

A PROSPECTIVE, LONGITUDINAL STUDY OF THE RELATIONSHIP OF PSYCHOLOGICAL WORK TO DURATION OF SURVIVAL IN PATIENTS WITH METASTATIC CANCER

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SUMMARY

This study is a prospective, longitudinal investigation of the psychological factors associated with the duration of survival in patients with metastatic cancers of various kinds who were receiving group psychotherapy. A correlative approach rather than an experimental (trials) design was used in the study because our aim was to relate the psychological attributes of each individual to survival rather than to test the efficacy of the intervention.

Twenty-two patients with medically incurable metastatic cancer of various kinds received weekly group psychotherapy for up to 1 year, the great majority remaining well enough to attend the group for at least 8 months. During this time, they provided extensive verbal data, through written homework, and from notes taken by the therapists at interviews and during group sessions. These data were subjected to detailed qualitative analysis, as a result of which a number of psychological themes were defined. A quantitative rating was assigned to the data for each theme in each individual patient through team discussions. The scores for the individual themes were summed to produce a 'total psychological score', representing the degree of each patient's involvement with psychological self-help work. The values for each patient were then related to his or her survival duration.

Cox regression analyses showed that this composite score, and five of six major themes, were significantly related to survival duration. These themes were: ability to act and change; willingness to initiate change; application to self-help work; relationships with others; and quality of experience. In contrast, there was no relationship between survival and four standard psychometric measures taken at the onset of therapy. However, results on a 5-point scale measuring the subject's expectancy that psychological efforts would affect the disease showed a strong relationship to survival.

To control for differences in severity of disease as a factor possibly influencing psychological work, the analyses were repeated, using the survival duration predicted for each patient by a panel of oncologists as a covariate. Closely similar results were obtained.

Limitations on the interpretation of the results are discussed. Within these limits, it appears that there is a strong association between longer survival and psychological factors related to the involvement of cancer patients in psychological self-help activities. While causality cannot be inferred, reasons are given for believing that this is not a result of the disease influencing the patients' psychology, but rather the converse. Copyright © 2000 John Wiley & Sons, Ltd.

INTRODUCTION

It has long been thought that a cancer patient's mental attributes might affect the rate of progres-

sion of disease. Stolbach and Brandt (1988) reviewed the writings of physicians from the seventeenth and eighteenth centuries who reported that feelings of anxiety, disappointment and depression were possible precursors of cancer onset. In more recent times, work with animal models has clearly shown a relationship between psychological determinants and tumour growth (LaBarba, 1970; Sklar and Anisman, 1981; Visintainer *et al.*, 1983). Research on the relationship

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of human personality to cancer has not yielded consistent results, however. Prospective studies have implicated a number of possible risk factors, the most consistent finding being depression or repression of emotion (Shekelle *et al.*, 1981; Hislop *et al.*, 1987; Jensen, 1987; Temoshok, 1987; Gross, 1989; Kaasa *et al.*, 1989), a conclusion disputed by Kreitler *et al.* (1993) in their more recent review. Other factors which some have found to be protective included social support (Ell *et al.*, 1989; Waxler-Morrison *et al.*, 1991; Maunsell *et al.*, 1995), smaller numbers of severe or difficult life events (Ramirez *et al.*, 1989) and 'fighting spirit' (Greer *et al.*, 1979; Pettingale *et al.*, 1985). Other investigators failed to find similar relationships (Funch *et al.*, 1983; Jamison *et al.*, 1987; Cassileth *et al.*, 1988), and fighting spirit was not found to be protective in a recent, prospective analysis of 578 patients (Watson *et al.*, 1999).

More recently, evidence for an effect of psychological factors has been sought from intervention studies. This would seem to be a more promising approach. If the mind is to affect the regulation of cancer progression via endocrine or immune intermediary mechanisms, there must presumably be some *change* in mental status, resulting in a change in these physiological regulators; without such influences, the disease would continue to progress at the same rate. Psychological therapy would make change more likely.

Evidence from controlled trials of interventions is mixed, however. An influential analysis by Spiegel *et al.* (1989) demonstrated an 18-month average prolongation of life in women with metastatic breast cancer who attended a weekly support group for up to 1 year. Some anomalies in the survival curves for the control group in this experiment (unusually rapid deaths) have been pointed out by Fox (1998). A similar experiment which, unlike that of Spiegel *et al.*, was designed to test for prolongation of survival (Cunningham *et al.*, 1998) showed no effects of treatment and a more typical survival curve for controls. Fawzy *et al.* (1993) found a significant survival advantage for patients with malignant melanoma who had taken a brief, group psychoeducational course 6 years previously; however, this effect disappeared at a 10-year analysis (Fawzy, personal communication). Edelman *et al.* (1999), using an intervention similar to that of Fawzy *et al.*, failed to show an effect on the lifespan of woman with metastatic breast cancer. Richardson *et al.* (1990),

in an experiment primarily testing for compliance with medication and using a sequential cohort design, reported significant effects of a psychological intervention in patients with haematological malignancies. Other published studies with weaker designs have given either positive (Linn *et al.*, 1982) or negative results (Gellert *et al.*, 1993; Ilnyckyj *et al.*, 1994).

Thus we are at a point where, although there is some evidence for an effect of psychological interventions on average survival, it is not consistent. In addition, the available personality literature, based mainly on an analysis of mean group responses to psychometric tests, has also yielded no consensus as to which psychological attributes might promote survival. One problem may be that (in our experience) relatively few cancer patients respond to psychological help by making significant changes to their lives. Nevertheless, we have noted, as have others (e.g. Kennedy *et al.*, 1976; Achterberg *et al.*, 1977), that patients who do become very involved with psychological self-help methods often seem to survive longer than is medically expected. This potentially important phenomenon may be missed when group means are compared in randomized trials, the impact of a few being washed out in the mean results. Randomized clinical trials test the effects of an intervention against non-intervention controls. Our focus is not on testing the efficacy of a psychological intervention but on the subjects, with the aim of relating application to psychological self-help with survival duration. What evidence of this nature exists?

Early work by a number of investigators (Meares, 1980; Newton, 1982–1983; Simonton *et al.*, 1980) suggested that psychological interventions may enhance survival, although their conclusions were based on evidence that was essentially anecdotal. Since that time, there has been a plethora of 'New Age' speculation and assertion on this topic (e.g. Hay, 1984; Siegel, 1986), which is potentially confusing to the cancer patient population (Doan and Gray, 1992) and is often irritating to practitioners of evidence-based medicine. Among the more scientific investigations are two kinds of study. First, meta-analyses of cases of so-called 'spontaneous remission' (Everson and Cole, 1966; Challis and Stam, 1990; Stoll, 1992) or the disappearance of a malignant tumour in the absence of medical treatment that could have caused the remission. Such cases are said to be exceedingly rare and the medical

literature in this field has generally not considered the possibility that this event may be triggered by psychological change; i.e. the cases are considered in purely medical terms.

