Assessment of quality of life in cardiovascular therapy

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Introduction

Over the last two decades it has become apparent that traditional demographic and economic statistics used in western societies are inadequate measures of social change. The growth in measurements such as social indicators was a response to this awareness, and has become linked with the concept of 'quality of life'. There are however many dimensions to this concept, and although social indicators of well-being measure some aspects of the quality of life the terms are not interchangeable, for example, some research has described high levels of satisfaction or happiness in poor, black and ill people which may be explained by their limited expectations (Najman & Levine, 1981). To claim that these people have a high quality of life is to ignore political, cultural, and economic factors.

Unfortunately the distinction between quality of life and well-being is often ignored, and the term quality of life has become firmly established in the behavioural sciences and health field. Some of the scepticism surrounding the concept and measurement of well-being when presented as quality of life relates to this misnomer. In this article we will limit the term quality of life to describe well-being.

In western societies there has been a considerable decline in both mortality and morbidity from infectious diseases, an increased life expectancy and a rise in the prevalence of chronic disease (Figure 1). U.S. statistics show the considerable impact of chronic diseases on the population and the health care system: 30 million Americans are estimated to have some functional impairment due to chronic disease; 50% of these are unable to carry out major activities such as employment, work within the home or attend school; 67% of these are aged under 65 years, and 33% under 45 years. Chronic diseases account for 80% of health care resources, 60% of patient days of hospitalisation in short stay acute hospitals, and 52% of physician visits (Cluff, 1984). A prevalence disability survey in England estimated 17.9% of women and

12.5% of men in an inner city area had some functional limitation or activity restriction; the most frequently reported impairments were those of the sense organs, bones, central nervous, circulatory and respiratory systems (Patrick *et al.*, 1981).

Despite an increasing expenditure on health, competition for resources stimulated health workers to develop measures of the utilization and effectiveness of health care systems. In conjunction with experimental results health economists needed to devise measures of benefit or effectiveness of treatments. Simple cost benefit studies related to work productivity are less appropriate in chronic diseases with a large proportion of subjects not at work. However, methodological approaches were developed primarily by workers in the behavioural sciences and health economics, statistics and operational research fields.

Methods of measuring quality of life on treatment

Improvement of survival, and the alleviation of symptoms and restoration of function are the major goals of medical therapy.

In the last 10 years there have been many major trials of treatment in cardiovascular diseases (Table 1). Most of these studies showed only marginal benefits on mortality but only the Coronary Artery Surgery Study project attempted to evaluate any outcome measure other than mortality or morbidity (CASS, 1983). The unfavourable effects of treatment were not considered though in some trials, for example in mild hypertension, asymptomatic patients were given long term drug treatment. In many therapeutic processes, clinicians make decisions in which the patient's well-being is assessed together with survival, for example in cancer chemotherapy. The survival advantages offered may be slight and the sequelae of therapy drastic. In contrast in terminal disease, potent

Figure 1 Mean annual death rate (males): England and Wales from McKeown & Lowe (1974), with acknowledgements to Blackwell Scientific Publications Limited

Table 1 Major cardiovascular trials of last decade

Coronary drug project
Aspirin myocardial infarction study
Anturan reinfarction trial
Hypertension detection and follow-up program
Coronary artery surgery study
Multiple risk factor intervention trial
Coronary primary prevention trial

drugs are used that alleviate pain and may produce euphoria; these drugs may shorten survival but improve well-being.

To assess the effects of treatment we need to measure changes in symptoms and function and also other aspects of the patients' lives that might be relevant. For example, relief from chest pain may be accompanied by a decrease in anxiety, and greater social and physical mobility. It is also important to evaluate whether any benefit in one dimension is offset by an adverse treatment effect in another.

In the mild chronic diseases, the relationship between the disadvantages of therapy or the disease state, and the possible benefits of reduced mortality risk is not so clear and researchers have attempted to quantify these relationships via the Health Index model.

This model intends to reduce the measurement to one single statistic, an index. The alternative approach is that of health profiles that have been developed to describe many aspects

of quality of life without a single summary figure.

Health index

The attraction of a single index of health, based on a proportional score of perfect health, is that it can then be used to adjust the years of life lost or gained by a treatment programme—well years (Kaplan & Bush, 1982), or, more commonly as favoured by the economists, QALYS (Quality adjusted years of life). These are defined as years of perfect health. Decision and utility theory has been the major influence in the development of the health index approach.

