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Abstract

Improving the physical comfort and emotional and spiritual well-being of dying patients has become a national concern to individual patients, health professionals and family members who provide care, and policy makers who must decide how to allocate resources for end of life care. Data show that patients' preferences regarding type and site of terminal care often differ from what actually happens. Research on this discrepancy has focused primarily on structural factors such as access to hospital beds and funds for home care. Little is known about patient and caregiver characteristics that contribute to the degree of congruence between preferences and outcomes, or that diminish or sustain patient and caregiver well-being during terminal care.

This revised application, again submitted as an Investigator-initiated Interactive Research Project Grant, proposes a preliminary study to determine the feasibility of conducting a full-scale study to explain discrepancies between preferences and outcomes in type and site of end of life care, and patient and caregiver well-being. The full-scale study, which is guided by a stress and coping theoretical framework, will be proposed subsequently. The research focuses on patients with AIDS and cancer, living at home at study entry, and their primary family caregivers. This preliminary study will determine the feasibility of: a) identifying terminally ill patients with approximately 3 to 6 months to live, b) recruiting and c) retaining terminally ill patients and their primary family caregivers, until the patient dies or through six months. The preliminary study will also be used to refine the assessment protocol, including new measures of structural variables. This preliminary study will follow 44 dyads (88 dyads total) of terminally ill patients and their caregivers at Columbia/NY Psychiatric Institute and the University of California San Francisco. **The data collected in the preliminary study will be used in the full-scale study.**

A. SPECIFIC AIMS

Please note: NIH policy requires that a resubmission retain its original title. A more appropriate title for this revised application would be: AIDS & Cancer: Preferences & Outcomes during Terminal Care.

Improving the care of dying patients with respect to their physical comfort and emotional and spiritual well-being has become a national issue. It is of central concern to individual patients, to health professionals and family members who provide care, and to policy makers who must decide how to allocate resources for end of life care. Data show that patients' preferences regarding type and site of terminal care often differ from what actually happens. Research on this discrepancy has focused primarily on structural factors such as access to insurance, hospital beds, and home care. Little is known about patient and caregiver characteristics that contribute to the degree of congruence between preferences and outcomes, or that diminish or sustain patient and caregiver well-being during terminal care. The eventual goal of our research is to develop useful interventions to improve end of life care and quality of dying.

We plan a two-stage research agenda that includes a preliminary study, which we propose here, and a full-scale study, which we will propose in a subsequent application. The research will focus on patients with cancer and AIDS who are living at home at study entry and their primary family caregivers. The research will be carried out in New York and San Francisco. The purpose of this preliminary study is to determine the feasibility of the full-scale study and to refine the assessment battery. For this preliminary study, we will follow 44 dyads of terminally ill patients and their primary family caregivers at each of the two sites. Each dyad will be followed bi-weekly in home visits for up to six months. **The data collected from the 44 dyads at each site in the preliminary study will be used in the full-scale study.**

The specific aims of this preliminary study are to:

1. Determine feasibility of identifying terminally ill patients with approximately 3 to 6 months to live, using a strategy that takes optimistic bias into account;
2. Determine the feasibility of recruiting terminally ill patients and their primary family caregivers;
3. Determine the feasibility of retaining terminally ill patient/caregiver dyads until the patient dies or through six months, while interviewing them bi-weekly;
4. Refine the interview assessment for the full-scale study.

The specific aims of the subsequent full-scale study have been revised in response to the committee's comments. These aims now include type of care (palliative, curative); site of terminal care (home, assisted living facility, skilled nursing facility, residential hospice, and hospital); and structural factors (bed availability, financial resources for home services), as well as psychiatric, and stress and coping variables that were highlighted in our previous application. The specific aims of the subsequent full-scale study are to:

1. Examine the preferences and actualities regarding type and site of care:
 - a) describe degree of congruence between preferences and actualities over time for both patient and caregiver;
 - b) identify predictors of congruence including structural factors, patient's cognitive, psychiatric, and medical status; and caregiver strain and mood;

- c) describe stability or change of preferences over time;
 - d) describe relationship between patient and caregiver preferences over time.
2. Assess prevalence and course of depressive disorders and symptoms in patients and caregivers during the final months of life;
 3. Describe well-being (positive and negative mood) in patient and caregiver during the final months of life, and explain changes in well-being using a stress and coping model;
 4. Describe the relationship between congruence and well-being for both patients and caregivers; are disparities between preferences and actualities related to diminished well-being?

Secondary aims include determining the influence of ethnicity, disease (cancer, AIDS), and locale (New York, San Francisco) on preferences and actualities regarding type and site of care, describing changes in stress and coping variables as death approaches, and describing the frequency and circumstances surrounding desire for hastened death.

Justification for Submission as Investigator-initiated Interactive Research Project Grant

This proposal is submitted as an Investigator-initiated Interactive Research Project Grant representing a coordinated two-site collaboration between Susan Folkman, Ph.D., who will direct a research site at the Osher Center for Integrative Medicine at the University of California – San Francisco, and Judith Rabkin, Ph.D., who will direct a research site at the New York State Psychiatric Institute/Columbia University. The same study will be conducted at the two sites. The PIs have worked closely in the preparation of this proposal and will continue to work closely to ensure the standardization of the study protocol and data collection at the two sites (see Section D for details). There are three compelling reasons for using this funding mechanism: 1) The PIs have complementary expertise in depression and stress and coping, central concerns of the study. Dr. Rabkin is an expert in diagnosis and assessment of depression in the medically ill and has conducted numerous NIH-funded clinical trials and cohort studies with the medically ill. Dr. Folkman has developed and applied the theoretical model of stress and coping in numerous empirical studies, including two NIMH-funded longitudinal studies of AIDS-related caregiving. 2) Two sites are required to recruit the full sample of 220 dyads for the full-scale study within a reasonable time. We expect to recruit 3 to 4 dyads/month/site during both the feasibility study and the full-scale study. Having only one site would double the time needed for data collection. Further, for the preliminary study, two sites are needed to recruit the subsample of 44 qualified patients with AIDS or cancer within the allowed time. 3) Data will be centrally analyzed at UCSF, which increases efficiency.

B: BACKGROUND AND SIGNIFICANCE

The proposed preliminary study is designed to determine the feasibility of conducting the subsequent full-scale study. In this section we provide the rationale for the subsequent full-scale study.

