

Health status measurement instruments in chronic obstructive pulmonary disease

Yves Lacasse MD MSc, Eric Wong MD MSc, Gordon Guyatt MD MSc, Roger S Goldstein MB ChB, *Centre de Pneumologie, Hôpital Laval, Ste-Foy, Québec; Department of Medicine, University of Alberta, Edmonton, Alberta; Department of Medicine and Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario; Department of Medicine, University of Toronto, Toronto, Ontario*

Y Lacasse, E Wong, G Guyatt, RS Goldstein. Health status measurement instruments in chronic obstructive pulmonary disease. *Can Respir J* 1997;4(3):152-164. Chronic obstructive pulmonary disease (COPD) is associated with primary respiratory impairment, disability and handicap, as well as with secondary impairments not necessarily confined to the respiratory system. Because the primary goals of managing patients with COPD include relief of dyspnea and the improvement of health-related quality of life (HRQL), a direct measurement of HRQL is important. Fourteen disease-specific and nine generic questionnaires (four health profiles and five utility measures) most commonly used to measure health status in patients with COPD were reviewed. The measures were classified according to their domain of interest, and their measurement properties – specifications, validity, reliability, responsiveness and interpretability – were described. This review suggests several findings. Currently used health status instruments usually refer to the patients' perception of performance in three major domains of HRQL – somatic sensation, physical and occupational function, and psychological state. The choice of a questionnaire must be related to its purpose, with a clear distinction being made between its evaluative and discriminative function. In their evaluative function, only a few instruments fulfilled the criteria of responsiveness, and the interpretability of most questionnaires is limited. Generic questionnaires should not be used alone in clinical trials as evaluative instruments because of their inability to detect change over time. Further validation and improved interpretability of existing instruments would be of greater benefit to clinicians and scientists than the development of new questionnaires.

Key Words: *Chronic obstructive pulmonary disease, Dyspnea, Performance status, Quality of life, Questionnaires*

Instruments de mesure de l'état de santé dans la maladie pulmonaire obstructive chronique

La maladie pulmonaire obstructive chronique (MPOC) est non seulement associée à une déficience respiratoire primaire, à une incapacité et à un handicap mais aussi à des déficiences secondaires qui ne sont pas nécessairement limitées au système respiratoire. Parce que les principaux objectifs de la prise en charge des patients atteints de MPOC incluent le soulagement de la dyspnée et l'amélioration de la qualité de vie liée à la santé, une mesure directe de la qualité de vie liée à la santé est importante. Quatorze questionnaires spécifiquement adaptés à une maladie et neuf questionnaires généraux (quatre profils de santé et cinq mesures d'utilité) utilisés le plus couramment pour mesurer l'état de santé des patients atteints de MPOC ont été passés en revue. Les mesures ont été classées selon leur domaine d'intérêt, et leurs propriétés de mesure – spécifications, validité, fiabilité, réponse et interprétation – ont été décrites. La présente revue propose plusieurs résultats. Les instruments de mesure de l'état de santé couramment utilisés se rapportent habituellement à la perception des patients quant à leur performance dans trois domaines principaux de la qualité de vie liée à la santé : la sensation somatique, la fonction physique et liée à l'occupation et l'état psychologique. Le choix du questionnaire doit avoir une relation avec son objectif, en établissant clairement une distinction entre sa fonction évaluative et sa fonction discriminante. Dans leur fonction évaluative, seuls quelques instruments remplissent les critères de sensibilité, et l'interprétation de la plupart des questionnaires est limitée. Les questionnaires généraux ne devraient pas être utilisés isolément dans les essais cliniques comme des instruments évaluatifs car ils ne peuvent déceler les changements dans le temps. Des méthodes de validation plus approfondies et une amélioration de l'interprétation des instruments actuels seraient plus utiles pour les cliniciens et les chercheurs plutôt que le développement de nouveaux questionnaires.

Though the focus of treatment of patients with chronic lung diseases often includes physiological measurements of expiratory flows or exercise capacity, growing evidence that symptoms and overall health-related quality of life (HRQL) are poorly related to these physiological outcomes (1-3) has prompted investigators to include measurements of health status as end-points into their clinical trials. Over the past 15 years, investigators have developed a number of instruments to measure health status in patients with chronic obstructive pulmonary disease (COPD). The availability of a variety of questionnaires has led to confusion regarding the most appropriate instrument to use and how to interpret the results. The objectives of this study were to describe and classify currently available health status measurement instruments for patients with COPD.

METHODS

In contrast to the report published in this issue of the *Canadian Respiratory Journal*, reviewing the measurement properties of the Chronic Respiratory Questionnaire (CRQ) (4), this article is not the result of a systematic overview of the literature. This review does not attempt to be comprehensive, but uses the authors' judgement to select the most popular and widely used available instruments, and collect the most salient data on the instrument's measurement properties.

This report will assist interested individuals in identifying the primary articles and recent reviews of the measurement of HRQL in COPD (5-7). To retrieve papers reporting on the measurement properties of the questionnaires included in this review, computer searches of the English-language medical literature were conducted in the Science Citation database using the reference of the original article describing the questionnaire. When information on the measurement properties of a particular questionnaire was limited, the authors of the original report on the instrument were contacted for more detailed information. The basic terminology related to health status measure has been defined in a previous paper (8) and will not be repeated. When commenting on the responsiveness of the instruments on the basis of the results of trials in which the questionnaire was used, priority was given to randomized controlled trials. Such trials usually provide stronger evidence of responsiveness than nonrandomized trials. Throughout this text, in interpreting the coefficients of correlation, the strength of the correlations was qualified as

follows: coefficients ranging from 0 to 0.20 denote a negligible correlation; 0.21 to 0.35 a weak correlation; 0.36 to 0.50 a moderate correlation; and greater than 0.50 a strong correlation.

WHY SHOULD HRQL BE MEASURED IN COPD?

End-stage COPD is preceded by years of progressive disability and handicap associated with limited exercise capacity (9,10), and a variety of symptoms not necessarily confined to the respiratory system. For instance, when specifically asked to describe their symptoms, patients most frequently acknowledge breathlessness, fatigue, sleep disturbance, irritability and sense of hopelessness (11,12). Typically, affected patients rapidly enter into the vicious circle of dyspnea, inactivity and physical deconditioning (13), with consequent potentially devastating emotional responses, including depression (14).

Many investigators have found that measures of exercise capacity (either maximal or functional) correlate only weakly or moderately with quality of life instruments in chronic lung diseases (Table 1). Consequently, the measurement of exercise capacity cannot be used as a surrogate outcome for quality of life in respiratory rehabilitation; quality of life should rather be measured directly.

Health status measurement is a growing field. The authors' recent review of the health status measure instruments used in controlled clinical trials of respiratory rehabilitation (15) illustrates the evolution of measurement in pulmonary medicine over the past 20 years. In early trials (16,17) HRQL measurement was assessed by more or less structured interviews; questionnaires related to fixed personality traits; or health status measurement instruments borrowed from the psychosocial sciences which had most often been developed to measure psychological status in psychiatric patients. The most important limitation of these early strategies related to their validity – the capacity of an instrument to measure what it claims to measure (18).

Recognizing that chronic lung diseases may be as an important determinant in the deterioration of quality of life, some investigators have developed their own questionnaire or adapted existing instruments (19). The availability of disease-specific questionnaires has highlighted the limitations of these strategies. For instance, trials of theophylline in stable COPD patients in which health status was measured with nonvalidated diary questionnaires failed to show signifi-

TABLE 1
Correlations between fully validated health-related quality of life (HRQL) measurement instruments and functional exercise capacity

Reference	Study population	HRQL measure instrument	Functional exercise capacity measure	Pearson's coefficients of correlation
Mahler et al (1)	38 patients (32 COPD; 5 asthma; 1 interstitial fibrosis)	Baseline Dyspnea Index	12 min walk test	r=0.60; P<0.05
Guyatt et al (2)	43 patients (25 COPD; 18 chronic heart failure)	Chronic Respiratory Questionnaire (dyspnea)	6 min walk test	r=0.46; P<0.05
Jones et al (3)	141 patients (COPD and asthma; proportion not specified)	St George's Respiratory Questionnaire (symptoms)	6 min walk test	r=-0.26; P<0.01

COPD Chronic obstructive pulmonary disease

TABLE 2
An overview of the health status measurement instruments in chronic obstructive pulmonary disease (COPD)

Questionnaire	Quality of life domains				
	Overall quality of life	Somatic sensation	Physical function	Emotional function	Social interaction
Disease-specific questionnaires					
Medical Research Council Dyspnea Scale (25)		√			
American Thoracic Society Dyspnea Scale (26)		√			
Oxygen Cost Diagram (27)		√			
Additive Activities Profile Test Quality-of-Life Scale (28)			√		
Baseline/Transition Dyspnea Index (1)		√			
Modified Dyspnea Index (29)		√			
Chronic Respiratory Questionnaire (30)		√		Ö	
Pulmonary Function Status scale (31)		√	Ö	Ö	
Chronic Disease Assessment Tool (32)		√	Ö	Ö	
COPD Self-Efficacy scale (33)				√	
Medico-psychological Questionnaire for Lung Patients (34)				√	
St George's Respiratory Questionnaire (3,35)		√	Ö		Ö
Pulmonary Function Status and Dyspnea Questionnaire (36)		√	Ö		
University of California, San Diego Shortness of Breath Scale (37)		√			
Generic questionnaires – Health profiles					
Psychological Adjustment to Illness Scale (38,39)				√	Ö
Nottingham Health Profile (40)		√	Ö	Ö	Ö
Sickness Impact Profile (41)			√	Ö	Ö
Medical Outcome Survey – Short Form (42,43)		√	Ö	Ö	√
Generic questionnaires – Utility measures					
Quality of Well-Being (44)		√	Ö		Ö
Standard Gamble (45)	√				
Time Trade Off (45)	√				
Rating Scale (45)	√				
Health Utilities Index III (46)	√				

* Now called the Human Activity Profile

cant improvement in subjective effects of the drug (19). Subsequently, several trials in which disease-specific questionnaires were used concluded that theophylline was associated with significant changes in quality of life (20-22).