Second, there is a small literature analysing the psychological properties of so-called 'remarkable survivors', cancer patients who appear to have lived much longer than expected with or without remission of evident cancer (Kennedy *et al.*, 1976; Achterberg *et al.*, 1977; Roud, 1986–1987; Pennington, 1988; Huebscher, 1992a,b; Berland, 1995). A number of design weaknesses render the conclusions of these studies unreliable. The major flaw is that, in all cases, patients who apparently outlived their predicted life expectancies were selected retrospectively, meaning that there was no way of knowing how many patients showed similar characteristics but failed to survive. Inaccuracies and biases in recall are also unavoidable with such retrospective assessment. Furthermore, these measurements were typically carried out at a single time point; patients were not observed over any length of time, as is possible when a psychological intervention is used. The methods of psychological description were mainly clinical impression or interview. Only the studies by Pennington (1988) and Huebscher (1992a,b) apparently used rigorous qualitative methods to analyse interview transcripts (grounded theory, in both cases). In all of the studies, medical documentation was almost non-existent and inappropriate subjects (with medically curable cancers) were often included.

Our aim in the present study was to describe, in a more reliable and rigorous way, the individual variation in psychological responses to the predicament of life-threatening cancer, and to relate this variability to survival duration, using a case-oriented, correlative approach. To avoid the bias inherent in retrospective selection of a tiny proportion of 'remarkable survivors', we adopted a prospective, longitudinal design, the subjects being followed over an extended period before their ultimate fate was known. This does not appear to have been attempted before, probably because the focus has been on complete remission, which is generally thought to be rare. Rather than look only for 'cures', our approach was to document smaller variations in the length of life and to relate this to variations in psychological attributes. Furthermore, we used a psychological intervention (1 year of weekly group therapy) to increase the probability of relevant change, and to

allow frequent, regular data collection. Finally, because this was an exploratory, hypothesis-generating study, and it was not known what kinds of psychological work and change might prove to be related to survival, the main technique selected for characterizing patients' psychological state was a qualitative analysis of verbal data collected from a variety of sources: written homework, therapist notes and interviews. To this we added a quantitative dimension by rating responses in certain categories. The present report is concerned mainly with quantitative aspects of the relationship of psychological attributes to survival; a subsequent report will deal with the quality of the patients' experience in more detail.

METHODS

Subjects

The study population (Table 1) consisted of 22 subjects with cancers that were considered by a panel of oncologists' (below) to be medically incurable. These were metastatic in 20 cases (the remaining two patients having diagnoses of cholangiocarcinoma and multiple myeloma). The most common sites of the original cancers were breast, colon or rectum, and pancreas. The interval since diagnosis was variable. These patients had all shown some prior interest in helping themselves with psychological adjunctive techniques and had completed a six-session psychoeducational programme in which they had learned basic coping skills, relaxation, thought monitoring, mental imaging, goal setting and some communication skills (Cunningham *et al.*, 1991). Following this initial training, those who expressed a wish to do further work, and who met the medical criteria, were enrolled in a weekly therapy group for a planned 12 months. Once they had attended this group for 2 months they were considered part of the study. If, after initial enrolment, patients became too ill or were insufficiently interested to persist beyond 2 months (a further six individuals), they were not included in the study, because very little data was collected from them over such a brief period. It is of importance that there was no other selection exercised by the investigators, in contrast to the retrospective studies reviewed above. The final 22 patients were thus consecutively enrolled individuals who met the criteria of

Table 1. Main characteristics of study subjects

Patient	Gender	Age at study entry (years)	Length of time in group (months)	Primary disease	Sites of metastases	Oncologists' median survival prediction (first quartile, third quartile)	Actual survival from study entry in years (observed)
1	F	56	12	Colorectal	Rectum, peritoneal wall	1.00 (0.75, 2.10)	2.85
2	F	32	12	Osteosarcoma	Lung	1.30 (0.90, 1.75)	2.92
3	M	52	12	Adenoid cystic carcinoma (larynx)	Lung	2.00 (1.25, 3.75)	1.29
4	F	48	12	Breast	Mediastinal and hilar nodes	1.80 (0.90, 2.15)	> 5.62 ^a
5	F	48	12	Malignant melanoma	Abdomen, femoral and gluteal muscle	1.10 (0.85, 1.43)	> 4.74 ^a
6	F	61	12	Malignant melanoma	Lung	1.05 (0.75, 1.58)	1.82
7	F	46	12	Pancreatic	Liver	0.40 (0.30, 0.50)	2.07
8	M	47	8	Renal cell carcinoma and colorectal cancer	Abdominal wall	1.40 (1.20, 2.50)	1.35
9	F	44	8	Cholangiocarcinoma		1.00 (0.50, 1.30)	0.87
10	M	67	8	Pancreatic	Liver	0.30 (0.25, 0.50)	0.81
11	F	53	8	Colorectal	Liver	0.95 (0.50, 1.31)	1.72
12	M	63	12	Lymphoma	Axillary and inguinal lymph nodes	1.20 (0.70, 2.00)	2.54
15	F	62	4	Multiple myeloma		2.75 (1.63, 3.90)	> 4.63 ^a
16	F	35	12	Breast	Multiple vertebrae	1.12 (0.81, 1.50)	2.50
17	M	32	4	Pancreatic	Liver	0.40 (0.35, 0.70)	0.38
20	F	31	2	Breast	Lung, liver	0.80 (0.76, 1.15)	0.99
21	F	33	6	Cervical	Pelvis, bowel	0.40 (0.25, 0.81)	1.20
22	F	42	12	Colorectal	Ovary, lung	1.00 (0.80, 1.50)	1.63
23	F	34	12	Ovarian	Pelvis and abdomen, bowel	0.88 (0.45, 1.54)	> 2.79 ^a
25	F	54	12	Leiomyosarcoma	Abdomen, lung	0.65 (0.29, 1.00)	> 2.75 ^a
26	F	42	12	Breast	Multiple vertebrae	0.78 (0.48, 1.30)	1.59
28	F	49	8	Colorectal	Liver, lungs	0.75 (0.60, 1.00)	> 2.10 ^a

^a These subjects were still alive as of 31 December 1998, the date of these survival calculations.

sufficiently strong motivation and good health to spend 2 months or more in therapy. The subjects (Table 1) were mainly female, all were between the ages of 31 and 67 years and most had above-average education.

Intervention

The intervention was 1 year of weekly 2.5-hour group psychotherapy sessions, conducted by two of the authors (AJC and CP), with between four and seven patients in the group at any one time. New members were recruited into the group at intervals, over a period of 3.5 years, to replace those leaving. Thirteen of the 22 subjects attended the therapy groups for 12 months, five attended for 8 months, and the remaining four attended sessions for between 2 and 6 months, because of declining health in two cases and lack of interest in the other cases. A monthly support group was available to graduates.

The intervention had three components. The first was support, in the sense defined by Peteet (1982): patients were comforted and strengthened by the group in the face of life-threatening disease. Expression and clarification of feelings was encouraged, as was rational problem solving, frank communication with important others, monitoring and changing of cognitions and the daily application of coping skills. Patients were helped to become, as Spiegel (1986) put it, 'experts in living'. Fear of death and dying was openly discussed and group members who died were grieved for. The second aspect of the intervention was homework: there was an emphasis on taking responsibility, not for one's cancer or its outcome, but for the implementation of a personal programme of self-help. Patients were asked to practise coping skills, such as relaxation and meditation, and to complete 20 weekly sessions of written homework, which included questions and assignments over a wide range of psychological and spiritual/existential issues (examples: What makes me feel I really want to live? Which people are important in my life, and how much support do I feel each of them gives me? Draw a picture of an important aspect of your life at the following (specified) stages. Attend at least one community spiritual or religious meeting and write about how it affected you). The third facet of the intervention was group psychotherapy: patients' entrenched opinions and habit patterns were

explored and modifications suggested; e.g. common issues included guilt, denial, blaming physicians and others, exaggerated dependencies, feelings of helplessness and a perceived loss of entitlement to longer life.