Interest in end of life care is widespread

Medical professionals and the general public are becoming increasingly interested in palliative and home-based care at the end of life. The 4-part television special produced by Bill Moyers in the fall

of 2000, which received widespread news coverage and public attention, reflects this interest. Several factors play a role. One major influence is the change in the economics of medical care (Sankar, 1995). The emergence of managed care in the 1990's and Medicare constraints that limit hospital reimbursement for patients not receiving active treatment have led to patients being discharged from hospitals "sicker and quicker" (Schachter & Holland, 1995, p.92). In addition, Medicare now covers hospice care, usually in the home. Other contributing factors include technological innovations, major foundation support for palliative care service delivery and research programs, and growing recognition of the futility of "high tech" invasive procedures as applied to dying patients. Contemporary interest in home-based palliative care is reflected in, and in turn promoted by the development of a clinical subspecialty that emphasizes symptom control, patient participation in medical decision-making, psychosocial support and open communications about death and dying (McIntyre, 1999).

Palliative and curative care

Although the definition of palliative care is "in flux" (Lynn, 2001), the term refers in general to the relief of suffering, whether physical, psychological or spiritual (WHO, 1990). The hospice movement, first introduced in this country in the 1970s, is designed to provide such care. Hospice philosophy emphasizes advance planning, including the preparation of wills, advance directives, health care proxies and decisions about DNR orders. Family members are seen as integral partners and patient-controlled symptom management is emphasized.

There is no clear boundary distinguishing palliative from interventional (curative) care, which includes procedures to eradicate the underlying disease (e.g. chemotherapy) or extend life (e.g. mechanical ventilation), nor in the opinion of end of life experts should they be mutually exclusive (Corless, 2000; O'Neill et al, 2000). Sometimes the same procedure (e.g. blood transfusions) can be intended either to relieve suffering or extend life, and whether conceptualized as palliative care depends on intent. While palliative care is not inherently incompatible with interventional care, the model underlying hospice services in the United States is a "transitional" one (Lynn, 2001), in which hospice care replaces curative treatment. Formal resources provided through hospice are generally not accessible until the doctor, the patient and the family all agree on a prognosis of less than six months as well as renunciation of curative treatment efforts. These are the essential inclusion criteria for hospice care under Medicare regulations, which is the major payer of hospice in this country (Lynn, 2001).

Health care providers and patients alike may be caught among the conflicting goals of the "technological imperative" (to maintain life by all means), the "research imperative" (to eliminate death, disease by disease), and the "clinical imperative" (to accept death as an unavoidable biological reality) (Callahan, 2000). These incompatible belief systems contribute to delay in consideration of end of life issues including delay in hospice referrals by both physicians (Christakis & Escarce, 1996) and patients (Larson & Tobin, 2000). Even if physicians ultimately recommend cessation of further interventional treatment in favor of palliative care, many patients refuse. In a recent study of 173 cancer patients whose oncologists recommended hospice, only 27% accepted the referral (Navari & Stocking, 2000). Eventually the referral may be accepted, but usually too late in the dying process to realize the real benefits of hospice (the median survival in hospice of cancer patients with Medicare coverage declined from 26 days in 1994 to 19 days in 1998 (Lynn, 2001).

Insurance for interventional care is more generous than for hospice services, which typically are reimbursed at the rate of \$100/day per patient. Thus, even if palliative in intent, expensive medications or procedures such as parenteral nutrition may not be provided, and payment for home attendants is limited to less than 8 hours per day. Because most AIDS patients have enhanced Medicaid coverage that provides up to 24 hours/day home attendant coverage as well as other services such as homemakers to care for dependent children and other special benefits, they are less likely than others to choose formal hospice programs.

Preferences regarding site of terminal care may change with age and disease progression.

In opinion surveys of the general public, most people say they would prefer to remain at home as death approaches (Council on Scientific Affairs, 1996; Schachter et al., 1998). In several prospective studies of terminally ill patients, the majority also expressed this preference (Townsend, 1990; Dunlop, 1989; Pritchard, 1998; Cooke et al. 1998; Karlsen & Addington-Hall, 1998). However, in a study of patients over age 65 in a community long term care program, Fried and colleagues (1999) found that nearly half of their sample of 246 patients preferred terminal care in the hospital (more than double the rate usually found in surveys of the general population). In a study of “factors considered important at the end of life by patients, family, physicians and other care providers,” Steinhauser et al. (2000) conducted a cross-sectional stratified random national survey of 340 seriously ill patients in the Veterans’ Administration database, as well as 332 of their recently bereaved relatives, 341 physicians and 429 other care providers. Respondents were asked to rate the importance of 44 attributes of experience at the end of life. Thirty-five percent of patients agreed that dying at home was important, while 53% did not have a strong opinion. When asked to rank 9 preselected attributes, freedom from pain was ranked first, and dying at home was ranked last by patients, bereaved family members and physicians, and eighth by other care providers.

Structural, patient, and caregiver factors influence the actualities of type and site of terminal care

Structural characteristics of the health care system. Several major epidemiologic programs of research cumulatively have demonstrated that structural factors rather than patient preferences or illness characteristics are the strongest predictors of site of terminal care. The SUPPORT study gathered data from inpatients in 5 teaching hospitals who were in the advanced stages of one of 9 illnesses (excluding AIDS) between 1989-1994. Of the 479 patients who died within the observation period, the single strongest predictor of site of death was availability (proximity and number) of local hospital beds. The risk of in-hospital deaths decreased in regions with greater nursing home availability and use. For Medicare beneficiaries, percent dying in hospital varied from 23% to 54% across regions of the country (Pritchard, 1998). Similarly, in their analysis of 1995-96 Medicare records, Wennberg et al. (1999) found that “about one-third of the variation in the chance of a hospitalized death could be attributed to the number of hospital beds per thousand residents of hospital referred regions” (p. 178). More generally, they observed, “to the extent that end of life issues are addressed in practice, they are resolved in ways that depend on where the patient happens to live, not on the patient’s preferences or the power of care to extend life” (p. 176). This national study also found tremendous geographic variation in rate of hospital deaths, ranging from less than 20% to almost 50%. In 1995-96, 26% of Medicare deaths in San Francisco and 48% of Medicare deaths in New York occurred in hospitals. On a statewide basis between 1989 and 1997, the increase in home deaths in California was 85% (from 15% to 27%). During the same period of time in New York, the increase was 24% (from 17% to 21%) (www.chcr.brown.edu/dying/usa_statistics.htm).

Structural factors must be included when considering actualities of site of care. **However, two-thirds of the variance in site of care remains unexplained. Grande et al. (1998) called for a more intensive research design including longitudinal observations of patient and caregiver characteristics and their interactions to complement epidemiologic studies.**

Patient characteristics that influence type and site of care

Medical condition. Terminally ill patients typically experience multiple and fluctuating symptoms affecting a variety of systems and functions. In Coyle et al's. (1990) prospective study of 90 cancer patients, 44 different symptoms that interfered with activities were spontaneously reported by patients. It is often the accumulation of unexpected and multiple symptoms (e.g., itching, mouth sores, skin breakdown, constipation) that results in significant distress. Adequate pain management is one of the most important aspects of end of life care according to terminally ill patients (Singer et al.1999) and is often inadequate (McCarthy et al. 2000). Sometimes pain is managed well, but other symptoms receive less attention (Jones et al.1993). Frequently the caregiver is required to possess or develop a variety of skills to provide effective symptom management, and often needs professional training and support (Wrubel & Folkman, 1997). If such support is deficient, home care may not be feasible.

