Editorials

Why measure quality of life?

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The academic study of the patient's quality of life has received considerable attention of late, but has generated a controversy about the relevance and feasibility of such investigations. Advocates of quality-of-life research point out that it should represent the final common pathway of the health care effort and that some refocusing of our goals for health care delivery away from assessment of laboratory results and toward functional outcomes in patients is necessary if our society's health is to be maintained. But many respected experts in research and health planning take a contrary position. First, they argue that we would not be in the position of discussing the niceties of quality of life were it not for the rigorous scientific research that has yielded penicillin, immunizations, drug treatment for leukemia and the like. Second, they hold that evaluating quality of life is not feasible: the data are inherently too "soft", the measurement methods are too vague, and there is a real concern that hard science will be replace by unfettered consumerism.

Despite the apparent polarity between these two positions, I maintain that traditional basic science medical research and quality of life pursuits are complementary and synergistic. As a point of departure for this argument it is important to set forth, in general terms, what science knows and what it does not know in terms of the biologic process. The scientific method achieves clarity when it is possible to extract a process from its environment, control all the variables but one (the independent variable) and observe the effect that changes in the independent variable have on the dependent variables. The interpretation of results depends on the success with which the process under study can be isolated from its environment, the reliability and accuracy with which variables can be measured and, of critical importance, the proper selection of dependent variables. The more successfully these criteria are fulfilled the more narrow the statistical bounds and the more confidence we can have in the validity of the result *in the context of the experiment*. Critical to the extrapolation of a basic science result to the clinical setting is the understanding that the clinical process cannot be isolated from the environment, that the dependent variables that laboratory and clinical scientists select may differ, and that these variables are not the same parameters that patients find understandable or relevant.

The evolution of patient outcome from basic science can be described by a four-stage model: basic science (e.g., chemistry), basic biology (e.g., immunology), clinical study (e.g., pharmacology) and personal outcome (e.g., rehabilitation). At each level of development the biologic process is studied from a different perspective: the molecule, the cell, the organ, the disease and the patient. With each step out of the laboratory, the variables indicating response are harder to define and the environment is harder to control. The translation from one level to the next is not precise. Hence, molecular mechanisms do not always translate into cellular events. A critical disjunction occurs between clinical study and patient outcome. At the clinical study level a disease process may be understood in molecular detail and a treatment may have been developed. However, the treatment will not succeed unless three new and essential criteria are met. First, it must be possible to deliver the treatment to the patient in the real world. Second, there must be measures of outcome that are understandable and relevant to patients, whose perspective is emotional and personal, in contradistinction to that of the detached scientist. Third, the net effect of a treatment must be perceived by the patient to be of functional benefit. In other words, patients are unlikely to accept a treatment, whatever its scientific merit, if they see nothing in it for themselves.

The development of effective therapies brings into focus this disjunction between what the medical scientist can produce and what the patient needs and expects. If there were no effective treatments, then the aim of clinical science would be palliation of symptoms. Likewise, if treatment were uniformly curative and of short duration, and if the residual side effects were trivial, then quality-of-life issues would assume little importance. There are no quality-of-life studies related to the use of penicillin for pneumococcal pneumonia. However,

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in the intermediate ground, where treatment is toxic, of substantial duration and only partially curative, the quality-of-life issue must be squarely faced. Here the physician–scientist is anxious to measure the outcome of treatment with precision; therefore, end points are selected that are finite (e.g., survival or disease-free survival time) and measurable (e.g., changes in tumour diameter or enzyme levels).[1] Scientists are chary of data that do not at least simulate laboratory "hardness". As a result, physicians can compare trials and can give patients statistical estimates of survival duration or the extent of tumour response. What physicians cannot do is tell their patients, even in statistical terms, what effect treatment is likely to have on their lifestyle. Furthermore, because we lack practical measures of patient function we are unable to compare treatments, in a rigorous way, vis-à-vis functional outcome in patients. Thus, what we must do is develop "harder" measures of functional outcome in patients and incorporate them into clinical trials. To achieve this goal, the physician–researcher will have to accept, at least at the outset, that there will be a sacrifice in precision. The benefit will be a gain in relevance and an improved measure of the final common pathway in the chain of patient care.

