Title

A longitudinal study of psychological adjustment to the diagnosis of cutaneous malignant melanoma as a predictor of clinical status at follow-up

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A LONGITUDINAL STUDY OF PSYCHOLOGICAL ADJUSTMENT TO THE DIAGNOSIS OF CUTANEOUS MALIGNANT MELANOMA AS A PREDICTOR OF CLINICAL STATUS AT FOLLOW-UP

A Doctoral Dissertation presented

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ABSTRACT

One hundred and twenty-two patients seen at the University of California, San Francisco, and Children's Hospital, San Francisco, Malignant Melanoma Clinics were followed to evaluate a psychological factor, adjustment to the diagnosis of cutaneous malignant melanoma, as a predictor of clinical status at follow-up. Patients were interviewed on their initial visit to the Melanoma Clinics by a clinical psychologist. The interview covered a broad range of psychosocial topics, including the patient's adjustment to the diagnosis of melanoma. All interviews were videotaped for later coding to identify the patient's psychological adjustment responses. These responses were coded into two categorization schemes; Greer et. al. (1979) nominal categorization procedure, categorizes the patient on the basis of his or her verbatim responses, into one of four mutually exclusive psychological adjustment categories. A second approach, termed the profile of psychological adjustment derives a quantitative measure of each adjustment response-category for all subjects. Thus, each patient is assigned a profile of adjustment scores. The four psychological adjustment categories are: denial, fighting spirit, stoic acceptance and feelings of hopelessness/helplessness.

Use of contingency table and logistic regression analysis identified two statistically significant

gender-specific predictors of clinical status. Responses characteristic of stoicism among women and feelings of helplessness/hopelessness among men were significantly associated with outcome (P=0.05 and P=0.06, respectively). These findings are related to other, relevant longitudinal studies and their similarities and differences discussed. Limitations of study design and suggestions for future research are also discussed.

INTRODUCTION

A number of studies have explored the role psychological factors play in the development of cancer (for reviews see Crisp, 1970; Greer, 1979; Bahnson, 1980, 1981; Greer and Silberfarb, 1982; Levy, 1983). These studies have identified psychological factors such as personality types, mental states, and life stress as being associated with the onset of cancer. Overall, however, the findings have been inconsistent and, at times, contradictory, attributable, in large part, to weaknesses in the design and analysis of such studies. Limitations in evaluating psychological factors include the retrospective nature of the studies as well as inadequate assessment and control for known biological and epidemiological risk factors associated with disease occurrence. More detailed discussion of the methodological and analytic limitations of these studies can be found in excellent reviews by Fox (1978), Morrison and Paffenbarger (1981) and Temoshok and Heller (1984).

Studies of the effects of psychological factors on cancer prognosis or outcome are much less frequent; though it has been suggested that there is a greater theoretical reason to expect psychological factors to affect the course of disease than development (Fox, 1978; 1983). Moreover, prognositc studies, while not immune to some of the methodological and statistical pitfalls which plague

etiologic studies, avoid the major problem of retrospective assessment of the patient's psychological status by utilizing a prospective research design. In such studies, psychological status is assessed prior to disease recurrence and predictions can be made regarding which patients, on the basis of these psychological assessments, are at a significantly higher risk of relapse and mortality. Though seemingly a more productive avenue of investigation, few studies have examined the role of psychological factors as they influence the course of disease.

The following review of literature will describe, in detail, the findings from psychological studies of cancer progression. In addition, each study will be critiqued in terms of its research methodology and statistical analysis. Issues which also warrant consideration in interpreting study's findings will be presented as well.

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GENERAL LITERATURE REVIEW

In an early investigation of the relationship between psychological factors and cancer survival, Blumberg et. al. (1954) studied a wide variety of tumor types in an attempt to identify personality characteristics which would differentiate patients by the rate of tumor progression. Fifty patients were given the Minnesota Multiphasic Personality Inventory (MMPI) during a period of disease remission. Based on findings from a pilot study, patients with rapidly progressing tumors usually displayed two of the three following characteristics: highly negative F-K values (<=12), considered indicative of high defensiveness or a strong tendency to present the appearance of serenity in the presence of deep inner distress; D values (=>55), considered indicative of unrelieved anxiety or depression; and low Ma values (<60), suggesting an abnormal lack of ability to decrease anxiety through outward corrective action. Accordingly, if a patient met two of the above psychological criteria, they were classified as having a pattern of personality characteristics predictive of a decreased duration of survival following treatment.

The criterion variable, tumor progression, was determined by noting the average duration of survival for each tumor type based on actuarial statistics. The criterion variable was operationalized as follows: specific

tumor type were categorized as "Average Progression"; patients surviving less than 50% of the mean expected duration (the lowest quartile of survival) were categorized as "Fast Progression"; and patients surviving more than 50% of the mean excepted survival pattern (upper quartile of survival) were categorized as "Slow Progression." To illustrate, in acute myeloblastic leukemia the average survival period is from 4 to 6 months. Using the above criteria, average, fast and slow progression were defined as 2-8 months, 1 month, and 12-18 months, respectively. Other variables which might confound the relationship between the psychological characteristics and the tumor progression categories such as age, socioeconomic status, intelligence and the patients' knowledge of the extent of their disease, were controlled in the research design.

The results show that 22 of the 25 patients with fast progressing tumors and 17 of the 25 patients with slow or average progressing tumors were correctly categorized based on knowledge of the psychological predictors. The overall accuracy of classification was 78% (39 out of the 50 patients), or 28% better than could be expected on the basis of change alone ($P<.01$).

The authors suggest that these findings indicate that longstanding, intense emotional stress may exert a profound stimulating affect on the growth rate of tumors. Conversely, improved host resistance can be explained as the

ability to reduce or adapt effectively to stress induced by the environment or emotional conflicts.

Blumberg et. al. (1954) conducted a careful investigation relying on the use of a well-established, standardized, self-administered measure of personality, the MMPI. Further, methodological rigor can be seen in the control of potential confounding variables. The authors, moreover, were able to dispense with the need to control for site and stage of disease by utilizing an actuarial estimate of each patient's expected average duration of survival. There is, of course, some concern over the size of the patient population. From a statistical perspective, small sample sizes, in this case, 50 patients, have a larger standard error of measurement. Consequently, the chosen statistic is less reliable and more susceptible to random measurement error.

In general, the study design is methodologically sound and the results previously discussed merit serious attention. However, as with the findings from any investigation using small samples, the results need further confirmation and replication with a larger patient population.

Klopfer (1957) in a psychodynamically oriented study, investigated the relation between personality characteristics and rate of tumor progression.

Twenty-four patients, 23 men and 1 woman, diagnosed

with various tumor types comprised the study population. All patients had previously completed the Rorschach.

The criterion variable, the rate of tumor progression, was operationalized as either "fast" or "slow" tumor progression. Fast progression was defined as survival less than the 25th percentile of the mean expected survival period for persons of a similar age and tumor type. Slow tumor progression was defined as survival more than the 75th percentile of the mean expected survival period for persons of similar age and tumor type.

Based on a preliminary investigation of six patients, three with fast and three with slow progressing tumors, the author developed the Rorschach criteria for differentiating between the two criterion groups. These criteria were then applied to interpret the Rorschachs of the 24 patients in the study population. The Rorschachs were reviewed blind with only the patient's age and sex known. There was no information related to clinical disease status available to bias the Rorschach interpretations.

Results show that of the 11 patients with a fast progressing tumor, 9 were correctly classified by the Rorschach. Likewise, of the 12 patients with a slow progressing tumor, the Rorschach criteria correctly classified ten. One patient was unable to be categorized on the basis of their Rorschach responses and was therefore excluded from the analysis. Overall, the classification

concordance rate, defined as the number of patients predicted to have a specified disease status divided by the actual number of patients with that disease status, was 82% (19/23; P<.02).

Klopfer postulates that the connection between the personality organization reflected in the Rorschach responses of the patient and the rate of tumor progression can be explained as a symbiotic relationship between the patient and his cancer. More specifically, Klopfer argues that if a large quantity of the vital energy a patient has at his disposal is utilized for ego defense purposes, then the patient has less energy available to fight the cancer. Consequently, in patients with diminished energy resources, the rate of tumor progression will be accelerated. Conversely, if a minimum of vital energy is consumed by ego defensiveness, the patient's host resistance is increased and, as a result, the rate of tumor progression will be impeded. As an example, anecdotal evidence suggests that cancer patients who are affable, compliant, or "good people" die more quickly as the result of their disease. According to the present study's findings, this increased rate of tumor progression, culminating in decreased survival, is the cost patients pay for being "good." These patients have simply invested too much ego defensive energy in their attempts to maintain an agreeable personality. This study offers a good deal of insight into the personality of the

cancer patient as it relates to host resistance or, more appropriately, breakdown of resistance and rapid progression of the malignancy. While theoretically fertile, the empirical underpinnings of the present investigation are, however, somewhat weak. Each of these apparent limitations will be discussed in turn.

Of major significance is the use of projective techniques (Rorschach) to assess personality characteristics of the study population. It is well-established that projective techniques are difficult to evaluate and, as a result, are less reliable than other more standardized, object personality measures. The present findings, to a large extent, may be attributable to an idiosyncratic interpretation of the Rorschach rather than a true reflection of the patient's underlying personality characteristics. Furthermore, use of projective techniques results in data which are difficult to interpret in relation to the findings from previous studies, thus limiting comparability.

In addition, the criteria used by Klopfer which was able to discriminate between patients with fast as opposed to slow progressing tumors is not described. Without a careful, detailed description of the psychological variable, subsequent studies cannot attempt to confirm these findings. The lack of specification of the criteria used by researchers employing projective techniques has continued to

plague this area of research. Again, though the findings are indeed provocative, the use of projective techniques has resulted in another isolated body of data which defies replication.

From a statistical vantage point, the study population of twenty-three patients is considered extremely small. Small samples result in findings which are notoriously unreliable and unrepresentative of the population-at-large. Therefore, the findings should be considered as tentative and generalization of the results viewed as inappropriate pending further studies using substantially larger patient populations.

In conclusion, though the present study is thought provoking, weaknesses in the research design have resulted in findings of limited reliability and questionable validity.

Shrifte (1962), in another psychoanalytically-oriented investigation, studied the affect of unresolved "unpleasant feeling tension" on host resistance to cancer. She hypothesized that patients whose cancer is not arrested will differ from those whose cancer is in remission on the extent and quality of their underlying feeling tension. As used in the present study, "unpleasant, feeling tensions" were thought related to despair, prolonged frustration, and the inability to discharge feelings directly with accompanying high levels of anxiety.

To evaluate this hypothesis, thirty women aged 30 to 60 with a diagnosis of cancer of the cervix, similar socioeconomic status, and treated at the same medical center, were interviewed using the Rorschach scored with the DeVos system of analyzing for affective components. This scoring system permits a breakdown of patient responses into seven main categories and forty-seven sub-categories of feeling including, "extent of underlying unpleasant feeling tension," and "qualities of underlying unpleasant feeling tension" as well as eight qualities of hostility, twelve of anxiety and seven of bodily preoccupation. All patients were treated by hysterectomy, were ambulatory and on an out-patient status at the time of psychological assessment.

This criterion variable, course of disease, was operationally defined as whether the patient was disease-free over a subsequent two-year follow-up period. Specifically, patients who were disease-free over this period were classified as having a good cancer course. Patients who had a disease-recurrence were classified as having a bad cancer course. Patients for which it was difficult to determine disease-recurrence were excluded from the analysis. Based on the above criteria for classification of the patient's course of disease, 15 patients were determined to have a good cancer course and 7 patients were determined to have a bad cancer course.

Comparison between the two cancer course groups showed

no statistically significant differences with respect to either the extent or quality of underlying unpleasant feeling tensions. However, the two criterion groups were able to be differentiated on the basis of response to "bodily preoccupation." The disease-free group scored noticeably high on this measure whereas the disease-recurrence group displayed no bodily preoccupation at all. In interpreting this psychological variable, Shrifte considered the relapsers as being more reckless, ambitious and expending greater amounts of energy than those patients who were disease-free. In a statistical test of these judgements, the relapsers were mostly classified as expending more energy, whereas the disease-free patients were classified as exhibiting equal amounts of expenditure and conservation of energy. This difference was significant at the .005 level.