IMPORTANT DOMAINS OF QUALITY OF LIFE IN COPD

Defining quality of life remains a difficult task. Dimensions assessed by a representative group of quality of life instruments ranged from burden of symptoms to social functioning (23). The term HRQL is often used when widely valued aspects of life not directly related to health, such as income and freedom, are not considered (18). The concept of HRQL usually refers to the patients' perception of performance in at least one of four important domains: somatic sensation, physical function, emotional state and social interaction (24). These domains allow researchers to classify the areas explored by health status measuring instruments currently used in assessing COPD patients (1,25-46) (Table 2).

DISEASE-SPECIFIC QUESTIONNAIRES IN COPD

Disease-specific questionnaires focus on the areas of function that are relevant to a particular condition and, consequently, are likely to detect small changes. Fourteen currently used disease-specific questionnaires in COPD populations (1,25-37) were selected, and their specifications (Table 3) and measurement properties reviewed (Table 4).

These questionnaires focus on one or more of the four major domains of HRQL and are presented accordingly (20).

Somatic sensations: Dyspnea is the most frequent symptom presented by patients with COPD and is associated with a wide range of activities (11,12). Accordingly, most questionnaires measuring somatic sensations have focused on the measurement of dyspnea. Other somatic sensations reported by patients with COPD include fatigue and sleep disturbances (11,12).

Defining and measuring dyspnea: Dyspnea may be defined as "an increased sense of respiratory effort" (82). A review of the questionnaires in which dyspnea was measured (1,25-27,29-32,34,37) demonstrated that, most often, the correlations between HRQL scores and indexes of physiological functions were weak to moderate. This observation was thought to reflect the fact that patients with COPD of a similar severity may have different perceptions of the effects of their disease. For most questionnaires, inferences regarding their validity in the measurement of dyspnea would have been strengthened if the investigators had made a priori predictions regarding the magnitude of the correlations and then tested these predictions.

Instruments applied to measure dyspnea are heterogeneous measures examining different components of dyspnea, ranging from the stimuli preceding the development of dyspnea to the consequences of dyspnea (5). For instance, the earliest health status measures used in COPD (those of the British Medical Research Council [25] and the American

TABLE 3
Specifications of selected disease-specific questionnaires in chronic obstructive pulmonary disease (COPD)

Instrument	Measurement purpose	Questionnaire structure	Item scaling and total score	Administration
MRC Dyspnea Scale (25)	Discriminative	From a questionnaire initially designed to be used in epidemiological studies in the general population; measures the stimuli preceding the development of dyspnea Time frame not specified	Dyspnea scale with grades 1 to 5: grade 1 (breathlessness only on strenuous exertion) to grade 5 (too breathless to leave the house or breathless after undressing)	Self-completed or interviewer-administered; completed within 30 s
American Thoracic Society Dyspnea Scale (26)	Discriminative	Initially designed to be used in epidemiological studies in the general population; part of a series of yes-no questions related to: respiratory symptoms (cough, phlegm, breathlessness); past illnesses tobacco smoking; and occupational and family histories Time frame focuses on symptoms that are present or have ever occurred	Series of yes-no questions; no scoring system; the frequency of positive responses to individual questions is usually reported in epidemiological studies (47)	Self-completed or interviewer-administered; telephone interviews possible (47); completed within 20 mins
Oxygen Cost Diagram (27)	Both evaluative and discriminative	Measures only dyspnea; a list of everyday activities is positioned alongside a 100mm vertical scale proportionally to their oxygen cost (48); patients mark the line at a point above which they think their dyspnea would not allow them to go when at their best Time frame not specified	Item scaling: from 0 (sleeping) to 100 (brisk walking uphill)	Self-administered; completed within 1 min
Additive Activities Profile Test Quality-of-Life Scale (28)*	Discriminative	Measures the impact of physical or emotional disorders on lifestyle: 94 activities (numeral against each item) requiring low oxygen consumption (eg, getting in or out of a chair) to high oxygen consumption (eg, running a mile in 10 mins) are ordered Time frame not specified	For each activity, patients are asked to mark whether they are still doing it, have stopped doing it or never did it; scoring is by noting the highest numeral still being performed and then subtracting from it the total number of activities that the patient had quit	Self-administered; completed within 20 mins
Baseline Dyspnea Index (BDI) (1)	Discriminative	Measures three aspects of dyspnea: magnitude of the task that provokes dyspnea; magnitude of the effort needed to evoke dyspnea; and consequent functional impairment	Items: 0 (severe) to 4 (unimpaired); total (baseline focal score) range 0 to 12	Interviewer-administered; completed within 5 mins
Transition Dyspnea Index (TDI) (1)	Evaluative	Measures the same three aspects of dyspnea as the BDI Time frame not specified	Item scaling: -3 (major deterioration), 0 (unchanged), +3 (major improvement); total (transition focal score): range -9 to +9	Same as the BDI
Modified Dyspnea Index (29)	Discriminative	Measures three aspects of dyspnea: magnitude of the task that provokes dyspnea; magnitude of the effort (the vigour with which patients can perform their maximum task); consequent functional impairment at home and at work (forming a composite functional scale) Time frame not specified	Item scaling: 0 (severe) to 4 (unimpaired); total (focal score): range = 0 to 12	Interviewer-administered; completed within 15 mins
Chronic Respiratory Questionnaire (CRQ) (30)	Primarily evaluative	Four domains: dyspnea (five self-generated items); fatigue (four items); emotional function (seven items); mastery (four items) Time frame: two weeks	Item scaling: 7-point Likert scales 0 (no symptoms) to 7 (extreme symptoms); the total score within domain is reported; converting the total score on a 7-point scale is recommended	Interviewer-administered; duration of the first interview: 20 to 30 mins; subsequent interviews, 10 mins
Pulmonary Function Status Scale† (31)	Both evaluative and discriminative	64 items: five demographic and 59 divided into three domains: dyspnea; activities of daily living (subscales: self-care, mobility, household tasks, grocery shopping/meal preparation, daily activities, relationships); psychosocial behaviour (subscales anxiety, depression) Time frame: one month	Item scaling: different item scaling across domains, most often using Likert scales; total score by adding scores for each item and then dividing by the number of items answered with a value greater than 0; low scores indicate greater impact of COPD	Self-administered questionnaire; completed within 30 mins
Chronic Disease Assessment Tool (32)	Evaluative	106 items selected from existing questionnaires and divided into five sections: general health and medical history; environmental risk (air quality and tobacco exposure); Health Impact Measurement Survey (modification of the Arthritis Impact Measurement Survey [49] and of the CRQ [30]); Quality of Life Index (50); demographic data	Item scaling: derived from the original questionnaires	Self-administered; completed within 25 to 30 mins
COPD Self-efficacy Scale (33)	Both evaluative and discriminative	34 items representing situations in which patients are likely to have low confidence in managing breathing difficulty; five domains (factors): negative affect; intense emotional arousal; physical exertion; weather/environment; behavioural risk factors Time frame not specified	Item scaling: 5-point Likert scales ("Very confident" to "Not at all confident"); little information currently available on the scoring system	Self-administered; completed within 10 mins

Continued on next page

TABLE 3 (continued)

Instrument	Measurement purpose	Questionnaire structure	Item scaling and total score	Administration
Medico-psychological Questionnaire for Lung Patients (34)	Evaluative	52 items divided into four domains: well-being; experienced invalidity; displeasure; social inhibition Time frame "nowadays"	A 3-point scale follows all 52 items written as statements: correct / ? / incorrect; scoring system not provided by the author	Self-administered; completed within 15 mins
St George's Respiratory Questionnaire (3,35)	Both evaluative and discriminative	Three domains: symptoms (eight items); activity (16 items); impact (26 items) Time frame symptoms one year; other domains "these days"	Item scaling – symptom domain: 5-point Likert scales; other domains: yes-no questions; each domain is scored separately (0% to 100%); summary score: 0 (perfect health) to 100% (worst); scores calculated using weights attached to each item	Self-completed; completed within 20 mins
Pulmonary Function Status and Dyspnea Questionnaire (36)	Evaluative	164 items; two components: measurement of dyspnea intensity with 79 activities and changes attributed to COPD in functional activities related to 79 activities of daily living; six subscales: self-care; mobility; eating; home management; social; recreational Time frame "now as compared to before you developed breathing problem"	Dyspnea component: a Dyspnea Index is determined from 79 activities rated as causing severe or very severe dyspnea (0 to 79); functional ability component: an Activity Index is determined from the number of activities that have been modified (extreme change or omission) because of COPD (0 to 79)	Self-completed; completed within 10 to 15 mins
University of California, San Diego Shortness of Breath Questionnaire (37)	Evaluative	24 items: 21 activities of daily living that are associated with varying levels of exertion; three items about limitations caused by shortness of breath, fear of harm from overexertion and fear of shortness of breath	Shortness of breath scale: 6-point Likert scale indicating how frequently patients experience shortness of breath (0 [never] to 5 [not able to do])	Self-completed; completed within 5 mins

*Now called the Human Activity Profile; [†]Pulmonary Function Status Scale by Weaver, formerly called the 'Pulmonary Impact Profile Scale' (PIPS). MRC Medical Research Council

TABLE 4
Measurement properties of disease-specific questionnaires used in patients with chronic obstructive pulmonary disease (COPD)