General health policy model This ambitious model attempts to quantify the relationship between prognosis, survival and quality of life (Fanshel & Bush, 1970; Kaplan *et al.*, 1976; Kaplan & Bush, 1982).

Each individual is conceived of as being in a particular state of 'wellness' or life quality at a particular time. These states of 'wellness' defined from interview response to a large number of symptom and performance items are then weighted using ratings derived from a series of Household Interview Surveys to give a Quality of Well Being Score, bounded by 0 at death and 1 at perfect health. The major strength of the model is that the final expression of outcome—The Well Life Expectancy—takes account of prognosis. This movement of individuals in and

out of various states of well-being over a lifetime is represented mathematically as a Markov process. A person at high risk of coronary heart disease may be functioning very well at present but have a high probability of transition to a lower state. This probability is incorporated into the Well Life Expectancy by adjusting the Quality of Well Being score. Various treatments can be compared by their Well Life Expectancies (Figure 2).

Figure 2 Comparison of treatments by their Well Life Expectancies (from Kaplan & Bush, 1982)

There are however considerable drawbacks to the application of the model related mainly to the problems of determining prognoses and assuming that this depends only on the present state and not on previous states.

In one of the few applications of the General Health Policy model—a study of phenylketonuria—the likelihoods of changing between 15 states of dysfunction were assigned by a panel of 11 experts (Bush *et al.*, 1973). For most disease states it would be extremely unusual to obtain this kind of agreement between experts.

Data from a large and long term cohort study might provide working estimates of these transition probabilities, or the inclusion of Quality of Well Being scales into randomised controlled trials would provide estimates of changes in these scales over time (Kaplan & Bush, 1982).

Other approaches to constructing a single global index of health have also used decision theory methods to obtain ratings of the values attached to different health states between the endpoints of death and perfect health (Torrance, 1976; Llewellyn-Thomas *et al.*, 1984). A set of scenarios representing various states of disability, for example for patients receiving renal dialysis, are presented to the raters (patients, medical care workers, university graduates, stratified population sample) who have to choose between remaining in a certain state of health for a time up to death, or remaining in a better state for a shorter period of time and then dying. The

application of these approaches is very limited at present and has been mostly used in cost benefit analysis of health care programmes.

Health profiles

Although theoretically the health index model such as the General Health Policy Model offers a more comprehensive assessment of the overall effects of therapy, the practical difficulties of defining a single index and the considerable limitations on knowledge of disease prognoses make the application of this approach difficult in the clinical therapeutic situation.

The development of health profiles was a response to the awareness that quality of life measurements could be used both to identify the need for health care, and to assess changes due to health care programmes. These profiles differ considerably in assessing performance, behaviour, and feelings. Their suitability for use for specific diseases will be tested over the next few years as they are included in trials needing a quality of life outcome measurement.

The attraction of many of these general profiles is that they satisfy most of the established criteria of psychometric tests (American Psychological Association, 1974). These criteria are briefly summarized as they are important in establishing the credibility of measurements in the field of quality of life and they define the standards required of any measurement.

Repeatability is a measure of the consistency of the information, and can be established by test-re-test procedures. Reliability of the final score increases with the number of items in the score, and the repeatability of each item.

Stability is the degree of change in the score over a long period of time and is particularly important when assessing the impact of therapy at different ages.

Validity is the extent to which the score or item is a meaningful measure of a particular attribute. In quality of life measurements, it is difficult to agree on what objective criteria can be used to evaluate validity. Evidence from other types of validity is sought instead, such as *construct* validation which examines the relationship of a score to many variables to which it should and should not be related, and *convergent* validity which is the degree of correlation between different methods of measurement.

Sensitivity refers in this context to the ability of the measurement to detect the effects of therapy

and can be best assessed when changes in scores are correlated with clinical changes. There is very little information at present on the sensitivity of most general or disease specific instruments.

Most validations of general profiles have related to the ability of the profile to find cases rather than to detect changes in health status over time. Workers outside the behavioural sciences are often sceptical of these methods. A different approach to measurement is indeed required. Validation in quality of life measurements is considered an ongoing process with continual appraisal of the performance of these measures. Since quality of life assessments are newcomers in health trials, the models and instruments of these assessments are very largely in the experimental stage.

Consideration needs to be given as to what aspects of quality of life should be considered. Some authors advocate the investigations of all the variables that have been shown to determine quality of life (Najman & Levine, 1981).

