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Quality of Life Instruments in Oncology

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The objective of this article is to aid clinicians in understanding the current state of the development and application of quality of life (QOL) instruments as outcome measures in cancer clinical research and practice. As a result of the achievements of the past two decades, the concept of QOL has been defined and many reliable and valid measurement tools have been developed. The two main approaches to QOL assessment, psychometric-based and utility-based, are discussed together with a brief description of the strategies for meaningful interpretation of QOL profiles. QOL measures in oncology have the potential to be used to study populations in randomised clinical trials, to aid patient–clinician interactions in routine practice and to support policy decision making and economic evaluation of healthcare provision. © **1999 Elsevier Science Ltd. All rights reserved.**

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INTRODUCTION

DURING THE twentieth century we are witnessing a changing pattern of diseases in developed countries. The major health problems no longer come from acute and infectious diseases, but from chronic diseases that develop, persist, recur and require treatment over a long period of time. This change has led to a fundamental shift in health-related thinking. Health is now seen as the presence of positive physical, mental and social well-being, not merely the absence of disease [1]. Consequently, social scientists and clinicians have become increasingly interested in the measurement of health status, functioning and well-being and in the use of these measures as outcomes in healthcare research and practice [2].

Cancer is no exception to this changing disease pattern. With the advance of oncological science and practice, complex new treatments have been introduced, achieving cure in some, and prolongation of life in many, patients with a common cancer. For many patients, cancer has turned from a rapidly fatal illness into a chronic disease treated over the course of months and years with complex and toxic therapies. Oncology staff are now being required to monitor and address the adverse consequences of cancer illness and treatment on a patient's physical, psychological and social performance. It is becoming essential that outcomes from cancer treatment include measures of quality of life (QOL), as well as survival and objective response to treatment. Healthcare providers and governments in developed countries are increasingly concerned that scarce resources are used effectively and that outcomes are assessed broadly to ensure that choices are made reflecting both survival and quality of life.

The objective of this review is to aid the clinicians in understanding the current state of development and application of QOL measures in clinical research and practice and is not intended to be an exhaustive review of all available tools. It represents the views of physicians who use QOL instruments in their research and practice. We have attempted to describe, briefly and with the minimum of technical language, the theoretical basis for development of QOL tools and have focused on discussing the possible uses of these measures in different clinical situations. Throughout the text key references will be provided to assist readers who need further detail.

DEFINITION OF QUALITY OF LIFE (QOL)

The measurement of such an all-encompassing and subjective concept as QOL has become possible due to extensive contributions from behavioural, psychosocial and health services researchers. QOL has been defined as 'the subjective evaluation of life as a whole' [3] or 'QOL refers to patients' appraisal of and satisfaction with their current level of functioning compared with what they perceive to be possible or ideal' [4]. Both definitions emphasise the subjective and evaluative nature of the concept. There is a general consensus among researchers that QOL is a multidimensional construct

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that includes several key dimensions. At the minimum, QOL instruments should include: physical functioning (ability to perform self-care activities, mobility, physical activities and role activities such as work or housework); disease- and treatment-related symptoms (such as pain, shortness of breath, hair loss); psychological functioning (emotional distress, anxiety, depression); and social functioning (family interactions, time with friends, recreation activities).

More recently, attention has also been paid to spiritual or existential concerns, sexual functioning, body image, satisfaction with healthcare and with the doctor–patient relationship [5–7].

In general, the term QOL encompasses all aspects of patients' well-being and may include the impact of living standards, environmental factors etc. The term health-related quality of life (HRQOL) is more specific and more appropriate to clinical research and practice as it points only to those aspects of life which are affected by healthcare interventions. Therefore, HRQOL can be considered synonymous with subjective health status assessment, a term widely used in the social sciences, health services and general medical literature. The term quality of life (QOL) is more popular in the oncology literature and is extensively used instead of HRQOL or subjective health status. A possible explanation for this discrepancy is that it feels intuitively inappropriate to discuss 'health' in patients suffering from potentially fatal illness. Therefore, in this review we will use the term quality of life (QOL) to indicate health-related quality of life for brevity and consistency with the literature in oncology.