Instrument	Validity	Reliability/internal consistency	Responsiveness	Interpretability
MRC Dyspnea Scale (25)	Poor concordance between the level of dyspnea and maximal voluntary ventilation; coefficient of correlation not reported	No information available	Little potential for responsiveness in a homogeneous population of patients with COPD	Not known
American Thoracic Society Dyspnea Scale (26)	Limited information currently available in COPD; in a general population the frequency of symptoms was correlated to FEV ₁ (% pred) (47)	When administered by interviewers, showed good interobserver reliability (47)	Little potential for responsiveness in a homogeneous population of patients with COPD	Not known
Oxygen Cost Diagram (OCD) (27)	No correlations with FEV ₁ and FVC (27); weak correlations with P _I max and P _E max (r=0.28 to 0.25) (27); strong correlation with the 12 min walk test (r=0.60) (27) and the 6 min walk test (r=0.50) (2); correlation with the MRC scale: r=-0.53; with the BDI 0.54 (51) to 0.59 (2)	ICC* 0.68 (51)	No ability to detect change compared with the TDI (2,52-55)	Not known
Additive Activities Profile Test Quality-of-Life Scale (28)	Strong correlation with VO ₂ max (r=0.83; P<0.01)	Not known	Not known; limited clinical experience with the questionnaire exists	Not known
Baseline Dyspnea Index (BDI) (1)	Moderate to strong correlations with FEV ₁ , FVC, P _I max and P _E max (r=0.35 to 0.56) (1,51,56); strong correlation with the 12 min walk test (r=0.60) (1) and 6 min walk test (r=0.59) (2); strong correlations with other measures of dyspnea – MRC r=-0.70 (51); OCD r=0.54 (51) and 0.589 (2)	Interobserver reliability (weighted Kappa) BDI 0.65 to 0.72 (1,51)	Does not apply to the BDI (the TDI usually follows the BDI to measure change over time)	Little information available on the significance of difference in scores
Transition Dyspnea Index (TDI) (1)	No correlation with spirometry results (1); weak but significant correlation with the 12 min walk test (r=0.33) (1)	Interobserver reliability (weighted Kappa) TDI 0.63 to 0.65 (1)	Able to detect change over time in an observational longitudinal study (57) and trials of inspiratory muscle training (58,59); theophylline (52,60) and rehabilitation (61,62); as responsive as the dyspnea domain of the CRQ (30,62)	Little information available on the significance of any score
Modified Dyspnea Index (29)	Strong correlations with FEV ₁ , FVC, P _I max and P _E max (r=0.65 to 0.87); no correlation with the 12 min walk test (r=0.18); strong correlation with the Pneumoconiosis Research Unit Score: Spearman's rho=-0.62 (29); has not been validated against its precursor the BDI	Not measured during the development of the instrument	Not known; limited clinical experience with the questionnaire exists; used in a trial of negative pressure ventilation in severe COPD (54)	No information available on the significance of any difference in scores

Continued on next page

TABLE 4 (continued)

Instrument	Validity	Reliability/internal consistency	Responsiveness	Interpretability
Chronic Respiratory Questionnaire (CRQ) (4,30)	Discriminative function: moderate to strong correlations between the CRQ and corresponding domains of the Symptom Checklist (SCL-90) (63) and the Medical Outcome Survey (MOS-SF-36) (64,65); evaluative function: good agreement between predicted and observed correlations between changes in CRQ scores and changes in physiological measures and changes in patients' health status global ratings (30)	Test-retest reliability demonstrated in three independent studies (63,64,66); internal consistency not applicable for the dyspnea domain; Cronbach's alpha ranges from 0.71 to 0.87 for the other domains (63,65,67)	Ability to detect change demonstrated for all four domains in randomized controlled trials of respiratory rehabilitation in COPD (62,68-70) and in a number of trials of different interventions in COPD (4)	On a 7-point Likert scale, a difference in score of 0.5 represents the minimal clinically important difference; 1.0 represents a moderate change and 1.5 a large change (71)
Pulmonary Function Status Scale (31,72)	Strong correlations with the 12 min walk test ($r=0.62$; $P<0.001$); weak correlation with FEV ₁ /FVC ($r=0.29$; $P<0.01$) (72); strong correlation with the Sickness Impact Profile ($r=-0.54$; $P<0.01$); moderate correlations with measures of depression (Multiple Affect Adjective Checklist: $r=-0.40$; $P<0.01$) and self-esteem (Rosenberg's Self-Esteem Scale: $r=-0.41$; $P<0.01$) (72)	Test-retest reliability (one week) $r=0.67$ ($p=0.002$) (72); internal consistency Cronbach's alpha=0.81 (72)	Not known; limited clinical experience with the questionnaire exists	Not known
Chronic Disease Assessment Tool (CDAT) (32,73)	Content validity assessed by clinical experts; construct validity assumed on the basis of the validity of the original questionnaires used to develop the CDAT; no correlation with any other health status instrument or physiological measure has been provided to support construct validity of the scale	Internal consistency of the different sections demonstrated	Not known; limited clinical experience with the questionnaire exists	Not known
COPD Self-Efficacy Scale (33)	Validity assumed on the basis of the apparent validity of the self-efficacy theory; no correlation with any other health status instrument or physiological measure has been provided to support construct validity of the scale	Test-retest reliability $r=0.77$, $P<0.001$; internal consistency Cronbach's alpha=0.96	Not known; limited clinical experience with the questionnaire exists	Not known
Medico-psychological Questionnaire for Lung Patients (MPQL) (34)	Weak to moderate correlations between the well-being, experienced invalidity and displeasure domains of the MPQL and the results of 12 min walk test maximal exercise capacity and the number of hospitalization days over a 12-month period (34); no correlation between the social inhibition domain and any of the measured variables (34)	Test-retest reliability (unspecified interval): $r=0.36$ for the well-being domain; $r=0.65$ to 0.72 for the other domains; Internal consistency: Cronbach's alpha=0.69 (social inhibition) to 0.93 (well-being) (34)	In a nonrandomized trial of respiratory rehabilitation in COPD, change in MPQL well-being scores weakly correlated with changes in hospital days ($r=0.24$) and a dyspnea ($r=-0.29$); change in MPQL-experienced invalidity scores weakly correlated with changes in maximal exercise capacity ($r=-0.28$) and moderately correlated with change in a measure of leisure activity (74)	Not known
St George's Respiratory Questionnaire (SGRQ) (3,35)	Validated in a heterogeneous population of 141 patients with chronic airways diseases (including asthma and COPD) (3,75,76): SGRQ-symptoms versus MRC-cough, $r=0.59$; SGRQ-symptoms versus MRC-sputum, $r=0.49$; SGRQ-symptoms versus MRC-wheeze, $r=0.57$; SGRQ-activity versus 6 min walk test, $r=0.59$; SGRQ-impact versus Anxiety/Depression scale, $r=0.62$; the magnitude of these correlations agreed with a priori predictions	Coefficient of variation [†] 19%; ICC* 0.92 (3)	Change in SGRQ's total scores correlated with changes in: FEV ₁ (% pred), $r=0.22$; 6 min walk test $r=0.36$; MRC scale, $r=0.47$; Depression scale, $r=0.35$; Anxiety scale, $r=0.17$ (3); able to detect change (improvement and deterioration) over time in a randomized trial of nasal positive pressure ventilation (77)	Minimal clinically important difference: -4 units (derived from a mathematical model and then verified in asthmatics [35]); moderate and large treatment effects -8 and -12 units, respectively (78)
Pulmonary Function Status and Dyspnea Questionnaire (PSFDQ) (36)	Construct validity tested by dividing subgroups of patients on the basis of their subjective reports of impairment: patients reporting extremes of dyspnea and functional ability (most or least) differed significantly in the following variables: FEV ₁ , FEV ₁ /FVC, exercise capacity (VO _{2 max}). Strong correlation between the Dyspnea Index and the Geriatric Depression Scale ($r=0.55$; $P<0.001$); moderate correlation between the Activity Index and the Geriatric Depression Scale ($r=0.43$; $P<0.01$) (36)	Internal consistency Cronbach's alpha on the six subscales of the dyspnea dimension (36); no data on test-retest reliability	In a 12-week randomized placebo-controlled trial of nortriptyline in depressed patients with COPD using an early version of the PSFDQ, changes in the Activity Index were noted in the treatment group (70)	Not known
University of California, San Diego Shortness of Breath Questionnaire (37)	Moderate correlations with FEV ₁ ($r=-0.445$; $P<0.01$), ratings of perceived breathlessness ($r=0.474$; $P<0.001$), and the CES-D ($r=0.418$; $P<0.001$); strong correlation with the 6 min walk test ($r=-0.669$; $P<0.001$) (80)	Test-retest reliability (2 days) $r=0.94$ (37)	Able to detect change over time in a randomized controlled trial of respiratory rehabilitation in COPD (81)	Not known

*An intraclass correlation coefficient (ICC) compares the variability between patients (the signal) with the variability within patients over time (the noise); an ICC of 0.70 is considered to reflect good reliability; [†]Coefficient of variation: standard deviation/mean; as a reference: coefficient of variation of forced expiratory volume in 1 s (FEV₁)=8%. CES-D Center for Epidemiologic Studies' Depression Scale; FVC Forced vital capacity; MRC Medical Research Council; P_{I max} Peak inspiratory pressure; P_{E max} Maximal expiratory pressure; % pred Percentage predicted value; VO_{2 max} Maximal expiratory pressure

Thoracic Society [26]) were developed for discriminative purposes within the frame of epidemiological surveys and focused on predetermined activities provoking dyspnea. They offer little potential for the detection of small changes over time and are only useful to discriminate patients according to the level of activities associated with dyspnea. On the other hand, the Transition Dyspnea Index (1) and the dyspnea domain of the CRQ (30) focus on a set of activities selected during the administration of the questionnaires that are important for individuals. They offer potential for responsiveness but are inappropriate as discriminative instruments because the dyspnea rating among patients is made on different sets of activities. A major limitation of most dyspnea scales (with the exception of the CRQ) is that they are difficult to interpret.

