PATIENT ACTIVITY IN COPD

Quality of Life: Concept and Definition

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ABSTRACT

This paper will consider 4 topics: (1) the definition of health-related quality of life, (2) the measurement of health-related quality of life, (3) the relationship between exercise and health-related quality of life in the general population, and (4) the relationship between exercise and health-related quality of life in patients with COPD. The paper presents data from the National Health Interview Survey, the San Diego COPD Rehabilitation Trials, and the National Emphysema Treatment Trial (NETT).

INTRODUCTION

Evidence-based reviews suggest that patients with chronic obstructive pulmonary disease (COPD) benefit from exercise and rehabilitation programs (1). Benefits include reduced physical and psychological symptoms (2), improved exercise tolerance (3), fewer hospitalizations and physician visits, and more gainful employment (4). It has been argued that exercise enhances quality of life among COPD patients (5). However, there are a variety of different definitions and measures of life quality. The purpose of this article is to review the definition and measurement of health-related quality of life and to summarize some of the quality of life outcomes in our research program.

Methodologies to evaluate outcomes in chronic disease differ from those used for the assessment of acute disease. Treatments for acute disease, particularly infections, often involve identification of the etiology and eradication of the problem leading to a complete cure. In chronic diseases, which are never cured, the therapeutic goal might be to reduce disease burden. Biological tests used to assess acute diseases usually offer an incomplete picture for patients with COPD. Evaluating the impact of chronic disease requires a different set of tools (6). Patient interpretation, adaptation and behavioral response are of great clinical importance. We have argued that assessment of outcomes in COPD requires a different conceptualization known as the Outcomes Model (7, 8). In contrast to the Traditional Biomedical Model that requires identification of basic disease mechanism, the Outcomes Model emphasizes all medical and social factors that may affect the patient. Sometimes, the exact biological explanation for disability is unknown. For example, quality-of-life (QOL) outcomes in patients with pulmonary disease are not well predicted from measures of pulmonary function (7). The Outcomes Model accepts that biologic pathways may never be fully understood (9).

Definition of health-related quality of life

Diseases and their consequent manifestations are important for two reasons. First, illness may shorten life expectancy. In other words, those with specific diseases may die prematurely. Second, diseases may cause dysfunction, as well as symptoms, that lead to disabilities in an individual’s performance of usual activities of daily living. Clinical studies typically refer to health outcomes in terms of mortality (death) and morbidity (dysfunction) and sometimes to symptoms (10).

Over the last 30 years, medical and health services researchers have developed new quantitative methods and measures to assess levels of wellness. These measures are often called quality-of-life measures. Since they are generally used exclusively to evaluate health status in individuals with medical disorders that impair everyday functioning or cause symptoms, we prefer the more descriptive term “health-related quality of life” (11).

Figure 1 summarizes the number of publications under the topic of quality of life identified in PubMed between 1972 and 2005. In 1972, PubMed did not identify any publications under...
the “quality of life” topic heading. However, over the next 30
years, the number of articles that use the “quality of life” key-
word phrase grew dramatically. In 2005, PubMed identified 5345
such articles. In one year from 2004 to 2005, the number of arti-
cles listed under the quality of life keyword grew by 10% (over
600 articles). This rate of growth has been consistent for several
years. Quality of life is now a common outcome in studies of
patients with chronic lung disease. A PubMed search of all years
crossing COPD with quality of life (in January 2007) yielded
1607 references. Adding the term “rehabilitation” still leaves
567 citations.

**Measurement of quality of life**

Quality-of-life (QOL) measures are valuable for clinical stud-
ies for several reasons. First, QOL measures are used to quan-
tify the impact of a condition and to compare the effects of lung
diseases with the consequences of other chronic medical prob-
lems. Second, QOL measures can be used to evaluate changes
resulting from therapeutic intervention or the course of disease.
Third, QOL measures are necessary as a central component of
cost/effectiveness analysis (5). We will address each of these
issues in the following sections. We will first consider the ration-
ale behind common measures that have been used to quantify
health-related quality of life (7, 12–14).

**Distinctions among measures**

Table 1 lists some of the many measures for evaluating quality-of-life outcomes in studies of patients with lung dis-
ese. The table makes several distinctions between measures.
There are two major approaches to quality of life assessment:
profile and decision theory. The psychometric approach is used
to offer a profile summarizing different dimensions of quality
of life. The best-known example of the psychometric tradition
is the Medical Outcomes Study 36-Item Short Form (SF-36)
(15). The SF-36 includes 8 health concepts: physical function-
ing, role-physical, bodily pain, general health perceptions, vi-
tality, social functioning, role-emotional, and mental health. In
addition, a mental health summary score and a physical health
summary score can be calculated.