Cognitive impairment. Significant changes in cognitive functioning may occur as patients approach death (Council Report, 1996), ranging from increasing apathy and confusion to delirium, dementia and coma (van Gorp & Buckingham, 1998; Valcuikas,1995; Bruera et al.1992). The prevalence of cognitive changes is difficult to determine because in most instances, psychiatric consultations are only requested when patients present difficulties and even then, diagnostic labels vary from specific syndromes such as delirium to broad terms such as cognitive failure. As noted by Bruera et al. (1992), estimates of cognitive failure among cancer patients range from 8% to 85%, largely due to these methodological variations. Among patients with AIDS, mild cognitive impairment is far more common than dementia, an end stage diagnosis with an annual incidence estimated at 7% (Van Gorp & Buckingham, 1998).

Consequences of cognitive impairment may include difficult or reduced communication, increased difficulties with activities of daily living requiring escalating levels of assistance, and reduced competency to give informed consent to procedures or with respect to end of life decision making (Fainsinger & Young, 1991). In addition, such changes add to caregiver strain and thus contribute to the transfer of such patients to institutional care for their remaining time (Hinton, 1994).

Depression. Prevalence estimates differ widely, and are influenced both by the diagnostic criteria used and imminence of demise. As noted in the IOM report, "Approaching Death" (1997), "Some anxiety and depression are understandable responses to serious illness and loss. This contributes to disagreement about the nature and prevalence of clinical depression in the population of patients who are dying" (p. 243). Kathol et al. (1990) noted that depression has been identified in 2% to 45% of patients with medical illnesses depending on method of classification. Shuster et al. (1999) report 20% to 50% rates of "clinically significant depression" in the setting of terminal illness. In post-bereavement interviews with 3357 caregivers participating in the SUPPORT and HELP studies, retrospective ratings of patients' emotional state in the last three days of life showed that mild dysphoria or mild anxiety was common. However, 25% were reported to have moderate

depressive or anxiety symptoms, according to the caregivers' estimations (Lynn et al., 1997). The course of depressive symptoms as death approaches – whether it worsens or diminishes – is currently unknown.

Can depression be diagnosed in the terminally ill? Identifying depression in the medically ill can be complicated by somatic symptoms such as fatigue, anorexia, and insomnia common to both. Cognitive impairment (described above) may also complicate mood assessment. Further, it may be difficult to conduct standardized diagnostic evaluations when patients are very sick. Nevertheless, trained clinicians can distinguish between sadness and clinical depression by focusing on affective/cognitive diagnostic criteria, and by using recently developed standardized brief assessments, as shown in numerous studies of patients with AIDS (Rabkin et al., 1997; Williams et al., 1991), cancer (e.g. Chochinov et al., 1994,1997) and other terminal illnesses (e.g. Cohen et al., 2000). Identification of clinical depression in terminally ill patients matters both because clinical depression warrants and usually responds to treatment even in very sick patients (Block, 2000), and untreated depression may increase caregiver strain and undermine efforts to provide palliative care.

Caregiver factors: realities of home care and distress

Realities of home care. Arras and Dubler point out that "dying at home may be initially attractive in an abstract fashion to both patients and family members, but the reality is rarely benign..."(1995, p. 3). Caregivers and patients often underestimate the magnitude of the burden of caring for terminally ill, and the importance of sufficient medical/social/financial resources to ease the burden. In a study of domiciliary terminal care in Edinburgh cited by Thorpe (1993), 90% of cases in which admission became necessary was because of stress on relatives, exacerbated by lack of respite care or equipment.

Distress. As Schulz and Quittner (1998) note, "one of the most consistent findings in the caregiving literature is that caregivers report elevated rates of depressive symptomatology" (p. 108). Although the vast majority of caregiving studies focus on caregivers of patients with dementia, studies of caregivers of patients with other conditions such as ALS (Rabkin et al., 2000), AIDS (Folkman et al.,1994; Wight et al.,1998), brain injury (Marsh et al.,1998), cancer (Nijboer et al.,1999), and heart transplant (Dew et al.,1998) also show high levels of caregiver distress, suggesting that caregiving in virtually any illness context leads to high levels of distress in the caregiver. In a study of 31 informal caregivers of minority women with AIDS, a major concern of the caregivers was keeping the diagnosis secret because of the stigma of the disease in their communities. Further, although all the caregivers were active church members, none told anyone in their church about their caregiver role to a family member with AIDS, again because of fear of stigma which detracted from social support that might otherwise have been provided (Baker et al., 1998).

Effects of patient and caregiver distress on the other person

A number of studies have shown a relationship between patient and spousal distress including studies of patient-caregiver dyads in the contexts of cancer (Ben-Zur et al., 2001; Given, et al., 1993) rheumatoid arthritis (Manne & Zautra,1990), and amyotrophic lateral sclerosis (Rabkin et al., 2000). However, the cross-sectional design of these studies makes it impossible to determine whether the distress in one contributed to distress in the other. Not only is it important to understand factors that affect patients' mood so that steps can be taken to reduce distress and promote well-being, but in light of patients' concerns about being a burden to their caregivers (e.g., Hinton, 1994; Lo, personal

communication), it is quite possible that caregiver distress would be interpreted by the patient as a sign of this feared burden, which in turn could affect the patient's desire to remain at home. In an analysis of legal assisted suicides in Oregon in 2000, physicians reported an increase over the previous year in "the number of patients who were concerned about being a burden to family, friends and caregivers" (Sullivan et al., 2001).

To our knowledge, only one study has evaluated the effects of caregiver and patient distress on location of death. In Hinton's (1994) prospective study of 232 terminal cancer patients in hospice care who had been referred to a home care service and were alive at least one week, the best predictors of terminal admission (where patients died in hospital) were psychological distress among both the patients and the caregivers as rated just before the admission.

Psychological well-being during terminal care

The distress associated with caregiving and terminal illness leads inevitably to questions about factors that protect both the patient's and the caregiver's psychological well-being. We focus on two sets of explanatory variables: resources and coping. Stress and coping theory (Lazarus & Folkman, 1984; Folkman, 1997) provides the rationale for the selection of variables and the relationships we posit among them.