Rest dyspnea versus exercise-induced dyspnea: The Borg dyspnea (83) scale is useful for measuring exercise-induced dyspnea in the laboratory but has not proved useful for obtaining historical reports of dyspnea (37). Because the focus of this review is the measurement of symptoms in day-to-day activities (as opposed to exercise-induced dyspnea), it will not be discussed further.

Measuring other symptoms: The CRQ (30) contains a domain measuring fatigue, a symptom that has been reported as important by patients with COPD (11,12), as opposed to cough, sputum production and wheeze, which are measured by the St George's Respiratory Questionnaire (3,35). Because the latter has been developed for patients with COPD and asthma, the inclusion of cough and wheeze is appropriate.

Physical function: Functional status, defined as the patient's ability to perform activities of daily living (7), often defines the level of autonomy of affected patients and is of crucial importance in the delivery of health services. In a recent review, Lareau et al (7) summarized the psychometric properties of the questionnaires measuring functional status in COPD. Disease-specific questionnaires that measure physical function in COPD include the Additive Activities Profile Test Quality Of Life Scale Now called the Human Activity Profile (28), the Pulmonary Function Status Scale (31), the St George's Respiratory Questionnaire (3,35), and the Pulmonary Functional Status and Dyspnea Questionnaire (36). Both the St George's Respiratory Questionnaire and the Pulmonary Functional Status and Dyspnea Questionnaire have proved able to detect change over time.

Emotional function: Irritability and hopelessness are frequent complaints in patients with COPD (11,12). Depression prevalence rates in patients with moderate to severe COPD are approximately 42% (14,84). Depression prevalence rates as high as 76% have been reported (85). The prevalence of anxiety disorders in COPD is less clear. Investigators have reported anxiety rates ranging from 2% (85) to 34% (86,87). Most clinicians thus consider the measurement of anxiety and depression in clinical trials of COPD relevant (88). The variability of depression and anxiety prevalence rates may stem from the heterogeneity of the populations under study.

Depression has often been measured in COPD with the Center for Epidemiologic Studies' Depression Scale (CES-

D) (89), the Beck Depression Inventory (90) and the Zung Self-Rating Depression scale (91). The level of anxiety has often been assessed by the Spielberger's State-Trait Anxiety Inventory (92) and the Zung Self-Rating Anxiety scale (91). Although all these questionnaires are problem-specific (ie, 'depression-specific' and 'anxiety-specific'), they have not been specifically developed for use in patients with COPD. Many have been developed and validated in the context of epidemiological studies in the general population. Their validity with COPD is therefore limited. Their usefulness as evaluative instruments is also unknown because their ability to detect change over time has not been ascertained. A more complete review of these instruments was reported by Lader (93).

Self-efficacy: Negative attitudes and beliefs held by patients with COPD concerning themselves, their illness and its treatment correlate with reduced functional capacity (94). This finding is congruent with Bandura's self-efficacy theory. Self-efficacy refers to the personal conviction people have regarding whether they feel that they can successfully execute particular behaviours to produce certain outcomes (33,95). According to this theory, people who entertain doubts about their capabilities give up; those who have a strong sense of efficacy persist (95). In COPD, self-efficacy represents a mediator between chronic respiratory disease and unnecessary activity restriction (33). The findings by Kaplan et al (96) further support for the validity of this theory. The authors demonstrated that in a group of patients with COPD the efficacy expectations correlated significantly with health status and exercise tolerance.

The COPD Self-efficacy Scale was developed by Wigal and collaborators (33). In the original paper, the authors presented evidence of test-retest reliability, internal consistency and the description of item aggregation of the scale. Validity of the questionnaire was assumed on the basis of the apparent validity of the self-efficacy theory; no correlation with any other health status instrument or physiological measure has supported the construct validity of the COPD Self-efficacy Scale. Also, the psychometric measurement properties of the instrument remain unexplored.

Other disease-specific instruments: Other disease-specific questionnaires include items or even full domains measuring emotional dimensions related to COPD (Table 2). Data regarding the validity and responsiveness of the emotional function and mastery domains of the CRQ (30) exist (Table 4). Items specifically relating to anxiety and depression were not included in the St George's Respiratory Questionnaire (3), the authors arguing that a number of established measures existed for this area of health.

Social function: Social function refers to an individual's capacity to perform activities associated with her or his usual role, including employment, school, work or home-making (7). Occupational function in patients with COPD is often irrelevant (Table 2). Most patients with symptomatic COPD are elderly, retired patients over age 65 years. The St George's Respiratory Questionnaire (3,35) includes work-related items.

TABLE 5
Specifications of selected generic questionnaires in chronic obstructive pulmonary disease (COPD)

Instrument	Measurement approach and purpose	Questionnaire structure	Item scaling and total score	Administration
HEALTH PROFILES				
Psychological Adjustment to Illness Scale (38)	Discriminative and evaluative	46 items in seven domains Time frame past 30 days including today	Item scaling 0 (unimpaired) to 3 (severe) Individual domain score and overall score Score: sum of individual responses	Interviewer-administered; completed within 20 to 30 mins
Self-Reported Psychological Adjustment to Illness Scale (39)	Discriminative and evaluative	46 items in seven domains; Time frame past 30 days including today	Item scaling 0 (unimpaired) to 3 (severe) Individual domain score and overall score Score: sum of individual responses	Self-administered; completed within 20 mins
Nottingham Health Profile (40)	Discriminative and evaluative	Part 1 – 38 items in six domains; Part 2 – seven statements each address an area of daily life most often affected by health Time frame not specified	Item Scaling: Yes/No Predetermined weight for each item Scores calculated individually for each domain and converted to 0 to 100 scale Higher score = worse	Self-administered; completed within 20 mins
Sickness Impact Profile (41)	Discriminative and evaluative	136 items in 12 domains; three domains can be combined to form Physical Global Score; four other domains can be combined into Psycho-social Global Score; total score from all 12 domains Time frame 24 h	Items scaling: Yes/No Preassigned weight for each item Separate score for each domain, physical global score, psychosocial global score and overall score Score: 0 to 100 Lower score = worse	Interviewer-administered, self-administered or over the telephone; completed within 20 mins
Medical Outcome Survey – Short Form 36 (42,43)	Discriminative and evaluative	36 items in 8 domains; number of items per domain vary from two to eight; two summary health concepts; physical component summary and mental health component summary Time frame one week	Item scaling: Yes/No, or 2-, 3-, 5- or 6-point scale Predefined scoring scheme Domain score and overall score Score: 0 to 100 Higher score = better health Summary Concepts require special scoring system	Interviewer-administered, self-administered or over the telephone; completed within 5 to 10 mins
UTILITY MEASURES				
Quality of Well-being (44)	Discriminative and evaluative	Three dimensions each with multiple function levels and 23 symptoms or problem complexes Time frame four consecutive days	Series of questions to determine function levels for each dimension, and Yes/No response to symptoms/problem complexes Items are preference weighted to generate an overall score Score: 0 (death) to 1 (asymptomatic optimal functioning)	Interviewer-administered; completed within 15 to 20 mins
Standard Gamble (45)	Discriminative and evaluative	A gamble between present health state and a combination of probabilities of perfect health and immediate death No time frame Preference patient	Score: 0 (death) to 1 (full health)	Interviewer-administered; completed within 10 mins
Time Trade Off (45)	Discriminative and evaluative	Amount of shortened life span the patient is willing to trade for perfect health No time frame Preference: patient	Score: number of years converted to scale of 0 to 1	Interviewer-administered; completed within 5 mins
Rating Scale (45)	Discriminative and evaluative	Rates current health status on scale No time frame Preference patient	Score: 0 (death) to 100 (perfect health)	Interviewer-administered; completed within 5 mins
Health Utilities Index III (46)	Discriminative and evaluative	15 questions in eight dimensions Time frame four weeks Preference others	Each question has 4 to 6 levels of function Score: 0 to 1	Self-administered; completed within 5 to 10 mins

Disease-specific questionnaires in COPD – Summary:

Currently used COPD-specific health status instruments usually focus on patients' perception of performance in three major domains of health-related quality of life: somatic sensation, physical and occupational function and psychological state (Table 2). A limitation of many of the questionnaires is their unproved ability to detect change over time. Furthermore, when differences in scores have been demonstrated in the setting of clinical trials, the clinical relevance of these differences has been uncertain. Information regarding the interpretability of the CRQ (30) and the St George's Respiratory Questionnaire (35) exists. Comparisons of these two questionnaires are under way.

GENERIC MEASURES FOR COPD

Generic measures of quality of life have been used extensively in population research and in clinical research. They can be divided broadly into two groups: health profiles and utility measures. This paper reviews the measurement properties of four health profiles (38-43) and five utility measures (44-46) that are frequently used in research studies (Tables 5,6).