The decision theory approach attempts to weigh the differ-
ent dimensions of health in order to provide a single expres-
sion of health status. Supporters of this approach argue that

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<th>Measure</th>
<th>Targeted Measures</th>
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<tbody>
<tr>
<td>Chronic Respiratory Questionnaire</td>
<td>Profile</td>
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<td>UCSD Shortness of Breath (SOBQ)</td>
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<td>Decision Theory</td>
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<td>Quality of Well-being Scale (QWB)</td>
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<td>Health and Activities Limitations Index (HALex)</td>
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![Figure 1. Frequency of articles identified using the keyword “Quality of Life” in PubMed data base between 1972 and 2005.](image-url)
psychometric methods fail to consider that different health problems are not of equal concern. A minor itch is a symptom and coughing up blood is also a symptom. However, the importance of a minor itch and coughing blood are not equal. Simple symptom counts may miss the severity or impact of more serious complaints. A cough, for example, might result in a low overall score if it disrupts usual activities of daily living.

In an experimental trial using the psychometric approach, some aspects of quality of life may improve while others may worsen. For example, a medication might reduce coughing, but increase skin problems or reduce energy. When components of outcome change in different directions, an overall subjective evaluation is often used to integrate the components and offer a summary of whether the patient is better or worse off. The decision theory approach attempts to provide an overall single measure of quality of life that integrates subjective function states, preferences for these states, morbidity, and mortality. The profile methods do not offer a single number that is indexed between death and perfect health.

In addition to the distinction between psychometric and decision theory approaches, measures can be classified as either generic (top of Table 1) or disease targeted (bottom of Table 1). Generic measures can be used with any population, while disease targeted measures are used for patients with a particular diagnosis. Finally, measures can be separated by the purposes of their use. Most measures can be used to characterize populations and to study clinical changes. However, cost-effectiveness analysis requires a generic measure of benefit that scales outcomes on a metric ranging from death to perfect health. Thus, only generic, decision theory based measures can be used to evaluate cost-effectiveness.

A more detailed discussion of the different measures is available elsewhere (5). Readers interested in more detailed reviews may also consult Shumaker and Berzon (16), Walker and Rosser (17) and McDowell and Newell (18). The American Thoracic Society maintains a website (www.atsqol.org) that summarizes quality-of-life measures that can be used in outcomes research for lung disease. The site lists measures by disease and offers references on their use.

The next sections concentrate on example generic and disease specific measures that have been applied in our research program.

**Decision theory approaches**

Some approaches to the measurement of health-related quality of life combine measures of morbidity and mortality to express health outcomes in units analogous to years of life. The years of life measure can be adjusted for diminished quality of life associated with diseases or disabilities (19).

Measures of health outcome should consider future as well as current health status. Lung cancer, for example, may have very little impact on current functioning but may have a substantial impact on life expectancy and functioning in the future. Today, a person with a malignant tumor in a lung may be functioning very much like a person with a chest cold. However, the cancer patient is more likely to remain or become dysfunctional, or to die prematurely. Comprehensive expressions of health status need to incorporate estimates of future outcomes as well as to measure current status (9).

Quality of life data can be used to help evaluate the cost-effectiveness or cost/utility of health-care programs. Cost studies have gained in popularity because health-care costs have grown so rapidly in recent years. Not all health-care interventions equally return benefit for the expended dollar. Objective cost studies might guide policymakers toward an optimal and equitable distribution of scarce resources. Cost-effectiveness analysis typically quantifies the benefits of a health-care intervention in terms of years of life, or quality-adjusted life-years (QALYs). Cost/utility is a special use of cost-effectiveness that weights observable health states by preferences or utility judgments of quality (20). In cost/utility analysis, the benefits of medical care, surgical interventions, or preventive programs are expressed in terms of common QALYs (21).

If a man dies of COPD at age 60 and we expected him to live to age 80, we might conclude that the disease precipitated 20 lost life-years. If 100 men died at age 60 (and also had a life expectancy of 80 years), we might conclude that 2000 (100 men × 20 years) life-years had been lost. Yet, death is not the only relevant outcome of lung disease. COPD might also cause long term consequences and diminished quality of life. Quality-adjusted life-years take into consideration such consequences. For example, a disease that reduces quality of life by one-half will take away 0.5 QALY over the course of each year. If the disease affects 2 people, it will take away one year (2 × 0.5) over each year. A medical treatment that improves quality of life by 0.2 for each of 5 individuals will result in the equivalent of 1 QALY if the benefit persists for one year. This system has the advantage of considering both benefits and side effects of programs in terms of the common QALY units.