METHODS

There are two main approaches to assessment of QOL outcomes: psychometric-based and utility/preference-based measurement. They will be considered separately.

Psychometric-based measures

Definition, description and instruments. The basic idea of the psychometric theory is that unobservable constructs (QOL domains like physical functioning or emotions) are measured by a collection of representative questions. In practice the respondents are asked to indicate the presence, frequency or intensity of symptoms, feelings or behaviours. The responses to individual questions are aggregated (usually unweighted) to form scales, measuring particular construct or QOL domain. These instruments typically produce several numerical values for different QOL domains and are known as health/QOL profiles. Some questionnaires can also give an aggregated single score or QOL index.

The development of QOL instruments is based on principles of test construction and evaluation. The scope of enquiry must be prospectively defined reflecting the purpose of the measure, the definition of QOL, domains of QOL and possible specific (disease- or treatment-related) areas of interest. Then a common strategy is to generate a large pool of issues, relating to the defined scope of enquiry, from which to derive the most appropriate and sensitive test. The selection of items for the questionnaire is based on patients' as well as on health professionals' views. In the next stage the questionnaire is administered to a larger group of patients to collect data to test its psychometric properties [8, 9]. The instruments must demonstrate reliability, validity and responsiveness to clinically significant changes over time [10].

Reliability refers to the extent to which an instrument is free of measurement error. In practice, reliability is measured by yielding the same results in repeated applications in an unchanged population (test–retest reliability). For questionnaires with separate scales, that is multiple items related to a single dimension, another form of reliability called internal consistency, is important. This is assessed using Cronbach's coefficient alpha representing the degree to which items within a single scale are associated with one another. An alpha coefficient of above 0.80 is considered optimal for instruments intended to be used for group comparisons [11]. Validity is defined by the extent to which an instrument measures what it is supposed to measure, and refers to the degree of non-random or systematic bias. The above properties of the QOL instruments can usually be found in the reports describing the initial development and testing of the instruments or in their manuals.

A large number of well-constructed and psychometrically valid QOL questionnaires have been developed and are available for use with patients with cancer. These include generic measures of QOL and health status that have been used for non-cancer medical patients, instruments that have been especially developed for general cancer populations (cancer condition-specific) and cancer site-specific or treatment-specific instruments. Questionnaires designed to measure specific dimensions of QOL are often added to those in detailed studies, for instance, of anxiety and depression. Table 1 provides a few examples of commonly used measures in oncology. Researchers facing the difficult choice of a QOL instrument from the confusingly wide variety available, might find it useful to start with the now available compilations of QOL instruments. They are reference compendiums that usually provide brief information on the developmental history of the measures, target populations, examples of the questions and contact details [26, 27].

Generic, cancer condition-specific and cancer site-specific instruments have advantages and disadvantages and must be evaluated within the context of each particular study. Generic instruments allow comparisons to be made across conditions, but may not focus on the area of interest for a specific intervention. Disease- and site-specific instruments are likely to be more responsive to change, but are not comprehensive. Therefore, some researchers recommend that the approach to QOL measurement in cancer clinical trials should be inclusion of a more general 'core' questionnaire supplemented by a site-specific or even 'trial-specific' module or checklist of questions, constructed to address specifically the purpose of the trial [28].

The instruments included in Table 1 all have published development histories and share a number of additional characteristics that measurement specialists agree are essential for assessment in the cancer setting. They are all self-administered, multidimensional, relatively brief (taking less than 15 min to complete), with good reliability, validity, sensitivity to change and acceptability to patients.