Collection of psychological data

Data collection was prospective, carried out before the patient's ultimate fate was known, and longitudinal, typically over a period of 1 year (less for some, as indicated above). There were three main sources of verbal data: detailed process notes taken by the therapists during all group meetings; written homework supplied by the patient in response to the questions and assignments in the homework manual; and individual interviews (with the first author), wherever possible, approximately 1, 6 and 12 months after entry into the group. Notes were also taken at casual contact times (e.g. telephone calls). In collecting verbal data, there was a particular focus on the perceived effects of the interventions and self-help work, and on thoughts, emotions and behaviours of the subjects that might have relevance to the experience of adjusting to the cancer. However, patients spoke over a wide range of topics, including most aspects of their lives and functioning. Clinical inferences by the therapists were also an important part of the database. Records were kept of attendance and of homework completed.

Because of the existence of literature on the relationship between quality of life and related variables to outcome (Coates *et al.*, 1992; Wisloff *et al.*, 1997), we administered five self-report questionnaires at the beginning of the therapy. This was instituted a short time after the beginning of the project, and data are available for 17 of the 22 subjects. Two of the instruments used are in common use in psycho-oncology: the Profile of Mood States (POMS), a 37-item version (McNair *et al.*, 1971/1981; Shacham, 1983), which is a basic measure of affective state in several dimensions including anxiety and depression; and the Functional Living Index for Cancer (FLIC) (Schipper *et al.*, 1984), a 22-item measure assessing the physical, emotional and social aspects of cancer patients' quality of life. To these we added the Purpose in Life test (PIL) (Crumbaugh, 1968), which measures perceived meaning in life, and the Sense of Coherence (SOC) questionnaire, sometimes known as the Orientation to Life

questionnaire (OLQ) (Antonovsky, 1979), which assesses whether or not things are expected to turn out well.

The fifth instrument, an unpublished scale which we devised and called the Expectancy Questionnaire (EQ), was a simple, 5-point scale asking subjects about their expectations of the effects of the psychological therapy on the cancer. The five points on this scale were (in slightly abbreviated form): 0, no change in the cancer; 1, may be some slight slowing of cancer growth; 2, expect to make a real difference to the cancer although it may not visibly regress; 3, expect cancer will shrink noticeably; 4, the cancer will disappear.

Prediction of medical outcomes

This study used a heterogeneous sample of patients with diseases that are usually associated with different lengths of survival. We, therefore, had to ensure that any association between psychological variables and survival duration was not simply a result of disease severity acting on both. For example, if low psychological scores were found to be associated with poor survival, this might occur because these patients were too ill to do much self-help work. Controlling for the severity of disease at the start of the intervention would remove this factor. Various methods for predicting, at intake, a patient's likely survival time were considered. A literature search was undertaken for patients comparable with each of our subjects, but it proved impossible to match many of them precisely to populations studied in published trials. We could not readily enter individual prognostic factors into the analyses, such as site of metastases or interval from primary to metastatic diagnoses, because the factors that were important varied from one patient to another. We felt, therefore, that the best available estimates could be gained by submitting the medical details for each patient to an expert panel. In effect, we used a panel of oncologists, and their medical experience, to factor in the many prognostic features of a patient's history in order to produce a numerical estimate of the severity of the disease in the form of estimated expected survival. This survival estimate was then used as a covariate to control for the heterogeneity of the sample.

As a first step, the oncologist co-investigator (DH), who had not met the patients and was

blind to their psychological characteristics and progress, obtained from subjects' charts all relevant prognostic data describing their disease status at the time of entry into the study. This included information on tissue of origin and grade, metastatic spread, interval between primary and secondary disease, any tumour marker activity, treatment and general health details. Written consent for this had been provided. This prognostic information was given, at individual meetings, to 14 oncologists, none of whom had met the patients. We asked them to draw a survival curve, for each patient, on a blank graph provided, predicting the rate at which individuals like the subject would be expected to die. From the curve we could then read off the median predicted survival, i.e. the point at which 50% of such subjects would be expected to have died. Thus, for each experimental subject, we had a number of predicted survival curves; this number varied from nine to 14 because the oncologists had the option to decline making a prediction if they felt insufficiently experienced with the particular diagnosis. The median of these estimates was in turn calculated. Thus, we had a median estimate of the median, or 50% survival rates, medians being chosen over means to avoid the skewing of estimates by occasional high values.

To gain some estimate of the accuracy of the technique, the same panel of oncologists (with two missing) predicted the survival curves of 18 recently deceased patients, not included in the study, who also had a variety of types of metastatic cancer. The median survival for all patients in this sample agreed closely with the actual median (Barbera L, Bezjak A, Cunningham A, Tritchler D, in preparation. Physician prediction of survival in patients with metastatic cancer). This method of predicting survival (to control for survival differences owing to varying diagnoses), although the best we have been able to devise, remains uncertain. It has the advantage of allowing the consulting oncologists to take into account individual features of each patient, such as their age and previous disease history, thus providing a more relevant estimate than a comparison with normative population means.

We were also able to use these oncologists' estimates to rank the patients, despite their different prognoses, in order of the degree to which they outlived their predicted survivals. For example, if a subject died 18 months after study entry, and the median estimate of the panel members

was that 50% of similar patients would have survived only 9 months, he or she outlived expectancy by a factor of 2.0 (observed survival divided by the median survival predicted by the panel of oncologists). This ranking has been used to prepare a graphical comparison of the psychological attributes of each subject (Figure 1). For the six subjects still alive at the time of writing, this ratio is obviously an underestimate.

We maintained contact with all surviving patients after their year of therapy was over, through occasional telephone calls and through the attendance of many of them at monthly sup-

port group meetings; the date of death, where this occurred, was verified from their charts.

Qualitative analyses

An analysis of these data was carried out using non-numerical unstructured data searching, indexing and theorizing (NUDIST) (Richards and Richards, 1994) software to facilitate coding, organization and retrieval of the verbal data. A grounded method was used: dimensional analysis (Schatzman, 1991; Kools *et al.*, 1996). The first

Subject	O/M	Appraisal	Ability to change	Willingness to change	Application	Relations with others	Quality of experience	Total Psych Score
7.	5.17	●	◐	●	●	◐	●	●
5.	>4.31	●	◐	◐	◐	◐	●	◐
25.	>4.23	◐	◐	◐	●	◐	●	◐
23.	>3.17	◐	◐	◐	◐	◐	◐	◐
4.	>3.12	●	●	●	●	●	●	●
21.	3.01	◐	○	◐	◐	○	○	○
1.	2.84	◐	◐	◐	◐	◐	◐	◐
28.	>2.80	●	●	●	●	●	◐	●
10.	2.71	◐	◐	○	○	○	○	○
2.	2.25	○	○	○	◐	○	◐	○
16.	2.24	◐	◐	●	●	●	◐	●
12.	2.12	◐	◐	◐	●	○	◐	◐
26.	2.03	◐	○	◐	◐	◐	◐	◐
11.	1.81	◐	◐	◐	◐	◐	◐	◐
6.	1.73	◐	◐	◐	◐	◐	◐	◐
15.	>1.68	◐	◐	◐	◐	◐	◐	◐
22.	1.64	◐	○	○	◐	○	○	○
20.	1.24	◐	◐	◐	◐	◐	◐	◐
8.	0.96	◐	○	◐	◐	◐	◐	◐
17.	0.97	◐	○	○	○	◐	○	○
9.	0.87	◐	○	◐	◐	○	○	○
3.	0.64	◐	○	◐	○	◐	◐	○