Health profiles: Health profiles are useful because they provide information on many aspects of a patient's life. The first three instruments in Table 5 are multidimensional profiles that cover many health concepts (40-43). Of these three, Psychological Adjustment in Illness Scale (38) and Self-Re-

TABLE 6
Measurement properties of generic questionnaires used in patients with chronic obstructive pulmonary disease (COPD)

Instrument	Validity	Reliability/internal consistency	Responsiveness	Interpretability
HEALTH PROFILES				
Psychological Adjustment to Illness Scale (PAIS) (38)	Discriminative: in nonpulmonary populations good correlations between seven domains and four other psychological test scores ($r=0.31$ to 0.81) (39)	In nonpulmonary populations, inter-rater reliability = 0.33 to 0.83 for total and domain scores (38)	In patients with duodenal ulcer undergoing therapy for eradication of <i>Helicobacter pylori</i> there were significant improvements in PAIS-SR overall scores as well as in three of six domain scores (97)	Little information available on the significance of any difference in score
Self-Reported Psychological Adjustment to Illness Scale (PAIS-SR) (39)	Evaluative: unable to locate any study on validity testing	Internal consistency reliability coefficient 0.47 to 0.87(39)		
Nottingham Health Profile (40)*	Limitation: designed to detect moderate to severe problems only; ceiling effect on mild conditions (98). In COPD and asthmatics: Discriminative: no significant correlation with FEV ₁ (99); significant correlations between dyspnea on VAS and all domains ($r=0.22$ to 0.60) 6MW and S, E and PM ($r=-0.24$ to -0.52) and PaO ₂ and E, P, and PM ($r=-0.22$ to -0.39) (100); Evaluative: significant correlation between FEV ₁ and E ($r=-0.46$, 0.44) (99); poor correlation with FEV ₁ ($ r = 0.03$ to 0.16) except between ER and FEV ₁ in one group ($r=0.32$) (101)	In non-COPD patients, test-retest reliability: Part 1 – Spearman's r from 0.75 to 0.88; Part 2 – Cramer's alpha from 0.55 to 0.86 (102)	Able to detect changes in patients before and after combined heart and lung transplantation (103) but unable to detect changes in COPD or asthmatic patients (99,101)	Discriminative: distinct profile of patients with chronic airflow obstruction compared with normal population (101); little information available on the significance of any difference in score
Sickness Impact Profile (SIP) (41) [†]	Discriminative: in COPD, total SIP versus 6 min walk test $r=-0.64$; significant correlations between TS, PGS, PSGS and FVC or 6 min walk test and between FEV ₁ or PEFR and PGS (104) In nonspecific pulmonary diseases: small but significant correlation between FEV ₁ and TS, PGS after adjusted for age ($r=-0.29$ to -0.26) (105) Evaluative: asthmatics: Correlations with validated disease-specific questionnaire was poor for TS, PGS and PSGS: $ r <0.30$ (106)	In nonpulmonary specific populations, reliability by Pearson r value was 0.88 to 0.92 (14)	COPD: significant worsening in FEV ₁ , FVC and PaCO ₂ with nonsignificant worsening in TS (107) Asthmatics: significant improvement in night time asthma attacks and daytime bronchodilator use only in treated patients, and significant improvement in TS in treatment and placebo groups but not between groups (108) NPP: PGS and PSGS detect deterioration preferentially but not improvement (109)	Discriminative: distinct profiles for COPD patients (88) and pulmonary patients of different degrees of impairment (105); however, confidence intervals tend to be wide for each group (104) Evaluative: little information is available on the significance of any difference in score
Medical Outcome Survey – Short Form 36 (SF-36) (42,43)	Discriminative: in COPD: good correlations with BDI in six domains (0.42 to 0.91) except RE and MH. Significant correlations with FEV ₁ and PI max in five domains ($r=0.30$ to 0.65) except RE, MH and P (110) Evaluative: in nonpulmonary populations, significant correlations with self-reported scales in all domains and health constructs (111)	In nonpulmonary populations; Cronbach's alpha ranged from 0.73 to 0.96 (112); test-retest reliability $r=0.63$ to 0.81 (112)	In nonpulmonary populations good correlations with changes in self-reports (111). Hip replacement patients had significant change in scores in the appropriate domains before and after surgery (113)	Discriminative: different profiles between different levels of severity of COPD patients and normal population (114); distinct profiles seen in asthma and other nonpulmonary diseases (115). Evaluative: little information available on the significance of any difference in score
UTILITY MEASURES				
Quality of Well-being (44)	Discriminative: in COPD, moderate to strong correlations with FVC, FEV ₁ and exercise tolerance ($r=0.34$ to 0.54) (116); Evaluative: moderate correlations with exercise tolerance ($r=0.40$) weak correlations with change in oxygen saturation ($r=0.28$); poor correlations with FVC, and FEV ₁ ($r=0.03$ to 0.11) (116)	Interday correlations in COPD patients 0.80 to 0.98 (117)	Able to detect changes over time after education with or without exercise in patients before lung transplant (118) but unable to detect improvement after pulmonary rehabilitation (81)	Little information available on the significance of any difference in score
Standard Gamble (45)	Discriminative: asthmatics – poor correlations with FEV ₁ , FVC and PEFR (0.10) and symptoms (0.17 to 0.21) (119); Evaluative: asthma, weak but significant correlations with PEFR and FVC (0.23 to 0.24) (119); in pulmonary rehabilitation poor correlation with 6MW (unpublished data)	In nonpulmonary populations, internal reliability 0.70 to 0.92; test-retest reliability 0.80 (120)	In asthmatics detected significant differences before and after treatment with salbutamol but not salmeterol and not between groups (119)	Little information available on the significance of any difference in score

Continued on next page

TABLE 6 continued

Instrument	Validity	Reliability/Internal consistency	Responsiveness	Interpretability
Time Trade Off (45)	Little information is available	In nonpulmonary populations; internal reliability 0.77 to 0.88; test-retest reliability 0.63 to 0.80 (120)	Little information is available	Little information available on the significance of any difference in score
Rating Scale (45)	Discriminative: asthmatics – weak correlations with FEV ₁ (0.22) and symptoms (0.26 to 0.33) (119) Evaluative: asthmatics – weak but significant correlations with symptoms (0.23 to 0.24) (119);	In nonpulmonary populations: internal reliability 0.86 to 0.94; test-retest reliability 0.77 (44)	In asthmatics, detected significant differences before and after treatment in salmeterol and salbutamol groups and between groups (119)	Little information available on the significance of any difference in score
Health Utilities Index III (46)	Discriminative: significant difference in utility score between teenagers in control group and group of extremely low-birth-weight infants (121) Evaluative: little information is available	Test-retest reliability in general population: for eight attributes, kappa 0.14 to 0.73. index score (intraclass correlation coefficient) 0.77 (46)	Little information is available	Little information available on the significance of any difference in score

BDI Baselines Dyspnea Index; E Energy; ER Emotional reaction; FEV₁ Forced expiratory volume in 1 s; FVC Forced vital capacity; MH Mental health; MW Minute walk; NPP Nonpulmonary population; P Pain; PEFR Peak expiratory flow rate; PM Physical mobility; PGS Physical Global Score; PSGS Psycho-Social Global Score; RE Role-emotional; S Sleep; TS Total score; VAS Visual Analogue Scale

ported Psychological Adjustment in Illness Scale (39), focus only on the psychological aspects of health.

All of the instruments have proved helpful in distinguishing different populations and examining differences between patients within the same population. The first three instruments in Table 5 have been validated in COPD patients (99,100,104,110). However, the Nottingham Health Profile was designed to discriminate among patients with moderate to severe illness (98). Therefore, it may not be able to discriminate among patients with mild disease.

In an evaluative setting, only the first three instruments in Table 5 have been validated against other measures (99,101,106). Another instrument, the Medical Outcome Survey – Short Form 36 (SF-36), has not been validated in pulmonary patients. The other two instruments showed weak correlations with physiological measures such as the forced expiratory volume in 1 s (FEV₁) (101,106).

The Sickness Impact Profile (SIP) has shown strong evidence of reliability (41). In the remaining questionnaires, there were a few domains in which measures of reliability correlated poorly (38,39,102,112). Trials in COPD patients in which SIP or Nottingham Health Profile was used sometimes identified significant changes in physiological parameters such as FEV₁ without accompanying changes in quality of life assessments (99,101,107). The SF-36 (111,113) and Self-reported Adjustment to Illness Scale (97) are responsive in nonpulmonary patient populations. Whether the instruments are responsive in COPD patients remains to be seen.

The SIP (88,104,115), SF-36 (111,112) and Nottingham Health Profile (103) had distinctive profiles for COPD patients compared with the normal population. The SIP (105) and SF-36 (114) had different profiles for pulmonary patients at different levels of impairment. However, the minimal important difference in the domain scores or the overall scores have not been established, this limitation being most evidence in all five instruments when considering change over time.

In summary, all five health profile instruments listed in Table 5 have similar properties when they are used in a discriminative setting. In an evaluative setting, most of the

instruments have not demonstrated good responsiveness in COPD patients. Therefore, in a clinical trial of COPD patients, it is best to use a combination of a generic health profile to reflect quality of life and a disease-specific instrument to detect small changes.

Utility measures: Utility measures use a preference-based or value-based approach to express the HRQL of an individual using a single number. This number incorporates the overall assessment of HRQL and the values attached to it. This number is usually between 0 and 1. The two extreme values are anchored to specific states, most commonly death (0) and full health (1).

There are two different approaches to obtaining the preference weight which can come directly from the patient or from other people. In two common measures, the Standard Gamble (45) and Time Trade Off (45), the preference comes from the patient. In these measures, the patient trades a specific health state for full health by risking death or by shortening his or her life span.

In the second approach, the preference weight is obtained from other people, most commonly through the use of a multi-attribute questionnaire. A series of health states of increasing severity are compiled based on limitations in different dimensions of HRQL. Either the general population or specific population groups are asked to rate these states on a scale. Based on the responses, preference weights are assigned to the different states. During a study, the patient's utility value of a certain state will be determined by the preference weight assigned to the state, made up of the combination of limitations in the dimensions identified by the patient. This is the basis of the Quality of Well-being (44) and the Health Utilities Index III (46). The advantage of the utility measures is that they allow comparison among different diseases. In addition, the single value summarizing the overall health state and its associated values facilitates economic analyses.

In a discriminative setting, only the Quality of Well-being scale has been validated in COPD patients and demonstrated good discriminative power (116). Both the Standard Gamble and the Rating Scale did not demonstrate strong discrimina-

tive ability in asthmatic patients (119). The Health Utilities Index III is a relatively new instrument with only one study showing its discriminative power in adolescents (120). In the evaluative setting, the Standard Gamble (119), Rating Scale (119) and Quality of Well-being (116) have all been validated against other measures. However, only weak correlations were seen compared with physiological measures such as the FEV₁ and forced vital capacity (116,119).