Of the several different approaches for obtaining quality-adjusted life years, most are similar (22). The most commonly used methods are the EuroQol (EQ-5D), the Health Utilities Index (HUI), the Quality of Well-being Scale (QWB), and the Health and Activities Limitations Index. In this report, we emphasize the Quality of Well-being Scale because it has been applied most often in outcomes studies of COPD patients.

**Quality of well-being scale**

The QWB combines preference-weighted values for symptoms and functioning. The preference weights were obtained by ratings of 856 people from the general population. These judges rated the desirability of health conditions in order to place each on the continuum between death (0.00) and optimum health (1.00). Symptoms are assessed by questions that ask about the presence or absence of different symptom complexes. Functioning is assessed by a series of questions designed to record functional limitations over the previous 3 days, within three separate domains (Mobility, Physical Activity, and Social Activity). The 4 domain scores are combined into a total score that provides a numerical point-in-time expression of well-being that ranges.
from zero (0) for death to one (1.0) for asymptomatic optimum functioning.

The QWB has been used in numerous clinical trials and studies to evaluate medical and surgical therapies in conditions such as chronic obstructive pulmonary disease (23), HIV (24, 25), cystic fibrosis (26, 27), diabetes mellitus (28), atrial fibrillation (29), lung transplantation (30), arthritis (31, 32), end-stage renal disease (33), cancer (34), depression (35, 36), and several other conditions (22). Further, the method has been used for health resource allocation modeling and has served as the basis for an innovative experiment on rationing of health care by the state of Oregon (37, 38). Studies have also demonstrated that the QWB is responsive to clinical change derived from surgery (30) or medical therapies in conditions such as rheumatoid arthritis (39), AIDS (25) and cystic fibrosis (26). The self-administered form of the QWB (QWB-SA) was developed more recently. It has been shown to be highly correlated with the interviewer-administered QWB and to retain the psychometric properties (40). General information about the QWB can be found at: [http://orpheus.ucsd.edu/famed/hoap/MEASURE.html](http://orpheus.ucsd.edu/famed/hoap/MEASURE.html)

**Integrating cost with outcome data**

While treatment programs provide health benefits, they also have costs. Resources are limited, and good policy requires that they be used wisely. Methodologies for estimating costs have now become standardized (21). From an administrative perspective, cost estimates include all costs of treatment and any costs associated with caring for side effects of treatment. Typically, economic discounting is applied to adjust for using current assets to achieve a future benefit. From a social perspective, costs are broader and may include, for example, costs of family members staying off work to provide care. Comparing treatment programs for a given population with a given medical condition, cost-effectiveness is measured as the change in costs of care for the program compared to the existing therapy or program, relative to the change in health measured in a standardized unit such as the quality-adjusted life year (QALY). The difference in costs over the difference in effectiveness is the incremental cost-effectiveness and is usually expressed as the cost/QALY. Since the objective of all therapeutic interventions is to produce QALYs, the cost/QALY ratio can be used to show the relative health benefits from investing in different programs (22).

Rehabilitation service providers must compete with other health care providers for limited resources. In order to compete successfully, it will be necessary to document that behavioral services provide a benefit to the consumer. One of the advantages of using QALY outcomes is that the common metric allows for comparisons among very different types of services. All providers in the health-care system have the common objectives of increasing length of life and improving quality of life. General quality-of-life outcomes, such as QALYs, allow evaluations of the relative value of investing in each of these specialties in comparison to the resources that they use. Several different governments have proposed allocating resources based on formal cost-effectiveness evaluations (38). For example, the Australian government now requires evidence of effectiveness, as do a variety of European governments. In Ontario Canada Quality-Adjusted Life Years have been considered as a basis for formulary decisions (41). Similar proposals have been considered in the United Kingdom (42). The use of QALYs has increased dramatically in recent years. Just a decade ago QALYs were rarely cited in the medical literature. Today, QALYs are identified in nearly 300 articles per year.

For most clinical outcome studies, it is advisable to include disease-targeted approaches in addition to generic measures of health outcome. These measures are typically more sensitive to changes in a particular disease or illness process. One example of a measure designed specifically for COPD patients is the UCSD Shortness of Breath Questionnaire.