From the above listed questionnaires, two relatively new instruments—the European Organization for Research and Treatment of Cancer (EORTC) QOLQ-C30 and the FACT-G, have received growing attention in the research arena and appear to be excellent candidates for broader use in other clinical settings [29]. In addition to their rigorous development, these instruments share a common format in that they contain a generic or core set of questions that can be

Table 1. *Examples of instruments for measuring QOL in cancer patients*

Generic instruments that may be used in oncology	Medical Outcome Study (Short Form) MOS SF-36 [12] Nottingham Health Profile (NHP) [13] Sickness Impact Profile (SIP) [14]
Cancer (condition) specific instruments	Cancer Rehabilitation Evaluation System—Short Form (CARES-SF) [15] EORTC Core QOL Questionnaire (EORTC QLQ C-30) [16] Functional Assessment Of Cancer Therapy (FACT) [17] Functional Living Index—Cancer (FLIC) [18] Linear Analogue Self-Assessment (LASA) [19] Linear Analogue Self-Assessment (LASA) [20] Rotterdam Symptom Checklist (RSCL) [21] Spitzer QOL Index (QOLI) [22]
Cancer site-specific instruments	Breast Cancer Chemotherapy Questionnaire (BCCQ) [23] EORTC Lung Cancer Module (EORTC QLQ-LC13) FACT-breast, bladder, bone marrow transplantation (BMT), colorectal, head and neck, lung, ovarian, prostate, HIV.
Psychiatric diagnostic tools	Hospital Anxiety and Depression Scale [124] General Health Questionnaire [25] Zung Depression Scale [24]

augmented by site-specific modules. This modular approach to QOL measurement in cancer was developed by the EORTC QOL Study Group [30] who in 1986 set out to develop an assessment tool to monitor the QOL of patients entered onto international clinical trials. The resulting generic cancer measure is known as a 'core' questionnaire—EORTC QLQ-C30 and is currently widely used in clinical trials [16]. Site-specific modules incorporating questions addressing disease- and treatment-specific problems have been developed for lung, breast, head and neck, colorectal, oesophageal, pancreatic cancer and multiple myeloma [8, 9]. In a parallel effort in the U.S.A., Cella and colleagues have developed a QOL measurement system which is referred to as the Functional Assessment of Cancer Therapy (FACT) scale [17]. Recently it has been extended to include a questionnaire for other chronic diseases and renamed the FACIT system (Functional Assessment of Chronic Illness Therapy). It has site- and treatment-specific modules for breast, bladder, brain, colorectal, cervix, oesophageal, head and neck, lung, ovarian, prostate and pancreatic cancer patients, as well as those with anaemia, fatigue or undergoing bone marrow transplant and biological treatment.

At the end of the table, we have included examples of several psychiatric diagnostic tools. These instruments have a longer developmental history than many QOL questionnaires. They were constructed and validated in the 1960s–1970s as self-report screening instruments for mood disorders and were later demonstrated to be useful and valid in cancer populations [31, 32]. Strictly speaking, they should not be classified as QOL instruments because they measure only one QOL dimension [33]. However, unlike the multidimensional QOL instruments which are largely descriptive tools, the psychiatric questionnaires have the unique property of being able to identify potential cases of depression or anxiety.

Clinical meaning of QOL results and interpretation strategies

The QOL instruments have been developed as descriptive research tools and their relative novelty makes the clinical interpretation difficult, both for absolute scores and differences in scores. At the same time this issue is of crucial importance if we want to make the transition from studying QOL in the research setting to incorporating QOL assessment across the course of care of individual patients. Exceptions are the above-mentioned psychiatric diagnostic tools, the results of which have easily understandable clinical and practical meaning. These questionnaires can function like other routine tests used in clinical medicine (for example haemoglobin concentration, hormone levels, X-rays, etc.). Threshold levels for the identification of potential cases of pathological psychological distress have also been suggested for the emotional functioning scales of SF-36 and RSCL [31, 34, 35]. However, the clinical meaning of scores on newer concepts such as level of physical activity, social functioning, or even severity of symptoms is far from clear. Furthermore, the research in this area has been hampered by the lack of a 'gold standard' against which to calibrate the new measures.