Demographic variables such as work, education and income status.

Social variables such as membership and participation in social and family groups, work satisfaction, pursuit of leisure interests.

Psychological variables such as emotional state, cognitive performance, psychological morbidity.

Performance variables such as aspects of self care, mobility, confinement.

Sexual variables such as libido, potency.

The objectives and design of the trial, the nature of the disease and therapy, and practical and methodological feasibilities of measurement will influence the choice of quality of life measures. These considerations can be illustrated in trials of therapies in angina and hypertension.

Results of quality of life measurements **Quality of life measurements in angina**

Several studies have been reported in which a quality of life outcome has been included.

Coronary artery surgery study (CASS)

The main objective of the CASS study was to assess the effects of surgery on mortality in a randomised group of patients with stable

ischaemic heart disease (80% of these had angina) over the 5-year-period 1975–1979. Although a variety of 'descriptors' were included in the trial which reflected outcomes other than survival, there was no formal statement of those aspects of quality of life in which the effects of therapy might be measured over such a long time period. Patient functioning was assessed by single item measures of chest pain, presence of heart failure, limitations of activity, employment status, recreational status, drug therapy, days of hospitalisation, smoking status, and participation in a supervised exercise programme (CASS, 1983).

In the surgical group there was less chest pain and less limitation of activity, better performance on treadmill testing and fewer angina relieving drugs were employed. Although the investigators were aware of bias in their questionnaire administration, they felt sufficiently confident of their methods to claim that patients undergoing surgery had a significantly better quality of life. The reliability and validity of their measurements was not established, improvement on exercise is not necessarily an indicator of an improved quality of life and psychological well-being and social functioning were not examined in this study.

The coronary artery bypass graft study (CABG)

The Coronary Artery Bypass Graft Study (CABG) used standard psychiatric evaluations—Psychiatric Evaluation from Cat-16 Personality Factor Questionnaire, and Rosenman-Friedman standardized interview—to obtain data on emotional state, behaviour, social role, personality and type A coronary prone behaviour, as well as single item measurements of employment, sexual activity and smoking habits (Kornfield *et al.*, 1982). These data were obtained pre-operatively, and at 9 months and 3.5 years post-operatively. Additionally at 3.5 year follow-up patients were also given a questionnaire which asked them to rate change on a five point scale from much worse to much better, for single items defining pleasure, nervousness, mood, job satisfaction, family relationships and sexual satisfaction. No controls were employed. Improvements were noted in most items in the self-reported questionnaire though sexual satisfaction showed the lowest improvement, and sexual activity had decreased considerably in the 3.5 year post-operative period. This study illustrates some of the difficulties encountered in a simple before and after treatment design for a single group of patients. Improvement is almost always reported by participants in a trial (Mann,

1984). Randomization either to a placebo or to alternative treatments allows these effects to be separated out.

The selection of certain instruments in this study to measure psychological variables may also not have been appropriate. Many scales are constructed to measure attributes that are likely to be permanent. Most patients' ratings in the Type A coronary prone behaviour assessment were unchanged over time, and this may be because Type A personality is unlikely to change.

Trials of anti-anginal drug treatment

In two ongoing double-blind randomized controlled trials of placebo and dermal glyceryl trinitrate patches certain aspects of the quality of life are being measured. The assumption has been made that an overall improvement in behavioural well-being is associated with better control of chest pain.

Practical considerations of time and cost required the use of an existing instrument that could be self-administered. Since no specific instrument for angina has been developed, choice was limited to a general profile that both included areas of special interest in angina such as physical activity, and psychosocial dimensions that might be affected by the relief of chest pain and improved tolerance to therapy.

In these trials the Sickness Impact Profile (SIP) is being employed. The SIP is a standardised questionnaire of 136 items describing the impact of sickness on behaviour in 12 categories (Table 2). Scores may be obtained for the overall profile, for each of the 12 categories, and for a category combination to give a physical dimension and a psychological dimension score. The scores are not simple additions of items but are predetermined weights based on estimates of the relative severity of each dysfunction obtained by ratings from health service professionals and a sample of general practice patients (Bergner *et al.*, 1981).

The SIP can be used as a self-administered questionnaire; it has been translated into colloquial English by members of St. Thomas' Hospital for use in a longitudinal study of disability (The Functions Limitation Profile (Patrick, 1981)). This version is being used in the present trials.