The patient is going to have to put up with more tests, albeit without additional blood-letting. If the evolved measure is to be relevant, the questions posed will have to be sharply focused on important and often sensitive aspects of day-to-day living.

Methodologic challenges

The medical social scientist faces major methodologic challenges in developing a measure of the quality of life. First, the investigator must achieve a consensus on the relevant factors of quality of life among physicians, nurses, patients, family and others who are concerned about the patient. Whether the proposed index is designed to explore one disease in particular (e.g., breast cancer) or a family of illnesses (e.g., cardiovascular diseases), if patients and health care providers are unable to find common ground for the definition of parameters and end points the effort will fail. Second, the questionnaire must be compact enough to enable repeated use, but comprehensive enough to adequately evaluate components of quality of life. Third, each component of the questionnaire must be interpretable by all patients in the study group; a question, for example, that focuses on the workplace may be meaningless to the housewife. Fourth, the instrument must be sensitive enough to detect changes in the overall quality of life and in its component factors. It should be possible to detect such trends early enough to initiate intervention, when appropriate, or to judge the effect of alterations in treatment design. Fifth, and perhaps most vexing, is the necessity of comparing quality of life between patients. Does the baseline quality of life of a farmer differ from that of a city dweller? Does the quality of life of a housewife change differently from that of a businessman with a similar illness? Are there parameters of quality of life such as vocational function or psychologic state that take on greater importance in some patients or in some diseases?

If these problems can be tackled and a test instrument constructed, then what steps must be taken to bring it into use, to make it an acceptable measure? Since the research strategies of clinical medicine and psychosocial studies differ, the validation procedure selected will likely represent a new approach for all participants. It will be necessary to have all members of the study team believe that each step in the validation process is useful.

Quality-of-life indices

There is no uniform approach to the design of a quality-of-life measure. One can envision global indices for the quality of life as well as indices narrowly specific to particular clinical problems. An approach to the universality problem is to design an instrument in which patients serve as their own internal controls. In such a model the baseline score becomes less important than the trend in scores over time. Questions in such a document are designed to elicit relative answers (e.g., "a great deal" or "not very much") rather than absolute values (e.g., "I worked 6 hours today"). Defining the component structure is critical. If one seeks an all-inclusive measure, then the problem becomes infinite and the questionnaire boundless. On the other hand, if the instrument is designed to concentrate on day-to-day aspects of functional living, then factors such as vocational function, psychologic state, social and familial interaction, and somatic state (e.g., pain and nausea) may encompass enough of the patients' practical concerns to provide a relevant questionnaire. One can employ techniques such as the "Q sort", which is designed to estimate a rank ordering of the importance of these component factors.[2] Statistical maneuvers such as factor analysis and discriminant analysis can be used to test the hypothesis that the questionnaire in fact measures what it is designed to measure.[3,4]

If a quality-of-life questionnaire is to become credible to a medical scientist, then it must be validated with rigour. To rush a half-baked index into unfettered clinical use risks discrediting the entire effort. Correlation studies with validated psychometric, physical, functional and other relevant measures must be undertaken on multiple representative samples of the target population. The use of multiple observer experimental designs serves to "harden" softer data. Predictive studies and longitudinal analyses of patients whose disease outcomes follow expected courses all serve to build the case for validity and relevance.

The functional impact of illness is becoming better understood in greater depth than it was with measures such as the New York Heart Index[5] and the Karnofsky Scale,[6] which measured only physical parameters of illness. Breast cancer, chronic obstructive lung disease and rheumatic diseases are now being studied for their broader psychosocial impact.[7-11] There is acceptance now that unmistakable physiologic responses to treatment for heart failure do not always translate into functional improvement.[12] The functional motivation underlying home dialysis programs is being measured. Pioneering attempts at medical quality-of-life assessment have been made, but most have practical or methodologic short-

comings.[13-16] This is not to discredit the approach; rather, the effort must continue and needs support.

