J Clin Epidemiol Vol. 45, No. 2, pp. 117–125, 1992
Printed in Great Britain

0895-4356/92 $5.00 + 0.00
Pergamon Press plc

FUNCTIONAL STATUS AS AN OVERALL MEASURE OF HEALTH IN ADULTS WITH CYSTIC FIBROSIS: FURTHER VALIDATION OF A GENERIC HEALTH MEASURE

STEVEN L. SHEPHERD,[1] MELBOURNE F. HOVELL,[1,*] DONALD J. SLYMEN,[2] IVAN R. HARWOOD,[2] C. RICHARD HOFSTETTER,[4] LAURA E. GRANGER[5] and ROBERT M. KAPLAN[6]

[1]Center for Behavioral Epidemiology, Graduate School of Public Health, San Diego State University, [2]Division of Epidemiology and Biostatistics, Graduate School of Public Health, San Diego State University, [3]Department of Pediatrics, School of Medicine, University of California, San Diego, [4]Department of Political Science, San Diego State University, [5]Department of Internal Medicine, Southern California Permanente Medical Group, San Diego and [6]Division of Health Care Sciences, School of Medicine. University of California, San Diego, California, U.S.A.

(Received in revised form 24 July 1991)

Abstract—We studied the validity of a generic health measure in a population with a chronic, life-shortening illness. Thirty-seven adults with cystic fibrosis (CF) and 46 of their healthy peers completed a questionnaire which included 12 questions on functional status from the RAND Health Insurance Study. For the CF group, the questionnaire and a medical chart review yielded data on 7 additional health variables, including pulmonary function. After data collection, members of the CF group were followed for 5 years, by which time 11 had died.

The functional status of the CF group was significantly lower than that of the comparison group. Within the CF group, functional status correlated significantly with 6 of the 7 other health variables. Analysis using the Cox proportional hazards model showed that functional status alone was a significant ($p < 0.001$) predictor of a CF subject's survival time; in a multivariate model a non-significant trend suggested that lowered functional status may be associated with an increased risk of early death even after adjustment for pulmonary function and percent ideal body weight. These results extend previous findings and suggest that functional status can be used as an overall measure of health in a wide variety of studies.

Cystic fibrosis Adults Health status indicators Health surveys Morbidity Prospective studies

INTRODUCTION

Interest in the development and use of generic or non-disease-specific measures of health has been growing rapidly. Among the reasons for this are the ability of generic health measures to facilitate comparisons between heterogeneous patient populations or diverse medical interventions; their reflection of aspects of health that are important to patients but may not be captured by traditional physiologic measures (such as complications, comorbidity and treatment side-effects); and the potential for appropriately selected generic measures to be fruitfully incorporated into routine clinical practice [1–5]. So important do some reviewers now consider

*All correspondence should be addressed to: Melbourne F. Hovell, Ph.D., Center For Behavioral Epidemiology, Graduate School of Public Health, San Diego State University, San Diego, CA 92182-0405, U.S.A.

generic health measures that at least one group has stated that their inclusion is "crucial" to the proper design of many clinical trials [6].

For any measure to be of use, however, it must be reliable and valid. In the case of generic health measures it helps further if broad applicability can be demonstrated. One of the most comprehensive efforts to develop reliable, valid and practical generic health status measures has been that involved in the planning of the RAND Health Insurance Study (HIS) [7]. One measure used in the HIS was functional status—"the performance of or the capacity to perform a variety of activities normal for people in good health" [8]. Analyses have shown a 14-item questionnaire assessing functional status to have high 4-month test–retest reliability and strong associations with a variety of other health measures in community-dwelling adults below 62 years of age [9].

Many of the items used to assess functional status in the HIS were later incorporated into the Medical Outcomes Study [10]. The results of this more recent study demonstrate that differences in functional status scores permit differentiation between patients with and without common chronic disorders, that different chronic disorders are associated with different functional limitation profiles, and that patients with greater numbers of chronic disorders have greater decrements in functioning [11]. At least one additional study has shown that functional status as assessed by the RAND HIS method is correlated cross-sectionally with diastolic blood pressure in patients with hypertension and with glycoslyated hemoglobin in patients with diabetes, and that in both cases the measurement of functional status can add significantly to the prediction of these same physiological measures at a 6-month retest [12]. Despite this prognostic use of the RAND functional status measure, however, this instrument's ability to predict mortality in a chronically ill population or to do so in relation to a more traditional physiologic measure has, to our knowledge, not yet been studied.