**Subjects are arranged in descending order of observed/median predicted survival and their scores on each of the themes are represented by circles with graded shading representing ranges in scores as described in legend. ● 80 - 100% ◐ 60 - 79% ◑ 40 - 59% ○ 20 - 39%*

Figure 1. Diagrammatic representation of rating for each patient on each theme. Subjects are arranged in descending order of observed survival divided by the median survival predicted by the panel of oncologists (labeled as O/M). Thus, an O/M score of 5.17 means that the patients lived 5.17 times longer than predicted. Their scores on each of the psychological themes are represented by circles with graded shading representing ranges in scores in the themes listed in Table 2.

step developed a vocabulary of concepts or categories from the extensive raw data; these were coded and clustered into a provisional index tree of some 55 categories. As a model was gradually developed, this number was reduced by collapsing closely similar categories and by a decision to focus the analysis around psychological perceptions, attitudes and behaviours within individuals (excluding e.g. the subject's social circumstances, although retaining documentation of his or her reactions to it). This resulted in 26 final categories. A key process in understanding a phenomenon through dimensional analysis is the process of dimensionalizing, i.e. naming the main components and describing their various attributes. Therefore, the 26 categories were combined into the six major themes shown in Table 2 (example: 'Application to self-help work'). These themes have been connected in a simple model that forms the core of our analysis of the process of striving to overcome cancer and will be reported in detail elsewhere.

Quantitative rating of psychological features

For each of the categories to be rated, all relevant data were assembled and summarized by one team member. The adequacy of this summary was checked by a second member. We developed quantitative ratings, on a scale of 1–5, for each of these categories, with written descriptions of patterns that would qualify as '1', '3' or '5'. An assessment of the strength or intensity of that category could now be made for each subject. For example, in the category 'Dedication to self-help work', a rating of '1' was given when the subject was not at all committed to self-help work and invested little or no time in it; a rating of '5' applied when the work was the top priority in the life of a subject who was sufficiently self-motivated to go consistently beyond assigned homework. The score for a theme was the sum of scores for its component categories. Table 2 shows how the 26 categories were combined into

Table 2. Main psychological themes assessed

Psychological theme	Components (categories)
1. Appraisal of threat and need to change	Appraisal of threat Perceived need to change Awareness of changes needed Secondary gain
2. Ability to act and change	Ability to act (<i>vs</i> resistance to acting) (lack of) Emotional repression (lack of) Avoidance of challenge (lack of) Control needs
3. Willingness to initiate change	Intrinsic interest in exploring new behaviours Perceived ability to change Outcomes expected from self-help work Wishes, plans and goals
4. Application to self-help work	Amount and nature of work carried out Dedication to self-help work Spiritual work carried out Reinforcing experiences during work
5. Relationships with others	Experiences of intimacy Relations with therapy group (lack of) Judgementalism; forgiveness Lasting effects of self-help work on relations
6. Quality of experience	Self-worth Peace of mind Ability to cope with distressing emotions Social openness Spiritual awareness Integration of self-help work into life

six themes. These themes were then used for our calculations of the relationship of psychology to survival. We also summed the ratings for all 26 categories to give a total psychological score.

Figure 1 is a visual display of the ratings for each theme in each subject. It shows graphically the association between theme scores and survival ratio. As can be seen from the figure, different symbols have been assigned to ratings of 80–100%, 60–79%, 40–59% and 20–39% of the possible score for a theme (the lowest rating assigned for a category was 20%, meaning that the subject obtained a rating of only 1 for each of the categories contributing to the theme). To minimize personal bias in assigning ratings, a team discussion process was used. All of the salient information for each subject on each category to be rated was scrutinized and rated independently by either three or four persons. Two of the raters were the therapists, who had detailed clinical knowledge of the subjects, while the other raters were blind to the subjects. All had to be satisfied that the verbal data supported the rating ultimately assigned by discussion to consensus.

Statistical analyses

Relationships between the psychological variables were estimated using Pearson's correlation coefficients. Cox regression analysis was used to relate the six qualitatively derived psychological themes, the total psychological score, the psychometric scores at the beginning of therapy, the medical estimate of survival and age to the actual survival measured in years. Results are presented as risk ratios from the regression equations with the associated *p*-values. The risk ratio indicates the decrease in risk of death that results from a 1-unit increase in the measure being tested. To further illustrate the size of the effect, Kaplan–Meier plots are presented for two of the significant measures divided at their respective medians. A log rank test was calculated to compare the survival in the upper and lower halves of the population.

Two-variable Cox regression models were examined to test whether the results observed for the qualitative and psychometric measures were changed when the medical estimate of survival or the age of the subject were controlled for.

RESULTS

Distribution of ratings on the qualitatively derived themes

Figure 1 shows the ratings of each patient on each theme. The 22 patients were arranged in order of the ratio of the observed survival divided by the survival predicted by the panel of oncologists. In all but four cases this ratio was greater than 1, indicating that the observed survival was longer than that predicted by the oncologists. The median ratio of the observed time over the predicted time was 2.25. Several patterns are obvious from this visual display; in particular, there was a strong tendency for those subjects with best survival ratios to have the highest scores. All ratings of 80–100% in any theme occurred in the top half of the figure, as did all total psychological scores of 60% or more. While a high psychological score was always associated with prolonged survival, the reverse was not always true; some individuals with low psychological scores lived longer than predicted. As we move down the figure, there was a trend towards lower ratings, the poorest survivors having the lowest psychological scores. It is also apparent that the different themes were highly inter-correlated. The Pearson correlation coefficients, ranging from 0.64 to 0.97, are shown in Table 3.

Qualitative themes and survival

Cox regression analyses showed that all of the qualitative themes, with the exception of appraisal of threat and including the total psychological score, were significantly related to observed survival (Table 4). These results are unlikely to be independent of each other because of the high inter-correlation of the themes (see above). The possible independence of the themes in relation to survival was not explored further here because of the limitation of the small sample size.

In order to illustrate the effect of total psychological score, the population was divided into half at the median total score. The Kaplan–Meier curves for the two halves of the population are presented in Figure 2, along with a log rank test comparing them. Of the 11 subjects whose total psychological score was less than the median, all died within the study period, with a median survival of 1.29 years (range 0.39–2.92). Of the 11

Table 3. Pearson correlation coefficients for the qualitatively derived psychological themes

	Appraisal	Ability to act	Willingness to change	Application	Relationships	Quality of experience
Ability to act	0.81					
Willingness to change	0.90	0.92				
Application	0.75	0.82	0.91			
Relationships	0.65	0.88	0.81	0.77		
Quality of experience	0.64	0.84	0.82	0.76	0.87	
Total score	0.85	0.96	0.97	0.91	0.91	0.91

subjects with a total psychological score greater than the median, only five have died, with a median survival of 2.85 years (range 1.72– > 5.62).