Psychological, spiritual, and social resources that help patients and caregivers cope with the patient's terminal illness

Spiritual resources. Spiritual resources refer to formal religious beliefs, attitudes, and practices as well as beliefs about a higher power or force in the universe and associated attitudes and practices. Spirituality is defined as the search for meaning and purpose in life, and provides the experience of individual transcendence and connection to universal order (Richards, et al 1999; Klass, 1995; Prest & Keller;1993, Tillich, 1963). It is often present for those who are approaching death (Byock, 1996, 1997; Speck, 1993; Kaczorowski, 1989; Hay, 1989), even for those without formal religious belief systems (Richards & Folkman, 1997; Speck, 1993). The inability to find meaning can be a source of distress for the dying as well as the caregiver (Committee on the End of Life Care, 1997). Some studies show spiritual resources are negatively associated with distress (Acklin et al.,1983; Baider et al.,1999; Yates et al.,1981), although other studies show no relationship (Smith et al., 1983; Franks et al.,1990; Rabkin et al., 2000). It is unclear under what circumstances and for whom spiritual resources are protective, and whether spiritual beliefs increase as the patient's death approaches.

Social support refers to emotional, informational, or advisory support that is either perceived or actually offered during times of stress. Support that is provided through the relationship between the caregiver and the patient during caregiving is of particular importance to the proposed study. Typically, the caregiver is thought of as providing support to the patient, but the patient may be an equally important source of support for the caregiver (Folkman et al.1994; Pakenham et al.1995; Spaid et al., 1994; Stanton & Snider, 1993; Williamson & Schulz, 1990). In a study of social support among AIDS caregivers (Soskolne et al. 2000), caregivers were asked to describe a stressful event related to caregiving and identify the person who was most helpful. The ill partner was named as the most helpful person in approximately 50% of the events. LeBlanc and Wight (in press) showed that reciprocity between caregivers of men with AIDS and their care recipients was common and protective. In one of the few studies to examine spousal social support, coping, and mood in a

sample of people with cancer, Manne et al. (1999) found that patients who received more spouse support reported more positive mood and were more likely to cope by focusing on the positive aspects of the cancer diagnosis and treatment.

But the relationship between patient and caregiver can also be a source of distress (e.g. Cantor, 1983). Newsom and Schulz (1998) found that nearly 40% of disabled patients reported some distress in relation to help they had received. Marital conflict was associated with this finding among those who needed the most care. In a review of the cancer literature, Lederberg (1998) notes that patients underestimate their spouses' distress, and spouses underestimate the value patients placed on their support. This may also apply to caregivers who are adult children.

Coping

Coping refers to thoughts and behaviors that patients and caregivers use to deal with instrumental problems related to the patient's illness (problem-focused coping), manage distress (emotion-focused coping) (Lazarus & Folkman, 1984), and maintain positive well-being (meaning-focused coping; Folkman, 1997; Park & Folkman, 1997).

Coping and mood during terminal care. Most of the empirical literature on coping and illness, whether from the perspective of the patient or the caregiver, does not focus specifically on terminal illness. However, studies of coping during earlier stages of illness consistently show that denial-like, escape-avoidant coping is associated with increased distress in patients and caregivers (e.g., Carver et al.1993; Epping-Jordan et al.1999; Compas et al.1999; Manne et al.1999; McCaul et al.1999; Schnoll et al., 1998; Stanton & Snider, 1993). Other kinds of coping appear to be especially effective in diminishing distress including positive reappraisal (Carver et al.1993; Dunkel-Schetter et al., 1992), fighting spirit (Chen et al., 1996; Greer et al., 1979, 1990; Morris et al., 1977; Schnoll, et al.,1998), benefit-finding and benefit-reminding (Affleck & Tennen,1996), and problem-focused coping such as logical analysis, information seeking, problem solving (Vitaliano et al.,1990) and instrumental coping (Pruchno et al.,1989).

Coping and positive mood. Coping theory and research traditionally has been concerned with the regulation of distress (e.g., Vaillant, 1977; Pearlin & Schooler, 1978; Lazarus & Folkman 1984). However, recent research suggests that positive mood co-occurs with distress, and may have important adaptational functions. A study of caregiving in the context of AIDS revealed that caregivers experienced substantial levels of positive psychological mood during periods when they also experienced high levels of distress (Folkman, 1997). Other investigators have reported similar findings in illness contexts (Viney, 1986; Wortman & Silver, 1987). A prospective 2-year cohort study of 2,282 older Mexican Americans who reported no functional problems at baseline found that positive affect was protective with respect to functioning and mortality, independent of adverse effects due to depressive symptoms (Ostir et al., 2000). This study, and recent laboratory research by Fredrickson (1998), suggests that positive mood, independent of depressive symptoms, may have important adaptational significance.

The surprising findings about the co-occurrence of positive and negative mood and the possible adaptational significance of positive mood leads to questions about coping processes that support positive mood as opposed to coping processes that regulate distress. Thus far, it appears that coping processes that serve this function are meaning-based, utilizing the individual's values, beliefs, and goals (Folkman & Moskowitz, 2000). The investigation of this class of coping processes is still in

its earliest phases. It is not yet known for whom and under what conditions denial-like coping is adaptive in relation to mood, or what kinds of coping specifically support positive mood, as opposed to coping strategies that regulate distress.

End of Life Issues and Culture/Ethnicity

Ethnic and cultural groups vary in their attitudes about illness and death along essential dimensions. Representative issues often influenced by cultural expectations include assumptions about who in the family is responsible for making health care decisions and what the patient should be told about a terminal diagnosis. Who should be informed about terminal illness? Is death an acceptable subject for discussion? Is truth-telling valued if hope is thereby diminished? To what extent if at all should aggressive efforts be made to extend survival at the end of life?

Ethnic membership alone cannot accurately predict attitudes. As Kalish and Reynolds noted in their classic study, *Death and Ethnicity*, "At the same time that our data show substantial ethnic differences, we are also aware that individual differences within ethnic groups are at least as great as, and often much greater than, differences between ethnic groups" (1976, p. 49). Acknowledging this variability within groups, rather consistent trends have been observed in the clinical and empirical literature with regard to DNR orders and life support at the end of life. In general, Black and Hispanic patients and families are more likely than white families to request aggressive treatment for terminal family members (Caralis et al., 1993; Blackhall et al., 1995, 1999) Some groups assume doctors would not suggest the option if a case was hopeless.

Others have found that Black compared to white patients are less inclined to complete advance directives (Garrett et al., 1993), sign DNR orders, and are less likely to accept palliative and hospice care. This pattern among Black respondents of seeking maximum possible medical treatment, despite providers' perceptions of its futility, may, at least in some instances, reflect distrust of the medical system and suspicions that this system is motivated to withhold care from minority and poor populations (Koenig & Gates, 1995; Rothchild, 1998).

Why are we studying AIDS and Cancer?

