.8 (55, 56). The advantages of distributional methods are that they are often easily obtained, do not require a clinical anchor, and provide an idea of the data distribution. Confidence intervals are established for precision which cannot be done for anchor methods. However, few agree on such an approach as the benchmark for clinical relevance and some debate the appropriateness of a 0.2 SMD as the definition of MID (57, 58). The distribution approach remains abstract to clinicians though the SMD can be translated into the numbers needed to treat (NNT), as long as the reliability is acceptable (Cronbach alpha +/> 0.7) (59, 60). However, distributional approaches are best used in conjunction with anchor methods in determining important changes in QOL scores (60). There have been attempts to correlate important differences between distributional methods and anchor-based methods. One standard error the mean or $^{1}/_{2}$ standard deviation difference between pre-and post-test mean QOL scores correlates with an effect size of 0.5 if reliability by Cronbach alpha is >0.75 and 0.2 if the Cronbach alpha is >0.9 (59–61).However, patients need to be in the moderate and not extremes of QOL for this relationship to hold true (62,

63) The MCID from anchor-based methods have not been directly compared to the distributional approach for most QOL questionnaires.

The MCID is “the smallest difference in a score corrected for random noise within a domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects or excessive costs, a change in patient management”(53). Unlike distributional methods, anchor methods are patient-centered. One way MCID is determined is to use individual rated global perceived improvements or diminished QOL. By using this anchor approach proportional response outcome (“responder’s analysis”) is possible which is not possible with distributional methods (7, 53). Population based approaches use external outcomes as anchors to define treatment responses. For example, a 10- point improvement in a QOL questionnaire might be associated with a 20% improvement in function and survival. The MCID, therefore, is a 10- point improvement in the questionnaire scale. The results can be expressed in absolute changes in the scale or relative changes (as a percentage) of the total score. The absolute changes are easier to analyze (64–66). Another commonly used anchor method is to use the global impressions of patient perceived change (scales such as −7 to +7) which is dichotomized and used to construct receiver-operating characteristics curves for cut off values which are used to determine sensitivity and specificity (5, 53, 67–70).

There are drawbacks to anchor methods. Meaningful important changes are not bidirectional, are anchor dependent and not immutable (52, 71–73). The lack of bidirectional symmetry in QOL is observed with well-known QOL tools such as the SF-36 and the Functional Assessment of Cancer Therapy (52, 74). It is unlikely that there will be one MCID for all populations (61, 75, 76); however, because of limited research, the few available MCIDs are often being applied liberally outside of the specific populations from which they were derived. If one is using a global assessment of QOL by patients, the threshold chosen for cut off in the Likert scale (e.g. −7 to +7) will influence the MCID. Anchors do not take into account precision such that the MCID can be within measurement error (63, 77). There can be also be differences between population-based anchors and individual perceived global changes and disease course. For instance, the SF-36 QOL changes follow more closely patient global anchors and physician assessment of response than actual disease course in rheumatoid arthritis (78). Global anchors are subject to response shifts as patients experience their illness. Moreover, global anchors are subject to regression toward the mean. Patients with worst QOL will shift responses toward the mean or less severe rating over time without any intervention (77, 79).

Because of the limitations with both anchor-based and distribution-based approaches, it is recommended that several methods be used to determine the MCID in QOL questionnaires rather than relying on a single approach (52, 71, 77).

Palliative care QOL questionnaires are in general tested psychometrically but the majority lack responsiveness (clinemetrics) (40, 80). Most clinicians depend on statistically significant differences for reporting outcomes and have misinterpreted statistical difference as clinically important. Most have interpreted sound psychometrics of a QOL measure as an indicator of its clinical usefulness. Validity and reliability are only the first step in

developing a QOL questionnaire. It is useful clinically when responsiveness is established. It is important that palliative care specialists understand how to interpret QOL changes and understand the clinimetrics of these measures. This will be critically important in a value-based and population-based reimbursement systems in which utility will become important to public and private payers and to policy makers.

6. What is utility and is at relevant to palliative care?

When QOL is used in palliative care the endpoint should have relevance both clinically and economically. QOL questionnaires are adapted to reflect health states or levels which have utility when determining economic outcomes to palliative. Palliative interventions should improve QOL even if they do not improve survival and thus have a positive influence on quality adjusted life years saved(QALYS). The utility of the intervention will be determined by the cost of the intervention in relationship to the change in health state. Interventions which have a small benefit but large cost will not have value in population based health. It will be difficult for palliative care specialists to convince policy makers and payers to support palliative interventions without including utility or cost effectiveness (81–84). This is the major future challenge in palliative care. For if palliative care thrives in a value based or population based reimbursement health care system, the specialty will have to show value.