Cystic fibrosis (CF) is an inherited, life-shortening disorder; in 1986 the projected mean life expectancy for a child born with CF was 26 years [13]. Multiple organ systems are affected but most CF-related morbidity and mortality is due to chronic lung infection; in one recent series of CF adolescents and adults three-quarters of all hospital stays and 97% of all deaths were caused by pulmonary disease [14]. The purpose of our study was 2-fold: to assess the validity of a RAND-derived index of functional status as a measure of overall health in adults with CF. And second, to assess the ability of functional status to predict mortality in this same population and to do so in relation to a routinely used physiologic measure—pulmonary vital capacity. A demonstration of validity and prognostic value in this population should further extend both clinical and research acceptance of this or related easily administered measures of health.

METHODS

Subjects

Patients at the University of California, San Diego, Cystic Fibrosis Center (UCSD) were eligible for participation if they were 18 years of age or older, English speaking, and had confirmed diagnoses of CF on the basis of positive sweat tests. Of 55 patients meeting these criteria, 37 (28 men and 9 women; mean age 27.2) agreed to participate. This participation rate is similar to that obtained in other studies of patients with CF involving the use of questionnaires [15, 16] or medical chart reviews [17] (less-than-100% "participation" rates in this latter methodology resulting from incomplete data in some available charts). A detailed sociodemographic description of the participants has been published [18]. Participants did not differ statistically from eligible non-participants with respect to such medical and sociodemographic variables as mean age, proportion that was male, mean percentage of predicted slow vital capacity, mean percentage of ideal body weight, mean number of days hospitalized in the preceding year, or mortality rates 1 and 5 years after recruitment [18]. Medically and sociodemographically the participants appear reasonably representative of other populations of CF adults described in the literature [18].

The analysis described here is part of a larger study intended to assess prospectively the possible differential relationship between stress and health in groups with varying baseline health or stress-exposure characteristics. Because of this larger study's design, data on functional status were available from a comparison group of 46 adults recruited from local colleges and businesses and free of self-reported chronic disease [18]. The CF and the healthy comparison groups did not differ significantly with respect to major sociodemographic variables (e.g. age and

socoieconomic status) and a variety of psychosocial variables (e.g. social support) [18].

The study protocol was approved by the human subjects committees of the University of California, San Diego and San Diego State University. All subjects were volunteers and provided informed consent.

Instruments and variables

Data were obtained by means of mailed questionnaires composed of closed-ended questions. Among these were 12 questions assessing functional limitations (Table 1). Ten were taken verbatim from RAND's Revised Functional Limitations Battery [8]. An eleventh RAND question (question No. 8, Table 1) was added on the basis of recommendations aimed at improving sensitivity [8]. Question No. 11 was created by us to assess self-imposed limitations in functional status, a problem we have commonly observed in this study population.

The RAND-recommended response options to the functional limitations questions make it possible to determine the duration of a functional limitation (existing for less or more than 3 months), but the frequency in our study of answers indicating short-term limitations was very low and all answers were recoded to indicate only the presence or absence of a limitation. Following the approach used by RAND researchers, a Functional Status Index (FSI) was created [9]. Questions were placed in one of four categories of limitations—mobility, physical activity, social role activity, or general—and the total number of categories in which a limitation existed used as the FSI score. Possible scores ranged from 0 to 4.

Additional health variables obtained or calculated from the mailed questionnaires included number of disability days during the preceding year, number of days hospitalized during the preceding 2 years, percent of ideal body weight, a self-rating on a 5-point scale of the subject's health compared to other adults with CF, an index of current life satisfaction [18], and an acute symptom index reflecting the frequency of occurrence during the preceding 2 years of 16 minor, non-specific acute physical symptoms (e.g. headaches or joint soreness). The questions in this latter index were also based on instruments developed for the RAND HIS [19].