Most major studies of the terminally ill have focused on patients over age 65, have used Medicare records, and/or have selectively included patients with cancer (Fried et al., 1999). Inclusion of cancer patients allows us to examine the relationships between our fine-grained clinical approach and previous epidemiologic studies of similar patients. Inclusion of AIDS patients provides information about a younger population of patients and their caregivers, and about the relative effects of different (enhanced) benefit structures and care needs. In addition, inclusion of both AIDS and cancer allows us to identify characteristics that do and do not cross these disease categories, both of which constitute major public health challenges and societal burden.

Clinical estimation of survival

Medicare hospice regulations require physicians to make a 6-month prognosis to establish patient eligibility (Lynn, 2001). Such prediction is difficult and often inaccurate (Christakis, 1999; Christakis & Lamont, 2000; Vignano, 2000). This is reflected in the median survival time in hospice programs, which appears to be declining as more patients are enrolled (Lynn, 2001). In a sample of 6451 Medicare patients admitted to hospice, Christakis & Escarce (1996) found median survival to be 36 days. In the SUPPORT study, patients were given a 50/50 statistical chance of living more than 2 months on the day before they died (Lynn 2000). More recently, Christakis & Lamont (2000)

studied doctors' prognoses in 468 patients at time of hospice referral and found median survival to be 24 days. While errors include both over-and under-estimates of survival, the former are far more common, with 63% in the Christakis & Lamont study overestimating survival compared to 17% who were over-pessimistic.

Is HIV/AIDS still suitable for a study of terminal illness?

Since the advent of combination antiretroviral therapy (ART) in the mid-1990's, AIDS deaths have plummeted in all groups of patients with access to treatment. Between 1995 and 1998, annual deaths declined from 50,000 to 17,000 nationally (Pallela et al., 1998). Newly identified cases remain stable at about 40,000 per year; with incidence unchanged and survival extended, the number of identified HIV+ people continues to rise. Morbidity and mortality rates in New York City have followed the national pattern, with 32,000 people living with AIDS in 1995 and 36,200 in 1998 (S. Forienza, personal communication, February 2001) while annual deaths have declined 72% from 7,046 to 1,978 during this period (Chiasson, 2000). However, by the end of 1998, mortality rates may have reached a plateau, according to data from New York City (Chiasson, 2000), Chicago (Ahmad, 2001), and nationally (Lee et al., 2001).

The new drug regimens have, for most people, transformed the course of AIDS from the fulminant, rapidly fatal disease seen in the 1980s to a chronic disease that is manageable, at least for a time, for many but not all patients. Nevertheless, death remains a risk and reality, now more often preceded by a longer period of terminal disease than seen earlier in the epidemic (Selwyn, 2000). During this period of progressive disability, intermittent acute illness episodes may occur along with chronic symptoms, eventually requiring palliative care in addition to illness-specific treatments (Greenberg et al., 2000). Corless et al (2000) refer to a "long-term continuum of care," most provided on an outpatient basis. Ultimately, failure of ART and salvage therapy mark "the traditional period of transition from acute or chronic care to palliative and end of life care" (Corless et al 2000).

There has been a concomitant shift in causes of morbidity and mortality from the often lethal opportunistic infections and Kaposi's Sarcoma characterizing the earlier phase of the epidemic, to include a sizeable proportion of deaths from non-HIV-specific conditions such as liver disease and cancers (Bauer, 2001). Recent studies both in Europe and here have documented the increasing prevalence of chronic viral hepatitis (Martin-Carbonero, 2001) and the proportion of deaths among HIV+ patients without an AIDS diagnosis has increased over time (Mocroft et al 2001). In a French study, non-AIDS-related deaths predominated in 1998-1999, most notably non-Hodgkins lymphoma, other malignancies and hepatitis (Bonnet, 2001). Finally, an American study of mortality between 1995 and 1998 in an inner-city hospital found that patients still had relatively high mortality rates from opportunistic infections despite access to ART, but 38% died of bacterial infections and hepatic and renal diseases (Ahmad, 2001).

Because the shift in the trajectory of survival in AIDS is relatively recent, established mortality predictors do not exist although, as noted, shifts in cause of death have been documented internationally. Three potential independent predictors of 1-year mortality have been proposed by Vlahov and colleagues, based both on the cumulative literature and their own data with HIV+ patients in residential health care facilities (personal communication, 2/16/00).

Virologic treatment failure and CD4 count. Studies of prognostic indicators of death in the era of ART show that HIV RNA viral load, in addition to CD4 cell count, is a significant indicator of

disease progression and death, and is almost universally used as a surrogate endpoint marker in clinical treatment studies of antiretroviral drugs. Some patients fail to respond to ART either because of infection with a resistant viral strain, a history of serial monotherapy leading to resistance, or treatment-emergent resistance after initial response to ART. Given the extensive documentation of the association between virologic response and improved survival, it is likely that virologic failure even after salvage therapy in combination with low CD4 count is a predictor of one-year mortality.

Functional status. Earlier studies have found that impairment in activities of daily living (IADL and ADL) predicted mortality (e.g. Justice et al, 1996). In a retrospective study of patients in a residential care facility, any impairment of functional status and especially restricted ambulation predicted 6-month mortality (Selwyn et al.,2000).

Liver disease. Chronic viral hepatitis and concurrent hepatitis C (HCV) infection are increasingly prevalent among HIV+ patients, especially injection drug users. Not only is HCV an independent cause of morbidity and mortality, but impaired hepatic function limits the efficacy of antiretroviral medications metabolized through the liver. Further, antiretrovirals themselves may themselves be hepatotoxic (Sulkowski, 2000). HCV responds to current therapy in about 40% of patients treated with dual therapy (interferon alpha and ribavirin). Nonresponse is elevated in HIV-co-infected patients and re-treatment success for nonresponders to monotherapy, even with combined therapy, was found to be less than 20% in a meta-analysis (Cummings, 2001). Impaired liver function due to HCV, antiretroviral drugs or other causes (e.g. alcoholism) may thus predict 1-year mortality.

Desire for hastened death

The literature on hastened death is dominated by studies of physician, patient, and public attitudes about euthanasia and physician-assisted suicide. There is a striking paucity of studies that prospectively examine patient desires vis à vis what actually happens, or the context associated with these preferences and outcomes.

Even less is known about caregiver-assisted death. A computer search revealed only one such study (Cooke et al., 1998), which happened to come from Folkman's longitudinal study of caregiving partners of men with AIDS. In that study, 17 (12%) bereaved caregivers reported their partners received an increase in medication that was intended to hasten death, and 14 (82%) of these increases were administered by the caregiver himself. Little is known about the frequency with which hastened death is desired or discussed with family caregivers, the conditions under which such discussions or requests are made, or the conditions under which such requests are enacted. The proposed study is positioned to address these questions.