The SIP has been extensively tested and shown to have good validity and high reliability. There is some experience of use with it in clinical trials comparing levels of dysfunction in different groups of patients and their tolerance to therapy. Some SIP categories have been shown to correlate with clinical changes in rheumatoid arthritis

Table 2 Sickness impact profile (SIP)

12 categories	Number of questions
Ambulation	12
Mobility	10
Body care	} 23
Movement	
Social interaction	20
Communication	9
Emotional behaviour	9
Alertness behaviour	10
Eating	9
Work	9
Sleep and rest	7
Household management	10
Recreation and pastimes	8
	136

(Deyo & Inui, 1984), and to discriminate between clinically different groups of breast cancer patients (Selby *et al.*, 1984). Its sensitivity to the effects of drugs has not yet been reported.

Questions to measure possible side effects of previous and current therapy and an index of activity are also included. This index has been derived from the work of Fanshel & Bush (1970) and describes a degree of disability in terms of function and the patient's perception of changes in function due to the disease state or its therapy. The index has been used in trials of anti-hypertensive drugs in Europe, and there is some preliminary evidence that it is sensitive to drugs.

Quality of life measurements in hypertension

In short term trials of anti-hypertensive drugs, we need to study those aspects of well-being relevant to hypertension and its treatment which are likely to be fairly immediately responsive to the effects of therapy. The areas of interest are suggested by the considerable literature documenting the symptomatic and psychological consequences of hypertension.

Mild hypertension *per se* is unlikely to produce symptoms. Early studies suggesting this (Ohler, 1927) did not take account of such factors as awareness of hypertensive disease, high anxiety levels in patients referred to hospital clinics, and the high levels of reported symptoms in the general population (Bulpitt, 1982). A wide range of symptom side effects can be produced by drug treatment (Table 3). Studies of treated and untreated hypertensives have suggested an impairment of cognitive function.

Table 3 Frequently reported side effects of hypotensive drugs

<i>Class of drug</i>	<i>Symptoms</i>	<i>Psychomotor/psychosensory functioning</i>
<i>Diuretics</i>	Impotence, decreased libido, lethargy, constipation, nausea, dizziness	
<i>β-adrenoceptor blocking drugs</i>	Dyspnoea, lethargy, dizziness, vivid dreams, cold extremities, blurred vision, blocked nose	Prolongation of complex reaction time Reduction of verbal memory Psychosensory impairment
<i>Centrally acting drugs</i>		
Methyldopa	Diarrhoea, tiredness, weakness of limbs, weight gain, dry mouth, vivid dreams	Reduction of verbal memory
Clonidine	Tiredness, sleep disturbance, dry mouth, constipation	
Reserpine	Tiredness	Depression
<i>Adrenergic neurone blocking drugs</i>		
Guanethidine	Failure of ejaculation, diarrhoea, postural hypotension, blurred vision	
Bethanidine	Impotence and failure of ejaculation, postural hypotension, weak limbs	
<i>Vasodilators</i>		
Hydrallazine	Palpitations, flushing, impotence, headache	
<i>Angiotensin converting enzyme inhibitors</i>		
Captopril	Skin rash, loss of taste, taste disturbance	
<i>Calcium antagonists</i>		
Verapamil	Constipation, dizziness, headaches, nausea	
Nifedipine	Headaches, flushing, dizziness, ankle swelling, nausea	

Certain aspects of intelligence are negatively associated with hypertension (Wilkie & Eisdorfer, 1971; Schultz *et al.*, 1979) and reduced memory function has been shown both in patients taking β-adrenoceptor blocking drugs (Lichter *et al.*, 1984; Solomon *et al.*, 1983), and in untreated hypertensives (Franchesci *et al.*, 1982).

Psychological well-being may be affected both by drug therapy and by labelling the patient with a diagnosis of hypertension. The MRC trial found no increase in psychiatric morbidity between labelled hypertensives (treated and untreated) and normotensives (Mann, 1984); but other studies on more general aspects of psychological well-being have reported an increase in depressive symptoms, worry over health, decrease of self-esteem, problems of marital adjustment and greater absenteeism

from work for both aware hypertensives and normotensives who think they have hypertension (Macdonald *et al.*, 1984). A British study found that 29% of hypertensive patients attending an outpatient clinic considered that hypertension or its treatment had affected their lives. The most frequent reason given was tiredness followed by inability to walk far, headaches, and a poor sex life (Bulpitt & Fletcher, 1985).