Shrifte concludes that the patients with a poor course of disease possessed a pattern of functioning indicative of " . . . undischarged, dammed up, wasted, unused vitality" (p.394). The patients who remained disease-free displayed the opposite characteristics.

This study, while raising some interesting questions, has a number of methodological weaknesses which severely limit the reliability, validity and interpretation of the findings. Foremost, the independent variable, psychological assessment, is obtained through the use of a projective

technique, the Rorschach. Project techniques have well-known measurement errors. Moreover, such evaluation instruments yield data which, if not confirmed by other, more standardized measures, are difficult to interpret. Therefore, without additional corroborating evidence to establish some measure of convergent validity, the findings are highly suspect. In view of this weakness, projective techniques should be avoided. In addition, there is no control for the patient's stage of disease. Stage of disease is a well-established prognostic determinant in cancer of the cervix. Without such information, we cannot proceed to evaluate the psychological component, above and beyond that accounted for by pathological characteristics of the disease, in predicting recurrence.

In terms of the data analysis, the extremely small patient sample of twenty-two women contrasted on seven main categories and forty-seven sub-categories of the DeVos scoring system for the Rorschach can, in fact, raise the issue of the use of multiple non-independent statistical tests. In this instance, statistical differences are more likely to be attributable to chance rather than being "true" differences. Indeed, the only significant findings resulted from post hoc analysis which were poorly described and the independent variable poorly operationalized.

In summary, the findings are of questionable reliability and validity. Furthermore, attributable in

large part to the psychoanalytic jargon used to characterize the patient's personality, the findings are also difficult to interpret.

Paloucek and Graham (1966) studied the affect of the psychosocial factors on the survival rates of patients with cervical cancer. The authors postulate that patients with a bad psychosocial background would have a poor prognosis in terms of survival following treatment for cancer of the cervix.

To evaluate the hypothesis, two series of patients were interviewed. The first group consisted of 47 patients with cancer of the cervix. The second group consisted of 59 patients with gynecologic malignancies including cancer of the cervix (41 patients), uterine corpus cancer (14 patients) and ovarian cancer (4 patients).

The psychosocial interview used to classify the patients in terms of their background is not described, although a number of factors and their respective frequencies are presented in tabular format. Among these factors: poor childhood, determined according to the stability and security of the marriage; promiscuity; patient's prognosis, the patient's estimate of the future with regard to her medical status; physician prognosis; despair; and recent debilitating social experiences.

The primary analysis pertains to the 88 patients with cancer of the cervix. The criterion variable is the

five-year survival rate. The authors, unfortunately, considered the sample too small to permit statistical analyses and, as such, none are presented. However, they do present the percentage of patients within each of the psychosocial classifications who experienced a poor or favorable prognosis. For example, 71% (35/49) of the patients who on the basis of the psychosocial interview were classified as having a "good" marriage survived five years after treatment. This is in contrast to 56% (22/39) of the patients classified as having a "bad" marriage. Overall, those patients, in addition to a "good" marriage, also having a good childhood, not promiscuous, no despair and less precipitating factors were more likely to have a better five-year survival rate.

The authors conclude that while there are discernable differences in the proportion of patients classified as having a good or poor psychosocial background in relation to the five-year survival rate for cervical cancer, these differences are not considered sufficiently striking. They emphasize that the patient's psychosocial background may not be the same before and after treatment, or if it is, in any event, it may not be a prominent determinant of survival.

The present study is fraught with numerous research design and statistical problems. To begin, determination of the psychosocial factors which would predict survival are derived entirely from a non-descript patient interview. In

addition, there exists the potential for interviewer bias as the interviewer had knowledge of the patient's disease status prior to conducting the initial 47 interviews. Further, the authors cite a number of epidemiological factors, e.g., obesity, nulliparity, age, etc., which exert an affect on gynecologic cancers. These factors, however, are associated with disease etiology, and none are identified as having an influence on recurrence or survival. If, indeed, these factors do affect prognosis, the authors fail to control for these potential confounding affects either in the study design or analysis. Relatedly, there is no description of the distribution of the stage of the disease or type of treatments the patients received. These factors have been shown to exert a direct influence on prognosis. Control of both of these factors is necessary in order to yield unambiguous and valid conclusions.

In terms of the data analysis, there is little that can be said, simply because no statistical analyses are presented. Rather, the percentage of patients classified as having good or bad psychosocial backgrounds are contrasted in terms of their five-year survival experiences. This descriptive analysis is totally unwarranted. Simple tests of the difference between the percentages would be acceptable. Moreover, the data lend themselves to a risk ratio analysis in which the risk of having a poor five-year survival rate can be calculated based on the percentage of

patients with good and bad psychosocial characteristics. In summary, research design and statistical problems are legion. Consequently, interpretation of the findings is painstakingly tedious and relatively unproductive.

In an excellent study, Stavraky et. al. (1968) explored the role of psychological factors in disease progression. Two hundred-and-four patients diagnosed with a wide range of tumor types were administered two psychological measures, the MMPI and the Differential Diagnostic Technique (DDT) as well as an intelligence test, the Verbal Component of the Wechsler Adult Intelligence Scale (WAIS). The MMPI is a well-known, standardized, self-report psychological instrument for assessing an individual's personality. The DDT, a projective technique, provides a measure of the individual's basic personality characteristics which might otherwise be masked by psychological defenses. The DDT yields two psychological measures for comparison; the Differential Index (DI) and the Control Index (CI). The DI is a measure of personality organization which delineates whether hostility or dependency is the predominant trait. A score of zero represents a normal balance between the two drives, a positive score represents less control of dependency than of hostility, and a negative score represents less control of hostility than dependency. The CI assesses overall control of emotional drives. A positive score represents

over-control, or rigidity of personality, a negative score is indicative of loss of emotional control, and a score of zero is indicative of a normal balance.

Outcome was defined as the length of patient survival from the date of first admission for treatment. Site and stage-specific life tables were calculated for breast and cervical cancer. For lung cancer patients, the small size of this sub-sample did not permit stratification by stage of disease so only one life table was calculated for the entire sample of lung cancer patients. Another sub-sample, "miscellaneous cases," contained no single tumor type with a sample large enough to permit the use of a life table.

Based on the life table calculations, the patient population was divided into three outcome groups designated as: Least Favorable (LF), Most Favorable (MF) and Average (A) outcome. The LF outcome group was defined as those patients within each site and stage-specific category who had survival times in the shortest quartile (<25 %tile). Those patients with survival times in the longest quartile (>75 %tile) were classified as the MF outcome group. The remaining patients were classified as Average outcome. The minimum period of follow-up after psychological testing was 40 months and the maximum period was 66 months.

To evaluate the potential for confounding attributable to epidemiologic and biological variables, the comparability of the LF, MF and Average outcome groups were examined in

terms of their sex distribution, age, socioeconomic status, site and stage of disease. Age was the only variable on which all three groups were comparable. Of the remaining four variables, however, only social class and stage of disease were found to be associated with the psychological measures. As the sample size did not permit controlling for both variables, matching was used with only stage of disease. In addition, a group of 159 normal subjects were also asked to complete the psychological test battery. This group provided normative test scores and thus served as a referent, or normal control group, with which the psychological scores of the three cancer outcome groups could be contrasted.

In a careful analysis, Stavraky et. al. compared test scores of the LF, MF, and Average outcome group and the control group on the combined DDT score and two separate DDT scales, the DI and the CI. A normal distribution of scores for both indices was generated using the responses from the normal control group. For the CI and the DI, the normal ranges around zero were +5 and +7, respectively. In terms of the CI, the MF outcome group contained a greater proportion of abnormally low scores (-5) than its control group. This difference was not statistically significant. For the DI, the MF outcome group contained a greater proportion of abnormally low scores and the LF outcome group a small proportion of high DI scores than the respective

control groups. Neither difference was, however, statistically significant. When the CI and the DI scores were considered jointly, a statistically significant difference was detected between patients with normal CI's and DI's in the MF outcome group vs the control group (0% vs 27%; P<.05). Although the LF group also had a small proportion of patients with normal CI's and DI's than its control group, the difference was not as striking (15% vs 23%: P=n.s.). In general, the DDT analysis suggests that the entire patient population had abnormal scores, with the MF group differing from the other cancer outcome groups in terms of the direction of hostility without loss of emotional control.

Comparison of MMPI test results between the four groups detected no significant differences. In addition, the authors attempted to cross validate the earlier findings of Blumberg et. al. (1954) which showed that a pattern of MMPI scores could predict rate of tumor progression. Using the Blumberg criteria, the present study failed to substantiate these earlier findings.

In terms of intelligence, the MF group contained a considerably larger proportion of patients with an above-average IQ than its control group (57% vs 32%). This difference was not, however, found to be statistically significant.

The authors suggest that the entire patient population

evidenced some degree of psychological abnormality. In particular, the findings suggest that patients with the most favorable survival outcome were more frequently hostile than cancer patients who survived an average length of time following treatment. Further, the combination of hostility and above-average intelligence is particularly outstanding in the MF group. From these findings, it is concluded that while the evidence does not support the findings from previous studies demonstrating that patients with a poor outcome show the greatest degree of psychological abnormality, they do, however, suggest that patients with the most favorable outcome are the antithesis of the "hopelessness" or "giving up" reaction described by Schmale (1966) and Engel (1965).

The authors are to be commended for conducting a study which is methodologically advanced over its predecessors. They provide a careful description of the psychological measures and the operationalization of the outcome criterion of survival. Moreover, the use of survival data based on a life table actuarial approach provides a referent or standard which permits valuable contrasts between the three cancer outcome groups. In addition, the inclusion of a "normal" control group to serve as a referent for evaluation of the cancer outcome groups psychological test scores represents a major improvement over the methodologies employed in past studies. Finally, the authors identified

potential confounding variables and adequately describe efforts to control for their distorting affects through matching techniques.

There is, however, a problematic issue which needs to be considered further. Of major significance is the inclusion of a projective technique, the DDT, as a measure to assess personality. Little is presented in the way of substantive psychometric properties such as the inter-rater reliability and the validity of the instrument. This point becomes of crucial importance as the use of the standardized psychological test, the MMPI, did not yield corroborative findings. Thus, there is no way to assess the convergent or divergent validity of the personality patterns identified with the use of the DDT. In summary, the use of projective techniques while perhaps theoretically appropriate, are methodologically indefensible and, as a consequence, result in data which are difficult to interpret and evaluate in relation to the findings from other studies of this type. This caveat is especially apropos when studying a phenomenon which is intrinsically difficult to quantity such as "personality."

Davies et. al. (1973) investigated the psychological adjustment of patients diagnosed with advanced malignancies. The association between psychological factors and length of patient survival was not the primary objective of the study. There are, however, some findings which

directly address this issue and therefore the study will be reviewed expressly for the sole purpose of explicating these relevant findings.

The study population consisted of 46 patients, 21 men and 25 women, with a mean age of 49 years who were receiving treatment for metastatic or widely invasive malignant diseases considered incurable. Twenty-two patients had a diagnosis of solid tumors while the remaining 24 had been diagnosed with leukemia or lymphoma.

Psychological status was assessed by means of a semi-structured interview as well as a battery of self-report instruments administered two or three days following admission to the hospital. The interview covered a broad range of relevant topics such as: patient's subjective feelings about the illness, knowledge of the disease, concerns over death and modes of adaptation to the illness. Based on the interview, a psychiatrist completed a 46-item checklist assessing the patient's mood, attitude, defense mechanisms, degree of distress and adaptational capacities. Moreover, the interviewing psychiatrist made a judgment as to the intellectual impairment of each patient based on memory deficits, orientation, concentration and abstraction, and a brief mental status examination. Further, the psychiatrist also rated the patient's overall physical condition using the Karnofsky Performance Status Scale which uses a 10-point inventory scale ranging from "no

evidence of disease" to "dying rapidly."

In addition, each patient completed a battery of self-report instruments which included the Cornell Medical Index, a 195-item inventory of physical and emotional symptoms; the Lazare-Klerman Personality Inventory, a 140-item inventory yielding scoring for 20 personality traits, the Locus of Control and the Multiple Affect Adjective Checklist.