In recent years, several important methodological steps have been made towards making the interpretation of QOL scores more meaningful and understandable to the medical professionals. The minimal clinically important difference in QOL scores have been defined as "the smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side-effects and excessive cost, a change in the patient's management" [36]. Different methods for determining the clinical meaningfulness of QOL scores have been investigated. They can be divided into two broad categories: distribution-based and anchor-based interpretations [37].

In the anchor-based interpretations the changes seen in QOL measures are compared, or 'anchored', to other clinical changes or results [36, 38, 39]. This approach is appealing to clinicians and is likely to have an impact on their understanding and interpretation of QOL results. It can also be expected that as QOL assessment becomes more common in clinical settings, intuitive familiarity will develop both through individual and collective experience, as has occurred for more established measures of disease activity and severity.

The most commonly used distribution measure is the effect size in which the importance of the change is scaled by comparing the magnitude of the change to the variability in stable subjects [40]. There are different ways of calculating effect sizes but, for example, one approach is to divide the

observed change in scores over time by the standard deviation of the baseline scores. The resulting number between 0 and 1 is empirically interpreted according to Cohen's operational definition as small = 0.20, moderate = 0.50 and large = 0.80 [41]. Another common approach is to use reliability coefficients to calculate standard error of measurement and 95% confidence intervals (CI) around individual scores [42]. The norms-based interpretation compares the particular individual or group scores with the distribution of the instrument scores in different populations characterised by known criteria, including general population, gender, age ranges, diagnosis, clinical severity groups, etc. [43]. Normative data from large population samples from different countries are available for SF-36 and the developers recommend its use together with 95% CI around individual patient scores [44]. From the cancer-specific instruments, interpretative information is available for EORTC QLQ-C30. King summarised 14 studies using EORTC QLQ-C30 and suggested effect-size based guidelines for interpretation of the clinical relevance of QOL scores [45]. The interpretation of the clinical significance of QOL scores can be facilitated by the reference data in the general Norwegian population and Danish women [46, 47]. A study of the subjective significance to the patients of changes in QOL scores using the EORTC QLQ-C30 has suggested that a mean change of 5 to 10 on the multi-item scales is perceived as 'a little' change, 10 to 20 as 'a moderate' change and greater than 20 as 'very much' change [48].

Uses of QOL assessment

QOL measures have the potential to be used to study populations in clinical trials and practice and to aid patient–clinician interactions and clinical decision making [49].

Clinical trials. The initial and subsequently most wide application of QOL instruments in oncology has been in clinical studies—both descriptive and randomised trials. Descriptive studies have suggested that QOL scores may have prognostic significance in advanced cancer. This has been shown separately in several different types of cancer and with a range of different validated self-reported multidimensional QOL instruments [50–55]. In general, poor QOL has been associated with shorter survival in univariate analysis. The prognostic significance of the QOL scores remains after allowance for conventional prognostic factors, including performance status, suggesting that the QOL scores bring additional unique prognostic information. These findings provide the most powerful evidence for the external validity of the QOL instruments and may have important implications for the stratification of patients into prognostic groups in future clinical trials.