The possible synergism between functional-outcome studies and basic biology is exemplified by this hypothetical example. Suppose a clinical trial comparing two treatments reveals that one group obtains an advantage in survival and disease-free survival time, whereas the second group appears to have a superior quality-of-life outcome. If there were no measurements of the quality of life, then the treatment offering increased survival time would become the new standard, and its approaches would be encouraged. Ultimately we might encounter a powerful and effective treatment that produces a cured but functionally disabled population or that has a low rate of compliance. However, the quality-of-life data might well provide the basic scientist with clues that would enable a modification of the treatment. For example, a cancer chemotherapy schedule that involved daily hospital treatment for 3 years is likely to produce a poor outcome in terms of quality of functional life. Altering the drug's half-life to allow weekly treatment is a basic science maneuver that, in this case, would have a direct functional impact.

We tread on new and unfamiliar ground. Quality-of-life studies will force us to come out from the comfort of technologic medicine into a world that is less concrete and less controllable but more human. The relevance and validity of some of our most trusted measures will be reassessed. Out of it all we will be better physicians, more sensitive to the vigour, complexity and adaptability of the human soul.

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Atrial fibrillation and embolism

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In the 1950s the problem of recurrent embolism secondary to chronic rheumatic heart disease complicated by atrial fibrillation was identified.[1,2] Mitral valvotomies uncovered atrial thrombi with alarming frequency. The prevention of recurrent embolism could be approached in three ways: by reversion to sinus rhythm with quinidine therapy, by surgical resection of the auricle and by long-term anticoagulation therapy.[1] Despite the alleged benefits of anticoagulants, it was felt that the mere presence of auricular fibrillation or rheumatic mitral stenosis did not justify long-term anticoagulant administration.[1]

In the 1960s it became fashionable to treat most patients who had chronic atrial fibrillation by means of cardioversion.[3] Failure of the patients to maintain a sinus rhythm, despite prophylactic quinidine therapy, made this procedure of dubious value. Consequently, the enthusiasm for direct-current conversion waned. The failure to maintain sinus rhythm may be closely linked to an accelerated repolarization of the myocardium, so it is possible that amiodarone, a drug that delays atrial repolarization, may prove more beneficial than quinidine.[4] In any case, anticoagulants were then reserved for patients with a history of embolism, and few received such therapy for chronic atrial fibrillation alone.

To date there has been little change in treatment. Although some have suggested that, unless there is a contraindication, long-term oral anticoagulant therapy should be used to prevent recurrent embolism, a firm belief remains that these drugs are indicated only in patients with a history of embolism or with mitral valve disease.[5] Indeed, most physicians advocate this treatment only after an embolic event has occurred. However, they seldom apply even this rule, for the patients are often elderly, and it is assumed that their strokes are a natural consequence of ageing.

The danger of death from embolism in cases of chronic atrial fibrillation has been well documented recently. Despite the frequency of chronic atrial fibrillation, though, few patients are receiving long-term therapy with anticoagulants. A review of the relation between embolism and atrial fibrillation supports the need for anticoagulants in the prevention of stroke.

Review of studies of atrial fibrillation

Mortality in an insured population

Among 3099 life insurance applicants who had atrial fibrillation, only 10% had chronic fibrillation.[6] A normal mortality rate was observed in cases of paroxysmal atrial fibrillation in which no cardiovascular impairment was identified, but the mortality rate associated with atrial fibrillation was increased 12.9 times for those with mitral stenosis compared with 3.2 times for those with coronary heart disease. The ratio of observed to expected deaths showed increased mortality among those with chronic atrial fibrillation, ranging from 7.0 for those with coronary disease ($P = 0.003$) to 17.4 for those with mitral stenosis ($P < 0.001$). The risk ratio for those less than 50 years of age was 16.1. Among those over the age of 60 years it was 3.3. The insurance application selection process tends to produce a bias towards a basically healthy segment of the population with an above average income, because most of the people with a very high risk would be eliminated, either through rejection or because of a high premium rating. This bias is the opposite of that in the patients in a general hospital, yet even in this relatively asymptomatic, healthy population, chronic atrial fibrillation carried a significant risk.

Epidemiologic assessment of the risk of stroke

The Framingham study involved 5184 patients aged 30 to 62 years who were followed for 24 years.[7] Since it was clinically difficult to separate thrombotic from embolic strokes the patients with the two types were

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