In an attempt to reduce the number of variables being studied and develop more global personality dimensions, the 46-item checklist which the interviewing psychiatrist completed based on the semi-structured interview was subsequently intercorrelated and subjected to a factor analysis with a principal factor solution using a varimax rotation. This statistical technique produced four principle psychological factors which accounted for 46% of the variance. These factors were labelled as adaptive, apathetic-given up, dependency, and accepting illness based on the loading of individual psychological items.

Results showed that only one of the psychological factors, apathetic-given up, was significantly corrrelated with patient survival time ($r=-0.41$; $P<.05$). This factor loaded high on such items as apathy, aloofness, uninvolvement, hopelessness, low anxiety and low observed motivation to get well. In addition, this factor also demonstrated significant correlations with a greater degree

of illness ($P<.05$), the presence of a hematologic disorder ($P<.05$) and reduced sleep ($P<.05$).

With respect to the self-report inventories, there were few intercorrelations between the personality factors and these indices with the notable exception of the personality factor of the "apathetic-given-up." This factor correlated highly with greater anxiety, hostility and depression as measured by the Multiple Affect Adjective Checklist, and, with greater pessimism and negatively correlated with greater aggression as measured by the Lazare-Klerman Personality Inventory. A second variable identified as significantly related to patient survival was impaired cognitive functioning as determined by deficits in memory during the interview. Moreover, these patients also demonstrated less disturbed sleep, were better liked by the nursing staff, were less apathetic and adapted more easily.

Davies et. al. conclude that patients with mild cognitive impairments may experience a diminution of interests and concerns as well as an altered perception of time which helps them to reduce their anxiety and despair over their disease. In discussing the finding of the association between the apathetic-given-up personality factor and survival time, Davies et. al. point out that although this clinical picture has been described by earlier investigators as associated with a less favorable outcome, interpretation of the results is not a straight forward

matter. While this factor was correlated with earlier mortality, it is also, in addition, correlated with a greater degree of physical illness. Therefore, the authors suggest that perhaps the psychological state, as well as early mortality, are both a consequence of the disease process.

Davies and associates conducted a thoughtful study, which unfortunately, did not focus on the relationship between psychological factors and patient survival. The authors, however, deserve credit for utilization of more advanced data-analytic techniques such as factor analysis to collapse the large number of psychological variables into a manageable number of principal factor dimensions.

There are, nonetheless, problems with the statistical design which warrant further inquiry. Most important, as patient survival was not the primary criterion variable, the authors provide little more than bivariate correlational analyses between the four personality factors and survival time. It would have been more informative and heuristic to report the difference in survival for those patients scoring high and low, respectively, on the psychological factor of apathetic-giving-up. In addition, there is little corroboration for the significance of this factor as the standardized personality inventories did not correlate with survival. Finally, the small sample makes the statistical parameters unreliable.

In conclusion, while the findings are provocative, the plausible alternative explanation for these results, suggested by Davies et. al., is that both the psychological factor and mortality are determined by the disease process. As such, the findings should be interpreted with caution till further studies with larger study populations can replicate and substantiate these results.

Derogatis, Abeloff and McBeth (1976) as part of a larger study investigated whether levels of psychological symptoms were related to disease progression.

The study population consisted of 23 patients, 13 women and 10 men, ranging in age from 32 to 79, diagnosed with a variety of malignancies. All patients were informed of the extent of their illness and were in-patients at the time of psychological assessment.

Assessment of psychological status was accomplished through the administration of the Symptom Checklist-90 (SCL-90). The SCL-90 is a self-report system inventory which is well validated and has been used in previous studies to assess psychological functioning in cancer patients. The SCL-90 consists of ninety items which reflect nine primary symptom dimensions, such as: Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation, and Psychoticism. Each item is rated by the patient on a five-point scale of distress ranging from "not-at-all" to

"extremely." In addition, the SCL-90 yields three global indices: the General Severity Index (GSI), the Positive Symptom Total (PST), and the Positive Symptom Distress Index (PSDI).

The criterion, prognosis, represents an independent clinical prognostic rating made by the patient's physician. The prognostic rating for each patient was divided into three categories of estimated life expectancy (survival): <3 months, >3months, or >12 months. By relying on clinical judgments to develop the prognostic categories, there was no need to control for site- or stage of disease or type of treatment as these factors would have been taken into consideration in the physician's decision making process in ascribing a prognosis.

Each SCL-90 symptom dimension and global indice was divided at the median resulting in patients who were classified as high and low scorers on each symptom dimension as well as the three global indices. A series of Chi-square analyses compared the three prognostic categories for patients with high and low scores on each of the symptom dimensions and global indices. Of the twelve statistical analyses, only Depression and the Global Severity Index yielded significant differences ($P<.025$ and .05, respectively). In both cases, a disproportionate number of patients with scores above the median were classified in the worse prognostic group of less than three-months estimated

survival.

The authors conclude that patients experiencing greater psychological distress, particularly that of a depressive nature, were also those patients suffering from the most severe degrees of physical disease.

Though basically a well-designed and implemented study, there are four problematic methodological and statistical issues which warrant further consideration. With respect to the study methodology, the study design is cross-sectional which prohibits ascertainment of the direction of causality between psychological symptoms and the prognostic categories. Second, there exists a serious potential for patient response bias. Psychological assessments were conducted one week after patients were admitted to the Oncology Service and fully informed of the extent of their disease. Consequently, this knowledge may have resulted in patients with the most severe conditions (<3 months estimated survival) reporting significantly higher SCL-90 depression and severity scores. Therefore, the causal direction for the observed association between psychological symptomatology and prognosis can reasonably be assumed to be from prognosis to reported psychological symptoms. To control for this bias, patients should be evaluated prior to becoming aware of the extent of their disease or before any prolonged contact with a medical staff.

A particularly thorny analytic issue concerns the use

of non-independent multiple statistical tests. In the present study, Derogatis and associates divided the psychological symptom dimensions and global indices at the median in order to develop "high" and "low" score groups on these measures. Moreover, there were three prognostic categories developed from physicians' prognostic ratings of each patient. Thus, the findings are the result of twelve 2x3 contingency table analyses. Of the twelve tests, only two yielded significant results.

When multiple factors (12 SCL-90 indices) of two groups (high and low scorers) are repeatedly tested for statistically significant differences, one or more of these factors may attain significance by chance alone. Employing multiple tests, in effect, changes the chosen alpha level so that each test is conducted at a numerically higher level of significance. The likelihood of identifying spurious associations attributable to the elevated Type I error is therefore increased.

Lastly, a related statistical issue concerns the use of a small sample. In the present study, there were 23 patients in the study sample. In a single contingency table analyses there would be six cells (2 for the psychological variable and 3 prognostic categories). There is a direct relationship between the cell size and reliability of the statistic. That is, as the ratio of patients-per-cell decreases (usually five is the lower limit), the reliability

of the Chi-square statistic decreases as well. This problem is, of course, amplified by the use of multiple statistical tests discussed earlier. Specifically, not only is one test unreliable but rather, there are 12 non-independent unreliable tests. Only by increasing the sample size to sufficiently permit a valid and reliable test can this problem be surmounted.

In a benchmark study, Greer, Morris and Pettingale (1979) investigated how particular coping responses adopted by cancer patients may influence prognosis.

This was a five-year prospective, multi-disciplinary study involving 69 consecutive women patients all less than 70 years of age. All patients had a diagnosis of Stage I or Stage II breast cancer according to the TNM classification. All patients were treated by simple mastectomy, although a random sample of 25 patients also received a routine course of post-operative prophylactic radiation therapy to ipsalateral axillary lymph nodes. Clinical and psychological evaluations were conducted pre-operatively, 3 and 12 months post-operatively, and annually for an additional four years.

Psychological assessments of each patient were obtained through the use of a structured interview schedule as well as standardized psychological tests. The structured interview covered such areas as patient delay in seeking medical care, characteristic response to stressful life

events, symptomayology or psychological stress. The standardized psychological test battery included the Hamilton Rating Scale, which yields a measure of depression; the Caine and Foulds hostility and direction of hostility questionnaire; the Eysenck Personality Inventory which assesses extroversion and neuroticism; and the Mill Hill vocabulary scale which assessed intelligence. In addition, patients' psychological responses to the diagnosis of cancer was assessed by asking them how their lives have been affected by it. The psychological responses were categorized according to patients' verbatim statements into four mutually exclusive categories: Denial, defined as apparent rejection of any evidence about the diagnosis; Fighting Spirit, defined as highly optimistic attitude accompanied by a search for greater information about the disease; Stoic Acceptance, defined as ignoring the illness and any symptoms as far as possible and professing to carry on a normal life; and feelings of Hopelessness / Helplessness, defined as complete engulfment by knowledge of the diagnosis and accompanying feelings of impending death and emotional distress. Moreover, as a reliability check of the information elicited from patients, a spouse or close friend, when possible, was also interviewed separately to verify and corroborate patients' responses.

Two criterion measures were employed: recurrence-free survival over the five-year follow-up as well as cancer

mortality during this period.

In the study design, potential confounding variables, such as site and treatment, were eliminated by restricting the study population to only women with breast cancer. Treatment was also uniform and the sub-sample who received radiation therapy did not differ from the mastectomy treated patients in terms of psychological responses or outcome at five-year follow-up. Stage of disease was not controlled, as both Stage I and Stage II patients were included in the study sample.

Of the original sample, two patients were excluded due to suicide and myocardial infarction leaving 67 patients. Of the 67 patients, 33 (49%) had survived the follow-up period without disease recurrence, 16 (24%) had survived with a disease recurrence, and 18 (27%) had died as a result of breast cancer. An additional 10 patients did not have a psychological assesssment so they too were excluded from the analysis, leaving only 57 patients for statistical analysis. Of the remaining 57 patients, 28 were recurrence-free and 29 had a disease-recurrence or were dead as a result of disease-recurrence.

Results showed no statistical differences between the disease-free and disease-recurrence groups on any of the psychological measures. In terms of psychological response to diagnosis, however, there was a statistically significant association between patients' response to the diagnosis as

assessed 3 months post-operatively and outcome at five-years. Specifically, 75% (15/20) of the patients classified as reporting responses of "denial" or "fighting spirit" were disease-free. In contrast, only 35% (13/37) of the patients who were classified as evidencing responses of "stoic acceptance" or "hopelessness / helplessness" were found to have a disease-free follow-up period ($P<.03$). Using mortality as the outcome measure and comparing these patients who died as a result of breast cancer with recurrence-free patients demonstrated that 88% (14/16) of the women who died manifested responses of "stoic acceptance" or "hopelessness / helplessness" whereas only 46% (13/28) of the recurrence free survivors displayed these responses ($P<.025$).

The authors conclude by noting rival plausible explanations for these findings. They discount each of the alternative explanations, however, and suggest instead that the psychological responses adopted by patients affected their outcome. In addition, it is suggested that future studies endeavor to refine and test the reliability and validity of the psychological response to cancer diagnosis categories.

While basically a sound methodological investigation, there are, nonetheless, some issues which warrant further consideration. Foremost is the subjective manner in which patients' psychological responses to breast cancer diagnosis

were obtained. If, these responses were determined by categorizing each patient's verbatim statements and making independent ratings by two judges, then, there should be some quantitative measure of inter-rater reliability reported. It may well be that the reliability of classifying patients was variable across the different psychological categories; some were good, and others, less reliable. This information is not specified. Moreover, as the reliability between raters were presumably not perfect, the authors did not specify what procedure was used when the rates disagreed on which category a patient's verbatim statements should be coded in. In essence, more information relating to the psychometric properties of this coding schema is necessary before it can be adequately evaluated. To the authors credit, they emphasize the need for further studies to establish the reliability and validity of these psychological response categories.

In a similar vein, the authors assert that the psychological response categories are mutually independent. However, there is no evidence reported which substantiates that claim. To obtain such information would require comparing a standardized psychological test results with the psychological response categories to determine if the pattern of responses on the tests are different for each of the psychological response categories.