A review of the CF subjects' medical charts was performed to obtain data on pulmonary function. At the UCSD CF Center the measure of pulmonary function obtained most frequently is slow vital capacity (SVC)—the total volume of air that can be exhaled without regard to rapidity after a maximum inhalation. Measured with a spirometer and expressed as a percentage of expected for a patient's height, sex and age, SVC is assessed for all patients during routine annual evaluations and at all clinic visits. The data for this study consist of the most recent SVC value entered in each patient's medical record prior to the administration of the mailed questionnaire.

The vital status of the CF subjects has been monitored since the administration of the mailed questionnaires and the number of months each patient has survived entered into

Table 1. Question content and scoring method of the Functional Status Index

Scoring method:	Total number of categories in which any item received a yes
Possible score range:	0 (no limitations in any category) to 4 (at least one limitation in every category)

Category of limitation: *Mobility*

1. When you travel around your community, does someone have to assist you because of your health?
2. Do you have to stay indoors most or all of the day because of your health?

Category of limitation: *Physical Activity*

3. Does your health limit the kind of vigorous activities you can do, such as running, lifting heavy objects, or participating in sports?
4. Do you have any trouble either walking several blocks or climbing a few flights of stairs, because of your health?
5. Do you have trouble bending, lifting, or stooping because of your health?
6. Do you have any trouble either walking one block or climbing one flight of stairs because of your health?

Category of limitation: *Social Role Activity*

7. Are you unable to do certain kinds or amounts of work, housework or schoolwork because of your health?
8. Does your health cause you to be slow, inefficient, or to tire easily in your work, schoolwork, or major activity?
9. Does your health keep you from working at a job, doing work around the house, or going to school?
10. Do you need help eating, dressing, bathing or using the toilet because of your health?

Category of limitation: *General*

11. Because of your health, do you sometimes make decisions not to do things you normally do, such as exercising or going out for entertainment?
12. Does your health limit you in any way from doing anything you want to do?

Adapted with permission from Ref. [8].

the data set. As of 60 months 11 patients had died, all from pulmonary disease.

Statistical analysis

Validity can be assessed several ways [20]. The approach most commonly used in evaluating health measures is to assess construct validity. This involves assembling empirical evidence that a measure is related as expected to other measures that tap dimensions of the same construct (e.g. health). To this end we first sought to determine if there was a difference (as would be expected) in functional status between the adults with cystic fibrosis and those with no chronic disorder. This was accomplished by comparing mean FSI scores using a t-test and the percentage of each group affected by each category of functional limitation using contingency table analysis. We next determined the extent to which the FSI scores in the CF group were correlated in the expected direction with our other available health measures. Specifically, higher FSI scores (indicative of more functional limitations) were expected to be associated with lower self-rated health, lower current life satisfaction, more frequent acute symptoms, and greater numbers of disability and hospital days. Higher FSI scores were expected to be negatively correlated with slow vital capacity and percent ideal body weight.

A second type of validity is criterion validity—the extent to which a measure correlates with an acknowledged "gold standard." A subset of criterion validity is predictive validity, which refers to the ability of a measure to accurately forecast a criterion measured at some point in the future. Criterion validity generally cannot be determined for health measures because there is no single definition for "health." But in the case of a life-shortening disease such as CF, it could be argued that survival time represents at least a proxy for such a gold standard.

The value of the FSI and SVC scores in predicting the CF subjects' survival time from the date of questionnaire administration was examined by fitting the Cox proportional hazards model [21] using the Cox model program (2L) in the BMDP statistical software package. Two-sided tests for significance were carried out using the likelihood ratio test. Confidence intervals were constructed based on the normal theory method. Our approach to these analyses was to evaluate first the significance within the model of the FSI score alone and SVC alone, then to evaluate whether one made a significant contribution in the presence of the other. Because low weight can also influence survival in adults with CF [22], the latter analysis was performed while controlling statistically for percent ideal body weight (IBW) using the CF group mean of 89.