A questionnaire had been developed for use in short-term trials of anti-hypertensive drugs to detect changes in symptoms, activity and perception of illness, (the Activity Index previously described), and psychiatric morbidity. The symptoms included should vary with the drugs in the trial. In a European multicentre trial of three drug regimes (an angiotensin converting enzyme inhibitor versus either a β-adrenoceptor blocking

drug or a centrally acting drug), 28 questions about symptoms were included, these included symptoms such as sleepiness, blurred vision and dry mouth that have previously been reported in the drugs under consideration.

Psychiatric morbidity was assessed by the Symptom Rating Test (Kellner & Sheffield, 1973). This is a 30 items check list providing both an overall score, and separate somatic, depression, anxiety and inadequacy scores. In future trials an extended version of the SRT (Kellner, 1983) will be used. This includes extra items for hostility and cognitive scores, both of interest in hypertensives, and excludes the inadequacy score.

The questions relating to symptoms have previously been shown to be repeatable and treatment sensitive (Bulpitt & Dollery, 1973; Bulpitt *et al.*, 1979). The SRT is sensitive to psychotropic drugs and to the duration of use of them. Higher scores have been found in studies of patients with certain disorders - peptic ulcer, hyperprolactinemia, vasomotor instability in menopausal women and various psychosomatic disorders (Kellner, 1982).

The questionnaire is designed to be self-administered. This is particularly important in short-term trials where trained interviewers are not used. In the European multicentre trial a proportion of questionnaires were administered in error by a member of the patient's medical care team. Although the responses on symptoms at entry to the trial were similar for both the self-administered and interviewed groups, the interviewers tended to report much more improvement at the end of the trial than did patients. The overall psychiatric morbidity was much lower in the interviewed group, and the amount of reported disability less (Bulpitt & Fletcher, 1985).

Use of these questionnaires in a variety of trials with different objectives and designs are planned and will provide data on quality of life such as the effects of different pharmacological classes of anti-hypertensive drugs (ACE inhibitors, β -adrenoceptor blocking drugs, calcium channel blocking drugs), and in normotensives, a sample of hypertensives and normotensives registered by GPs in an inner city area, diabetic hypertensives, and untreated hypertensives (both newly diagnosed and patients taken off therapy).

In addition memory function will be tested in hypertensives and their age/sex matched controls. The Wechsler-Russell tests of short and long term memory may not be sufficiently sensitive to impairment of higher cerebral function, and other tests derived from experimental psychology will also be employed.

Discussion

Models of cardiovascular disease which take account of both survival, and quality of life are of considerable interest to epidemiologists, economists and planners. The use of such models however is restricted by problems in assigning probabilities to complex events, and also in defining a single index of health. A more limited but realistic approach is the inclusion of measures of the quality of life in randomised trials of treatment.

The smaller the differences between treatments that reduce mortality and morbidity, the greater the importance of considering many aspects of quality of life. Measures of the quality of life are best utilized in controlled randomized trials. The major problem in designing a clinical trial with a quality of life assessment is in deciding what aspects of quality of life to measure, and how to do so.

Choice of areas to investigate in the quality of life

At present little is known of the impact of diseases and their therapy on quality of life. Clinical impression and literature reports point to important areas of further investigation. Patients' past experiences and their future expectations of the benefit of therapy should also be considered. The length of treatment will influence the choice of area to investigate, for example in a 3 month trial major changes in occupation or residence are unlikely to occur even if the treatment does markedly improve the patient's physical and mental well being. Similarly variables that relate to social support or relationships may not be apparent as short-term changes. The chronic effects of treatment, such as in hypertension, are very important and long-term studies are required.

Measurements of aspects of quality of life

Measurements of quality of life need to be reliable, valid, appropriate to the disease and therapeutic situation, and most important, sensitive to the effects of therapy. Although several well-established general profiles are available, these were not designed for the assessment of changes due to therapy. Selecting certain items from a profile is not recommended as validation procedures usually refer to the complete profile. Development of a specific health profile for a particular study has the advantage of allowing the investigators to define the appropriate areas of interest, but considerable experience with any profile in trials is needed before reliance is placed on the results.

Trial design

Evaluation of a quality of life outcome is at least as dependent on good trial design as any other outcome. Questionnaire responses are more affected by bias than many other clinical measurements. This bias may be due to a variety of influences, for example in single-blind or open studies the patient's or doctor's knowledge or expectations of particular therapies. Double blind randomised controlled trials using questionnaires which are either self-administered or administered by trained interviewers will minimise this bias, and will also allow the effects of treatment to be separated from other effects, such as the fact of inclusion in a trial.