All five measures demonstrated good reliability except for some attributes of the Health Utilities Index III (46,117,119). The responsiveness of Standard Gamble was disappointing; although it could detect changes before and after a treatment in pulmonary patients, it was unable to detect differences among treatment groups though these differences were noted in physiological measures and disease-specific quality of life instruments (119). The Rating Scale (119) and the Quality of Well-being (81,118) showed better responsiveness. Responsiveness data were not available for pulmonary patients in the Time Trade Off and Health Utilities Index III. Little information was available for any of the five instruments regarding the minimally important clinical difference of the instruments in either a discriminative or an evaluative setting.

In summary, information on the measurement properties of the utility measures is limited; these instruments have demonstrated weak discriminative ability and poor responsiveness to change. Although it is very attractive to use these instruments as part of an economic analysis, caution must be exercised in the interpretation of the data. It is recommended that utility measures be used in conjunction with other measures of quality of life in clinical trials.

DISCUSSION

Selection of a questionnaire for clinical research: The most appropriate clinical application of any questionnaire must be in the context of whether it is discriminative, evaluative or both (122). A discriminative instrument is one that can distinguish among groups of patients. Accordingly, the most important properties of a discriminative instrument should be its validity, reliability and interpretability. An evaluative instrument is one that measures changes in individuals or groups over time. Accordingly, the most important properties of a discriminative instrument should be its validity, responsiveness and interpretability. The requirements for maximizing one of the functions (discrimination or evaluation) may influence the choice of questionnaire (122). Because it focuses on specific areas of HRQL, a disease-specific questionnaire is more likely to be responsive to change than a generic instrument designed to measure all important aspects of HRQL (18).

Respiratory rehabilitation has illustrated the application of health status measurement instruments in COPD. In some trials of respiratory rehabilitation, the validity of the health status measurement instruments in a population with chronic lung disease has not been clearly ascertained beforehand. When valid health status measures were used, they sometimes consisted of generic instruments unlikely to detect small but clinically important changes over time. The conclu-

sions from an important, well designed, randomized, controlled trial illustrate this point. Toshima and collaborators (123) reported a trial of comprehensive rehabilitation versus education in patients with COPD. This paper and two other articles (81,124) reported short and long term follow-up results. One hundred and nineteen patients were randomized to either an eight-week comprehensive rehabilitation program (including upper and lower extremity exercise training, chest physiotherapy, psychological support and didactic education) or to a four-session didactic education program. The outcome measures included incremental and steady-state treadmill exercise tests, a self-efficacy scale, the Quality of Well-being Questionnaire (44), the CES-D (89) and the University of California, San Diego, Shortness of Breath Questionnaire (37), all health status instruments that had been proved valid in COPD populations. Immediately after the program, significant changes from baseline, favouring the group that had received exercise therapy, were noted in exercise capacity, self-efficacy for walking and shortness of breath scores. The clinical significance of these changes was uncertain. There were no significant between group differences in the general measures of quality of life or depression. The authors concluded that the Quality of Well-being Questionnaire (a generic instrument) may not have been sensitive enough to detect changes in quality of life attributable to rehabilitation (81). Clearly the choice of questionnaires must match the study objectives; valid questionnaires that are able to detect change over time are essential in clinical evaluative studies of respiratory rehabilitation.

In selecting a questionnaire to be used in clinical research, the investigator should first answer the following questions: Do I want to evaluate an intervention or discriminate among patients? Which of the domains am I most interested in measuring (symptoms, function, emotion, etc)? What is the time frame of the study? These should help the investigator identify the most appropriate questionnaire or questionnaires for the study. In a rehabilitation trial, a generic questionnaire can help to characterize the patients at baseline, whereas one or more selected disease-specific (and responsive) questionnaires can be used to evaluate the effect of the intervention on symptoms (Baseline and Transition Dyspnea Index [1], CRQ [30]) or the impact of the disease (St George's Respiratory Questionnaire [3,35]). When selecting a questionnaire it is also important to also consider the mode, ease and duration of administration (18).

Exercise capacity or health-related quality of life? Our objective was not to discourage the use of exercise testing (or other physiological outcomes such as FEV₁) as end-points in clinical trials in COPD. Exercise capacity testing constitutes an invaluable tool in many respects, but it serves different purposes in measuring different constructs (Table 1). Whereas exercise capacity testing is intended to measure the impairment, ie, the loss or abnormality of physiological function (125,126), and disability, ie, the lack of ability to perform an activity in the manner considered normal for a human being (125), quality of life has more to do with handicap – the disadvantage for a given individual, resulting

from impairment or disability, that limits or prevents fulfilment of a role that is normal for that individual (125).

The use of laboratory exercise testing has been summarized in two broad categories: diagnostic and management (127). An initial exercise test is useful in describing the physiological consequences of the disease and may disclose a coronary or peripheral arterial disease limiting or even contraindicating vigorous training in some patients with COPD. More importantly, exercise testing is useful in the clinical management of patients participating in a respiratory rehabilitation program. For instance, an initial incremental exercise test is helpful in assisting with the prescription of an appropriate level of training (128,129). Also, retesting provides physiological evidence that a training response has occurred and may be useful in the adjustment of intensity levels during the program (127). Exercise testing may be useful in motivating the patient to continue the activities (127). The measurements of health status and exercise capacity are complementary.

Future direction: Health status measurement has become an important part of identifying the impact of a management strategy and is likely to become of increasing interest. Physicians and nonphysician health professionals are likely to continue clinical research aimed at improving the comprehensive and integrative care of patients with COPD. We suggest that future research includes further validation and a better definition of the interpretability of existing instruments rather than the development of new questionnaires.