**UCSD shortness of breath questionnaire (SOBQ)**

The SOBQ is self-administered and asks subjects (43) to rate their breathlessness for 21 various daily activities (plus 3 overall items) on a 6-point scale from none at all (0) to severe (4) to maximal or unable to do because of breathlessness (5). For activities that they do not typically perform, respondents are expected to estimate their breathlessness for that activity. The 21 activities of daily living (ADLs) are grouped according to factor analysis into 4 categories of ADLs: Rest and Light ADLs (Factor 1), 8 questions; Moderate ADLs (Factor 2), 5 questions; Walking (Factor 3), 4 questions; and Strenuous ADLs (Factor 4), 4 questions. The score on each of the 24 items is summed to produce an overall summary score.

The QWB-SA and the UCSD SOBQ have been applied in a variety of investigations of physical activity in COPD patients. These include population studies, observational investigations, and clinical trials. The following sections review some of these applications.

**ESTIMATION OF HEALTH-RELATED QUALITY OF LIFE AND PHYSICAL ACTIVITY IN THE POPULATION**

A variety of methods have been used to estimate the relationship between health-related quality of life and self-reported physical activity in the adult population. One effort involves the use of the National Health Interview Survey (NHIS). In collaboration with John Anderson from the University of California, San Diego we built a data set that allows imputation of the QWB for the NHIS for the years 1989–2002. This unique data set includes more than 2,000,000 cases. Details of the method are published elsewhere (44). The analysis suggests a systematic relationship between the number of episodes of vigorous activity and estimated QWB score. There is a systematic relationship between physical activity and QWB score up to about 3–5 episodes of self-reported vigorous physical activity per week. Those who are unable to engage in vigorous activity have the lowest QWB scores. Interestingly, there is a slight drop-off in QWB scores for those who engage in vigorous activities 7 or more times per
week (see Figure 2). It is worth noting that because of the very large sample size, all differences are statistically significant.

**Exercise endurance in patients with COPD**

We have conducted several studies involving rehabilitation for patients with chronic lung disease. One of these experiments randomly assigned 119 COPD patients to either comprehensive rehabilitation or to an education control group. Pulmonary rehabilitation consisted of 12 4-hour sessions distributed over an 8-week period. The content of the sessions was education, physical and respiratory care, psychosocial support, and supervised exercise. The education control group attended 4 2-hour sessions that were scheduled twice per month. These education sessions did not include any individual instruction or exercise training. Topics included medical aspects of COPD, pharmacy use, breathing techniques and a variety of interviews about smoking, life events and social support. Lectures covered pulmonary medicine, pharmacology, respiratory therapy, and nutrition. Outcome measures included lung function, maximum and endurance exercise tolerance, symptoms of perceived breathlessness, perceived fatigue, self-efficacy for walking, Centers for Epidemiologic Studies Depression (CES-D) score, and the Quality of Well-being scale. The patients were evaluated at the baseline and then again after 2, 6, 12, 24, 36, 48, and 60 months.

Figure 3 shows the differences between those in pulmonary rehabilitation and the education control groups over the first year of the study. The top portion of the figure shows changes in exercise endurance. Those randomly assigned to rehabilitation had significantly higher endurance at 2, 6, and 12 months. This is complemented by differences in breathlessness where those in the rehabilitation program were less breathless at the end of the treadmill exercise after 2, 6, and 12 months. Similarly, patients in the rehabilitation group were significantly lower in perceived muscle fatigue at each follow-up period (lower section of Figure 4) (45).

There were no differences between groups for measures of lung function, depression, or general quality of life. However,
both groups experienced reductions in quality of life. For exercise variables, benefits tended to relapse toward baseline after 18 months of follow-up. In other words, activity changes are not well maintained over the course of time. The trial did not show significant changes in quality of life as measured using the QWB.

In a more recent study, 160 patients with chronic lung disease participated in a comprehensive rehabilitation program. In comparison to baseline, there was a significant improvement in quality of life as measured by the QWB, following the rehabilitation program. At the end of the program the patients were randomly assigned to a program designed to improve compliance and maintenance of the rehabilitation lessons or to routine follow-up. Outcome measures included quality of life, symptoms, healthcare utilization, measures of pulmonary function, measures of psychological function, and survival.