Summary

In addition to structural characteristics of the health care system, patient and caregiver characteristics may influence both their preferences regarding terminal care and what actually happens. The fine-grained analysis that we propose, based on intensive longitudinal clinical assessments, will complement existing large scale surveys. The proposed study will describe the degree to which patient and caregiver treatment preferences match actual outcomes, identify factors associated with observed disparities, and relate the impact of such disparities to patient and caregiver well-being. In addition, the study will illuminate processes that sustain patient and caregiver well-being throughout terminal care.

C. PRELIMINARY STUDIES

This collaboration brings together two scientists with complementary and overlapping areas of expertise: Dr. Rabkin, New York State Psychiatric Institute/Columbia University, and Dr. Folkman, who has been co-director of the UCSF Center for AIDS Prevention Studies (CAPS). As of May 1, 2001 Dr. Folkman becomes director of the UCSF Osher Center for Integrative Medicine, but will maintain close ties with CAPS. Dr. Folkman has conducted extensive research on caregiving and mental health in the context of terminal illness. She is widely recognized for her expertise in coping theory and research, most recently in the context of AIDS-related caregiving and bereavement. Dr. Rabkin has conducted extensive studies of depression in medically ill patients including diagnosis and treatment. The findings of their respective programs provide an important foundation for the proposed research.

San Francisco (Susan Folkman, Ph.D., PI)

Empirical research. Over the last 12 years, Dr. Folkman has conducted an NIMH-funded program of research on stress and coping in a cohort of caregiving partners of men with AIDS, and more recently in maternal caregivers of children with HIV and other chronic illness that is ongoing. The first study involved three groups of gay men: 86 HIV+ caregiving partners of men with AIDS, 167 HIV- caregiving partners of men with AIDS, and 61 HIV+ men in primary relationships with healthy partners. Each man was followed for two years with bimonthly psychosocial interviews and semi-annual physical and psychiatric assessments. Data collection began in 1990 and was completed in 1994, with a retention rate of 83%. A 3-year follow-up study with semi-annual assessments was completed in 1997. Findings regarding mood, coping, and spirituality during and subsequent bereavement described throughout Section B provide important background for the proposed research. More than 40 publications have resulted from this research. The research team involved in the gay men's study, including Ms. Anne Richards, who was the project director and qualitative analyst, Dr. Michael Acree, project biostatistician, Dr. Judith Wrubel, qualitative analyst, and the project assistants will be moving with Dr. Folkman to the Osher Center for Integrative Medicine, and continue with the proposed research.

Theory development. One of the most surprising findings from the study of caregiving partners was that positive mood co-occurred with negative mood throughout caregiving and bereavement. The only time positive mood was not as frequent as negative mood was during the weeks immediately preceding and following the partner's death (Folkman, 1997). Other researchers have reported similar findings (e.g., Viney, 1986; Wortman & Silver, 1987), but have not paid much attention to them. Recently, there has been growing interest in the general adaptive functions of positive emotions (e.g., Fredrickson, 1998), but little attention has been given to the role that positive emotions may play under conditions of intense stress. The full-scale study will examine these adaptive functions in relation to caregivers' and patients' preferences and outcomes regarding type and site of care.

A second set of findings related to positive emotion indicated the coping processes that generated them were different than the coping processes that regulated distress (Folkman, 1997). Coping processes that generated positive emotion were meaning-based; they drew on underlying values, goals, and beliefs (religious, spiritual, or about the world). Coping theory and research has been occupied primarily with the ways coping regulates distress (Lazarus & Folkman, 1984; Pearlin &

Schooler, 1978; Vaillant, 1977). The full-scale study will make an important contribution to coping theory because it will systematically assess both kinds of coping.

New York: Judith Rabkin, Ph.D., PI

Dr. Rabkin has been engaged in NIMH-supported AIDS research for the last 12 years, including epidemiologic cohort studies and clinical trials to treat depression and related symptoms in HIV/AIDS patients. More recently, her work has been extended to ALS patients, addressing similar issues regarding prevalence of depressive symptoms and disorders, their change over time with illness progression, and resilience factors. Throughout this period she has been affiliated with the HIV Center for Clinical and Behavioral Studies at Columbia, which will continue to serve as a resource for methodological issues.

Prevalence of depressive disorders in HIV+ men and women. Dr. Rabkin has been principal investigator (at Cornell) or co-investigator (at Columbia) of two 5-year NIMH-funded longitudinal cohort studies of HIV+ men and women. It was necessary to develop specific assessment methods for participants with significant medical symptoms and/or medication side effects, in order to differentiate these from the somatic symptoms of depression. In addition, these studies included many assessment instruments in multiple domains: psychosocial, psychiatric, neurocognitive, somatic. Experience with this broad range of measures has informed the selection of the current assessment battery, while the diagnostic experience will be usefully applied in the current study of very ill patients.

Treatment of depression in HIV+ patients. Since 1989, Dr. Rabkin has conducted placebo controlled randomized double blind clinical trials of conventional antidepressants (imipramine, fluoxetine, sertraline) and other medications (dextroamphetamine, testosterone) in the treatment of major depression among HIV+ patients (Rabkin et al., 2000; Rabkin et al., 1994a; 1994b; Rabkin 1999a, 1999b).

End of life studies. Dr. Rabkin has been interested in end of life issues for the past decade, working first with people with HIV/AIDS, and more recently, patients with amyotrophic lateral sclerosis. In the earlier work, she and colleagues examined factors associated with maintaining hope among those with a presumably fatal diagnosis (Rabkin, Remien et al., 1993; Rabkin, Williams, et al., 1990). She also has conducted several studies of the prevalence and correlates of suicidality among AIDS patients (Rabkin et al., 1993), and attitudes, plans and acts concerning hastened death (Rabkin et al., 1993; Goggin et al., 2000). More recently, she and colleagues assessed prevalence of depression, attitudes and plans regarding hastened death among ALS patients (Rabkin, Wagner et al., 2000).

Dr. Rabkin is currently co-principal investigator of a newly NIMH-funded longitudinal study of late stage ALS patients and caregivers. Dr. Albert, the principal investigator, will serve as co-principal investigator on this project. The home visits and interviews that she and colleagues are conducting provide practical guidance in the design of the proposed study. One important observation is that these very sick patients are able to complete the interview and rating scales without discomfort, and indeed say they enjoy their study participation, which was not perceived as burdensome.

Drs. Richard Rabkin and Martin McElhiney have worked for the past several years with Dr. Rabkin as study psychiatrist and project director respectively, and will continue in these roles in the proposed study.