RESULTS

Of the 37 CF subjects, 51% had an impairment in at least one category of functioning. Of the 46 comparison subjects, 9% had a functional limitation. The mean number of categories of functional limitation (FSI score) for the CF subjects was 1.3; that of the comparison subjects, 0.13 ($p < 0.001$). The percentage of the two subject groups affected by each category of limitation is shown in Table 2. For three of the four categories of limitation, a significantly greater number of CF subjects was affected.

Table 3 shows the Pearson correlations for the eight health variables available for the CF subjects. The FSI was significantly correlated in the expected direction with six of the other seven health variables; the absolute values of these significant correlations compare favorably with those between the FSI and five similar health variables in a study by RAND researchers of adults selected from the general population [9].

Table 2. Distribution of functional limitations by category of limitation

	Number (and percentage) of subjects with any limitations in this category		
Category of limitation	CF subjects ($n = 37$)	Healthy comparison subjects ($n = 46$)	p-Value
Mobility	2 (5.4)	0 (0)	0.2*
Physical activity	15 (40.5)	1 (2.2)	<0.001†
Social role activity	15 (40.5)	1 (2.2)	<0.001†
General	17 (45.9)	4 (8.7)	<0.001†

*Two-sided Fisher's exact test. †Uncorrected chi-square test for association.

Table 3. Pearson correlation coefficient matrix for all health variables measured in the CF subject group

Variable	Pearson correlation coefficient (p-value)							
	1	2	3	4	5	6	7	8
1. Functional Status Index*	—							
2. Self-rated health compared to CF peers*	0.63 (0.001)	—						
3. Current Life Satisfaction index*	0.51 (0.001)	0.40 (0.001)	—					
4. Slow vital capacity†	−0.57 (0.001)	−0.47 (0.002)	−0.44 (0.003)	—				
5. Acute Symptom Index*	0.53 (0.001)	0.20 (0.114)	0.18 (0.150)	−0.29 (0.042)	—			
6. Disability days during preceding year*	0.71 (0.001)	0.62 (0.001)	0.34 (0.025)	−0.66 (0.001)	0.50 (0.001)	—		
7. Hospital days during preceding 2 years*	0.56 (0.001)	0.25 (0.065)	0.11 (0.260)	−0.55 (0.001)	0.30 (0.034)	0.68 (0.001)	—	
8. Percent ideal body weight†	−0.22 (0.094)	−0.36 (0.015)	−0.25 (0.70)	0.53 (0.001)	0.001 (0.497)	−0.37 (0.015)	−0.18 (0.143)	—

*Higher scores indicate more functional limitations, worse self-rated health, lower current life satisfaction, higher frequency of acute symptoms, more disability days, and more hospital days, respectively.
†Higher scores indicate greater vital capacity and higher relative weight, respectively.

Results from the Cox proportional hazards model for the CF subjects are shown in Table 4. They show the FSI score by itself to be a highly significant ($p < 0.001$) predictor of survival time. The same is true of SVC. When both FSI and SVC were entered into the model and the effects of low weight controlled for statistically (Model 3), the independent predictive power of both variables was reduced ($p = 0.049$ for SVC; $p \leqslant 0.127$ for FSI). This is not surprising given the limited statistical power of a multivariate model incorporating three variables and based on only 11 deaths.

Figure 1 shows the survival curves derived from the Cox model for two different levels of functional status at baseline. Figure 2 shows curves for three different levels of pulmonary function at baseline. And Figs 3 and 4 show survival curves with both FSI and SVC included and controlling statistically for the effects of percent ideal body weight. Figure 3 shows the differing survival probabilities associated with FSI scores of 1 and 3 at baseline, given a slow vital capacity of 70, whereas Fig. 4 shows the differing survival probabilities associated with slow vital capcities of 100, 70 and 40, given a functional status index score of 1. When compared visually to the curves in Figs 1 and 2, the curves in Figs 3 and 4 suggest the increased refinement made possible in determining survival probabilities when FSI and SVC are used together rather than separately.