Selection of patients can also be biased; compliance is an indication of the effect of treatment on well-being and trials that exclude non-compliant patients will show more favourable responses to treatment. Similarly, patients who leave trials because of adverse effects must complete an evaluation at exit. Questionnaire design must also take account of differing levels of education and intelligence; patients should not have to be of above average intelligence to be able to complete a questionnaire.

It is also important to use standardised methods when inviting patients to participate. These should describe the aims of the study, how to fill in the questionnaires and promise full confidentiality. Place and time of completion should also be standardized, for example, in trials of anti-hypertensive drugs patients should complete the questionnaires before their blood pressure is taken.

In randomized trials baseline measurements are essential and usually obtained in a placebo run-in period. The timing of repeat measurements will be influenced by changes in therapy but over-familiarization due to too frequent

assessments should be avoided. Most problems in the statistical testing of changes in score measurements over time, such as the regression to the mean effect, are minimized by having a randomized controlled group. Appropriate tests for highly skewed data must be selected.

Conclusions

Methods of measuring aspects of quality of life in disease states and their therapies are very much in the experimental stage. Claims that a treatment improves the quality of life need to be viewed with caution, and assessed critically with respect to the choice of aspects, the validation of the measurements and the design of the trial. For example, a recent study suggested that quality of life could be easily evaluated from a physician administered questionnaire based on the frequency of angina, type of activity producing angina, and the use of medications (Peduzzi *et al.*, 1984). Although the reduction of symptoms is highly relevant, a comprehensive evaluation of quality of life should include many other aspects of function and feelings.

The issue of the relative merits of objective and subjective measurements is frequently raised; workers outside the behavioural sciences tend to regard only objective measurements as scientifically valid. Subjective assessment however is an essential component of quality of life; perceptions of health and expectations of health care influence the response to treatment, and may be of aetiological significance.

The development of Quality of Life models is an attempt to describe the interactions between disease, and social, cultural and psychological factors, and to provide a more comprehensive assessment of the effects of treatment.

References

- American Psychological Association (1974). *Standards for educational and psychological tests*. Washington, DC: American Psychological Association
- Bergner, M., Bobbitt, R. A., Carter, W. B. & Gilson, B. S. (1981). The Sickness Impact Profile; development and final revision of a health status measure. *Med. Care*, **19**, 787-805.
- Bulpitt, C. J. (1982). Quality of life in hypertensive patients. In *Hypertensive Cardiovascular Disease: Pathophysiology and Treatment*, ed Amery, A., pp 929-948. Hague/Boston/London: Martinus Nijhoff Publishers.
- Bulpitt, C.J. & Dollery, C. T. (1973). Side effects of hypotensive agents evaluated by a self-administered questionnaire. *Br. med. J.*, **3**, 485-490.
- Bulpitt, C. J. & Fletcher, A. E. (1985). Quality of life in hypertensive patients on different anti-hypertensive treatments: rationale for methods employed in a multicenter randomized controlled trial. *J. Cardiovasc. Pharmacol.*, **7**, (suppl), 5137-5145.
- Bulpitt, C. J., Hoffbrand, B. I. & Dollery, C. T. (1979). Contributions of drug treatment to symptoms of hypertensive patients. In: *Mild Hypertension: Natural History and Management* eds. Gross, F. & Strasser, T. pp 291-302. London: Pitman Medical.
- Bush, J. W., Chen, M. & Patrick, D. L. (1973). Cost effectiveness using a health status index: analysis of the New York State PKU screening program. In *Health Status Indexes*, ed Berg, R. pp 172-208