In the era of value-based healthcare, the difference in QALYS before and after an intervention is calculated to estimate its benefits on quality and quantity of life. QALYS is determined by multiplying the length of time (years) with the score for being in a health state during that time. The health state is estimated by QOL questionnaire scores, adjusted for the relative weight for each QOL domain based on patient preferences. Some QOL questionnaires, such as EQ-5D, assessment of QOL and SF-36 transformed to the SF-6D, already have relative weights established based on population based studies, and are particularly useful for utility analyses. The difference in QALYS with or without an intervention generally provides an estimated value between −1 and 1, where 0 indicates a health state as bad as being dead for 1 year, 1 indicates full health, and a negative score indicates a health state worse than death. Cost-effectiveness is assessed by dividing the cost of an intervention by the difference in QALYS, and is sometimes used to make decisions regarding the value of interventions within health care systems. In this sense utility is quite patient centered because they “vote” on interventions by their perceived QOL and benefits.

The QOL measure SF-36 transformed into a utility tool (SF-6D) has 6 QOL domains each with 2–6 health levels. These six domains are physical function, role limitation, social function, pain, mental health and vitality. Values of health range can from 0.35 to 1.0 with this tool (85). The SF-6D MID is 0.03 (mean) and effect size 0.051 (86, 87).

The Assessment of QOL Instrument has been transformed into a utility questionnaire consisting of 5 dimensions (illness, independent living, social relationships, physical function, psychological well-being); 4 dimensions are combined into a multiplicative model weighted for community values. The value in health states range from 0.04 to 1.0. Utility scores of <0.37 with this instrument predict a two-fold increase in readmissions for hospitalized patients (88).

The EQ-5D is the most commonly used utility tool internationally. There are 3 and 5 level Likert question forms (EQ-5D-5L and EQ-5D-3L). There is less of a ceiling effect with the EQ-5D-5L questionnaire. Scores range from −0.59 to 1 with negative values being worse than death and 1 being perfect health. There are population differences in preference values (89). The MID between the SF-6D and EQ-5D are not equal and differ in absolute values. Both separate health status as very good, good, fair, bad and very bad but there is disagreement between the SF-6D and EQ-5D particularly at the lower end of the scale (poor health status) (90, 91).

QOL questionnaires with similar domains as the EQ-5D or SF-6D can be mapped on to these utility measures in clinical studies(92–94). Mapping facilitates the use of QOL questionnaires for both clinical outcomes and cost-effectiveness analyses if domains between the QOL questionnaire and utility tool are congruent. QOL questionnaires used to map utility measures also need to have MCIDs established. Mapping between questionnaires is more accurate if multiple predictors are used. Important characteristics include the following: a population that complete a utility measure (e.g. EQ-5D) and QOL questionnaire, similar patient characteristics across studies for which patients complete the utility measure and the QOL questionnaires, an adequate number of patients completing both questionnaires, clinical effectiveness or health outcomes are well-defined, and outcomes are important to the population (25, 95, 96).

There are several draw backs to mapping QOL questionnaires to utility tools. Mapping regression between tools is population dependent. Furthermore, regression algorithms differ between populations such that “one sized does not fit all” (96). Certain commonly used questionnaires such as the IPOS and IPOS-S do not map at all to the EQ-5D and cannot be used for utility if the EQ-5D is used (97). In more general terms, patient views of utility are different than the health care system. Patients are concerned about whether palliative interventions of any sort will benefit them and not be costly to them personally. Utility measures for the most part is blind to family financial toxicity and are focused on medical system economics. QALYS assumes a linear value on the length of life yet patients frequently value time greater near the EOL than at the beginning of their terminal illness, or they may value it in a different way which cannot be measured by fixed utility questionnaires. The metrics of quality of death, as previously mentioned, are missed by the EQ-5D and SF-6D. Dissecting the most valuable components of a complex intervention like palliative care that contributes the greatest value to QOL cannot be detected by utility tools (34).Palliative specialists have an urgent need to develop utility measures for their specialty.