Table 4. Estimates for the CF subject group of regression coefficients and tests of hypotheses for the FSI and SVC scores from the Cox proportional hazards model

Variable	Coefficient	Relative risk		p-Value*
		Point estimate	95% confidence interval	
Model 1				
FSI	1.031	2.8	1.6, 4.9	<0.001
Model 2				
SVC†	−0.076	0.47	0.33, 0.67	<0.001
Model 3				
FSI	0.451	1.6	0.85, 2.9	0.127
SVC†	−0.053	0.59	0.33, 1.04	0.049
IBW	0.0015	1.01	0.94, 1.07	0.962

*Likelihood ratio test.
†Reported values are for a 10-unit change in SVC.

DISCUSSION

Research implications

The growth of interest in generic health measures in recent years has not been without its problems. Among these are a tendency to create new measures for studying new hypotheses or applications (a tendency counter to the very concept of *generic* measures) and a frequent failure to fully validate such newly developed measures [2]. For these reasons measures which have been previously used and validated are of great value. Several instruments meet these criteria but among the easiest to

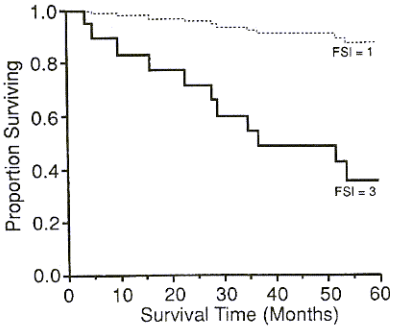

Fig. 1. Length of survival of CF adults by two representative FSI scores.

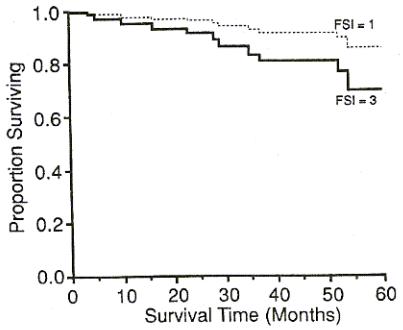

Fig. 3. Length of survival of CF adults by two representative FSI scores, adjusted for pulmonary function (SVC = 70) and percent ideal body weight (IBW = 89).

administer and score are those developed for the RAND Health Insurance Study [3]—in particular the RAND Functional Status Index. The Index has been shown to be a valid overall measure of health in a general population [9], and measures of functional status that are closely related have been validated in populations with common chronic illnesses [11].

Our results support and extend those of these earlier investigations. The FSI discriminated well between the adults with CF and those free from chronic disease. This is not surprising, given the potential severity of cystic fibrosis. However, because of the availability to us of data from a healthy comparison group, and because relatively few studies of functional status among persons with chronic illnesses have included comparison groups [11], we thought it important to verify that the FSI did indeed have such discriminative capability. The mean FSI scores of the two groups differed significantly, and in three out of four categories of functional limitation a significantly greater portion of the CF group was affected (Table 2). The only category in which a significant difference did not exist was in mobility limitations. This corresponds to previous findings that mobility limitations are the least common of functional limitations, probably representing the greatest degree of ill-health, and are the least sensitive category of limitations for use when attempting to determine differences in health status between groups [9].

The FSI also correlated as expected with virtually all the health measures available for subjects in the CF group. In particular, it correlated highly ($r = -0.57$; $p = 0.001$) with our measure of pulmonary function. This correlation is comparable with those obtained between measures of pulmonary function and an alternate generic health measure in patients with COPD [23] and CF [24], and is consistent with findings that the RAND measure of functional status correlates with physiologic health measures in subjects with hypertension and diabetes [12]. These demonstrations of construct validity contribute to a growing body of evidence that functional status can be used as an overall health measure in a wide variety of groups: the general population [9], those with common chronic diseases [11], and, as in our study, those with less common chronic diseases.

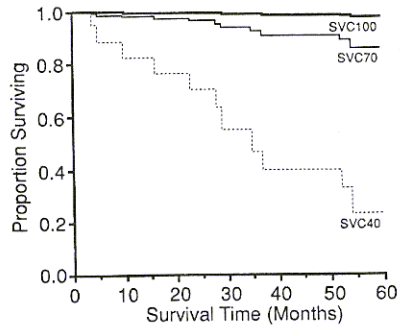

Fig. 2. Length of survival of CF adults by three representative values for SVC.