In randomised clinical trials QOL generally has been used as a secondary outcome measure in addition to traditional measures such as objective response to treatment and survival. A number of early clinical trials yielded interesting results which stimulated further research. These studies showed that more aggressive anticancer treatment can be associated with improved QOL when compared with less intensive treatment, even in the palliative setting and despite toxicity [56, 57]. Patients were observed to report improved QOL even when no traditional objective response was detectable and there was no survival benefit [58]. The last finding formed the basis of the move to design and conduct clinical trials of palliative anticancer treatment with QOL as a primary endpoint [59, 60]. In recent years the number of clinical trials incorporating QOL measures has substantially increased. Many clinical trials groups in Europe, the U.S.A. and Canada adopted policy statements encouraging the use of QOL evaluations in research protocols [61–64]. The methodology for measuring QOL in clinical trials must be as robust as the methodology used for more traditional outcomes. This is not a simple task. It requires a clear understanding of the reasons for measurement with the a priori stated research hypothesis and the purpose to which the data will be described. The data collection involves extensive initial organisation and training of data managers. Several papers published in the last 2–3 years provide guidelines on how to design, organise, analyse and standardise reporting of clinical trials with QOL as primary or secondary outcome [65–67]. The interpretation of the findings of clinical trials with QOL endpoints remains a challenge. Researchers' intuitive beliefs and judgements of QOL would inevitably influence the inferences they make about their research findings and the implementation of rigorous scientific methods in QOL research is of critical importance [68].

Clinical practice. One of the accomplishments of the 'QOL movement' at the level of individual patient–physician interaction has been to encourage rethinking of values to be taken into account in clinical decision making. It led to increased awareness of the many effects of the disease and its treatment on patients' lives and to increased attention to the communication skills needed for achieving inclusion of patients' views into shared decision making [49, 69–71]. The role of formal QOL measurement for individual patients in routine clinical practice, alongside traditional clinical, instrumental and laboratory examinations, is not yet established [72].

The potential use of QOL instruments in clinical practice can be viewed in two ways. One is identification of cases of pathological distress using psychiatric diagnostic tools and the other is providing descriptive information on multiple QOL domains through the application of multidimensional instruments. Both applications can provide information over time and thus help monitor problems.

There is now ample evidence that medical professionals underestimate patients' psychological distress and may fail to detect cases with clinically significant depression or anxiety [73]. Screening questionnaires for psychological distress increase the likelihood of identifying patients who might require specific interventions [74, 75] and may augment the doctor–patient relationship [76]. Although we know that the performance of these measures is superior to the detection rate of doctors and nurses [77], they are rarely used in routine clinical practice [78].

The situation with the use of multidimensional QOL instruments in clinical practice is similar. Clinicians probably address QOL issues informally in their daily practice, but it is not known how systematically clinicians ask QOL questions, what they ask and to what extent the answers are incorporated into treatment decisions. Formal assessment of QOL of individual cancer patients in everyday clinical practice may provide clinicians with additional information, which may help earlier detection of morbidity and earlier intervention, and it may also facilitate communication between oncologists and their patients. However, there is little systematic research addressing these questions.

Several barriers have hampered the practical use of QOL measures for individual patients including: the logistic barrier and cost of collection and analysis of large amounts of data;

the conceptual barrier of determining the clinical meaning of QOL scores; the theoretical concerns whether instruments developed for group comparisons can be used for individual patients; and the lack of research data on the possible benefits for the individual patients [79, 80].

Current information technology makes it possible to use QOL questionnaires in electronic format [81, 82]. Data can be collected, stored and scored automatically, allowing the doctors to have immediate information about their patients' present QOL as well as cumulative QOL information from previous clinic visits. Individual patients' QOL profiles can be presented in a meaningful format, similar to that of other widely used laboratory and instrumental tests. The computer-based administration of standard QOL instruments in a hospital and outpatient clinic setting is well accepted by a wide range of patients [83]. With the wider use of the Internet the administration of electronic QOL questionnaires may potentially be extended to patients' homes.

There is a clear need for more research on the possible benefits of QOL measurement as an intervention in itself before its use is widely recommended. Several studies were conducted in patients with chronic diseases outside oncology, addressing the impact of patient-based health status reports on patients' care and QOL [84–89]. Those studies suggested that the health status reports provided accurate and useful information, facilitated communication, but in general did not improve patients' functional status and QOL. The only published study in oncology addressed the feasibility of introducing individual QOL assessment using a general cancer questionnaire (EORTC QOLQ-C30) into the daily routine of an outpatient oncology clinic and the potential impact of such assessments on doctor–patient communication [90]. The results were encouraging, confirming the feasibility of the procedure and suggesting that the intervention appeared to stimulate physicians to initiate discussions on specific aspects of the health and well-being of their patients.