REFERENCES

- Mahler DA, Weinberg DH, Wells CK, Feinstein AR. The measurement of dyspnea. Contents, interobserver agreement, and physiologic correlates of two new clinical indexes. *Chest* 1984;85:751-8.
- Guyatt GH, Thompson PJ, Berman LB, et al. How should we measure function in patients with chronic heart and lung disease? *J Chron Dis* 1985;38:517-24.
- Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation. The St George's respiratory questionnaire. *Am Rev Respir Dis* 1992;45:1321-7.
- Lacasse Y, Wong E, Guyatt GH. A systematic overview of the measurement properties of the Chronic Respiratory Questionnaire. *Can Respir J* 1997;4:131-9.
- McCord M, Cronin-Stubbis D. Operationalizing dyspnea: Focus on measurement. *Heart Lung* 1992;21:167-79.
- Eakin AG, Kapla RM, Ries AL. Measurement of dyspnea in chronic obstructive pulmonary disease. *Qual Life Res* 1993;2:181-91.
- Lareau SC, Breslin EH, Meek PM. Functional status instruments: outcome measure in the evaluation of patients with chronic obstructive pulmonary disease. *Heart Lung* 1996;25:212-24.
- Guyatt GH. Measuring health-related quality of life: General issues. *Can Respir J* 1997;4:123-130.
- Killian KJ, Leblanc P, Martin DH, Summers E, Jones NL, Campbell EJM. Exercise capacity and ventilatory, circulatory, and symptom limitation in patients with chronic airflow limitation. *Am Rev Respir Dis* 1992;146:935-40.
- Jones NL, Jones G, Edwards RHT. Exercise tolerance in chronic airway obstruction. *Am Rev Respir Dis* 1971;103:477-91.
- Kinsman RA, Yaroush RA, Fernandez E, Dirks JF, Schocket M, Fukuhara J. Symptoms and experiences in chronic bronchitis and emphysema. *Chest* 1983;83:755-61.
- Guyatt GH, Townsend M, Berman LB, Pugsley SO. Quality of life in patients with chronic airflow limitation. *Br J Dis Chest* 1987;81:45-54.
- Casaburi R. Exercise training in chronic obstructive lung disease. In: Casaburi R, Petty TL, eds. *Principles and Practice of Pulmonary Rehabilitation*. Philadelphia: WB Saunders, 1993:204-24.
- Light RW, Merrill EJ, Despars JA, Gordon GH, Mutalipassi LR. Prevalence of depression and anxiety in patients with COPD. Relationship to functional capacity. *Chest* 1985;87:35-8.
- Lacasse Y, Wong E, Guyatt GH, King D, Cook DJ, Goldstein RS. Meta-analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. *Lancet* 1996;348:1115-9.
- McGavin CR, Gupta SP, Lloyd EL, McHardy GJR. Physical rehabilitation for the chronic bronchitis: Results of a controlled trial of exercises in the home. *Thorax* 1977;32:307-11.
- Cockcroft AE, Saunders MJ, Berry G. Randomised controlled trial of rehabilitation in chronic respiratory disability. *Thorax* 1981;36:200-3.
- Guyatt GH, Feeny DH, Patrick DL. Measuring health-related quality of life. *Ann Intern Med* 1993;118:622-9.
- Alexander MR, Dull WL, Kasik JE. Treatment of chronic obstructive pulmonary disease with orally administered theophylline: A double-blind, controlled study. *JAMA* 1980;244:2286-90.
- Jaeschke R, Guyatt GH, Singer J, Keller J, Newhouse MT. Mechanism of bronchodilator effect in chronic airflow limitation. *Can Med Assoc J* 1991;144:35-9.
- Jaeschke R, Guyatt GH, Willan A, et al. Effect of increasing dose of beta-agonists on spirometric parameters, exercise capacity, and quality of life in patients with chronic airflow limitation. *Thorax* 1994;49:479-84.
- McKay SE, Howie CA, Thomson AH, Whiting B, Addis GJ. Value of theophylline treatment in patients handicapped by chronic obstructive lung disease. *Thorax* 1993;48:227-32.
- McSweeney AJ, Creer TL. Health-related quality-of-life assessment in medical care. *Disease-a-Month* 1995;41:1-71.
- Shipper H, Clinch J, Powell V. Definition and conceptual issues. In: Spilker B, ed. *Quality of Life Assessment in Clinical Trials*. New York: Raven Press Ltd, 1990:11-24.
- Fletcher CM, Elmes PC, Fairbairn AS, Wood CH. The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. *BMJ* 1959;ii:257-66.
- American Thoracic Society. Recommended respiratory disease questionnaire for use with adults and children in epidemiological research. *Am Rev Respir Dis* 1978;118(Suppl):7-53.
- McGavin CR, Artvinli M, Naoe H, McHardy GJR. Dyspnoea, disability, and distance walked: Comparison of estimates of exercise performance in respiratory disease. *BMJ* 1978;ii:241-3.
- Daughton DM, Fix AJ, Kass I, Bell CW, Patil KD. Maximum oxygen consumption and the ADAPT quality-of-life scale. *Arch Phys Med Rehabil* 1992;63:620-2.
- Stoller JK, Ferranti R, Feinstein AR. Further specification and evaluation of a new clinical index for dyspnea. *Am Rev Respir Dis* 1986;134:1129-34.
- Guyatt GH, Berman LB, Townsend M, Pugsley SO, Chambers LW. A measure of quality of life for clinical trials in chronic lung disease. *Thorax* 1987;42:773-8.
- Weaver T, Narsavage G. Reliability and validity of Pulmonary Impact Profile Scale. *Am Rev Respir Dis* 1989;139:A244.
- Moody LE. Measurement of psychophysiological response variables in chronic bronchitis and emphysema. *Appl Nurs Res* 1990;3:36-8.
- Wigal JK, Creer TL, Kotses H. The COPD self-efficacy scale. *Chest* 1991;99:1193-6.
- Cox NJM, Hendriks JCM, Dijkhuizen R, Binkhorst RA, van Herwaarden CLA. Usefulness of a medicopsychological questionnaire for lung patients. *Int J Rehab Res* 1991;14:267-72.
- Jones PW, Quirk FH, Baveystock CM. The St George's Respiratory Questionnaire. *Respir Med* 1991;85(Suppl B):25-31.
- Lareau SC, Carrieri-Kohlman V, Janson-Bjerklie S, Ross PJ. Development and testing of the pulmonary functional status and dyspnea questionnaire (PFSDQ). *Heart Lung* 1994;23:242-50.
- Eakin EG, Sassi-Damborn DE, Ries AL, Kaplan RM. Reliability and validity of dyspnea measures in patients with obstructive lung diseases. *Int J Behav Med* 1995;2:118-34.
- Morrow GR, Chiarello RJ, Derogatis LR. A new scale for assessing patient's psychosocial adjustment to medical illness. *Psychological Med* 1978;8:605-10.
- Derogatis LR. *Psychological Adjustment to Illness Scale*. Baltimore: Clinical Psychometric Research, 1977.
- Hunt SM, McKenna SP, McEwen J, Backett EM, Williams J, Papp E. A quantitative approach to perceived health status: A validation study. *J Epidemiol Comm Health* 1980;34:281-6.
- Bergner M, Bobbitt RA, Carter WB, Gilson BS. The Sickness Impact Profile: Development and final revision of a health status measure. *Med Care* 1981;19:878-85.
- Ware JE Jr, Sherbourne CD. The MOS 36-item short form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;40:473-83.
- McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-item short form health survey (SF-36). II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care* 1993;31:247-63.
- Kaplan RM, Bush JW, Berry CC. Health status: Types of validity and the Index of Well-being. *Health Serv Res* 1976;11:478-507.
- Torrance GW. Social preferences for health states: An empirical evaluation of three measurement techniques. *Socio-Econ Plan Sci* 1976;10:129-36.
- Boyle MH, Furlong W, Feeny D, Torrance GW, Hatcher J. Reliability of the Health Utilities Index - Mark III used in the 1991 cycle 6 Canadian General Social Survey Health Questionnaire. *Qual Life Res* 1995;4:249-57.
- Helsing KJ, Comstock GW, Speizer FE, et al. Comparison of three standardized questionnaires on respiratory symptoms. *Am Rev Respir Dis* 1979;120:1221-31.
- Durmin JVG, Passmore R. *Energy, Work and Leisure*. London: Heinemann Educational Books, 1967:30-46.
- Liang M, Larson M, Cullen K, Schwutz J. Comparative measurement efficiency and sensitivity of five health status instruments for arthritis research. *Arthritis Rheum* 1985;28:542-7.
- Spitzer WO, Dobson JH, Chesterman E, et al. Measuring the quality of life in cancer patients. *J Chronic Dis* 1981;34:585-97.
- Mahler DA, Wells CK. Evaluation of clinical methods for rating dyspnea. *Chest* 1988;93:580-6.
- Kirsten DK, Wegner RE, Jorres RA, Magnussen H. Effects of theophylline withdrawal in severe chronic obstructive pulmonary disease. *Chest* 1993;104:1101-7.
- Eaton ML, Green BA, Church TR, McGowan T, Niewoehner DE. Efficacy of theophylline in 'irreversible' airflow obstruction. *Ann Intern Med* 1980;92:758-61.
- Shapiro SH, Ernst P, Gray-Donald K. Effect of negative pressure ventilation in severe chronic obstructive pulmonary disease. *Lancet* 1992;340:1425-9.
- Sassi-Damborn DE, Eakin EG, Ries AL, Kaplan RM. Treatment of dyspnea in COPD - A controlled clinical trial of dyspnea management strategies. *Chest* 1995;107:724-9.
- Mahler DA, Harver A. A factor analysis of dyspnea ratings, respiratory muscle strength, and lung function in patients with chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1992;145:467-70.
- Mahler DA, Tomlinson D, Olmstead EM, Tosteson ANA, O'Connor GT.