D. Methods

Overview of the Preliminary Study

The primary objective of this preliminary study of terminally patients and their primary family caregivers is to determine the feasibility of identifying patients with approximately 3 to 6 months to live; recruiting these patients and their caregivers; and retaining the patient-caregiver dyads for up to six months. A second objective of the preliminary study is to refine the assessment protocol for the subsequent full-scale study. Assuming that modifications to the assessment protocol will involve shortening or elimination of existing measures rather than addition of major new measures, we plan to include the data from the preliminary study in the subsequent full-scale study. Patients will include approximately 50% with cancer and 50% with AIDS. Patients and caregivers will be interviewed biweekly in their homes. The study will be carried out at two sites: New York Psychiatric Institute/Columbia University, and the University of California, San Francisco.

Sample size

The sample will consist of 44 dyads/site. We are not doing any hypothesis testing in this preliminary study, which leaves the determination of sample size more a question of pragmatics than power. We took three considerations into account: First, our combined experience and the experience of colleagues suggest that a reasonable recruitment goal for a study like this is approximately 3 to 4 dyads/month/site. Second, patients with AIDS and cancer may differ in terms of structural factors including insurance, availability of hospital beds, and funds for paid home care. We therefore felt it important to assess feasibility separately for each disease. Because the AIDS census is limited compared to the cancer census, recruitment of the AIDS dyads may go more slowly. Finally, we want to complete the entire preliminary study within three years.

Taking these three considerations into account, and allowing for the planning, training, and implementation of the study at its outset, the study design should allow us to recruit 44 dyads at each site (22 dyads with cancer and 22 with AIDS), and follow them for up to 6 months. Allowing for 10% to 15% attrition, this would provide approximately 37 – 40 dyads/site, or 18 – 20 dyads/disease/site. This sample size should be sufficient for addressing the feasibility questions, and for providing data that can be used to refine the assessment protocol.

Participants

Potential participants are: a) adult, non-demented patients who have a survival prognosis of **3 to 6** months, are receiving their care at home at study entry, and have an identified family member or significant other who is primarily responsible for care, and b) the identified family caregiver. Details of and rationale for inclusion/exclusion are in Section E.

Estimating Survival

Physicians tend to bias their predictions optimistically for a variety of reasons (see Section B). Based on our review of the literature and personal communications (February 2001) with Nicholas Christakis, an authority on this question, we plan to suggest two techniques for identifying patients with 3 to 6 months to live.

Technique #1: We will ask health care providers to identify patients with 6 to 12 months to live instead of asking them to identify patients with 3 to 6 months to live. Because of the expected optimistic bias, we expect that identified patients will live less than the predicted time, thereby

coming closer to our goal of having patients with 3 to 6 months to live. How close we get to the goal will be one of the important pieces of information to come from this preliminary study.

Technique #2: Following Christakis (1999; personal communication, February 2001), we will also present the request in probabilistic terms by asking providers to identify patients with a 50% chance of living 6 months. Christakis reports that this approach increases accuracy of prognosis.

Ideally, we would do an experiment in which we would randomly assign providers to each technique. However, some will be making multiple referrals while others will be making only single referrals, making it difficult with a small sample size to determine whether the two techniques differ in their effectiveness. Instead, we will offer both techniques. We will ask providers' reactions to the two approaches and find out which they prefer and why. The information will be used to refine the approach for the full-scale study.

Recruitment procedures

We have established arrangements with medical providers in acute care and home care settings in San Francisco and New York City (letters of support at end of Section E.). Each health care site will have a local clinical "point person" to identify patients who appear to meet eligibility criteria. Where possible, the study recruiter will also attend weekly clinic meetings in which cases are reviewed to identify potential participants. The treating physicians will be asked to confirm eligibility and the appropriateness of approaching the patient regarding study participation. Note that this system does not depend on physicians to recruit or refer participants.

Patients who are considered approved will be contacted by the clinic staff member, who will briefly describe the study and ask permission to have a research staff member contact him/her about possible participation. The research staff recruiter will then telephone the patient and explain study goals and procedures. The patient will be asked to identify his/her primary family caregiver. The recruiter will speak with the caregiver and explain study goals and procedures. Patients and caregivers who refuse to participate will be asked their reasons for non-participation, which will be recorded, as well as basic sociodemographic information.

Participant burden

The participants in this study represent a vulnerable population. The patients are terminally ill, and their caregivers may be seriously taxed both psychologically and physically. We will train interview staff carefully to be responsive to patient and caregiver limitations (see Training section below). In addition, we have taken great care to choose measures judiciously, to use short versions whenever possible, to keep the interviews to 1 hour or less, and to allow for participant limitations as follows:

- Self-report questionnaires will be read aloud if patient or caregiver prefers;
- An attenuated battery will be used for patients who are very ill, consisting of modified visual analog scale (VAS) format covering variables assessed previously by separate measures;
- If the participant is too fatigued to complete the interview, we will follow up by phone or in person within the next 48 hours. If the unfinished portion consists only of self-report measures, the participant will be asked to complete the questionnaires and return by mail within 48 hours;
- If the patient is transferred to an institutional setting, we will go to the institution to interview the patient if he/she is able and willing;
- If the patient becomes too ill to participate, we will still interview the caregiver.

Measures

The measures are presented in full in Appendix 1 (Patient Version) and Appendix 2 (Caregiver Version). A listing of the measures is provided here:

DEPENDENT VARIABLES

Congruence: Is what you want what you get?

Congruence between preferences for type and site of care and actualities – i.e., agreement or correspondence -- is now the key dependent variable of our study. There are no extant measures of it that are immediately applicable. We will use the start-up period of the preliminary study to refine the elements of the congruence variable and their measurement. We will begin with the following measures:

Type of care.

Treatments, services, and assistive devices will be assessed with a checklist of treatments (e.g., medications, chemotherapy, antiretroviral therapy, pain management). Formal (paid) services and hours available will be assessed (e.g., home attendants, visiting nurse service, physical therapy, nutritional counseling, pastoral care), as well routine informal assistance (e.g. neighbors, church groups). We will ask about assistive devices (e.g., wheel chair, hospital bed, commode). For each treatment, service, and assistive device that is listed, the participant will be asked the following questions at each visit:

1. Has it been recommended? (By whom: physician, social worker, etc.)
2. Is it wanted?
3. Is it affordable?
4. Is it being used?
5. Has it been refused by the patient?

Preferences regarding services. We will ask patients and caregivers which of the above services, treatments, and assistive devices they would prefer in an ideal world and which they would prefer given the existing situation.

Directives re preferences (asked of patient and caregiver). Have these preferences been communicated in:

- 1) DNR order
- 2) Health proxy
- 3) Discussion with physician
- 4) Discussion with each other

Intent of treatment. Patients and caregivers will be asked to rate each treatment (as appropriate) on two dimensions using visual analog scales. This approach reflects the belief that the two dimensions are not mutually exclusive.

- 1) To what extent is the intent curative or to extend life?
- 2) To what extent is the intent is to provide comfort and symptom relief (palliative care)?