Population level and policy decision making. At this level a key issue was the recognition that QOL is an important and valid outcome which should be incorporated into programme evaluation and resource allocation. A critical impetus for inclusion of QOL considerations in policy decision making was the 1985 statement by the Food and Drug Administration (FDA) that QOL should be considered one of two requirements for approval of new anticancer agents [91]. An example of QOL information affecting policy is the introduction of erythropoietin for patients on chronic renal dialysis in Canada and subsequent political decisions about its funding from the government-managed healthcare system [92]. Of course new drugs are not inexpensive and policy decision-makers need to weigh the costs against the benefits of the interventions. Psychometric QOL measures are less suitable for this purpose and utility-based measures with cost–utility analysis are preferable. They will be discussed in detail separately.

The psychometric measures of QOL, however, can be very useful to describe morbidity at population level and to monitor changes in morbidity as an additional outcome when assessing the effect of medical interventions or service delivery interventions. With the wider use of electronic methods of QOL data collection it is practically feasible to incorporate QOL indicators into large databases (such as Cancer Registries).

The future of psychometric measures—computer-adaptive assessment of health status

The QOL questionnaires have been developed for assessment of groups of respondents. They use a fixed set of questions, regardless of how appropriate any specific item is for a given individual respondent. The items are selected to represent a moderate range of activities/symptoms at a moderate level of difficulty/severity. This leads to several problems such as burdening some patients with questions irrelevant to their present condition and still not addressing problems specific and relevant to the individual patient. Modern psychometric methods like Rasch models and the Item Response Theory have great potential to achieve precise and efficient measurement of health status at individual patient level [93, 94]. The basic idea of these methods is that a particular response to a particular item depends on the type of item (item 'difficulty') and on the underlying (latent) health status (person's 'ability'). Both item 'difficulty' and respondent's 'ability' is measured on the same scale or 'ruler'. Combining the Item Response Theory with a computer algorithm allows individualised selection of items to provide the most precise information for the particular respondent and to score all items on a common scale. For example, the computer-adaptive assessment of a particular health status domain will start with one item, usually with moderate 'difficulty', the response to which will be used as an initial estimate of the respondent's score. On the basis of that estimate, the computer selects the next item which will be the most useful in achieving an accurate score. In the next step, the response to the second item is used to select item 3 until a preset level of precision is reached. The main requirements for the technique are (1) construction of the item bank with a large number of questions within different domains of interest; (2) calibration of items; and (3) computer assisted administration [95].

The advantages of computer-adaptive QOL assessment are numerous: individually tailored questionnaires, precise measurement of specific domains, reduction of test time, rapid scoring and feedback of results, comparability of scores across studies and diseases. Computer-adaptive testing so far has been applied successfully for educational and aptitude tests. Its application to health status assessment is still in the early stages of research, but it certainly has the potential to produce more precise and efficient QOL measures in the not so distant future. The Item Response Theory can also be applied for testing the cross-cultural equivalence of questionnaires and for the comparison and scoring of different QOL questionnaires on the same ruler [96].

Interactive computer systems can be used in a more simple way to collect patient-specific information. Patients can be asked to choose their most important problems from a list of symptoms and functional impairments and further questions can be then asked to assess the frequency and severity of the problems. This approach is identical in principle to the medical interviewing systems, but with additional structured questioning on functional, emotional and social issues [97]. We are currently in the initial phases of evaluating this approach using derived domains from standard QOL instruments. Combining standard QOL questionnaires with branching questions for more precise evaluation of problem areas has the potential to increase the sensitivity and the clinical usefulness of the data for the individual, reduce the time for completion and at the same time allow for standardised scores and comparisons within and between patients.