7. What is the evidence that palliative care improves QOL?

A meta-analysis of recently published studies which measured the effect of specialist palliative care services in various locations (hospital, hospice or community setting) on QOL 8 studies, 3 of which had a small but statistically significant difference favoring palliative care and four studies had nonsignificant differences. (98). The effect size (by SMD) was 0.16 (95% confidence interval 0.01–0.31). By sensitivity analysis the SMD was 0.57 (95% confidence interval-0.02 to 1.15). For patients receiving specialist palliative care early the effect size was 0.33 (95% confidence interval 0.05–0.61). A second study analyzed 10

palliative care studies of which 3 were randomized controlled trials. The quality of the studies was moderate to low and the great majority of patients had cancer. The effect size was estimated in half of the studies which was 0.27. The effect size was greater in the observation studies than the randomized trials (99). A third study measured QOL at the EOL using the Good Death Inventory (100). Of the 10 domains, 3 were improved (favorable place, maintained hope and pleasure, living in a comfortable environment) with an effect sizes of 0.1, 0.1 and 0.09 respectively. The benefits were greater in those with worse performance score (ECOG 3 and 4) with an effect size of 0.54.

These population-based effect sizes may seem disappointing regarding the benefits of palliative care on QOL. The effect size seemed in certain cases to be less than the MID previously discussed. However, the population standard median differences are made up of individuals who dramatically improve, those who have modest improvements, and those whose QOL remains stable or those that worsen. Certain groups appear to benefit more than others. Those seen earlier by palliative care had greater improvement in their QOL. Those with poor performance score at the EOL benefitted more than those with good performance scores though this is likely related to the questionnaire used to measure QOL and perhaps regression towards the mean. The real difficulty in gauging QOL benefits of palliative care is the lack of individual responses expressed in those achieving MCID. This would allow us to gauge proportionate or percentage responses (101).This is a significant problem in interpreting the present studies.

8. Which QOL tools should be considered in palliative care?

A recent systematic review of QOL questionnaires in palliative care recommended three measures which had adequate psychometrics (40), including the McGill QOL Questionnaire, the QOL at the End of Life questionnaire and the Quality of Death and Dying questionnaire (102–104). The reviewer found that the weakest psychometrics for these questionnaires was responsiveness. A survey of questionnaires used by palliative care specialists in Europe found that the European Organization for Research and Treatment of Cancer QOL questionnaire (EORTC-QLQ-C30) and the Patient Care Outcome Scale (I-POS) were most commonly used (42).

8.1 McGill QOL Questionnaire

The McGill QOL Questionnaire contains 16 items each having 11 responses per item (0–10) included in the questionnaire are psychological symptoms, existential well-being, support, physical symptoms. These domains were validated by factor analysis. The time required to complete the questionnaire was 10–30 minutes. The recall was 2 days. There are sub scale scores are available. This measure has been validated in inpatient palliative care patients. The reliability (Cronbach alpha) was greater than 0.7 except for physical symptoms which was 0.62. It had an intra-class correlation coefficient of 0.62–0.85 as a second measure of reliability. It has been validated by the Spitzer QOL Index and was externally validated against pain intensity. Pain intensity correlated with a 0.56 change in the existential subscale and 0.66 in the total scale. The effect size differences were significant for good to average days and average to bad days for the physical symptoms and support domains (104–107).

The McGill QOL questionnaire has been shortened. The shortened form has been validated in 190 terminally ill patients. The time to complete the questionnaire was 3.3 minutes. The Cronbach alpha ranged from 0.46 to 0.86 when compared to the long form of the questionnaire. There was a strong correlation with the multiple domains of the original McGill QOL Questionnaire. Scores were externally validated to hemoglobin levels. The construct validity was supported also by principal component analysis (108).

8.2 QOL at the End of Life Questionnaire

This questionnaire contains 25 items with 5 responses per item. Domains include outlook, inspiration, spiritual activity, religion, community. Recall is at 1 week and 1 month. It requires a structured interview. There is a total and sub section scoring system. The populations for which this was validated included those with heart failure, COPD, cancer and end-stage renal disease and so a diverse population which is an advantage. The internal consistency was greater than 0.7. It correlated with the Functional Assessment of Chronic Illness- spiritual subscale (>0.6) and preparation subscale (o.4–0.6). It moderately correlated with the Missoula-VITAS QOL Index (103).