All patients were evaluated prior to the pulmonary rehabilitation and then again after the 8-week program had been completed. Following the second evaluation, patients were evaluated at 6 months, 12 months, and 24 months. In an analysis by Heppner and colleagues, the patients were further divided into those who were regular walkers and those who walked irregularly. Regular walking was defined as walking most days or every single day while irregular walking was defined as walking some days, rarely, or never. The core psychosocial measures included the QWB scale, the UCSD Shortness of Breath questionnaire and a measure of self-efficacy for walking. Quality-of-life results are summarized in Figure 4. Regular walkers maintained better QWB quality-of-life scores than irregular walkers. Similarly, those who walked on an irregular basis had more shortness of breath than those who walked on a regular basis (46).

Our group has produced other evidence that walking compliance is related to better health outcomes. In one of our earlier studies, COPD patients were randomly assigned to one of five groups. One group underwent an intervention designed to increase compliance with physical activity using cognitive-behavior modification. Cognitive-behavior modification combines traditional behavior modification with cognitive therapy. Cognitive-behavior modification is believed to be superior to either the behavior modification alone or the cognitive component alone. The second and third groups received a behavioral and a cognitive intervention, respectively. The fourth group got attention while the fifth group received no treatment. All patients were evaluated at baseline and followed over the course of 12 weeks.

Cumulative time spent walking was measured using patient reports in a diary. Those in the cognitive-behavior modification group accumulated significantly more walking time than those in control groups. Compliance with physical activity was associated with changes in endurance as evaluated on a treadmill after 12 weeks. Further, these changes in endurance were associated with changes on the QWB scale. All 3 groups experiencing a cognitive or behavioral intervention showed improvements on the QWB while those in the 2 control groups declined on the QWB (47). Cost-effectiveness analysis demonstrated that the behavioral activity interventions were a reasonable use of resources in relation to other alternatives in health care (48).

**Correlational studies of exercise tolerance and QOL**

A variety of other evidence supports relationships between measures of exercise endurance and measures of health-related quality of life. The UCSD trials demonstrated systematic relationships between the QWB and the 6-minute walk at 6-month follow-up (49). There were similar relationships between the 6-minute endurance walk and the UCSD Shortness of Breath questionnaire. Perhaps more important are relationships between changes in exercise performance and changes in outcomes. Figure 5a compares patients who decreased their performance.
on the 6-minute walk between baseline and 12-month follow-up and those who increased their performance.

As the figure shows, those who increased their endurance improved their QWB scores by about 0.03 units. Studies using the QWB suggest that a change of 0.03 units is a meaningful clinical difference. It is equivalent to the benefits of cataract surgery or the medical treatment of rheumatoid arthritis. Figure 5b shows that those who improved their 6-minute walk performance had significantly greater improvements on the UCSD Shortness of Breath questionnaire.

Data from the National Emphysema Treatment Trial (NETT) offer similar results. The NETT evaluated patients on a variety of measures at baseline and again after completion of the rehabilitation program. Changes in 6-minute walking scores were divided into quintiles. There was a systematic relationship between level of improvement on the 6-minute walk and changes in the QWB. In particular, there is a difference between those in the first and fifth quintiles of 6-minute walking time. This difference was about 0.04 QWB units. The relationship between quintiles of improvement in 6-minute walk and scores on the UCSD-SOBQ were also linear and quite systematic. For the QWB, the differences of about 0.04 exceed the estimated MCID for the QWB of 0.03 units (7). Comparing patients in the first and fifth quintiles, this improvement translates into about 1 QALY for each 25 patients who obtain maintain the benefit for one year.

SUMMARY

Data summarized in this paper suggest that quality of life is an important outcome for patients with COPD. Quality-of-life measures help calibrate the effect of treatment. Standardized quality of life measures can allow the estimation of the treatment effect size. Sometimes, it is valuable to compare the size of the treatment effect in relation to alternative interventions. Measures, such as the QWB, can be translated into a standardized unit of outcome that can be reported in terms of quality adjusted life-years. These estimates can be useful in studies of treatment cost-effectiveness.

Data from a variety of studies suggest that improvements in exercise endurance are associated with improvements in quality of life. Unfortunately, long-term compliance with physical activity is often poor. Better methods for enhancing compliance with exercise interventions are needed. Correlational studies show a clear relationship between compliance with physical activity and quality-of-life outcomes for patients with COPD. These studies do not allow us to determine whether the association is causal. Future studies, including more systematic experimental trials, are needed to evaluate the impact of physical activity interventions upon quality-of-life outcomes for patients with COPD.

REFERENCES

6. Holman H, Lorig K. Patients as partners in managing chronic disease. Partnership is a prerequisite for effective and efficient...


42. Williams A. Cochrane Lecture. All cost effective treatments should be free. or, how Archie Cochrane changed my life! J Epidemiol Comm Health 1997; 51(2):116–120.