UTILITY-BASED MEASURES

Definition and description

Health utility measures were originally devised for use in the economic evaluation of healthcare provision [98]. For this purpose a QOL measure was required which can produce a single index, capable of comparing one QOL/health state to others and ideally applicable across different healthcare fields [99]. This requirement is distinct from the psychometrically derived health status profiles, which are more descriptive and more often disease-specific as described above.

Utility assessment has its roots in the mathematical decision theory which characterises how a rational individual should make decisions when faced with uncertain outcomes. Utility values are numbers that represent the strength of an individual's preference for a particular health state under conditions of uncertainty [100]. Utility is expressed as a single value between 0—the poorest imaginable health (often death), and 1—perfect health. This can then be used to describe the usefulness (the derivation of the term utility) of health gains or losses which result when medical interventions prolong life, influence the quality of life, or both.

In deriving utilities the task is to present people with imaginable health states, and to allow them to express their relative preferences comparing these states with others [100]. Deriving preferences has been a difficult area of methodology for some years [101]. Utilities may be measured by means of one of several techniques (summarised in Table 2). Some researchers divide them into two categories: utility measures truly based on the decision theory and preference measures which use rating scales. The utility measures are methodologically advantageous as they have interval scale properties, but their concept may be difficult for many people to understand. The rating scales elicit preferences, which are similar to measuring the importance and the value a person explicitly places on a health state or QOL dimension. Preference methods are simple to understand, are clearly linked to patient-reported values, are less time-consuming and thus less costly, but they do not necessarily have interval properties [102]. Utility values can be similar internationally using consistent techniques and populations [103]. However, different techniques yield differing results for many reasons including the place of uncertainty, the complexity of the task of valuing health states, and the imprecision of individual estimates [104, 105].

Utility scores may be generated by patients, clinicians or the general population. The choice of sample population to value health states has proved controversial. The patient population has experience of particular health states, but their utilities are not comparable with those from another sample, hence less helpful for policy decision making. Those with illness hold very different views from those without in their preparedness to take risks [106]. The 'well' are also a heterogeneous group, so different population sizes and types yield very different results [107]. Utilities derived from the general population aim to represent a societal perspective in healthcare decision making [108]. The duration of health states, which health state precedes and follows another, and the interaction with other events in life (having a young family for example), may also influence the utility of health states [109].

In practice, health utility can be assessed by using measures with population-based utilities already derived for the described health states. They include the EuroQol [110] and the Index of HRQOL [111]. There is a clear need for more [112]. Another approach is to derive utilities specific to the health states in the study in question, but this is a complex and time-consuming task [100]. Using prior derived utilities is a more feasible approach [113]. Utilities can be derived from psychometric measures with a good example being the work with SF-36 [99].

Uses of health utility measures

Health utility measures combined with the time course of disease generate a quality of life adjusted outcome expressed as Quality-Adjusted-Life-Years (QALYs). QALYs are used as indicators of effectiveness that combine the impact of morbidity and mortality. A single Quality-Adjusted-Life-Year (QALY) is 1 year of life in a health state with utility 1.0, or 2 years on a state with utility 0.5, 10 years at 0.1, etc. This can then be used as the unit of outcome measurement in randomised clinical trials for comparison of quality-adjusted survival (Q-TWiST) or used in cost–utility analysis. The value of such an approach remains controversial with some doubting the usefulness of single utilities to describe multidimensional concepts like QOL.

Q-TWiST analysis is Quality-Adjusted Time Without Symptoms and Toxicity. This is not an economic analysis, but another approach to including the concept of QOL in measuring outcome. From Kaplan–Meier survival analysis the time spent in each of three health states is summarised—time with treatment toxicity, time without symptoms or toxicity (TWiST), and time with disease symptoms after relapse

Table 2. Techniques for obtaining utilities

Methods	Description	Notes
I. Rating scale methods		
Anchored analogue scales	If you had physical function A and emotional function B, how would you place your QOL on this scale from death to perfect health?	The EuroQol Thermometer is an example [103]
Magnitude estimation	How many times worse is it to have health state A than B?	
II. Based on decision theory		
Time trade-off	How long in good health would you trade for period A with QOL profile B?	Various forms exist
Standard gamble	What risk of immediate death would you accept to escape from health state A to perfect health?	Used in developing utilities for the SF6D derived from the SF-36 [99]. Probably fits best with utility theory.