Though most histopathological and epidemiological

factors of importance are controlled in the study design and, treatment effects are evaluated in the analysis, the sample was not stratified by the stage of disease. Irrespective of other factors, women with Stage II breast cancer have a markedly higher rate of disease-recurrence and, consequently, mortality than women with the Stage I disease. As the psychological response categories which demonstrated statistically significant differences between those patients who had a recurrence and those disease-free were obtained from information collected at the three-month post-operative interview, it is conceivable that by this time women were aware of the extent of their disease and this knowledge may have influenced their answers, resulting in patient response bias. For instance, patients' awareness that they had a more advanced disease may have influenced them to report more "hopelessness / helplessness" and were less likely to report a "fighting spirit."

Finally, the small patient population (57 cases) makes statistical analyses unreliable and, indeed, may have prohibited stratification by stage of disease. Though identifying significant findings, the confidence interval or standard error (SE) surrounding the statistic is large. This range of confidence around the chosen statistic is, to a large extent, determined by the size of the sample; as N increases, the SE decreases. In this case, the findings must be interpreted cautiously as the standard error is

undoubtedly large.

In summary, the findings of Greer et. al. (1979) are extremely provocative. Due to methodological and statistical weaknesses in the study, however, the findings are in need of replication using a larger patient population.

Derogatis, Abeloff and Melisaratos (1979) undertook a study to further evaluation the relationship between psychological factors and length of survival in cancer patients. The present investigation was conducted as part of a larger prospective three-year study evaluating the psychological impact of chemotherapy on patients diagnosed with metastatic breast cancer. The study population consisted of thirty-five women receiving treatment for metastatic breast cancer on an out-patient basis at the time of the study. Each patient's initial psychological evaluation was conducted during her second visit to the Out-Patient Department of the Johns Hopkins Oncology Center.

Psychological evaluation consisted of a structured interview as well as two standardized, self-report measures: the SCL-90R and the Affect Balance Scale (ABS). The interview assessed the patient's psychosocial adjustment, attitudes and expectations concerning the disease and its treatment.

Of the self-report measures, the SCL-90R has been previously described. In brief, it is a symptom inventory

which has been used to study mental status in other studies of cancer patients. The ABS measured the patient's mood and affect. It is a 40 item adjective checklist that describes the patient's mood state in terms of four positive and four negative mood dimensions and the balance between them.

In addition, the interviewer and the treating physician were asked to complete the Global Adjustment to Illness Scale (GAIS) which provides global impressions of the patient's psychosocial adjustment. The GAIS represents psychological adjustment on a scale of 1 to 100, with a brief narrative describing the patient's quality of adjustment at each 10-point increment. The rater, based on clinical impressions, assigns the patient some value between 1 and 100. The Patient Attitude, Information, and Expectancy Form (PAIE) was also completed by the interviewer to record and quantify the accuracy and quality of the patient's appreciation of her illness and its treatment. Each judgment issue was represented on a 7-point scale and ratings were summed to produce an overall score.

The criterion, survival, was operationally defined such that patients who died as a result of their disease within one-year from the baseline psychological interview were categorized as short-survivors. Conversely, patients who lived for one-year or longer were termed long-term survivors. According to this criterion, 13 patients were determined to be short-term survivors whereas 22 were

identified as long-term survivors. The mean survival time for the short and long-term groups was 8.6 and 22.8 months, respectively ($P<.001$).

Results show that the long-term survival group (LSG) differed significantly from the short-term survival group (SSG) on a number of self-report symptom and mood measures. In general, the LSG reported higher levels of psychological distress with the specific symptom dimensions of anxiety ($P<.10$), hostility ($P<.01$), psychoticism ($P<.01$), and global indices such as the general severity index ($P<.10$) and positive symptom total ($P<.10$) being identified as significantly higher than the SSG. With respect to mood states, the LSG manifested significantly higher scores on all four negative affect dimensions: namely, anxiety ($P<.10$), depression ($P<.05$), guilt ($P<.05$), and hostility ($P<.10$), as well as the negative affect total score ($P<.01$). The affect balance index of the LSG was also significantly lower ($P<.05$) than the SSG's indicating a mood balance that reflects the negative end of the scale. In contrast to the higher scores of the LSG on the negative mood states, the SSG has higher scores on three of the four positive mood states; specifically, joy, contentment and affection. None of these differences reached statistical significance, however.

Results of the physician's psychological assessment using the GAIS and the PAIE demonstrated that the LSG had a

mean GAIS which was significantly lower than the SSG, indicating that the physician perceived the LSG as less well adjusted to their illness. Further, physicians rated the LSG as possessing significantly more negative attitudes toward their illness and its treatment. Relatedly, the interviewers' ratings showed that the LSG displayed significantly poorer attitudes towards their physicians as well.

In order to evaluate whether the observed difference in survival between the LSG and the SSG could be explained by factors associated with the disease per se, the authors compared the medical characteristics of the long- and short-term survivors. Only two statistically significant differences were identified. One, more of the SSG (85%) than the LSG (55%) had previously received chemotherapy ($P<.10$). And, second, the mean duration of previous chemotherapy was significantly longer for the SSG as compared to the LSG, being 407 days vs 181 days, respectively ($P<.05$).

The findings, based both on self-report measures and physician and interviewer assessments, clearly differentiate the short from the long-term survivors. The long-term survivors had a psychological profile characterized by more distress, a greater sense of alienation, less positive mood states, and they were clearly capable of communicating dysphoric feelings, particularly those emotions of anger and

hostility.

In synthesizing the findings from the present as well as previous research, the authors assert that a common psychological profile emerges which apparently influences patient survival. Specifically, cancer patients whose coping styles facilitate external, conscious expression of negative emotions and psychological distress survive for longer periods of time. Patients whose coping styles involve suppression or denial of affect or psychological distress, conversely, have been shown to have shorter survival periods. In conclusion, DeRogatis and associates suggest that future studies should attempt to confirm these findings using larger study populations with a single histological tumor type while controlling for the stage of disease.

Derogatis and colleagues have conducted an excellent investigation. They are to be commended for using both, observer ratings (physician and interviewer) and standardized, self-report measures to establish by means of convergence the psychological characteristics of long- and short-term survivors. This method, whereby the data derived from one approach augments and substantiates data garnered by a second approach, increases the reliability of the findings. In addition, inclusion of a single histological type of cancer, metastatic breast cancer, within the study eliminates potential confounding associated with the use of

multiple tumor types. Relatedly, the authors' control for medical characteristics through post hoc analyses is also commendable.

There are, nonetheless, three statistical issues which warrant further explication. First, the authors prefer to use alpha levels which are numerically higher than customarily considered appropriate for evaluating statistical significance. Whereas most studies, by a convention-rule, employ .05 or lower as the chosen alpha level, the present study has elected to employ .10 as its criterion. The rationale for this selection is not specified and, as a direct consequence, a number of psychological factors attain significance which, under conventional statistical standards, would not be the case. For example, of the 11 SCL-90R and ABS dimensions which are reported as being significantly different between the long- and short-term survivor groups, 5 are significant by virtue of the elevated alpha criterion. Moreover, of the 3 clinical judgments found to be significant, one is statistically significant at this increased alpha level. Overall, of the 14 significant differences identified between the two patient survival groups, 6 of these tests, or greater than 40%, are significant above the commonly accepted alpha level of .05 for determining statistical significance. The effect of this arbitrary selection of a statistical criterion is to yield a greater number of

statistically significant differences between the two patient groups which may not reflect a true difference at all. Second, such an approach limits comparability with the findings from earlier studies which chose to use the commonly accepted criteria of .05 or lower, since no doubt a number of other variables would have attained significance had these studies selected the more lenient .10 criterion, thus, perhaps altering the psychological profiles which emerged as significantly associated with patient survival.

A second issue, one that repeatedly plagues this body of research, concerns the use of a small study population. The present study bases its findings on a sample of 35 cases. As has been noted throughout this review, small samples produce large standard errors or confidence intervals which, as a consequence, make the chosen statistic less reliable.

Finally, the use of multiple statistical tests can result in the identification of spurious statistical associations. In the present study, the authors chose to test for statistically significance differences between the long- and short-term survival groups on a number of psychological factors. Only considering the SCL-90R and the ABS, the two groups are contrasted by t-tests on a total of 21 psychological dimensions (12 from the SCL-90R and 9 from ABS). Repeated statistical tests are likely to attain significance by chance alone. This problem is compounded,

moreover, by the use of an inordinately high alpha level which results in more tests yielding statistically significance differences between the patient groups of long- and short-term survivors.

In summary, while the findings are in accord with earlier investigations and, as such, merit serious consideration, they require further substantiation and replication using larger patient populations and a more sophisticated data-analytic approach which eliminates the need for, and the resultant problems inherent in, the use of multiple statistical tests.

GENERAL SUMMARY AND CRITIQUE OF METHODS AND STATISTICS

Summary

Based on this review of the research literature, a number of psychological factors have been identified as being associated with an increased risk of tumor progression and, consequently, decreased duration of survival following treatment for cancer.

Shrifte (1962) and Klopfer (1957) reported that cancer patients who were more likely to experience disease recurrence or had decreased survival intervals, respectively, could be characterized, on the basis of projective techniques, as expanding large amounts of energy to maintain ego defenses in the face of their illness. In such instances, this expenditure of energy had resulted in a diminution of vital energy available for host resistance to combat tumor growth. Consequently, the malignant process progresses more rapidly resulting in earlier mortality. These findings are difficult to evaluate, however, as the use of projective techniques to assess personality characteristics is clearly of questionable reliability and validity.

Blumberg and associates (1954) reported finding a statistically significant relation between a profile of MMPI scores characterized by strong defensiveness, unrelieved tension and lack of ability to decrease anxiety and tumor

progression. Conversely, Stavraky et. al. (1968) in a subsequent investigation was unable to replicate these findings.

Derogatis et. al. (1976) identified greater psychological symptomatology, particularly of a depressive nature, among patients who had the most severe disease conditions. This study, however, utilized a cross-sectional design and estimated prognosis based on physician's judments which does not directly address the issue of whether or not psychological factors influence, in a prospective sense, actual cancer outcome.

In a subsequent study, Derogatis et. al. (1979) reported that short term as contrasted with long term survivors could be differentiated on the basis of a psychological profile characterized by an inability to communicate dysphoric feelings, particularly anger and hostility. Likewise, Davies et. al. (1973) reported that patient survival was inversely correlated with a psychological factor termed "apathetic-given up." However, the latter study suggests that the psychological state as well as the duration of survival are both a function of the malignant disease process. In addition, the researchers reported no relationship between psychological symptomatology and prognosis.

Greer and Morris (1979) reported that psychological coping styles characterized by "feelings of hopelessness /

helplessness" and "stoic acceptance" were predictive of less favorable outcomes; namely, greater likelihood of disease recurrence and mortality over a five-year follow-up period. In addition, these authors also report finding no relationship between cancer outcome and depressive symptomatology as measured by a standardized, self-report symptom inventory. Contrariwise, Paloucek and Graham (1966) while discerning differences between cancer patients with good and poor five-year survival rates on the basis of psychosocial factors, conclude that these differences are not of sufficient magnitude to suggest that psychological factors play a prominent role in cancer prognosis.

CONFLICTING FINDINGS IN STUDIES OF PSYCHOLOGICAL FACTORS AND CANCER PROGNOSIS

Studies exploring the role of psychological factors (PF) in cancer prognosis have endeavored to identity a single factor or set of psychological factors which would predict prognosis above and beyond that accounted for by known biological and epidemiological variables. While, to some extent, the studies reviewed have identified statistically significant differences between cancer patients who had a favorable prognosis and those who did not, other studies have failed to replicate these findings. Much of this research has produced inconclusive, inconsistent, at times contradictory and often confusing results. The cumulative findings from this research are, overall, difficult to

interpret, of questionable reliability and validity, and of limited generalizability. In general, psychological studies of cancer prognosis suffer from several methodological and statistical weaknesses which may contribute to the marked inconsistency in the research findings.