Because the subjects in this study have a range of cancer diagnoses that might have considerably different survival experiences, which in turn could influence psychological work, we tested the relationship of the qualitatively derived themes, controlling for the expected survival estimated by the oncologists' panel. The results are given in Table 5 and were virtually unchanged from the uncontrolled analyses. Again, all themes, except appraisal of threat, were significantly related to survival at levels very similar to the uncontrolled analyses. The medical estimate was significant at $p = 0.05$ when

tested alone (data not shown), and remained significant at similar levels when included together with a qualitative theme (Table 5).

As a final test of the qualitative themes, the Cox regressions were repeated, controlling for the age of the subject. Age was not significant when tested alone and did not change the results of the qualitative themes when included in the models with them (data not shown).

Psychometric measures and survival

Psychometric data were available for 17 of the 22 subjects. Of the five psychometric measures,

Table 4. Results from Cox regressions relating qualitative and psychometric data to survival time (years)

Variables	Risk ratio ^a	Inter-quartile range (IQR) ^b	Risk ratio over IQR ^c	<i>p</i> -value
Ratings of qualitative data ($n = 22$)				
Appraisal	0.98	25	0.62	0.17
Ability to act	0.94	15	0.41	0.008
Willingness to change	0.97	30	0.46	0.03
Application	0.96	35	0.27	0.02
Relationships	0.95	25	0.31	0.008
Quality of experience	0.95	33	0.17	0.001
Total psychological score	0.95	27	0.26	0.007
Psychometric data ($n = 17$)				
POMS	1.01	12	1.08	0.87
FLIC	0.99	27	0.81	0.54
EQ	0.50	1	0.5	0.03
OLQ	0.99	28	0.84	0.66
PIL	0.99	11	0.88	0.66

^a In all cases (except POMS, which is reversed), as the score for a variable increases, the risk of death decreases. In the second column, the change in the risk of death is shown for 1% unit change in the variable. Thus, a 1% increase in total psychological score translates into a 0.05 (5%) decrease in the risk of dying.

^b The third column shows the IQR, i.e. the difference between the third and the first quartile.

^c The fourth column shows the relative risk of dying associated with a value at the third compared with the first quartile. Thus, a subject at the third quartile of the total psychological score has 0.26 the risk of dying compared with someone in the first quartile.

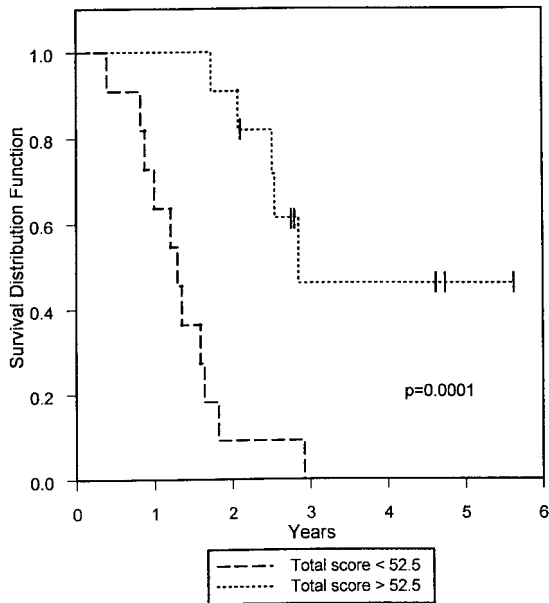


Figure 2. Kaplan–Meier survival curve for the total psychological score split at the median. ($n = 11$ in both groups and the p -value is taken from the Log Rank test.) The vertical ticks represent patients who are still alive (censored).

only the Expectancy scores taken at the onset of therapy showed a significant relationship with survival ($p = 0.03$; see Table 4). The effect of the

Table 5. Results from Cox regressions relating qualitative and psychometric data to survival time (years) and controlling for medical prediction of survival

Variables	p -value	
	Theme	Medical prediction
Ratings of qualitative data ($n = 22$)		
Appraisal	0.17	0.06
Ability to act	0.005	0.04
Willingness to change	0.02	0.05
Application	0.005	0.02
Relationships	0.003	0.04
Quality of experience	0.001	0.05
Total psychological score	0.004	0.04
Psychometric data ($n = 17$)		
POMS	0.34	0.24
FLIC	0.37	0.34
EQ	0.02	0.23
OLQ	0.47	0.35
PIL	0.46	0.35

Expectancy scores, as illustrated in Figure 3, was shown by dividing the data at the median Expectancy score and presenting the Kaplan–Meier curves. In this case, the median (Figure 3) did not split the sample into two equal groups because the Expectancy scores only ranged from 1 to 4 and there was a large number of ties. All five subjects with scores less than the median have died, with a median survival of 0.99 years (range 0.39–1.64). Seven of the 12 subjects with scores greater than or equal to the median have died, with a median survival of 2.29 years (range 1.20– > 4.74). Controlling for either the medical estimate of survival (Table 5) or age (data not shown) in the Cox regressions did not change the results.

DISCUSSION

The aim of this study has been to generate hypotheses about psychological factors that may influence the progression of cancer in patients. A correlative method was needed. We used what Tashakkori and Teddlie (1998) called a type 4 mixed qualitative/quantitative design: a

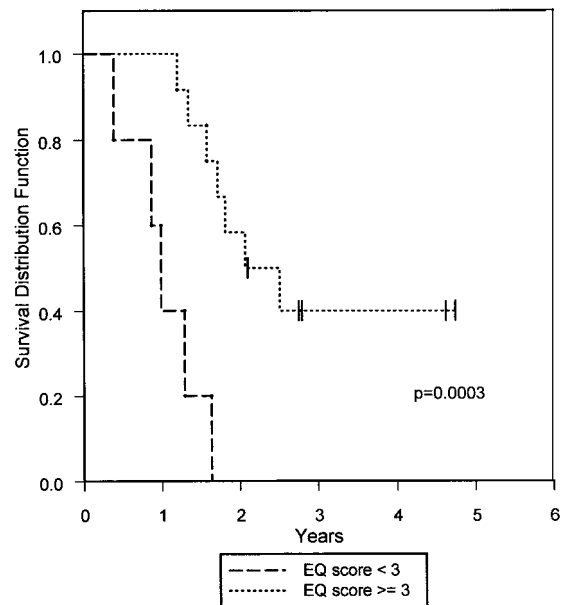


Figure 3. The Kaplan–Meier survival curves for the Expectancy Questionnaire split at the median. (The upper curve, $n = 12$, had scores \geq the median of 3 and the lower curve, $n = 5$, had scores $<$ the median of 3; the p -value is taken from the Log Rank test. The vertical ticks represent patients who are still alive (censored).

qualitative analysis of verbal data derived from each patient, followed by a quantitative rating of the emergent themes. This labour-intensive, exploratory approach was chosen because the attributes related to survival are not yet known. As is noted in the 'Introduction', several decades of research using psychometric tests have not yielded consistent correlations between personality or behavioural variables and survival in cancer patients. Our sample size (22 patients), while small by trial or survey standards, is large for such a detailed qualitative analysis, and comprises data collected and analysed over about 5 years.