- Changes in dyspnea, health status, and lung function in chronic airway disease. *Am J Respir Crit Care Med* 1995;151:61-5.
58. Harver A, Mahler DA, Daubenspeck JA. Targeted inspiratory muscle training improves respiratory muscle function and reduces dyspnea in patients with chronic obstructive pulmonary disease. *Ann Intern Med* 1989;111:117-24.
 59. Lisboa C, Munoz V, Beroiza T, Leiva A, Cruz E. Inspiratory muscle training in chronic airflow limitation: Comparison of two different training loads with a threshold device. *Eur Respir J* 1994;7:1266-74.
 60. Mahler DA, Matthay RA, Snyder PE, Wells CK, Loke J. Sustained-release theophylline reduces dyspnea in nonreversible obstructive airway disease. *Am Rev Respir Dis* 1985;131:22-5.
 61. Reardon J, Awad E, Normandin E, Vale F, Clark B, ZuWallack RL. The effect of comprehensive outpatient pulmonary rehabilitation on dyspnea. *Chest* 1994;105:1046-5.
 62. Goldstein RS, Gort EH, Stubbing D, Avendano MA, Guyatt GH. Randomised controlled trial of respiratory rehabilitation. *Lancet* 1994;344:1394-7.
 63. Wijkstra PJ, Tenvergt EM, vanAltena R, et al. Reliability and validity of the Chronic Respiratory Questionnaire (CRQ). *Thorax* 1994;49:465-7.
 64. Martin LL. Validity and reliability of a quality-of-life instrument. The Chronic Respiratory Disease Questionnaire. *Clin Nurs Res* 1994;3:146-56.
 65. Waterhouse JC, Harper R, Marsh F, Jones NMB, Brazier JE, Howard P. Measuring quality of life in chronic obstructive pulmonary disease. Can we assess change? *Eur Respir J* 1994;7(Suppl):419s.
 66. Larson JL, Covey MK, Berry JK, Wirtz S, Kim MJ. Reliability and validity of the Chronic respiratory disease questionnaire. *Am Rev Respir Dis* 1993;147:A530.
 67. Güell R, Casan P, Sangesis M, Morante F, Belda J, Guyatt GH. The Spanish translation and evaluation of a quality-of-life questionnaire in patients with chronic obstructive pulmonary disease. *Arch Bronconeumol* 1995;31:202-10.
 68. Simpson K, Killian K, McCartney N, Stubbing DG, Jones NL. Randomised controlled trial of weightlifting exercise in patients with chronic airflow limitation. *Thorax* 1992;47:70-5.
 69. Wijkstra PJ, van Altena R, Kraan J, Otten V, Postma DS, Koëter GH. Quality of life in patients with chronic obstructive pulmonary disease improves after rehabilitation at home. *Eur Respir J* 1994;7:269-73.
 70. Güell R, Morante F, Sangesis M, Casan P. Effects of respiratory rehabilitation on the effort capacity and on the health-related quality of life of patients with chronic obstructive pulmonary disease. *Eur Respir J* 1995;8(Suppl):356s. (Abst)
 71. Jaeschke R, Singer J, Guyatt GH. Measurement of health status: ascertaining the minimal clinically important difference. *Controlled Clin Trials* 1989;10:407-15.
 72. Weaver TE, Narsavage GL. Physiological and psychological variables related to functional status in chronic obstructive pulmonary disease. *Nurs Res* 1992;41:286-91.
 73. Moody L, McCormick K, Williams A. Disease and symptom severity, functional status, and quality of life in chronic bronchitis and emphysema (CBE). *J Behav Med* 1990;13:297-306.
 74. Cox N, Hendriks J, Binkhorst R, van Herwaarden C. Symptoms, physical performance and psychosocial parameters before and after pulmonary rehabilitation. *Int J Rehab Res* 1992;15:140-7.
 75. Quirk FH, Jones PW. Patients' perception of distress due to symptoms and effects of asthma on daily living and investigation of possible influential factors. *Clin Sci* 1990;79:17-21.
 76. Quirk FH, Baveystock CM, Wilson R, Jones PW. Influence of demographic and disease related factors on the degree of distress associated with symptoms and restrictions on daily living due to asthma in six countries. *Eur Respir J* 1991;4:167-71.
 77. Meecham Jones DJ, Paul EA, Jones PW, Wedzicha JA. Nasal pressure support ventilation plus oxygen compared with oxygen therapy alone in hypercapnic COPD. *Am J Respir Crit Care Med* 1995;152:538-44.
 78. Jones PW, Lasserson D. Relationship between change in St. George's Respiratory Questionnaire score and patients' perception of treatment efficacy after one year of therapy with nedocromil sodium. *Am J Respir Crit Care Med* 1994;149:A211.
 79. Borson S, McDonald GJ, Gayle T, Deffebach M, Lakshminarayan S, Van Tuinen C. Improvement in mood, physical symptoms, and function with nortriptyline for depression in patients with chronic obstructive pulmonary disease. *Psychosomatics* 1992;33:190-201.
 80. Eakin EG, Prewitt LM, Ries AL, Kaplan RM. Validation of the UCSD Shrotness of Breath Questionnaire. *J Cardiopulmon Rehab* 1994;14:322. (Abst)
 81. Ries AL, Kaplan RM, Limberg TM, Prewitt LM. Effects of pulmonary rehabilitation on physiologic and psychological outcomes in patients with chronic obstructive pulmonary disease. *Ann Intern Med* 1995;122:823-32.
 82. Killian KJ. The objective measurement of breathlessness. *Chest* 1985;88:84S-90S.
 83. Borg G. Psychophysical bases of perceived exertion. *Med Sci Sports Exer* 1982;14:377-81.
 84. Gift AG, McCrone SH. Depression in patients with COPD. *Heart Lung* 1993;22:289-97.
 85. Agle DP, Baum GL, Chester EH, Wendt M. Multidiscipline treatment of chronic pulmonary insufficiency: Psychologic aspects of rehabilitation. *Psychosom Med* 1973;35:41-9.
 86. Karajci B, Rifkin A, Doddi S, Kolli R, Mutalipassi LR. The prevalence of anxiety disorders in patients with chronic obstructive pulmonary disease. *Am J Psychiatry* 1990;147:200-1.
 87. Yellowlees PM, Alpers JH, Bowden JJ, Bryant GD, Ruffin RE. Psychiatric morbidity in patients with chronic airflow limitation. *Med J Aust* 1987;146:305-7.
 88. McSweeney AJ, Grant I, Heaton RK, Adams KM, Timms RM. Life quality of patients with chronic obstructive pulmonary disease. *Arch Intern Med* 1982;142:473-8.
 89. Radloff LS. The CES-D Scale: A self-report depressive scale for research in the general population. *J Appl Psychol Measur* 1977;1:385-401.
 90. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561-71.
 91. Zung WWK. The measurement of affects: Depression and anxiety. *Mod Probl Pharmacopsychiatry* 1974;7:170-88.
 92. Spielberger CD, Gorsuch RL, Lushene RE, Vagg PR, Jacobs GA. STAI: Manual for the State-Trait Anxiety Inventory (form Y). Palo Alto: Consulting Psychologists Press, 1983.
 93. Lader M. The clinical assessment of depression. *Br J Clin Pharm* 1981;1:5-14.
 94. Morgan AD, Peck DF, Buchanan D, et al. Effect of attitudes and beliefs on exercise tolerance in chronic bronchitis. *BMJ* 1983;286:171-3.
 95. Bandura A. Self-efficacy mechanism in human agency. *Am Psychologist* 1982;37:122-47.
 96. Kaplan RM, Atkins CJ, Reinsch S. Specific efficacy expectations mediate exercise compliance in patients with COPD. *Health Psychol* 1984;3:223-42.
 97. Wilhelmsen I, Berstad A. Quality of life and relapse of duodenal ulcer before and after eradication of *Helicobacter pylori*. *Scand J Gastroenterol* 1994;29:874-9.
 98. Kind P, Carr-Hill R. The Nottingham Health Profile: A useful tool for epidemiologists. *Soc Sci Med* 1987;25:905-10.
 99. Van Schayck CP, Dompeling E, Rutten MPMH, Folgering H, Van den Boom G, Van Weel C. The influence of an inhaled steroid on quality of life in patients with asthma or COPD. *Chest* 1995;107:1199-205.
 100. Alonso J, Ant JM, Gonzalez M, Fiz JA, Izquierdo J, Morera J. Measurement of general health status of non-oxygen-dependent chronic obstructive pulmonary disease patients. *Med Care* 1992;30:MS125-35.
 101. Van Schayck CP, Rutten-van Molken MPMH, Van Doorslaer EKA, Folgering H, Van Weel C. Two-year bronchodilator treatment in patients with mild airflow obstruction. *Chest* 1992;102:1384-91.
 102. Hunt SM, McEwen J, McKenna SP. Measuring health status: A new tool for clinicians and epidemiologists. *J R Coll Gen Pract* 1985;35:185-8.
 103. O'Brien BJ, Banner NR, Gibson S, Yacoub MH. The Nottingham Health Profile as a measure of quality of life following combined heart and lung transplantation. *J Epidemiol Comm Health* 1988;42:232-4.
 104. Jones PW, Baveystock CM, Littlejohns P. Relationships between general health measured with the Sickness Impact Profile and respiratory symptoms, physiological measures, and mood in patients with chronic airflow limitation. *Am Rev Respir Dis* 1989;140:1538-43.
 105. Schrier AC, Dekker FW, Kaptein AA, Dijkman JH. Quality of life in elderly patients with chronic nonspecific lung disease seen in family practice. *Chest* 1990;98:894-9.
 106. Marks GB, Dunn SM, Woolcock AJ. An evaluation of an asthma quality of life questionnaire as a measure of change in adults with asthma. *J Clin Epidemiol* 1993;46:1103-11.
 107. The Intermittent Positive Pressure Breathing Trial Group. Intermittent positive pressure breathing therapy of chronic obstructive pulmonary disease: A clinical trial. *Ann Intern Med* 1983;99:612-20.
 108. Jones PW and the Nedocromil Sodium Quality of Life Study Group. Quality of life, symptoms and pulmonary function in asthma: Multicentre treatment with nedocromil sodium examined in a controlled multicentre trial. *Eur Respir J* 1994;7:55-62.
 109. MacKenzie CR, Charlson ME, DiGioia D, Kelly K. Can the sickness impact profile measure change? An example of scale assessment. *J Chronic Dis* 1986;39:429-38.
 110. Mahler DA, Mackowiak JI. Evaluation of the short-form 36-item questionnaire to measure health-related quality of life in patients with COPD. *Chest* 1995;107:1585-9.10
 111. Ware JE Jr, Kosinski M, Bayliss MS, McHorney CA, Rogers WH, Raczek A. Comparison of methods for the scoring and statistical analysis of SF-36 health profile and summary measures: Summary of results from the Medical Outcomes Study. *Med Care* 1995;33:AS264-79.
 112. Brazier JE, Harper R, Jones NMB, et al. Validating the SF-36 health survey questionnaire: New outcome measure for primary care. *BMJ* 1992;305:160-4.
 113. Katz JN, Larson MG, Phillips CB, Fossel AH, Liang MH. Comparative measurement sensitivity of short and longer health status instruments. *Med Care* 1992;30:917-25.
 114. Viramontes JL, O'Brien B. Relationship between symptoms and health-related quality of life in chronic lung disease. *J Gen Intern Med* 1994;9:46-8.
 115. Lyons RA, Lo SV, Littlepage BNC. Comparative health status of patients with 11 common illnesses in Wales. *J Epidemiol Community Health* 1994;48:388-90.
 116. Kaplan RM, Atkins CJ, Timms R. Validity of a quality of well-being scale as an outcome measure in chronic obstructive pulmonary disease. *J Chronic Dis* 1984;37:85-95.
 117. Anderson JP, Kaplan RM, Berry CC, Bush JW, Rumbaut RG. Interday reliability of function assessment for a health status measure: the quality of well-being scale. *Med Care* 1989;27:1076-84.
 118. Manzetti JD, Hoffman LA, Sereika SM, Scierba FC, Griffith BP. Exercise, education, and quality of life in lung transplant candidates. *J Heart Lung Transplant* 1994;13:297-305.
 119. Rutten-van Molken MPMH, Custers F, et al. Comparison of performance of four instruments in evaluating the effects of salmeterol on asthma quality of life. *Eur Respir J* 1995;8:888-98.
 120. Torrance GW. Utility approach to measuring health-related quality of life. *J Chronic Dis* 1987;40:593-603.
 121. Saigal S, Feeny D, Rosenbaum P, Furlong W, Burrows E, Stoskopf B. Self-perceived health status and health-related quality of life of extremely low-birth-weight infants as adolescence. *JAMA* 1996;276:453-9.
 122. Kirshner B, Guyatt G. A methodological framework for assessing health indices. *J Chronic Dis* 1985;38:27-36.
 123. Toshima MC, Kaplan RM, Ries AL. Experimental evaluation of rehabilitation in chronic obstructive pulmonary disease: Short-term effects on exercise endurance and health status. *Health Psychol* 1990;9:237-52.
 124. Toshima MT, Blumberg E, Ries AL, et al. Does rehabilitation reduce depression in patients with chronic obstructive pulmonary disease. *J Cardiopulmon Rehabil* 1992;12:261-9.
 125. World Health Organization. International Classification of Impairments, Disabilities, and Handicaps. Geneva: World Health Organization, 1993:27-9.
 126. American Thoracic Society. Evaluation of impairment/disability secondary to respiratory disorders. *Am Rev Respir Dis* 1986;133:1205-9.
 127. Jones NL. Clinical Exercise Testing. Philadelphia: WB Saunders, 1988:123-34.
 128. Casaburi R, Patessio A, Ioli F, et al. Reductions in exercise lactic acidosis and ventilation as a result of exercise training in patients with obstructive lung disease. *Am Rev Respir Dis* 1991;143:9-18.
 129. Vallet G, AhmaVdi S, Serres I, et al. Comparison of two training programs in CAL patients: Standardized versus individualized method. *Eur Respir J* 1997;10:114-22.



Hindawi
Submit your manuscripts at
<http://www.hindawi.com>