Methodological and Statistical Considerations in the Design and Analysis of Psychological Studies of Cancer Prognosis

The objective of this section is to identify and summarize the weaknesses in research design and data analysis. The research design issues to be addressed include: definition and measurement of the psychological factors, response bias, inappropriate operationalization of cancer prognosis, and control of potential confounding co-variates. The data analytic issues to be discussed include: use of small patient samples and multiple between-group statistical comparisons.

Definition and Measurement of the Psychological Factors

A major consideration in the design of the psychological studies of cancer prognosis is, as in any experimental paradigm, the definition and measurement of the independent or predictor variables, in this case, the psychological factors of interest. Psychological factors such as coping style, psychological symptomatology and personality dimensions have been shown to be related to cancer prognosis. Such psychological phenomena are, however,

intrinsically difficult to define and quantify.

The review of the research literature has identified three variants of this problem related to the definition and measurement of the psychological factors in studies of cancer prognosis. Of major importance is the use of projective techniques to assess personality characteristics of the patient population. It is well-established that projective techniques yield a large measurement error, are difficult to evaluate and, as a result, are less reliable than other, more standarized, objective personality inventories. Thus, rather than identifying underlying personality characteristics, projective techniques, to a large extent, may reflect the idiosyncratic interpretations of the evaluator. While perhaps theoretically appropriate, especially within the paradigmatic framework of a dynamically-oriented study, the use of projective techniques are methodologically indefensible for evaluating research hypotheses. As a consequence, the use of these techniques yields data which is not readily interpretible. The findings, moreover, are difficult to replicate as well as to evaluate relative to the results from other studies.

A related issue concerns the use of ad hoc psychological measures. These measures are usually developed specifically for administration within the confines of a particular study because more standardized psychological measures are inappropriate or unavailable for

testing the study hypotheses. The problem stems not from the development of such measures, but rather, from a lack of information adequately describing the measure's psychometric properties. Such information is needed to evaluate its reliability and validity. In general, study-specific measures designed to assess some aspect of psychological functioning should be well-described and accompanied by supporting psychometric data. Without the necessary psychometric information use of such measures results in findings which are difficult to interpret, of questionable reliability, and of limited comparability with other studies.

Likewise, when a structured interview schedule or particular questions are used to elicit patient responses which characterize the patient's psychological functioning, these interviews are, or parts thereof, should be explicitly described in detail. Lacking such description results in similar problems of interpretation, unreliability of the findings, and lack of comparability with other studies.

Response Bias

Patients' knowledge of the seriousness of their condition may bias self-report on psychological inventories. If, for example, a patient is informed that his condition requires radical or extensive treatment, this information may tacitly convey a dire prognosis to the patient which may be

reflected in their psychological evaluation. In general, this issue is more problematic in cross-sectional study designs (e.g., Derogatis et. al,, 1976) which do not use the actual disease outcome but instead estimate prognosis and identify associations between psychological symptoms and estimated prognosis. Response bias, then, can increase the likelihood of identifying spurious associations attributable to the patient's knowledge of disease severity which may directly influence self-report of psychological symptoms and behaviors.

Interviewer Bias

In the study design in which patients are interviewed, there exists the potential for interviewer bias. This subtle bias can arise as the interviewer becomes aware of the extent or seriousness of the patient's disease (e.g., Paloucek and Graham, 1966). With this knowledge, the interviewer may inadvertently alter the interview as to elicit information which may conform to the study hypotheses. The resultant associations between psychological factors and cancer prognosis may reflect this bias and, as such, do not represent "true" relationships.

Inappropriate Operationalization of the Outcome Variable

Most studies of psychological factors and cancer prognosis, to the investigator's credit, have chosen to operationalize

cancer outcome in terms of disease recurrence or duration of survival. One study (e.g., Derogatis et. al., 1976), however, utilized a cross-sectional research design. In this study, estimated prognosis was related to patient's self-report of psychological symptoms. Such a design skirts the issue of whether or not psychological factors affect actual outcome as the direction of causality cannot be ascertained. That is, the findings may be attributable to the malignant disease process or, perhaps, reflect a response bias (see above discussion of Response Bias).

Control of Potential Confounding Co-Variates

There is an abundance of information which has established the relationship between epidemiological and biological characteristics of the tumor and rate of disease progression resulting in disease recurrence and mortality. The most important of the biological factors, in general, are the site of the tumor and the stage of disease. Epidemiological factors of importance include: sex of the patient, age and socioeconomic status. Usually, studies of psychological factors and cancer progression have included a heterogeneous patient sample with various staged tumors within a single research design, to some extent, epidemiological factors are evaluated, but biological factors, however, are not. Inclusion of a heterogeneous patient sample need not necessarily be a problematic issue; if stratification or

other means of control (Miettmen, 1976) are utilized in the statistical analysis. This, unfortunately, is not the norm. To a large extent, stratification by type of tumor and stage of disease are prohibited by the use of small patient populations. Consequently, the inclusion of heterogeneous tumor types without partitioning the data analysis to control for differences in survival may obscure "real" differences, lead to spurious associations, and diminish comparability among other studies of psychological factors and cancer progression.

Data-Analytic Considerations

In any experimental design, statistics are employed as a means of quantifying and evaluating the research hypotheses under investigation. That is, statistics evaluate the likelihood that any observed relationship between psychological factors and cancer progression is not a chance phenomenon. Interpretation of the findings rests wholly on an evaluation of the significance of the observed statistical association. The reliability of the chosen statistic, be it a univariate measure (e.g., t-test), a bivariate measure (e.g., chi-square) or more complex multi-variate statistics, is a measure of the likelihood of identifying a similar relationship between the psychological factors and cancer progression should the study be replicated. A number of factors affect the reliability of a

chosen statistic. Two factors of importance, small sample sizes and the use of multiple between-group comparisons, can result in unreliable statistics which, as a consequence, may identify associations between the psychological factors and cancer progression which are, in fact, spurious. The review of the research literature has identified both of the aforementioned problematic data-analytic issues. Each issue will be discussed in turn.

The Use of Small Samples

Many studies of psychological factors and cancer progression have used extremely small samples. For example, of the studies reviewed, only one (Stavraky et. al., 1968) employed a study sample of more than one hundred patients. More common, the study samples have used between 33-88 patients. As noted in the prelude to this section, small patient samples yield statistics which are intrinsically unreliable. One measure more commonly utilized to evaluate statistical fluctuation or, reliability, is the Confidence Interval (CI). In experimental designs, the CI is customarily calculated for the 95% level of confidence. Simply described, the 95% CI is one where, if the study were repeated 100 times, 95% of the time the true value of the statistic would fall within this interval. Of course, the smaller (or, more narrow) the CI, the more reliable (or, less variable) is any one statistical test. The size or

width of the CI surrounding any chosen statistic is inversely related to the size of the patient sample. Specifically, as the size of the patient sample increases, the CI becomes more narrow. And, as noted, the wider the CI, the more possible values the true population parameter can assume with an increased probability of identifying a spurious relationship.

Therefore, in as much as investigators have relied mainly on small patient samples to evaluate the role of psychological factors and cancer progression, the resultant findings, while yielding statistical significance, must be cautiously interpreted in light of their limited reliablity. In addition, small patient samples have limited statistical power for detecting differences between patient groups; for example, "good" versus "poor" prognostic groups. Moreover, the small number of patients prohibits stratification of the patient sample by potential confounding variables; for example, stages of disease. Overall then, the findings from studies using small patient samples are in need of replication with larger patient populations.

Multiple Between-Group Comparisons

Studies of psychological factors and cancer progression have relied mainly on univariate statistics and contingency table analyses to describe the relationship between psychological

factors and outcome. Many such studies rely on multiple comparisons. When multiple factors of two groups (favorable and unfavorable cancer outcome) are tested for statistically significant differences, one or more of these factors may attain significance by chance alone. Employing multiple t-tests, for example, changes the chosen alpha level so that one is testing at a numerically higher level of significance. For instance, in studies of psychological factors and cancer progression which make only six such two-group contrasts (which is very few considering the number of psychological factors examined), the random possibility of identifying a single false-positive association (Type I error) is no longer .05; but rather, if the factors are mutually independent, the probability is elevated to .26. Most likely, these psychological factors are not independent, which further inflates the significance level. Consequently, the likelihood of identifying statistically significant, but spurious, differences between the groups increases as the number of tests is increased.

To protect against the identification of spurious findings, the customary statistical strategy is to decrease the size of the alpha level (p-value) required for attaining statistical significance. Unfortunately, there is no consensus among statisticians as to the best formula for adjusting the alpha level. A frequently described method is to divide the customary significance level (usually .05) by

the number of multiple comparisons (Brown and Hollander, 1975). Such an approach, however, is overly conservative and, as a direct consequence, it reduces the power of the test to detect real differences between the groups. Other, more appropriate, analytic approaches are described below.

Multivariate Statistical Analysis for Qualitative Data

Considering the large number of psychological factors, biological variables, and epidemiological factors which are included in studies of cancer progression, a multivariate statistical technique would be more appropriate and informative. Considering the categorical nature of the data, multivariate statistical approaches such as loglinear models, which are developed specifically for qualitative data would offer the most advantageous analysis. Loglinear models are the categorical response analogs to regression models for continuous response variates. Recently developed, these models are applicable to data in which one of the characteristics represents a dichotomous outcome and the other characteristic represents a classificatory variable. With respect to the studies of psychological factors and cancer progression, the model is readily applicable. The outcome in such studies is usually defined as either disease-recurrence or survival; that is, long or short survival. The psychological factors of interest can be classificatory variables in as much as a patient is

categorized as, for example, having a particular coping style or personality dimension.

The mathematical model suggested postulates a linear function of the effects of the various factors taken singly and in combination. Moreover, known biological and epidemiological prognostic determinants can be evaluated and controlled in such an analysis thereby reducing potential confounding attributable to these covariates. In addition, an extremely valuable asset of this model is the derivation of the "relative risk."

Relative Risk

In any experimental design, the use of statistics is one means of evaluating and quantifying whether or not an observed association is attributable to chance. If, for example, a statistically significant finding is identified between a psychological factor and cancer prognosis then, at some level, we are sanguine that this relationship did not occur as a chance phenomenon. However, the statistical significance of an association is not a measure of the strength of that association. The relative risk is such a measure.

The relative risk is a common epidemiologic measure of association which reflects the rate of an outcome among a group processing a certain characteristic relative to a group without that characteristic. The measure indicates

the likelihood that a member of a specified population will experience a similar outcome if he possesses the characteristic under study. Such a measure offers two advantages over other measures of association. First, the relative risk is invariant with respect to the marginals. And second, this is a readily interpretible measure which is commonly reported in medical journals. With regard to the latter feature of the relative risk, as statistical analyses assume greater complexity, the findings become increasingly difficult to interpret. The relative risk, though its derivation from a loglinear model may be difficult to understand, is intrinsically understandable and easily interpretible. Such a measure, therefore, is clearly advantageous for both statistical and interpretive reasons.

Krasnoff (1959) attempted to cross validate the findings of Blumberg et. al. (1954) which had demonstrated a significant relationship between a pattern of psychological characteristics derived from the MMPI and the rate of tumor progression. There are, however, research design differences between the two studies which delimit their comparability.

The present study population is comprised of both men and women (N=22) with a single historical tumor type, malignant melanona, in contrast to the Blumberg study which included only men, primarily from Veterans Administration Hospitals diagnosed with tumors at a wide variety of sites.

The two studies also differ in the degree of control they exert over potential confounding variables. In the present study, the patient's knowledge of his disease varied markedly whereas in the earlier study, each patient was informed of the nature and extent of his illness. In addition, all patients were considered as inoperable in the earlier study, while the present patient population received a variety of surgical treatments.

The criterion variable used by Blumberg was based on accumulated actuarial statistics in contrast to the Krasnoff study which used normative survival data. In the former study, the criterion groups, fast and slow disease

progression were operationally defined as survival less than the 25th percentile and above the 75th percentile of expected survival, respectively. Using the normative standards, survival less than 18 months was designated as "fast" progresssion while survival more than 72 months was designated at "slow" progression.

Of the total of 70 patients seen for psychological evaluation in the Krasnoff (1959) study, only 22 met the required survival criteria. Specifically, 6 patients were classified as having "fast" and the remaining 16 patients were classified as having "slow" progression tumors.