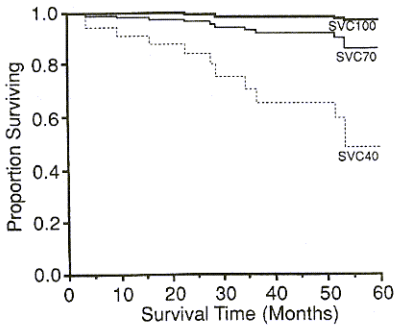

Fig. 4. Length of survival of CF adults by three representative values for SVC, adjusted for functional limitations (FSI = 1) and percent ideal body weight (IBW = 89).

As a further test of validity, and because the ability of the RAND measure of functional status to predict mortality had not previously been assessed, we analyzed the utility of functional status in predicting long-term mortality risk in the adults with CF. An initial univariate analysis showed that by itself functional status is a statistically significant predictor of survival time ($p < 0.001$; Model 1, Table 4), a finding of potential importance to investigators planning studies (e.g. epidemiological surveys) in which physiological measures will be unattainable. In a multivariate analysis incorporating two physiologic measures of recognized importance in this population—pulmonary function and relative weight, the ability of functional status to help predict survival in adults with CF was somewhat less striking, showing a non-significant trend only.

A possible explanation for the failure of functional status to achieve statistical significance as an independent predictor of survival time in this latter instance is inadequate statistical power—specifically, the use of a 3-variable model based on 11 deaths only. Given the consistent findings of the other analyses presented in this paper, it is our opinion that the multivariate analysis supports the presence of criterion validity for this measure in this group. Nonetheless, confirmation that functional status is a statistically significant independent predictor of survival time in adults with CF when adjusting for pulmonary function and weight will require a larger sample size encompassing more deaths. If the sample size is sufficient, additional physiological control variables such as FEV_1 or pancreatic sufficiency could be added. Or, given the recently verified close association in CF between genotype and clinical expression of the disease [25], adjustment could be made for genetic characteristics. Alternatively, the ability of functional status to help predict mortality risk could be examined in different clinical populations.

Clinical utility

There have been many previous attempts at developing valid assessment and prognostic schemes for patients with CF [26–28]. Despite their ability to aid in the prediction of either mortality risk or short-term changes in clinical status, all have been time-consuming and elaborate, requiring extensive physician evaluations as well as data from physiologic measures such as X-ray and pulmonary function scores, and none has been incorporated into widespread clinical practice. In contrast, the assessment of functional status takes but minutes and requires no physician input, thus making it a practical measure which could be obtained and recorded at all clinic visits.

There are several potential uses for this information. Nelson *et al.* have reported preliminary findings of a study assessing the feasibility and clinical usefulness of a simple office-based method for determining the functional status of patients in a private practice and at a Veterans Administration general medical clinic [5]. According to these authors, office-based assessments "frequently opened avenues of communication on clinical topics that would likely have gone unnoticed"—i.e. physicians were made aware of problems being experienced by their patients that might otherwise have gone unexplored. They also found that office-based functional assessments frequently "revealed substantially greater levels of dysfunction than previously recognized by the clinician".

Such revelations could be of benefit if followed by effective intervention. The diagnostic pursuit of previously unsuspected comorbidity might be one example of such an intervention. Depression, for instance, is associated with decreased functional status [29] and increased mortality risk [30], and the diagnosis and treatment of depression resulting from the identification of excessive functional impairment could conceivably lead to improved health and longevity in a patient with CF. But it may be unnecessary to identify the physiological cause of a given amount of functional impairment; it may be sufficient merely to improve a person's level of functioning. This possibility was demonstrated incidentally in a recent randomized controlled trial designed to study the safety of early hospital discharge in cases of uncomplicated myocardial infarction [31]; results after 6 months showed that early discharge tended to be associated with fewer rehospitalizations for cardiac reasons, a lower incidence of angina, and fewer reinfarctions. If the early hospital discharges in this study are viewed as interventions to promote an early return to function, it can be concluded that this non-disease-specific intervention produced quantifiable health benefits. Rubenstein *et al.* [32] have described a variety of function-enhancing interventions; which of these or others might benefit adults with CF is unknown, but the subject appears worthy of future research.