8.3 Quality of Dying and Death Questionnaire

This questionnaire assesses the quality of death from the perspective of bereaved caregivers or health care professionals. It contains 31 items with 11 potential responses per item (0–10). Domains are symptoms, personal care, preparation for death, moment of death, family, treatment preferences, whole person concerns. The questionnaire is administered by semi-structured proxy interview. The recall is retrospective. The Cronbach alpha for internal consistency is 0.89. Factor analysis did not support subscale construct based on the questionnaires domains. The study population were dying patients. Higher scores were associated with death at home, death in a preferred location, better rating of symptom treatment, adherence to patient preferences, family satisfaction with communication and care, availability of the healthcare team members (102).

8.4 Palliative Care Outcome Scale

This scale was constructed through agreement between staff and patient ratings for 8 of the 10 items. It was validated in 148 palliative care patients. Both staff completed and patient completed scales are available. The original scale has been expanded to include symptoms. The reliability is acceptable with a Cronbach alpha of 0.65 for patient completed questionnaires and 0.74 staff completed questionnaires. It has a construct validity with a range of Spearman correlations from 0.48 to 0.8 using the EORTC-QLQ- C30 and the STAS questionnaires. Test and re-test reliability is acceptable for 7 of 10 items. A change was noted in the scale scores with disease progression but this was not statistically significant (109, 110). It has been validated in patients with cancer using cognitive debriefing of both patients and oncologists. Factor analysis validated distinct domains which were emotional well-being, consequences of disease, received informational support, anxiety and burden of disease. This however has been disputed. A second study suggested that the measure consists of 2 factors (psychological well-being and 3 items related to professional care). Three items were considered independent (family anxiety, symptoms and pain). The author felt the POS better reflected quality of care rather than QOL (111). The experience with the

POS has been expanded to include patients with HIV, those with neurologic, pulmonary, cardiac and kidney diseases. It has been used as an outcome to study symptom prevalence and to audit quality of care (32, 112).

8.5 European Organization for Research and Treatment cancer QOL Questionnaire

The EORTC-QLQ-C30 has 9 multi item domains, 5 functional scales (physical, role, cognitive, emotional, social) and 3 symptoms scales (fatigue, pain, nausea and vomiting) (113). It contains a global scale for health and a QOL scale with the time frame of 1 week. There are several single item symptoms scales.

It was initially validated in 305 patients in 13 countries. It takes 11 minutes to complete. Only the functional scale, work and household work failed to meet reliability standards (Cronbach alpha of 0.7 or greater). Intrascale correlations were significant. Each scale appeared to assess distinctly different domains of QOL. It had discriminative validity based on the ECOG performance scale. There were statistically significant changes in the expected direction for physical and role function, global QOL well, fatigue, nausea and vomiting in patients who had either improved or worsened in their performance score. The psychometrics appeared to be consistent across countries and has been validated in terminally ill patients (114).

The measure has also been validated against the Hospital Anxiety and Depression Scale, the Edmonton Symptom Assessment Scale and the WHO-QOL Brief Scale. It has a Cronbach alpha greater than 0.7 in this second study except for social function (0.69), cognitive scale (0.57) and nausea and vomiting (0.69). This study confirmed that it discriminated patient groups by performance score and by treatment and education (115).

A review of 30 studies which used the EORTC-QLQ-C30 found that it improved prognostication by 5–8% over clinical variables alone in many cancers with nausea and vomiting, anorexia, dyspnea, role function and physical function adding to prognostication. Causative items clusters varied by disease. Minimal important differences have been established but these will differ based on the patient population (116).

The EORTC-QLQ-C30 has been adapted for patients in palliative care (EORTC-QLQ-C15-PAL). This questionnaire was reconstructed based on interviews with 44 patients and 66 healthcare professionals in palliative care. Item response theory was used to shorten the scale. Most important items in this modified scale were pain, physical function, emotional function, fatigue, global health status, QOL, nausea and vomiting, appetite, dyspnea, constipation and sleep. Four of the original subscales were shortened to reduce the question burden(117). In a more recent study, the measure was validated in 104 patients. The reliability was 0.7 or greater except for fatigue (0.58). It was found to have convergence validity against the original scale, the Brief Pain Inventory and Beck Depression Inventory Like the original scale, it discriminated performance status (118). One of the most important this scale is that minimal important differences in scale scores which has been established in patients with cancer (73). This questionnaire lends itself to mapping to the EQ-5D to gauge the cost-effectiveness of palliative care interventions.