Median survival of the 22 subjects was 2.25 times that predicted by the oncology panel (with six subjects still alive at the time of writing). This could either be the result of some selective factor, not obvious to the panel (and, therefore, probably psychological in nature), or be a result of attributes developed by the subjects while in therapy. Our argument for a relationship between the psychological properties of the subjects and survival duration is not, however, dependent on a comparison of the study group with the wider population, but rests on within-group comparisons. Regardless of any selection factors operating on the sample as a whole, there was a strong and highly significant relationship, by Cox regression analyses, between survival duration and a number of psychological themes obtained by the qualitative analysis: the ability to act and change; willingness to initiate changes; application to self-help work, relationships with others; and quality of experience. The one factor in which variations were not significantly related to survival was appraisal of threat, possibly because all of the subjects entering the study acknowledged the seriousness of the threat to their lives. The five significant themes, although differing greatly from one another in their clinical nature, were highly inter-correlated. It appears that, under the conditions of our experiment, all of these psychological factors fluctuate together. Alternatively, they may all be assessing one common, underlying quality. Together they form a complex of attitudes and behaviours, which we have called involvement in psychological self-help work. Our data thus support the anecdotal accounts and clinical experience that this kind of involvement is related to cancer survival. They do not prove a causal relationship, as is discussed below.

A number of aspects of the design limit the conclusions that can be drawn from this study,

however. The first is the possibility that those with more serious prognoses were less able to do the work required to achieve high psychological scores. To control for this, we entered into the regression equations an expert panel's estimate of probable survival duration. Controlling for this covariate did not change the significance of the relationship of psychological scores to survival. Applying the panel's estimates to each individual patient allows us to compare the degree of extended survival attained by patients with different kinds of disease, as is described in the 'Methods' section.

A second argument against the possibility that the psychological ratings were influenced by the seriousness of disease is based on the attendance and survival data (Table 1). Almost all of the study group were basically well for at least 6 months, which was long enough to acquire high ratings. These reflected the quality, not the quantity, of their engagement in psychological work. As Table 1 shows, all but four patients lived for at least 14 months after entry. Eighteen attended group sessions for at least 8 months, and three of the four who dropped out earlier than this survived for at least 1 year. There was only one early death in our sample, which occurred 4.5 months after entering the study (this man was well enough to make several trips between Canada and Germany during this time). We have observed clinically that motivation for action and change is, in any case, often at its highest when there are symptoms and a more immediate threat, and frequently wanes when people feel well. Results derived from the quality of life instrument (FLIC) also support the conclusion that our qualitatively derived themes were not simply covert measures of physical health at enrolment. No significant correlation was found on the FLIC, which specifically assesses physical health status among other things, between scores at entry and any of the themes or survival.

In contrast, an important limitation in our design lay in the need to delay psychological rating until the therapy was over. This was unavoidable; because it was the first experiment of its kind, we needed to collect data and analyse them qualitatively before the categories for rating could be finalized. With the categories now defined, it will be possible in future experiments to rate at an earlier stage, when health outcomes are less determined. However, because the aim of the experiment is to assess the response of patients to the

intervention, there is a limit to how early this can be done if involvement is to be assessed.

This design limitation leaves the study open to the criticism that the raters may have been influenced by having some awareness of the health status of the patients after their therapy. We attempted to minimize any such bias by using team consensus discussions to assign ratings, with at least one member of this team being unfamiliar with the patients. Blind rating of collected data could, in theory, circumvent this source of possible error, but would require deleting all therapists' inferences from the database. This would remove much of the most useful and subtle information about the subjects.

The generalizability of conclusions from our study is, however, severely limited by the self-selection of subjects for motivation to undertake a programme of psychological work. Although the subjects were consecutively enrolled patients who fulfilled the eligibility criteria (see 'Methods' section), they represent a very small proportion of those attending the hospital. It is currently unknown what proportion of patients not currently demonstrating motivation for this kind of work would be capable of a similar dedication to psychological self-help if further evidence for an effect on lifespan is found. The small number of patients is also an obvious limitation to confidence in the results; while the effects were large enough to have reached significance with small numbers, a similar outcome from further work will be needed to increase confidence in the psychology-survival relationship.

Our design, while imperfect, would appear to have a number of strengths by comparison with work carried out previously. First, its prospective and longitudinal nature; second, the thorough medical documentation of all participants, in contrast to the very limited or absent medical documentation in accounts of remarkable survivors; and third, the collection of psychological documentation based on weekly contact over a period of up to 1 year (around 100 h of contact per person), which contrasts with the usual single interviews in the remarkable survivor work or the psychometric tests of the personality-survival literature. The qualitative approach also allowed an initial openness to a wide range of factors that might influence good adaptation to cancer, and a gradual focussing of our data collection and analysis as patterns unfolded during the study.

As the qualitative analysis progressed, this focus became the subjects' interest and involvement in psychological work and change. Although we had prior clinical experience to suggest the importance of these qualities, we began the study with an interest in all aspects of the early lives and current life circumstances of patients, and with their personality traits in general. We also initially expected that the patients' reported behaviours might yield the most informative data. However, it became evident that the factors most critical to understanding subjects' adaptation were their ability or willingness to explore and implement new strategies and priorities; in other words, the focus shifted from the behaviour to its cognitive precursors. This parallels the shift of interest to cognitive processes in coping in the health psychology literature in general (Lazarus and Folkman (1984), Prochaska *et al.*, 1992). Within the theme of willingness to initiate change (Table 2), categories that emerged as important included outcomes expected from applying self-help strategies, perception of ability to make changes, and what we have called wishes, plans and goals. These were all familiar within the Health Action Process Approach of Schwarzer (1992) and the prior work of Bandura (1982), a social cognitive perspective emphasizing the complex set of expectancies and multiple stages of motivation and volition that guide attitudinal and behavioural change. The pathway from initial appraisal to willingness to change and the subsequent application to self-help work was strongly influenced, in turn, by what we described as the ability to act and change, a theme that included character traits concerned with defensiveness and resistance (or openness) to change. Individuals could be clustered into groups, according to their adaptational patterns, in a way that will be described in more detail elsewhere. In general, however, the dominant pattern associated with good outcome, in terms of both quality of experience and long survival, was an openness or flexibility, prompting a willingness to make substantial lifestyle changes, followed by a dedicated application to psychological self-help strategies. This is a pattern that also makes intuitive sense.

In marked contrast to the significant association of quantitatively derived data to survival, results from standard psychometric tests, including a quality of life instrument, obtained from 17 of the 22 subjects at the beginning of the therapy period, did not show any significant relationship

with survival in the present study. This is in agreement with the relatively large literature cited in the 'Introduction'. In those published studies, where significant prediction was achieved, additional data were generally obtained by interpersonal interactions such as interviews, as was the case in the present study (Greer *et al.*, 1979; DiClemente and Temoshok, 1985; Morris *et al.*, 1992; Edmonds *et al.*, 1999). While recent evidence from chemotherapy trials suggests that quality of life tests may predict survival (Coates *et al.*, 1992; Wisloff *et al.*, 1997), our experimental conditions differ from these reports in that our subjects received long-term group psychotherapy, presumably modifying their psychological status between the initial assessment and the time of death. In contrast to standard instruments, the expectancy score at the onset of therapy from the same small number of subjects showed a strong relationship to subsequent survival duration. It is unlikely that expectancy is a covert measure of physical health because, as was the case for the qualitatively derived psychological themes, it did not correlate significantly ($r=0.05$) with the FLIC. This intriguing result, which obviously requires replication with a larger sample, echoes the recent demonstration by Butow *et al.* (1999) that, after controlling for conventional prognostic factors, the strongest factor predicting survival duration in patients with metastatic melanoma was response on a 4-point self-report scale measuring the effects that patients expected from their treatment.