- Chicago: Hospital Research and Education Trust.
- Cluff, L. E. (1984). Chronic disease function, and the quality of care. *Quality of Life and Cardiovascular Care*, 1, 78-83.
- CASS Principal Investigators and their associates (1983). Coronary Artery Surgery Study (CASS): A randomised trial of coronary artery bypass surgery. Quality of life in patients randomly assigned to treatment groups. *Circulation*, 68, 951-960.
- CASS Principal Investigators and their associates (1983). Coronary Artery Surgery Study (CASS): a randomised trial of coronary bypass surgery. Survival data. *Circulation* 68, 939-950.
- Deyo, R. A. & Inui, T. S. (1984). Towards clinical applications of health status measures. Sensitivity of scales to clinically important changes. *Hlth Services Res.*, 19, 277-289.
- Fanshel, S. & Bush, J. W. (1970). A health status index and its application to health-services outcomes. *Oper. Res.*, 18, 1021-1066.
- Franchesci, M., Tancredi, O., Smirne, S., Mercinelli, A. & Canal, N. (1982). Cognitive processes in hypertension. *Hypertension*, 4, 226-229.
- Kaplan, R. M. & Bush, J. W. (1982). Health related quality of life measurement for evaluation research and policy analysis. *Hlth Psych.*, 1, 61-80.
- Kaplan, R. M., Bush, J. W. & Berry, C. C. (1976). Health status: Types of validity and the index of well being. *Hlth Services Res.*, 4, 478-507.
- Kellner, R. (1982). *Symptom rating test (SRT). A survey of studies*. Albuquerque. New Mexico: University of New Mexico.
- Kellner, R. (1983). *Abridged manual of the symptom rating test - seven scale version*. Albuquerque. New Mexico: University of New Mexico.
- Kellner, R. & Sheffield, B. F. (1973). A self-rating scale of distress. *Psych. Med.*, 3, 88-100.
- Kornfield, D. S., Heller, S. S., Frank, K. A., Wilson, S. N. & Malm, J. R. (1982). Psychological and behavioural responses after coronary artery bypass surgery. *Circulation*, 63, 24-28.
- Lichter, I., Richardson, P. J. & Wyke, M. A. (1984). Differential effects of atenolol and enalapril on tests of memory during treatment for essential hypertension. *J. Hypertension*, 2, 560.
- Llewellyn-Thomas, H., Sutherland, H. J. Tibshivani, R., Crampi, A., Till, J. E. & Boyd, H. F. (1984). Describing health states. Methodologic issues in obtaining values for health states. *Med. Care.*, 22, 543-552.
- Macdonald, L. A., Sackett, D. L., Haynes, R. B. & Taylor, D. W. (1984). Labelling in hypertension: a review of the behavioural and psychological consequences. *J. chronic dis.*, 37, 933-942.
- McKeown, T. & Lowe, C. R. (1974). *An introduction to social medicine*. Oxford Blackwell Scientific Publications.
- Mann, A. H. (1984). Hypertension: psychological aspects and diagnostic impact in a clinical trial. *Psychol. Med.*, monogr suppl 5.
- Najman, J. M. & Levine, S. (1981). Evaluating the impact of medical care and technologies on the quality of life: a review and a critique. *Soc. Sci. Med.*, 15F, 107-115.
- Ohler, W. R. (1927). The signs and symptoms of hypertension. *Am. Heart J.*, 2, 609-612.
- Patrick, D. (1981). Standardization of comparative health status measures: using scales developed in America in an English speaking community. In *Health Survey Research Methods*, ed. Sudman, S., Third Biennial Conference, Hyattsville MD. National Centre for Health Services Research. PHS Publications; No. 81-3268; 216-220.
- Patrick, D. L., Darby, S., Green, S., Horton, G., Locker, G. & Wiggins, R. D. (1981). Screening for disability in the inner city. *J. Epid. Comm. Hlth.*, 35, 65-70.
- Peduzzi, P. & Hultgren, H. (1984). Angina scoring method in the VA CAGB study. *Contr. clin. Trials.*, 5, 291.
- Selby, P. J., Chapman, J. A. W., Etazadi-Amoli, J., Dalley, D. & Boyd, N. R. (1984). The development of a method for assessing the quality of life of cancer patients. *Br. J. Cancer*, 50, 13-22.
- Schultz, N. R., Dineen, J. T., Glias, M. R., Pentz, C. A. & Wood, W. G. (1979). WAIS performance for different age groups of hypertensive and control subjects during the administration of a diuretic. *J. Gerontol.*, 34, 246-253.
- Solomon, S., Hotchkiss, E., Saravay, S. M., Bayer, C., Ramsey, P. & Blum, R. S. (1983). Impairment of memory function by antihypertensive medication. *Arch. gen. Psych.*, 40, 1109-1112.
- Torrance, G. W. (1976). Towards a utility theory foundation for health status index models. *Hlth Services Res.*, 11, 349-369.
- Wilkie, F. & Eisdorfer, C. (1971). Intelligence and blood pressure in the aged. *Science*, 1972, 959-962.