CONCLUSION

Our results suggest that the RAND measure of functional status has validity and applicability beyond that already demonstrated by its developers. This measure includes questions originally derived from the Quality of Well-being Scale [33] and which are similar to questions in several other generic health-related quality of life measures currently in use, as well as in the National Health Interview Survey and the Current Population Survey. Recent developments in health status measurement have improved upon the original RAND HIS measure by increasing sensitivity to minor variations in health and well-being [33, 34], but many of these newer measures retain at their core questions about functional status that are related to those examined in this study.

These newer generic health measures are suitable for inclusion in a wide variety of studies and settings, including epidemiological surveys, comparisons of patients with different or multiple diseases, and single- or multi-center studies comparing the effects of different interventions on patients with the same disease. The widespread use of such measures could, through the pooling of results, eventually produce invaluable information about the influence of diverse medical and social influences on health [1], particularly if incorporated within them were features such as the consistent measurement of functional status. Although no consensus now exists on which of several alternatives this consistent measure of functional status should be, the best candidates all include components related to those in the RAND FSI and examined here.

Clinically, office-based measurements of functional status have the potential for identifying patients suffering from previously unsuspected levels of dysfunction. It is conceivable that such identification could lead to interventions that improve patients' ability to function, that produce improvements in various physiological measures, and—in some instances perhaps—that improve longevity. All these possibilities remain to be tested, but the prospects are intriguing.

Acknowledgements—This work was supported in part by a grant from The San Diego Chapter of the Cystic Fibrosis Foundation. We thank Mark Welle, of the San Diego Xerox Reproduction Center, for photocopying the questionnaires used in this study, and Anita Jones for help in data collection.

REFERENCES

1. Ellwood PM. Shattuck lecture—outcomes management: a technology of patient experience. **N Engl J Med** 1988; 318: 1549–1556.
2. Spitzer WO. State of science 1986: quality of life and functional status as target variables for research. **J Chron Dis** 1987; 40: 465–471.
3. Read JL, Quinn RJ, Hoeffer MA. Measuring overall health: an evaluation of three important approaches. **J Chron Dis** 1987; 40 (Suppl. 1): 7S–21S.
4. Ware JE. Standards for validating health measures: definition and content. **J Chron Dis** 1987; 40: 473–480.
5. Nelson E, Wasson J, Kirk J *et al.* Assessment of function in routine clinical practice: description of the COOP Chart method and preliminary findings. **J Chron Dis** 1987; 40 (Suppl. 1): 55S–63S.
6. Guyatt GH, Veldhuyzen Van Zanten SJO, Feeny DH, Patrick DL. Measuring quality of life in clinical trials: a taxonomy and review. **Can Med Assoc J** 1989; 140: 1441–1448.
7. Brook RH, Ware JE, Rogers *et al.* Does free care improve adults' health? Results from a randomized controlled trial. **N Engl J Med** 1983; 309: 1426–1433.
8. Stewart AL, Ware JE, Brook RH. **Construction and Scoring of Aggregate Functional Status Measures:** Vol. 1. Santa Monica, CA: The RAND Corporation; August 1982: Publication No. R-2551-1-HHS.
9. Stewart A, Ware JE, Brook RH. The meaning of health: understanding functional limitations. **Med Care** 1977; 15: 939–952.
10. Stewart AL, Hays RD, Ware LR. The MOS short-form general health survey: reliability and validity in a patient population. **Med Care** 1988; 26: 724–735.
11. Stewart AL, Greenfield S, Hays RD *et al.* Functional status and well-being of patients with chronic conditions: results from the Medical Outcomes Study. **JAMA** 1989; 262: 907–913.
12. Kaplan SH. Patient reports of health status as predictors of physiologic health measures in chronic disease. **J Chron Dis** 1987; 40 (Suppl. 1): 27S–35S.
13. Fernald GW. Cystic fibrosis: increased longevity brings new priorities. **Diagnosis** 1989; 11(1): 19–30.
14. Penketh ARL, Wise A, Mearns MB, Hodson ME, Batten JC. Cystic fibrosis in adolescents and adults. **Thorax** 1987; 42: 526–532.
15. Moise JR, Drotar D, Doershuk CF, Stern RC. Correlates of psychosocial adjustment among adults with cystic fibrosis. **J Dev Behav Pediatr** 1987; 8: 141–148.
16. Cowen L, Corey M, Simmons R *et al.* Growing older with cystic fibrosis: psychologic adjustment of patients more than 16 years old. **Psychosom Med** 1984; 46: 363–376.
17. Corey M, Durie P, Moore D, Forstner G, Levison H. Familial concordance of pancreatic function in cystic fibrosis. **J Pediatr** 1989; 115: 274–277.
18. Shepherd SL, Hovell MF, Harwood IR *et al.* A comparative study of the psychosocial assets of adults with cystic fibrosis and their healthy peers. **Chest** 1990; 97: 1310–1316.
19. Manning WG, Newhouse JP, Ware JE. **The Status of Health in Demand Estimation: Beyond Excellent, Good, Fair and Poor.** Santa Monica, CA. The RAND Corporation; August 1981: Publication No. R-2696-1-HHS.
20. Kaplan RM, Bush JW, Berry CC. Health status: types of validity and the Index of Well-being. **Health Ser Res** 1976; 11: 478–507.
21. Cox DR, Oakes D. **Analysis of Survival Data.** New York: Chapman and Hall; 1984: 91–109.