We are aware of only one rigorous, published study that used a correlative design to relate psychological therapy to cancer progression. De Vries *et al.* (1997) assessed changes in the rate of growth of tumours coincident with a 12-week period of psychotherapy. A drop in this rate was found in five of 35 subjects. This approach uses an endpoint that might reasonably be thought to predict survival, and seems to suggest that psychological change can be rapidly translated into effects on tumours in some cases. We did consider using tumour markers or size as endpoints in this study, but opted instead for survival, that oncologists advised us was more definitive, because tumours sometimes fluctuate in growth rate or size for unknown reasons.

Finally, the null findings in our recently published randomized controlled trial (Cunningham *et al.*, 1998) need to be reconciled with the present

results. A hypothesis to explain this discrepancy derives from the present observation that prolonged survival is associated with considerable work and change. In the randomized trial, subjects were actively recruited, the initiative coming from the investigators. These subjects were not generally as highly motivated to do self-help work as those volunteers in the present study, who showed high levels of involvement. They resembled, rather, the subjects at the low end of the 'involvement' scale in our present study. However, it is intriguing to note (Cunningham *et al.*, 1998) that seven of the 66 subjects in the randomized trial (from the intervention group) took the trouble to seek psychotherapeutic help outside of the research protocol. These seven survived significantly longer than the rest of the group ($p=0.024$). While the number is too small to be more than suggestive, it is consistent with the present finding that motivation or drive to help oneself is associated with longer survival.

This comparison between the two studies also underlines the strengths and limitations of the two designs. Randomized trials test treatment efficacy more definitively. Correlative designs allow us to relate characteristics of individuals to outcomes, thus providing more information on what sort of changes might help patients. They have the advantage that valuable contributions can be made with relatively small numbers of patients, and they also avoid the inhumane process of randomizing patients who may desperately want the therapy on offer. If the relationship between therapy-induced psychological change and survival does exist, its validity will gradually become apparent with more studies of this kind being undertaken (as has happened for the smoking-lung cancer relationship).

In the next series of experiments, with the themes already defined, improvements will be possible, notably the earlier rating of patients during the intervention. We also plan to rate subjects at a number of time points, in order to relate change in psychology to outcome. This would strengthen the argument that therapy contributes something over and above the patients' initial attributes. Future work might be carried out with different patient populations, e.g. using a medically more homogeneous study group should decrease the influence of medical variables. The disease process in patients with primary cancer might prove more sensitive to psychological

factors because primary tumours are likely to be less well adapted to their host. If psychological attitude eventually proves to correlate reliably with survival, then it is probable, *a priori*, that change in attitude will promote change in survival duration. Prolongation of life through adjunctive psychological therapy may thus be more possible than has been generally believed in biomedical circles.

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REFERENCES

- Achterberg L, Mathews-Simonton S, Simonton OC. 1977. Psychology of the exceptional cancer patient: a description of patients who outlive predicted life expectancies. *Psychother Theory Res Pract* **14**: 416–422.
- Antonovsky A. 1979. *Health, Stress and Coping*. Jossey-Bass: San Francisco.
- Bandura A. 1982. Self efficacy mechanism in human agency. *Am Psychol* **37**: 122–147.
- Berland W. 1995. Unexpected cancer recovery: why patients believe they survive. *Adv J Mind Body Health* **11**: 5–19.
- Butow PN, Coates AS, Dunn SM. 1999. Psychosocial predictors of survival in metastatic melanoma. *J Clin Oncol* **17**(7): 2256–2263.
- Cassileth BR, Walsh WP, Lusk EJ. 1988. Psychosocial correlates of cancer survival: a subsequent report 3 to 8 years after cancer diagnosis. *J Clin Oncol* **6**: 1753–1759.
- Challis GB, Stam HJ. 1990. The spontaneous regression of cancer. *Acta Oncol* **29**: 545–550.
- Coates A, GebSKI V, Signorini D, Murray P, McNeil D, Byrne M, Forbes JF. 1992. Prognostic value of quality of life scores during chemotherapy for advanced breast cancer. *J Clin Oncol* **10**(12): 1833–1838.
- Crumbaugh JC. 1968. Cross-validation of Purpose-in-Life Test based on Frankl's concepts. *J Individ Psychol* **24**: 74–81.
- Cunningham AJ, Edmonds CVI, Hampson AW, Hanson H, Hovanec M, Jenkins G, Tocco EK. 1991. Helping cancer patients cope with, and combat, their disease: report on a group psychoeducational program. *Adv J Mind-Body Health* **7**: 41–56.
- Cunningham AJ, Edmonds CVI, Jenkins GP, Pollack H, Lockwood GA, Trichter D, Warr D. 1998. A randomized controlled trial of the effects of group psychological therapy on survival in women with metastatic breast cancer. *Psycho-Oncology* **7**: 508–517.
- De Vries MJ, Schilder JN, Mulder CL, Vrancken AM, Remie ME, Garssen B. 1997. Phase II study of psychotherapeutic intervention in advanced cancer. *Psycho-Oncology* **6**: 129–137.
- DiClemente RJ, Temoshok L. 1985. Psychological adjustment to having cutaneous malignant melanoma as a predictor of follow-up clinical status. *Psychosom Med* **47**: 81.
- Doan BD, Gray RE. 1992. The heroic cancer patient: reflections on the relationship between illusion and mental health. *Can J Behav Sci* **24**(2): 253–266.
- Edelman S, Lemon J, Bell DR, Kidman AD. 1999. Effects of group CBT on the survival time of patients with metastatic breast cancer. *Psycho-Oncology* **8**: 474–481.
- Edmonds CVI, Cunningham AJ, Lockwood GA. 1999. Psychological response to long term group therapy: a randomized trial with metastatic breast cancer patients. *Psycho-Oncology* **8**: 74–91.
- Ell K, Nishimoto R, Morvay T, Mantell J, Hamovitch M. 1989. A longitudinal analysis of psychological adaptation among survivors of cancer. *Cancer* **63**: 406–413.
- Everson TC, Cole WH. 1966. *Spontaneous Regression of Cancer*. Saunders: Philadelphia.
- Fawzy FI, Fawzy NW, Hyun CS, Elashoff R, Guthrie D, Fahey JL, Morton DL. 1993. Malignant melanoma. Effects of an early structured psychiatric intervention, coping and affective state on recurrence and survival 6 years later. *Arch Gen Psychiatry* **50**: 681–689.
- Fox BH. 1998. A hypothesis about Spiegel *et al.*'s 1989 paper on psychosocial intervention and breast cancer survival. *Psycho-Oncology* **7**: 361–370.
- Funch DP, Marshall J. 1983. The role of stress, social support and survival from breast cancer. *J Psychosom Res* **27**: 77–83.
- Gellert GA, Maxwell RM, Siegel BS. 1993. Survival of breast cancer patients receiving adjunctive psychosocial support therapy: a 10-year follow-up study. *J Clin Oncol* **11**(1): 66–69.
- Greer S, Morris T, Pettingale KW. 1979. Psychological response to breast cancer: effect on outcome. *Lancet* **ii**: 785–787.