[114]. These times can then be adjusted according to health utility estimates for QOL in each phase. Thus, a new survival time is calculated which is quality-of-life adjusted and then can be used in subsequent analysis [115]. The method was originally developed for assessment of the effectiveness of adjuvant chemotherapy in breast cancer [116]. A good example of its use is also a randomised trial of high-dose Interferon Alpha with observation in resected high-risk melanoma. The interferon arm had a longer relapse-free interval than the observation arm, but had substantial toxicity [117]. The overall benefit of this therapy was thus tied up in this balance. Q-TWiST analysis based on hypothetical extreme values of utility for toxicity and relapse, showed benefit for the interferon arm and thus provided support for the continuing use of adjuvant interferon at that time.

Usually the economic evaluation of medical interventions is expressed as cost per saved person's life or per year of extension of life. Combining utility measures such as QALYs with the cost of medical interventions gives cost–utility analysis. It is increasingly considered in cancer clinical trials by healthcare decision-makers who want to balance cost and benefits when allocating resources. One example of a clinical trial using cost–utility analysis is the study of effectiveness of adjuvant radiotherapy after conservative surgery when compared with surgery alone for stage I breast cancer. Radiation was associated with lower local relapse rates and better QOL, but higher costs [113]. Each observed outcome QOL state carried a utility, which had earlier been explicitly recorded in breast cancer patients. The benefit was expressed as years without recurrence adjusted for the utility and the costs were calculated for both arms. The results of the trial estimated the cost per QALY gained from radiotherapy of between US$ 88 000 and US$ 144 000. These costs per QALY are high, but are similar to others in breast cancer adjuvant therapy. The findings of the study are considered to support the continuing practice of adjuvant radiotherapy, but the authors emphasise that better selection of patients who are most likely to benefit is important in reducing the costs.

Economic evaluation is increasing in its prominence [118, 119], but remains controversial on ethical and political grounds [120]. However, in times when healthcare systems have to deal with the ever increasing costs of medical intervention, valid assessments of both patient-centred benefits and costs are important for rational allocation of resources.

Comparison of health utility-based QOL measures with psychometric instruments

Measuring HRQOL using psychometric techniques aims particularly to describe changes in health status to allow comparisons, aid communication and assist decision-taking, whereas for utility analysis the priority is valuation and allocation of resources. Health utility measures are usually generic, not disease-specific, intentionally to permit comparisons across different fields in healthcare. Disease-specific measures are potentially more sensitive in discriminating HRQOL in homogeneous populations with disease-specific problems as in the typical randomised phase III efficacy trial [121].

The simplicity of the utility measures and the judgements supplied with them can appeal to some clinicians and economists, but in essence the psychometric and evaluative measures of QOL differ in premise and technique. When compared they co-vary only moderately [105]. There is research into the unification of psychometric and economic principles [99, 122], but combination in a single measure could detract from both purposes [123], and perhaps each would be better chosen to address research aims, or in combination if necessary.

In summary, as a result of the achievements of the past two decades, nowadays we have many reliable and valid tools to evaluate QOL of patients with cancer. The development of QOL methodology continues towards more precise assessment using computer adaptive testing, implementation of electronic methods for data collection, integration of health profile measurement and patient preference weighting, rigorous statistical analysis and meaningful interpretation of QOL data. In parallel, we have observed increasing application of QOL instruments as outcome measures in clinical trials and growing interest in their use to aid patient–clinician interaction and policy decision making. The scientific rigour of QOL research will determine the extent to which the resulting data are accepted by clinicians, policy-makers and the public.

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