Tests between the two patient criterion groups on demographic factors demonstrated statistically significant differences on two factors: socioeconomic status and IQ. The fast tumor progression group was found to be significantly lower in socioeconomic status ($P=.05$) and verbal intelligence ($P<.05$). There were no significant differences between the groups in terms of age.

Using the MMPI criteria of Blumberg, the present study showed that for the slow progression patients, the MMPI correctly predicted 5 of the 16 patients for a cross classification concordance rate of 31%. For the fast progression group of patients, the MMPI criteria correctly categorized 3 of 6 patients for a concordance rate of 50%. Overall, the MMPI correctly classified 36% (8/22) of the patients into their respective tumor progression

categories. These findings differ markedly from the earlier results where Blumberg et. al. report a 78% cross classification concordance rate between the MMPI criteria and survival categories. Krasnoff concludes that the present data do not substantiate the earlier findings of Blumberg et. al. that disease progression, or survival, can be predicted on the basis of a pattern of MMPI scores.

The Krasnoff study suffers from an extremely small patient population (N=22). As noted in the previous critiques, a small sample has a wide confidence interval around the chosen statistic. Consequently, the statistic is subject to greater fluctuation and is, therefore, less reliable and less presentative of the "true" population parameter.

In addition, two variables, socioeconomic status and intelligence, were found to significantly differentiate between the two patient progression groups. These differences may reduce comparability between the present study population and that of the Blumberg study. Further analysis would be needed to determine if the populations are, in fact, comparable.

In summary, the attempt to cross validate Blumberg's findings is a worthwhile undertaking. However, the results from the present study, to a large extent, are questionable due to the extremely small patient sample and the apparent lack of comparability between the patient populations.

Therefore, it is suggested that the findings be interpreted with caution and should not be considered definitive.

In an investigative milestone, Rogentine et. al. (1979) attempted to identify psychological factors which would predict disease recurrence in patients diagnosed with cutaneous malignant melanoma.

Two consecutive series of patients were studied. All patients were Caucasian and had a pathologically confirmed diagnosis of cutaneous malignant melanoma. Patients ranged in age from 16 to 67 years. Fifty were men and seventeen were women. Fifty-five patients were diagnosed as clinical Stage II and twelve in unfavorable categories of clinical Stage I. All patients had undergone wide surgical excision of the primary lesion and regional lymph node dissection. As part of a larger, prospective randomized clinical trial conducted at the National Cancer Institute, patients were randomly assigned to one of four treatment groups: standard care, chemotherapy, immunotherapy, and a combination of immunotherapies. All patients were disease free at the time of the psychological evaluation.

Psychological evaluation of each patient was obtained within one week of the initial surgery and consisted of Recent Life Change Questionnaire (RLCQ), the SCL-90R and the Locus of Control Questionnaire. The primary question of interest on the RLCQ asked patients whether or not they experienced an illness which kept them either bedridden a

week or more or required hospitalization. All patients reported their current episode of cutaneous malignant melanoma and the subsequent hospitalization for surgical care. Patients were then asked to rate the amount of adjustment needed to cope with having malignant melanoma on a scale of 1 to 100. This score was designated the Melanoma Adjustment Score (MAS).

The criterion variable, clinical status, was defined as recurrence or disease-free at one year following lymph node dissection. Recurrence with all patients was radiologically and pathologically confirmed.

Potential confounding variables which might exert an influence on the relationship between the psychological factors and clinical status were controlled for in the design and analysis. Pathological and epidemiological risk factors for recurrence, such as clinical stage of disease, number of positive lymph nodes, tumor histology, Clark level, location of the primary lesion, age, set, and patient delay in seeking medical care have, to a large extent, have been identified as prognostic determinants in cutaneous malignant melanoma.

The major methodological innovation distinguishing the present study from earlier investigations, besides careful attention to covariate control, is the use of a cross validation research design. Specifically as it relates to the present study, the patient population was divided

roughly in half. In the first group of patients, the investigators attempted to identify significant relationships between the psychological measures and recurrence at one-year post-treatment. Subsequently, these predictor variables would then be applied, prospectively, to the second half of the patient population. There were 31 and 33 patients in each group, respectively. Three were not evaluable at the time of the analysis, however, they were included in the life table analysis.

The results showed that neither the SCL-90R nor the Locus of Control Questionnaire was able to discriminate between patients who experienced a disease-recurrence and patients who did not at one-year follow-up. Patient responses to the subjective question of the RLCQ, called the Melanoma Adjustment Score (MAS), did significantly discriminate between the patients without recurrence who reported significantly higher MAS scores than the patients who did relapse; 83 + 30 compared with 52 + 30, respectively ($P<.001$). Testing for differences on the MAS in group II and both groups combined confirmed the earlier findings ($P=.05$ and $P<.001$, respectively) that non-relapsers tended to report greater life adjustment in coping with malignant melanoma.

In both Group I and Group II, only one prognostic determinant was shown to predict disease recurrence, that was the number of positive lymph nodes. On the basis of a

clinical algorithm derived from Group I, two predictors of disease-recurrence were established; relapse would occur within one-year following surgery if a) the patient had =>7 positive lymph nodes, or b) if the patient had <7 positive lymph nodes but a MAS of <65. When applied prospectively to Group II, the researchers were able to correctly predict 9 of 11 relapsers and 16 of 22 non-relapsers for an overall classification concordance rate of 73% (P=.004).

In a converging line of analytic inquiry, based on the results of a two-variable discriminant function analysis of Group I, the derived coefficients were then applied prospectively to Group II. Of the 11 actual relapsers and 22 actual disease-free patients in Group II, the discriminant function analysis classified 8 patients and 16 patients as relapsers and disease-free, respectively, for an overall classification concordance rate of 72% (P=.017). When applied to the total patient population, the classification results showed that among the 29 actual relapsers, 18 were predicted to relapse and 11 to be disease-free, and, among the 35 disease-free patients, 30 were predicted to be disease-free and 5 to relapse. The overall classification concordance rate between predicted and actual disease status was 75% (P<.0001).

The authors suggest that the low scores on the MAS may reflect the use of psychological defense mechanisms, such as denial and repression. Conversely, high MAS values are

thought to represent a realistic appraisal of the illness. The exact meaning of the MAS, however, is not clear, as the authors hypothesize that it also may reflect coping styles or cognitive appraisal of life stress.

This study, more than any other, embodies excellent research design and a sophisticated data analysis. The use of cross-validation methodology whereby variables identified as significantly differentiating between the disease-recurrence and disease-free patients can then be applied in a predictive sense to the remaining patients to determine if they retain their discriminatory power represents a marked improvement over the research design of earlier investigations. Indeed, this methodology is almost equivalent to conducting two separate investigations, with the test of the identified predictors serving as a replication of the previous experiment. In addition, there is adequate attention accorded known biological and epidemiological risk factors for disease-recurrence. The control of these variables avoids questions of potential confounding and allows for a clear interpretation of the findings.

In terms of the statistical analysis, here again the investigators demonstrate a logical progression from simple unvariate statistical procedures used to identify differences in clinical status based on psychological and biological measures in the initial patient group, and then,

employ more sophisticated clinical algorithms and discriminant function analyses as a means of substantiating and amplifying the predictive or discriminatory power of these variables.

In conclusion, this study represents a significant methodologic milestone for research design and statistical analysis superior to previous studies in this area. The findings, accordingly, strongly suggest that a psychological factor is a independent, short-term prognostic determinant of clinical status for patients with malignant melanoma. Additional studies will need to establish the long-term potential of the MAS for predicting clinical status.

In a subsequent analysis, Fox (Temoshok and Fox; in press) addresses the issue of the long-term capability of the algorithm and discriminant function derived in the Rogentine et. al. (1979) study to predict two-and three-year relapse as well as mortality.

Applying the analytic methods employed in the earlier report, specifically, the algorithm and discriminant function developed from the patients in Group I, Fox investigated their capacity to correctly predict disease-recurrence and mortality among melamona patients followed for three years after treatment. In Group I, four additional patients experienced a relapse, three in the second year and one in the third year of follow-up, respectively. Applying the algorithm derived from earlier

research, it was found that of the first three, two were incorrectly predicted. The single three-year relapse was also incorrectly predicted. For Group II, four new relapses occurred in the second year of follow-up and three in the third year, respectively. Of the four second-year relapsers, three were incorrectly predicted. Of the three third-year relapsers, none were correctly predicted. Overall, for Group II, out of the seven new relapses in the second and third year of follow-up, only one was correctly predicted on the clinical algorithm.

The clinical algorithm was also applied to the prediction of disease mortality. In Group I, two relapsers died during the first year, an additional thirteen died during the second year and one died during the third year of follow-up. The algorithm correctly predicted mortality in 14 of the 17 relapsers. Contariwise, for Group II fourteen relapsers died over the three-year follow up period; however, only eight were correctly predicted using the clinical algorithm.

In the earlier report, Rogentine et. al. (1979) using the same two predictors, namely the number of positive lymph nodes and the Melanoma Adjustment Score, conducted a discriminant analysis on the patients in Group I and applied the co-efficients, prospectively, to Group II. In the present analysis, the same co-efficients were applied to Group I and Group II after a two- and three-year follow-up

to test the capacity of the co-efficients to predict disease-recurrence and mortality. In Group I, four new relapses were reported. Of these, three were correctly predicted. For Group II, of the seven new relapses over the three-year follow-up, only one, however, was correctly predicted.

A similar picture emerges with respect to the prediction of disease mortality. Of the eight new reported deaths in the second year, only three were correctly predicted. For the third year, two new deaths occurred and both were correctly predicted. Overall then, of the ten deaths reported for patients in both Group I and Group II over the three-year, follow-up period, the discriminant function co-efficient correctly predicted only five.

In summarizing these findings, Fox correctly points out the potential misleading nature of the results. For instance, with respect to Group I, four new relapses occurred in the three-year, follow-up period, of which only one was correctly predicted on the basis of the clinical algorithm. Even so, these data are combined with the original data from which the algorithm was derived, the classification concordance is still 17 of 21 cases or 81%. More appropriate perhaps would be to test the predictive power of the algorithm on the new relapses only. The problem, however, is that one cannot draw a valid conclusion from only four relapses.

A second problematic issue relates to studying disease mortality. Since death is almost always preceded by disease-recurrence, a high success rate for predicting relapse will increase the chance of a high success rate for predicting mortality. As more deaths occur, the number who relapse and the number who die come closer together. As such, the success rate of relapse prediction will more and more resemble the success rate of mortality prediction. The correlation between disease-recurrence and mortality will eventually increase to the point of unity; thus, diminishing the separate nature of these two variables. The data from Group II, with regard to the algorithm as will as the discriminant function, are subject to the same cautions and restrictions in interpretation.

Overall, the predictive capacity of both, the clinical algorithm and discriminant function for forecasting disease-recurrence, is markedly poorer than in the earlier report of Rogentine et. al. (1979). The findings suggest that perhaps the algorithm and discriminant function do not possess a long-term capability for predicting recurrence due to the eventual dominance of biological factors over time. Thus, while the Melanoma Adjustment Score may have short-term utility, biological factors may contribute more to predicting disease-recurrence over an extended period.

METHODS

Subjects

The study population consists of 122 patients with a pathology-confirmed diagnosis of cutaneous malignant melanoma seen at the University of California, San Francisco and Children's Hospital Malignant Melanoma Clinics between 1979 and 1981. Nearly all patients were seen within one month of biopsy. Patients were referred to the two Clinics for confirmatory diagnosis and treatment recommendations. Most patients were aware at the time they had melanoma, but few were aware of the severity of the disease or its prognosis. Patients whose initial consult with the Clinics was for a disease recurrence were excluded from the study population.

Patients ranged in age from 15 to 86; with a mean age of 45 years. Forty-eight percent fell within the age range of 30 to 49 years. Sex distribution was 54% male and 46% female. The demographic characteristics of the study population are comparable to the Clinics' patient population (Blois et. al., 1983), as well as to melanoma patients, in general (Pollack and Horn, 1980). Eighty-six percent of the patients were diagnosed as having clinical Stage I disease while 11% and 3% were diagnosed as clinical Stage II and Stage III, respectively. Patient follow-up ranged from 1 to

52 months with a mean follow-up period of 26 months. Twenty-six patients had a relapse during the follow-up period.