- Gross J. 1989. Emotional expression in cancer onset and progression. *Soc Sci Med* **28**: 1239–1248.
- Hay LL. 1984. *You Can Heal Your Life*. Hay House: Santa Monica.
- Hislop TG, Waxler NE, Coldman AJ, Elwood JS, Kan L. 1987. The prognostic significance of psychosocial factors in women with breast cancer. *J Chron Dis* **40**: 729–735.
- Huebscher RR. 1992a. Spontaneous remission of cancer. PhD Thesis, U.M.I. Dissertation Services, Ann Arbor, Michigan.
- Huebscher RR. 1992b. Spontaneous remission of cancer: an example of health promotion. *Nurse Pract Forum* **3**: 228–235.
- Ilnyckyj A, Farber J, Cheang MC, Weinerman BH. 1994. A randomized controlled trial of psychotherapeutic intervention in cancer patients. *Ann R Coll Physicians & Surg Can* **27**: 93–96.
- Jamison RN, Burish TG, Wallston KA. 1987. Psychogenic factors in predicting survival of breast cancer patients. *J Clin Oncol* **5**: 768–772.
- Jensen MR. 1987. Psychobiological factors predicting the course of breast cancer. *J Personality* **55**: 317–342.
- Kaasa S, Mastekaasa A, Lund E. 1989. Prognostic factors for patients with inoperable non-small-cell lung cancer, limited disease. *Radiother Oncol* **15**: 235–242.
- Kennedy BJ, Tellegen A, Kennedy S, Havernick N. 1976. Psychological response of patients cured of advanced cancer. *Cancer* **38**: 2184–2191.
- Kools S, McCarthy M, Durham R, Robrecht L. 1996. Dimensional analysis: broadening the conception of grounded theory. *Qual Health Res* **6**: 312–330.
- Kreitler S, Chaichik S, Kreitler H. 1993. Repression: cause or result of cancer? *Psycho-Oncology* **2**: 43–54.
- LaBarba RC. 1970. Experiential and environmental factors in cancer. A review of research with animals. *Psychosom Med* **32**: 259–276.
- Lazarus RS, Folkman S. 1984. *Stress, Appraisal and Coping*. Springer: New York.
- Linn MW, Linn BS, Harris R. 1982. Effects of counseling for late stage cancer patients. *Cancer* **49**: 1048–1055.
- Maunsell E, Brisson J, Duschenes L. 1995. Social support and survival among women with breast cancer. *Cancer* **76**(4): 631–637.
- McNair DM, Lorr M, Droppleman LF. 1971/1981. *Profile of Mood States Manual*. Educational and Industrial Testing Service, San Diego, California.
- Meares A. 1980. What can the cancer patient expect from intensive meditation? *Aust Fam Physician* **9**: 322–325.
- Morris T, Pettingale K, Haybittle J. 1992. Psychological response to cancer diagnosis and disease outcome in patients with breast cancer and lymphoma. *Psycho-Oncology* **1**: 105–114.
- Newton BW. 1982–1983. The use of hypnosis in the treatment of cancer patients. *Am J Clin Hypnosis* **25**: 104–113.
- Pennington S. 1988. *Healing Yourself*. McGraw: Toronto.
- Peteet JR. 1982. A closer look at the concept of support: some applications to the case of patients with cancer. *Gen Hosp Psychol* **4**: 19–23.
- Pettingale KW, Morris T, Greer S, Haybittle JL. 1985. Mental attitudes to cancer: an additional prognostic factor. *Lancet* **i**: 750.
- Prochaska JO, DiClemente CC, Norcross JC. 1992. In search of how people change: applications to addictive behaviors. *Am Psychol* **47**(9): 1102–1114.
- Ramirez AJ, Craig TKJ, Watson JP, Fentiman IS, North WRS, Rubens RD. 1989. Stress and relapse of breast cancer. *Br Med J* **298**: 291–293.
- Richards TJ, Richards L. 1994. Using computers in qualitative research. In *Handbook of Qualitative Research*, Denzin NK, Lincoln YS (eds). Sage Publications: Thousand Oaks, CA; 445–462.
- Richardson JL, Shelton DR, Krailo M, Levine AM. 1990. The effects of compliance with treatment on survival among patients with hematologic malignancies. *J Clin Oncol* **8**(2): 356–364.
- Roud PC. 1986–1987. Psychosocial variables associated with the exceptional survival of patients with advanced malignant disease. *Int J Psychiatr Med* **16**: 113–122.
- Schatzman L. 1991. Dimensional analysis: notes on an alternative approach to the grounding of theory in qualitative research. In *Social Organisation and Social Process*, Maines DR (ed.). Aldine de Gruyter: New York; 303–314.
- Schipper H, Clinch J, McMurray A, Levitt M. 1984. Measuring the quality of life of cancer patients: the Functional Living Index—Cancer: Development and Validation. *J Clin Oncol* **2**: 472–483.
- Schwarzer R. 1992. Self-efficacy in the adoption and maintenance of health behaviours: theoretical approaches and a new model. In *Self Efficacy*, Schwarzer R (ed.). Hemisphere Washington Pub. Co.
- Shacham S. 1983. A shortened version of the Profile of Mood States. *J Personal Assess* **47**(3): 305–306.
- Shekelle RB, Raynor WJ, Ostfeld AM, Garron DC, Bieliauskas LA, Liu SC, Maliza C, Ogelsby P. 1981. Psychological depression and 17-year risk of death from cancer. *Psychosom Med* **43**: 117–125.
- Siegel BS. 1986. *Love, Medicine and Miracles*. Harper & Row: New York.
- Simonton OC, Mathews-Simonton S, Sparks TF. 1980. Psychological intervention in the treatment of cancer. *Psychosomatics* **21**: 226–233.
- Sklar LS, Anisman H. 1981. Stress and cancer. *Psychol Bull* **89**: 369–406.
- Spiegel D. 1986. Psychosocial interventions with cancer patients. *Psychosoc Oncol* **4**: 83–95.

- Spiegel D, Bloom JR, Kraemer HC, Gottleib E. 1989. Effect of psychosocial treatment on survival of patients with metastatic breast cancer. *Lancet* **2**(8668): 888–891.
- Stolbach LL, Brandt VC. 1988. Psychological factors in the development and progression of breast cancer. In *Stress and Breast Cancer*, Cooper CL (ed.). Wiley: London.
- Stoll BA. 1992. Spontaneous regression of cancer: new insights. *Biotherapy* **4**: 23–30.
- Tashakkori A, Teddlie C. 1998. *Mixed Methodology. Combining Qualitative and Quantitative Approaches*. Sage Publications: Thousand Oaks, CA; 162.
- Temoshok L. 1987. Personality, coping style, emotion and cancer: towards an integrative model. *Cancer Surv* **6**: 545–567.
- Visintainer MA, Seligman MEP, Volpicelli J. 1983. Helplessness, chronic stress and tumor development. *Psychosom Med* **45**: 75–76.
- Watson M, Haviland JS, Greer S, Davidson J, Bliss JM. 1999. Influence of psychological response on survival in breast cancer: a population-based cohort study. *Lancet* **354**: 1331–1336.
- Waxler-Morrison N, Hislop TG, Meares B, Kan L. 1991. Effects of social relationships on survival for women with breast cancer: a prospective trial. *Soc Sci Med* **33**(2): 177–183.
- Wisloff F, Hjørth M. 1997. Health-related quality of life assessed before and during chemotherapy predicts for survival in multiple myeloma. *Br J Haematol* **97**: 29.