8.6 EQ-5D

The EQ-5D is a non-disease specific measure which describes health states and value of health related QOL which complements rather than replaces QOL measures (119). The EQ-5D consists of general health description which occurs in 5 domains and is divided into 243 health states plus “unconscious” and “dead”. Utility can be assessed by country specific algorithms. Domains include mobility, self-care, usual activities, pain, comfort, anxiety and depression (120, 121). As mentioned, it comes in a 3 and 5 level response per item questionnaire with the 5 level per item questionnaire less subject to a ceiling effect (122). It also has a vertical 20 cm VAS (visual analogue scale) with anchors “best imaginable “and “worst imaginable” health state (scaled 0–100). The questionnaire is relevant to both the healthy and seriously ill. It generates a single index value. The health state can be rated as even “worse than death” or undesirable as negative values. Utility was established through individual values in certain helps states and through “time trade off” methods which led to the negative values. QALYS was generated by using “time trade off” methods and the VAS scale. It discriminates functional classes which correlate with the Health Assessment Question score (122). The purpose of the EQ-5D is to monitor health status of patients over time, assess the seriousness of conditions or diseases at different times, provide evidence for medical effectiveness in improving health states and provide a measure of cost effectiveness per QALYS. The measure has been used to establish local, regional and national health states (119).

9. Expert commentary

Given that one of the key objectives of palliative care is to improve QOL, it should be measured routinely. There are many QOL questionnaires that have been developed to assess QOL in palliative care. Most have some degree of reliability and validity. What appears to be a significant gap in questionnaires particularly to palliative care is sensitivity to change. Almost no measure has established MCIDs which is critical to interventional studies. Very little has been done in utility or cost effectiveness in palliative care using QOL questionnaires and utility tools. QOL questionnaires can be useful in engaging patients in conversations around areas of their life which are deeply affected by serious illness. Measures are used as outcomes and quality audits but policy makers and payers are interested in utility and cost effectiveness. It will be important in the future that palliative care developed utility measures for health outcomes.

10. Five-year view

Currently, most of the QOL questionnaires in palliative care have fixed number of items. Consolidated effort from the research community is needed to further (1) validate existing QOL questionnaires at various stages along the disease trajectory, (2) define their MCIDs to allow proper power calculation for clinical trials and interpretation of findings, and (3) assess their clinical utility to facilitate cost- effectiveness analyses for various palliative care interventions. At the same time, active efforts are underway to develop newer QOL questionnaires that can be more personalized to the individual’s care goals based on computerized adaptive testing. Such approaches may reduce the number of items required

and thus question burden, and facilitate immediate recording and reporting in the electronic health record. A recent study demonstrated that routine patient reported outcome assessment not only has an impact on QOL but also survival(123). The benefits associated with such intervention will need to be further examined.

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11.

Key issues

- The World Health Organization defines quality of life as “an individual’s perception of their position in life in the context of culture and value system in which they live and in relation to their goals, expectations, standards and concerns.”
- QOL often changes as the disease progresses. Furthermore, an individual’s perception of his/her QOL may also evolve overtime (response shift).
- Palliative care plays an important role in enhancing patient’s quality of life by improving their ability to achieve personalized goals, such as symptom control and social support, while setting realistic expectations through impeccable communication.
- Multiple systematic reviews and randomized controlled trials have found that palliative care referral and specific palliative care interventions improve quality of life among patients with advanced diseases.
- QOL questionnaires may be used to assess patient care needs in clinical settings, provide quality monitoring in health systems, measure clinical outcomes in clinical trials, and estimate utility and cost-effectiveness of clinical interventions.
- Validity and reliability have been assessed for many QOL questionnaires in palliative care. Validity refers to the ability of a questionnaire to accurately assess what is sets out to measure. Reliability refers to the degree to which a questionnaire is reproducible.
- The responsiveness to change and minimal clinical important difference have not been determined for a majority of QOL questionnaires. Responsiveness to change examines the ability of a QOL questionnaire to reflect any improvement or deterioration over time. The minimal clinical important difference specifies what the magnitude of change is clinically meaningful.
- QOL questionnaires may be used to facilitate a utility analyses to assess cost-effectiveness of various interventions. To do this QOL questionnaire scores need to be weighed and transformed into health states to facilitate such analyses. More research is needed in the palliative care setting to assess utility and cost-effectiveness of various interventions.