22. Corey M, McLaughlin FL, Williams M, Levison H. A comparison of survival, growth and pulmonary function in patients with cystic fibrosis in Boston and Toronto. **J Clin Epidemiol** 1988; 41: 583–591.
23. Kaplan RM, Atkins CJ, Timms R. Validity of a quality of well-being scale as an outcome measure in chronic obstructive pulmonary disease. **J Chron Dis** 1984; 37: 85–95.
24. Orenstein DM, Nixon PA, Ross EA, Kaplan RM. The quality of well-being in cystic fibrosis. **Chest** 1989; 95: 344–347.
25. Kerem E, Corey M, Kerem BS *et al.* The relation between genotype and phenotype in cystic fibrosis—analysis of the most common mutation (ΔF_{508}). **N Engl J Med** 1990; 323: 1517–1522.
26. Taussig LM, Kattwinkel J, Friedwald WT, di Sant'Agnese PA. A new prognostic score and clinical evaluation system for cystic fibrosis. **J Pediatr** 1973; 82: 380–390.
27. Huang NN, Schidlow DV, Szatrowski TH *et al.* Clinical features, survival rates, and prognostic factors in young adults with cystic fibrosis. **Am J Med** 1987; 82: 871–879.
28. Brown-Ewing LJ, Finkelstein SM, Budd JR *et al.* A rule for the early detection of chronic changes in cystic fibrosis patient status. **J Clin Epidemiol** 1988; 41: 915–922.
29. Wells KB, Stewart S, Hays RD *et al.* the functioning and well-being of depressed patients **JAMA** 1989; 262: 914–919.
30. Murphy E, Smith R, Lindesay J, Slattery J. Increased mortality rates in late-life depression. **Br J Psychiat** 1988; 152: 347–353.
31. Topol EJ, Burek K, O'Neill WW *et al.* A randomized controlled trial of hospital discharge three days after myocardial infarction in the era of reperfusion. **N Engl J Med** 1988; 318: 1083–1088.
32. Rubenstein LV, Calkins DR, Fink A *et al.* How to help your patients function better. **West J Med** 1985; 143: 114–117.
33. Kaplan RM, Anderson JP, Wu AW *et al.* The quality of well-being scale: applications in AIDS, cystic fibrosis and arthritis. **Med Care** 1989; 27 (Suppl.): S27–S43.
34. Stewart AL, Ware JE (Eds). **Measuring Functioning and Well-being: The Medical Outcomes Study Approach.** Durham: Duke University Press; 1992. In press.