Measures and Procedures

Histopathology

Each patient was initially interviewed and examined by a physician, and the case was reviewed by Clinic consultants. All biopsy specimens were reviewed by a single pathologist. Based on physicians' consultation and the pathology report, two histopathologic indices were rated: Clark's level of dermal invasion and vertical thickness of the primary lesion in millimeters (Breslow's criterion). In addition, based on these histopatholoic indices, another prognostic index, the UCSF Summary Medical Risk was derived. Summary Medical Risk is a combined prognostic determinant derived from various histologic factors of the primary tumor. The main factors are Clark's level and tumor thickness. Additional factors of known prognostic importance, such as mitotic index and vascular invasion, and probable prognostic importance, such as cellular and mesenchymal host response, are also taken into consideration. The Clinics also routinely collect and store on a rapid retrival, computerized relational database demographic and other pathology data, such as patients' age, sex, tumor location, clinical stage and histologic type of

melanoma.

When seen at the Clinics, the patients were asked to participate in a psychological study of melanoma. Patients who signed standared research consent forms participated in a one-hour videotaped interview by a clinical psychologist. This structured interview covered a broad range of topic areas including: circumstances surrounding the patient's suspicion about a symptom or lesion, how and when the patient sought medical attention, the patient's thoughts and emotional reactions to the diagnosis of melanoma and coping with stressful situations.

Predictor Variable

The predictor or independent variables are the psychological adjustment reactions reported by patients when appraised of the diagnosis of cutaneous malignant melanoma. To categorize patients' psychological reactions based on a structured interview, the Psychological Adjustment to Melanoma Scale (PAMS) was developed. The PAMS is an attempt to refine the categorization of patient adjustment responses.

Scale Description and Development

The PAMS is comprised of four mutually exclusive psychological adjustment categories. The psychological

adjustment categories are: denial, fighting spirit, stoic acceptance, and hopelessness / helplessness. Each psychological adjustment category is characterized below. The categories which comprise the PAMS are an extension of the work of Greer and Morris (1979).

Denial: Apparent active rejection of any evidence of the diagnosis. Repression and suppression of the diagnosis. Such patients try to put the diagnosis and all thoughts of the disease "out of their minds," "to block it out," deliberately try to avoid thinking of it by engaging in other activities, e.g., running, throwing themselves into their replies and restrict discussion of the subject. They usually report no emotional distress.

Fighting Spirit: This psychological adjustment reaction is characterized by a highly optimistic attitude regarding the outcome of the disease. Such patients express a positive attitude and determination to control or actively deal with the disease. These patients have sought more detailed information from either their doctor, friends or have read about the disease. They plan to do whatever is necessary to "conquer" melanoma. Often no distress is reported as they channel their energies toward effecting a cure.

Stoic Acceptance: Such patients acknowledge the diagnosis but do not seek further information. These patients commonly ignore the illness and any symptoms or treatments as far as possible and profess to carry on a "normal life." Resignation and acceptance characterize this psychological adjustment response; such as, "It doesn't really bother me a great deal," "It's just one of those things in life," or "You just have to carry on." Recognition that they have melanoma is emotionally distressing at first, but their emotional reaction rapidly subsides as they adopt this stoic attitude.

Hopelessness/Helplessness: Patients exhibiting these feelings are usually completely engulfed by knowledge of the diagnosis. They consider themselves to be gravely or severely ill and sometimes as actually dying. They report feeling out of control, pessimistic, and have a reliance on external forces. Their lives are frequently disrupted by recurring preoccupation with melanoma and possible relapse or death. They are devoid of hope and exhibit a "giving up" attitude.

> Patients with this response will often manifest obvious emotional distress such as crying, depression and the uncontrolled feeling of anxiety or apprehension regarding the future. These emotional reactions tend to be of longer duration than those associated with the psychological adjustment response characteristic of Stoic Acceptance.

In addition, a second categorization procedure was used to derive a multi-dimensional quantitative profile of each patient's psychological adjustment to the diagnosis of melanoma. There are two fundamental differences between this alternative categorization procedure and the approach of Greer and Morris (1979). One is that the latter considers the four adjustment categories to be mutually exclusive while the former suggests that a patient's adjustment response is often reflective of characteristics respresentative of more than a single psychological adjustment category. And, second, each category is considered a continuum so that gradation of intensity with which each psychological adjustment response is manifest in the patient verbatim responses can be taken into consideration. Specifically, each psychological adjustment response manifest is rated on a four-point scale of intensity; ranging from none to strong.

Scale Development

Scale development was divided into two stages. The first stage focused on developing the Greer and Morris categorization procedure and obtaining psychometric

information regarding interrater reliability. A second, related stage focused on developing the multi-dimensional categorization procedure which would yield a profile of psychological adjustment responses. In Stage I, patient responses to questions inquiring about their thoughts, reactions, and feelings upon learning of the diagnosis of cutaneous malignant melanoma were recorded verbatim from videotaped, structured interviews and written on index cards. Each index card contained only the patient identification code number and his or her verbatim responses. No other descriptive or pathological information was included which might provide some indication as to the patient's prognosis.

Two judges, blind to the patient's medical status, independently were asked to assign each patient, on the basis of their verbatim responses to one of the psychological adjustment categories described above. Each judge was given a set of instructions which briefly described the research objectives and the descriptions of the psychological adjustment categories. Two decision rules were developed for this assignment procedure. One, in instances where a patient's responses could be characterized by two or more of the psychological adjustment categories, the judges were asked to assign the patient to the psychological adjustment category which best characterized the patient's dominant psychological mode of adjustment.

And, second, for cases in which the two judges disagreed on the patient assignment, a third judge blindly reviewed the patient's verbatim responses and made an independent assignment. If the referee-judge's assignment concurred with one of the other judge's, then that patient was categorized in the psychological adjustment category for which two of three judges agreed. In the event that all three judges disagreed on which psychological adjustment category to assign the patient, the patient was removed from the analysis as being too ambiguous to code with any degree of reliability.

Reliability

Reliability of the patient assignments to the psychological adjustment categories was measured by assessing the degree of concordance only between the two primary judges. Concordance (C) was determined by the following formula:

$$C = \frac{\text{Number of patients with concordant assignments}}{\text{Total number of patients}}$$

and multiplied by 100 to express concordance as a percentage (Selltiz et. al., 1976).

Stage II involved development of the quantitative multi-dimensional profile of psychological adjustment responses. Following assignment of patients' verbatim

responses to one of the four psychological adjustment categories, the two primary judges were asked once again to independently examine the patients' responses and to identify descriptors (actual words and phrases) for each psychological adjustment category which were of value in making their assignment. The lists were independently reviewed to eliminate redundant descriptors and a master list compiled for each of the psychological adjustment categories.

Next, six judges were asked to independently rate the degree of intensity with which each descriptor represented the particular psychological adjustment category.

The judges rated each descriptor on a four-point scale of intensity: 1) Not representative of the particular psychological adjustment category, 2) Weak 3)Moderate 4) Strong intensity.

Those descriptors which demonstrated high agreement from the judges as to which level of intensity they reflected were used to anchor a four-point numerical scale (see Guilford, 1954, for a review of numerical scales). Only descriptors on which 4 or more of the raters agreed represented a particular level of intensity were used as scale anchors. Again, the two primary judges were instructed to review the verbatim patient responses and assign a numerial rating for the degree to which each psychological adjustment category was manifest. If,

psychological adjustment responses were not applicable, the judges assigned a rating of 1 for those categories. For each psychological adjustment category which represented a patient's response, the judges (relying on the scale anchors) rated the intensity of the patient response on a scale of weak-to-moderate-to-strong. Thus, each patient's verbatim response is rated on all four of the psychological adjustment categories, yielding a profile of scale scores.

Reliability between judges for the multi-dimensional profile of psychological adjustment responses was determined by two evaluation procedures. It was necessary to evaluate, separately, the reliability of the two primary judges to assign a patient's verbatim response to the psychological adjustment categories, and, in addition, to determine a level of intensity within each psychological adjustment category manifest. The former procedure is an extension of the earlier concordance percentage. However, in this instance, since the judges were asked to identify which of the four psychological adjustment categories were manifest in a patient's verbatim response, there are four category assignments per patient, whether a psychological adjustment category is identified or not. Expanding the earlier formula to take account of the non-mutually exclusive nature of the judges' assignments, we get:

$$C = \frac{\text{Number of concordant patient assignments}}{\text{Total number of patients x number of psychological adjustment categories}}$$

multiplied by 100 to express inter-rater reliability as a percentage.

Second, for those patients with concordant psychological adjustment category assignments, evaluation of the reliability between judges as to the level of intensity of each psychological adjustment category is straightforward. In this instance, the formula is as follows:

$$C\ (\text{intensity}) = \frac{\text{Number of concordant levels}}{\text{Number of concordant psychological adjustment categories}}$$

multiplied by 100 to express C as a percentage.

While this allows for an overall measure of inter-rater reliability with respect to levels of intensity, an assessment of C (intensity) for each particular psychological adjustment category yields a psychological adjustment category-specific measure of inter-rater reliability.

Criterion Variable

All patients seen at the University of California, San Francisco, and the Children's Hospital Malignant Melanoma

Clinic who participated in the psychological study of melanoma were followed periodically. Clinical status, disease-recurrence or disease-free, was determined for each patient over the subsequent three-year period.

Objectives

The objectives of the present study are twofold. One, to evaluate the role of a patient's psychological adjustment to the diagnosis of cutaneous malignant melanoma as a predictor of clinical status at three-year follow-up. And, second, to determine which psychological adjustment categorization procedure, either the Greer and Morris approach or the multi-dimensional profile approach, has a greater capacity to predict clinical status.

RESULTS

Psychometric Findings

Results of the reliability studies between the two judges for the Greer et. al. (1979) nominal categorization procedure and the newly developed Profile procedure, in which a patient's verbatim responses are rated on a 1 - 4 scale of intensity for each psychological adjustment category, are based on a population of 117 patients.

Greer et. al. (1979) Nominal Categorization Procedure

There was 64% concordance between the judge's assignments of patients to psychological adjustment categories on the basis of patient's verbatim responses.

Profile of Psychological Adjustment Responses

The profile of psychological adjustment responses allows for a number of ways to evaluate inter-judge reliability (see Methods). A measure, comparable to that used for the Greer et. al. (1979) nominal categorization procedure, is to assess the overall agreement between judges in terms of distinguishing between the presence or absence of characteristics representative of a particular psychological adjustment category using the scale descriptors for guidelines.

The findings indicate that the judges exhibited a high

degree of agreement, 84%, in identifying the presence or absence of psychological adjustment categories, irrespective of the level of intensity of the categories. To evaluate the judge's reliability for each psychological adjustment category separately, a category-specific measure of agreement was computed. For the psychological adjustment categories of Denial, Fighting Spirit, Stoic Acceptance and Helplessness/Hopelessness, the category-specific reliabilities were 77%, 86%, 96%, and 83%, respectively. Thus, the judges, using the scale descriptors, were considerably more accurate in identifying patient responses characteristic of the psychological adjustment category of Stoic Acceptance and much less reliable in identifying Denial.

A second measure of reliability focuses on the judge's ability to assign a level of intensity for each psychological adjustment category identified. Overall agreement between the judges was 67%. Thus, for those patients on which the judges agreed on the assignment of a particular psychological adjustment category, 67% of the time they also assigned the same level of intensity. Category-specific reliabilities were also calculated for levels of intensity and were found to vary considerably; ranging from a high of 81%, for the psychological adjustment category of Denial, to a low of 50%, for the psychological adjustment category of Fighting Spirit. The categories of

Stoic Acceptance and Helplessness/Hopelessness had reliability measures of 63% and 71%, respectively.

Relation Between Psychological Adjustment and Clinical Status

To replicate the findings of Greer et. al. (1979). a contingency table analysis was conducted evaluating the relationship between the four mutually exclusive psychological adjustment categories as assessed by the method of Greer and his colleagues and clinical status at follow-up, either disease-free or disease-recurrence. Only patients with Stage I and Stage II disease were included in this analysis. Results show no significant relationship between the psychological adjustment categories and clinical status (see Table 1). Additional analyses for the total patient population (Stages I, II, and III) and for Stage I patients only yielded similar findings (see Table 2 and Table 3, respectively).

To evaluate the relationship between the psychological adjustment categories and clinical status for men and women separately, the sample as stratified by gender and another contingency table analysis was conducted, one for women and one for men. Due to the reduction in simple size available for each analysis, patients with disease Stage I, II, or III were included.

For men, there was no statistically significant relationship between the psychological adjustment categories

and clinical status at follow-up (see Table 4). For women, however, a marginally significant difference did emerge (see Table 5). Of the 53 women included in this analysis, seven had a disease recurrence and 46 were disease-free. Of the women categorized as manifesting a psychological adjustment response of Stoic Acceptance (N=17), 5 had a disease recurrence. Of all women who relapsed, 71% were categorized as Stoic. None of the other psychological adjustment categories made a significant contribution to the overall chi-square.

A stepwise logistic regression analysis was used to evaluate the capacity of the profile of psychological adjustment scores to predict clinical status at follow-up. In addition to the psychological scores, established or suspected epidemiologicial and biological prognostic determinants were also entered into the regression equation. Biological factors included tumor thickness in millimeters, stage of disease and tumor location. Location was dichotomized as "axial" (aggregating lesions of the head, neck and trunk) or "extremity" (aggregating lesions of the upper and lower extremities) in accordance with the suggestion of Cohen et. al. (1977) that axial tumors have a less favorable prognosis than lesions of the extremities. The patient's mean score for each psychological adjustment category was used to enter into the regression equation.

Clinical status at follow-up, the criterion, is a

dichotomous variable: either the patient is disease-free after treatment or the patient has evidence of disease pathology (recurrence). Included within this category are any type of disease recurrence, such as, localized, regional, metastatic disease or mortality, if confirmed as a consequence of melanoma. Of the 26 patients who relapsed, 16 died as a result of disease processes, 2 had metastatic disease, 3 had positive lymph nodes, 3 had a local recurrence within 5 cm. of the primary tumor and 2 were clinically suspicious with possible lymph node involvement. One patient died as a result of an unrelated condition and was excluded from the analysis.

None of the psychological adjustment categories were able to meet the .10 selection criterion of significance for inclusion in the regression model. All the variance in clinical status was accounted for a model which included two related biological predictors, tumor thickness and stage of disease and one epidemiological factor, sex (model chi-square= 30.38, P=0.0002, N=114).

Based on the findings identifying a significant relationship between the variable "gender" and clinical status, a second series of analyses were conducted in which the population was stratified by gender. For females only, none of the psychological adjustment scores entered at the first step were statistically significant. For males, however, a two risk factor model emerged (model chi-square=

11.93, P=0.03, N=63), which included a single psychological adjustment response, feelings of helplessness/hopelessness, marginally significant at the P= 0.06 level. The second factor, a biological variable, tumor thickness was also a highly significant predictor of clinical status (P=0.008). Comparing predicted with actual clinical status, using this two-factor model, 40 out of 45 patients with a disease-free status were accurately predicted (89% accurate prediction); 4 out of 18 cases of disease-recurrence were predicted accurately (22% accurate prediction). Overall, the concordance between predicted and actual clinical status was 70%.

DISCUSSION

The findings suggest that in addition to pathological characteristics of the disease, a non-biological factor, psychological adjustment to the diagnosis of cutaneous malignant melanoma may be a significant predictor of clinical status at follow-up. The patients who had responses characteristic of stoicism or feelings of helplessness/hopelessness were at greater risk of disease recurrence. It should be emphasized that although a psychological factor was a significant predictor of clinical status, the major prognostic determinant remains the biology of the tumor. Based on the logistic regression analysis, a biological predictor, tumor thickness, made a relatively larger contribution to explaining the variance in clinical status than did the psychological factor, psychological adjustment. To a large extent, however, biological determinants (e.g., tumor thickness) are constant, whereas psychological risk-factors may be modified.

The findings confirm the earlier results, reported by Greer and his colleagues (1979) and, to some extent, the findings from other recent longitudinal investigations as well (Levy, 1984; Weisman and Worden, 1977; Derogatis et. al., 1979; Stavraky et. al., 1968; Rogentine et. al., 1979). Caution is urged, however, in interpreting this body of research as there is considerable variability in the

operationalization and measurement of the independent variables as well as the criterion variables. Such variation, as Temoshok and Heller (1984) point out, reduces comparability between studies. Similarities and dissimilarities of each will be discussed in turn.

The present study design was most similar to that of Greer et. al. (1979). Both studies use a semi-structured interview to elicit information which was later coded to identify the patient's psychological adjustment response. The psychological adjustment categories used in the present study are an extension and more detailed version of those employed in the work of Greer et. al. (1979). The criterion variable, clinical status at follow-up, was, in both studies, any form of disease recurrence. Of course, Greer et. al. (1979) studied only females with breast cancer while our patient population consisted of men and women with cutaneous malignant melanoma. Stratification of the patient population, however, permitted us to approximate the Greer et. al. (1979) analysis by examining the relationship between psychological adjustments and clinical status for women only. Stratification yielded a sub-sample of 53 women; comparable in number to the Greer et. al. (1979) sample (N=57).

Our findings, moreover, not only corroborate those of Greer and his associates, but extend them as well. Specifically, we report that psychological adjustment "at

the time of diagnosis" is significantly associated with follow-up clinical status. This is in addition to the finding by Greer et. al. (1979), of no relationship between psychological adjustment at diagnosis and clinical status at follow-up, but rather a significant relationship was identified for patients' psychological adjustment responses based on their three-month, post-operative interviews. Thus, our findings both support and extend the work of Greer et. al. (1979).

Other investigators have identified similar associations. For instance, Weisman and Worden (1977) found that long-term survivors of cancer coped better with illness-related problems than did the short-term survivors. Stavraky et. al. (1968) identified a personality profile among those patients with the most favorable outcomes which the authors considered the antithesis of the "hopelessness" or "giving up" reaction. Derogatis et. al. (1979) identified a constellation of characteristics similar to stoicism. Patients whose coping styles involve suppression or denial of effect or psychological distress had shorter survival times. Rogentine et. al. (1979) found that patients who reported less psychological adjustment to the diagnosis of malignant melanoma were more likely to relapse at one-year follow-up. Levy (1984) found only one psychological factor, fatigue, related to nodal status in women with Stage I and II breast cancer. To a large extent,

the other, recent longitudinal studies identifying a relationship between a psychological factor and cancer outcome used different measurements of the predictor and the criterion variable. With respect to measurement of the predictor variable, Derogatis et. al. used multiple measures, most notably the SCL-90, the GAIS, and the PAIE; Levy (1984) used the POMS, Stavraky et. al. (1968) employed a projective technique, Rogentine et. al. (1979) used a simple quantitative measure of one variable from a Recent Life Change Questionnaire and Weisman and Worden (1977) used an interview. The variability in the measurement of the predictor variable may reduce comparability between studies. Likewise, 3 studies use length of survival as the outcome (DeRogatis et. al., 1979; Stavraky et. al., 1968; Weisman and Worden, 1977), one uses nodal status, whether positive or negative (Levy, 1984), and one (Rogentine et. al, 1979) uses disease recurrence. Thus, while similar, though not exactly so, findings have been identified in previous research, lack of comparable measures leads to findings which are less than comparable. On the other hand, such diversity yielding similar, albeit not exactly the same psychological constructs such as adjustment, suggests a convergence of evidence. However, the line between "convergence" and "divergence" is a fine one, which should be considered carefully in designing future studies.

Limitations of the Present Study

The present findings substantiate results reported by previous investigators. There are, however, a number of methodological issues which deserve further consideration. Each will be discussed in turn.

Sample Size

Our patient population is larger than most studies investigating the role of psychological factors in cancer outcome. By most standards, however, the patient population is small. Thus, while yielding significant results, caution is urged until the study is replicated with a larger patient population. A related issue involves the use of stratification. Stratification is an acceptable and effective means of partitioning the patient population whenever a variable is suspected of obscuring interpretation of the analysis. We chose to stratify our sample by the variable "gender" in order to have a truly comparable study to that of Greer et. al. (1979). By doing so, however, we reduce the statistical power to detect a true association between the predictor variable and the criterion. Such a statistical approach creates sub-samples which are considerably smaller than the total patient population. As our sample was not large to begin with, the findings derived from the stratification of the patients into sub-samples of males and females should be carefully interpreted.

Interviewer Style

While this subtle form of bias does not greatly affect our study, there is a possibility that different interview styles may result in eliciting different amounts of information which judges later used to categorize the patient's psychological adjustment response. Thus, a patient who is urged to discuss his or her reactions and feelings upon learning of the diagnosis of melanoma may supply a greater quantity of information which will yield, perhaps, a more accurate assessment of their psychological adjustment response. Interviewer differences may be a potential confounder which would have to be carefully controlled in any replication. However, in viewing the tapes, we feel that the different interview styles was a minimal problem.

Suggestions for Future Research

In accordance with the bio-psychosocial model of disease causation (Engel, 1977), future studies should strive to assess, not only known epidemiological and biological characteristics associated with disease-recurrence, but social factors which may exacerbate or modulate the stress of confronting cancer. In addition, if our understanding of how psychological processes influence cancer outcome is to go beyond associational relationships to causal

relationships, increased emphasis must be placed on identifying the physiological mediators linking psychological processes and disease-recurrence. These factors require careful and detailed operationalization (Temoshok and Heller, 1984) in order to produce results which are reliable, valid and comparable between studies. Clearly, such a research paradigm would necessitate an enormous expenditure of time, energy and financial resources. Equally apparent is the prodigious potential to derive valuable information which would have far-reaching implications for cancer treatment.

Psychological Adjustment Category	Clinical Status		Total
	Disease-free	Recurrence	
Denial	4	1	5
Fighting Spirit	22	5	27
Stoic	33	9	42
Helplessness Hopelessness	32	7	39

Total N=113

Chi-square= 0.17

P= 0.9

TABLE 1 - RELATION BETWEEN PSYCHOLOGICAL ADJUSTMENT CATEGORIES AND CLINICAL STATUS: STAGES I, II

Psychological Adjustment Category	Clinical Status		Total
	Disease-free	Recurrence	
Denial	4	2	6
Fighting Spirit	22	5	27
Stoi	33	11	44
Helplessness Hopelessness	33	7	40

Total N= 117

Chi-square= 1.34

P= 0.7

TABLE 2 - RELATION BETWEEN PSYCHOLOGICAL ADJUSTMENT CATEGORIES AND CLINICAL STATUS: STAGES I, II, III

Psychological Adjustment Category	Clinical Status		Total
	Disease-free	Recurrence	
Denial	4	1	5
Fighting Spirit	21	3	24
Stoic	32	7	39
Helplessness Hopelessness	29	4	33

Total N=101

Chi-square= 0.70

p= 0.8

TABLE 3 - RELATION BETWEEN PSYCHOLOGICAL ADJUSTMENT CATEGORIES AND CLINICAL STATUS: STAGE I

Psychological Adjustment Category	Clinical Status		Total
	Disease-free	Recurrence	
Denial	1	1	2
Fighting Spirit	12	4	16
Stoic	21	[illegible]	27
Helplessness Hopelessness	12	7	19

Total N=64

Chi-Square 1.7

P= 0.6

TABLE 4 - RELATION BETWEEN PSYCHOLOGICAL ADJUSTMENT CATEGORIES AND CLINICAL STATUS: MALES ONLY

Psychological Adjustment Category	Clinical Status		Total
	Disease-free	Recurrence	
Denial	[illegible]	[illegible]	[illegible]
Fighting Spirit	[illegible]	[illegible]	[illegible]
Stoic	[illegible]		[illegible]
Helplessness Hopelessness	21	9	21

Total N= 53

Chi-Square = 7.74

p= 0.05

TABLE 5 - RELATION BETWEEN PSYCHOLOGICAL ADJUSTMENT CATEGORIES AND CLINICAL STATUS: FEMALES ONLY

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