Site of care. Current site of care will be recorded. Sites of care will be classified as follows:

- 1) Home (including adult community/facility) without formal (e.g. health care agency) support
- 2) Home with formal support (e.g., Assisted living in adult residences; Visiting Nurse Service)
- 3) Home hospice
- 4) Residential or in-patient hospice
- 5) Skilled nursing facility
- 6) Acute care hospital

Preferences regarding site of care. We will ask patients and caregivers which of the above sites of care would be their preferred site in an ideal world and which site they would prefer given the existing situation.

Well-being: Depression and positive mood (Patient and caregiver)

Note: Assessed with respect to previous 2 weeks at each interview unless patient is too ill to complete, in which case only the Visual Analog Scales (VAS) will be administered.

Depression: Beck Depression Inventory: BDI-II and BDI-PC: 21 item self-report BDI-II (revised version, Beck et al., 1996) for caregivers at all scheduled occasions, and patients at the baseline visit. Thereafter, patients will be given the briefer BDI-PC (primary care) version (Steer, et al., 1999). The BDI-II is the research gold standard self-rating scale used to assess prevalence and severity of depressive symptoms. The 7-item BDI-PC is intended for medically ill patients, and has the advantages of brevity and exclusion of somatic symptoms.

Patient Health Questionnaire (PHQ) (Spitzer, Kroenke, & Williams, 1999) is a self-administered form of the earlier PRIME-MD (Spitzer, Williams, Kroenke, & al., 1994) developed for primary care patients. It inquires about symptoms and also their functional significance. It provides information about threshold mood disorders (DSM-IV diagnoses) and subthreshold disorders, and also yields a measure of depressive severity that can be used to track changes over time. It will be preceded by the 2-item SCID screen for major depression.

Positive and negative affect will be assessed with the 16-item, self-report modified version of the Bradburn Affect Balance Scale (Bradburn, 1969). We will also use the 4 items from the CES-D that describe positive mood.

Beck Hopelessness Scale (Beck et al., 1974) measures future expectations. A short (10-item) form will be used.

Endicott Quality of Life Enjoyment & Satisfaction Questionnaire (1993), short form, is a 16 item scale that will provide an overall rating of QOL.

Visual Analog Scales (VAS). These scales represent the simplest form of inquiry and will be used alone if patients are too ill to respond to the measures described above. The VAS will provide a common metric across all occasions, including those in which other data are missing because of patient illness. As recommended by Cohen and Mount (1992), we will use a 3-day time frame to maximize recall and to avoid very transient fluctuations often observed in very sick patients. The VAS scales assess positive and negative aspects of well-being. (e.g., “How weary have you been feeling?” “How optimistic have you been feeling?”) These items will be grouped and index scores created for each dimension. With respect to the validity of single item measures for the seriously ill, Chochinov et al. (1997) compared a standard interview and 3 brief screens for depression in 197 advanced cancer patients receiving palliative care. The most accurate screen was the single item asking “Are you depressed most of the day nearly every day?” It correctly identified all cases, with

no false positives. Given these findings, virtually any patient who can respond at all can be queried about mood.

INDEPENDENT VARIABLES

Structural variables

Structural variables will be assessed from two perspectives: at the individual level of patient/caregiver perceptions; and at the levels of state (New York, California), and where available, city (New York City, San Francisco) information.

Individual level:

Financial resources. The caregiver will be asked specific questions about the patient's health insurance and other benefits, and family financial resources (to reduce length of patient interview). Availability of beds in skilled nursing facilities, residential hospice units, and hospitals will be assessed in terms of patient and caregiver perceptions regarding availability of such beds.

State/local level:

Four sets of state/local data will be used to describe structural level variables that can affect type and site of care: Payment policies; Prevalence rates; Utilization rates; Cost information. The following data sources and references will be used to provide information about these four sets of variables:

1. Statewide Planning and Research Cooperative System (SPARCS): Data base
[Sparcs@health.state.ny.us](http://www.health.state.ny.us/nysdoh/sparcs/operations/who.htm), Bureau of Health Facility Planning
518-473-8144, or 800-638-3808. New York State Department of Health.
<http://www.health.state.ny.us/nysdoh/sparcs/operations/who.htm>
2. SPARCS: Hospital occupancy Quarterly Report.
Wysiwyg://195/http://www.health.state.ny.us/nysdoh/hoqr/main_1.htm
3. SPARCS: Summary of Hospital Data.
http://www.health.state.ny.us/nysdoh/sparcs/annual/t98_01.htm
4. SPARCS: Davis, Robert A. SPARCS coordinator. Annual Report, New York State Department of Health. Volume 1. 1998.
5. Office of Statewide Health Planning and Development (OSHPD): Data base
State of California, Healthcare information division, Healthcare information Resource Center
6. OSHPD: Annual Utilization Reports of Home Health Agencies and Hospices (1993-1997) and Hospitals and LTC (1989-1998), and Hospital Quarterly Data Trends, Accounting and Reporting Systems Section, 818 K Street, Room 4400, Sacramento, CA 95814. <http://www.oshpd.ca.gov>

Demographics/biographic: Age, sex, ethnicity; years of education completed; household income and composition; relationship to caregiver/patient; religion; work status; prior experience with death of close other. Extent of family accord regarding the patient's care plan and environmental resources will be assessed by the interviewer using a global 5-pt scale following the DSM-IV scoring system for Axis IV: Psychosocial and Environmental Problems (Cohen, Williams, & Rabkin, 1997).

Patient illness indicators

Cognitive Impairment

Mini Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) is a widely used brief, standardized assessment of mental status. A short form will be used after the baseline assessment.

Memorial Delirium Assessment Scale (Breitbart, Rosenfeld, Roth, & al., 1997): This brief, clinician-rated 10-item scale assesses the cardinal symptoms of delirium. It will be administered only when the interviewer considers it appropriate at the baseline visit or subsequently finds a marked change in the patient's mental status such as inability to focus or attend to the interview, disorientation to time or place, or significant decline in MMSE score.

Medical: Illness history and current medications; significant medication changes or changes in treatment plan will be recorded at each visit. (Information obtained from caregiver)

Karnofsky Performance Status (Yates, Chalmer, & McKegney, 1980). The interviewer uses this 100-point scale to rate the patient's level of physical functioning in the coming week.

Activities of daily living:

Lawton Instrumental Activities of Daily Living (Lawton & Brody, 1969) assesses performance on 8 everyday tasks instrumental to independent functioning.

Katz Index of Activities of Daily Living (Katz ADL) (Katz, Ford, Moskowitz, & al., 1963) assesses six self-care functions among patients with chronic disease and disability. It will be administered only to patients who cannot perform one or more activities on the Lawton IADL.

Somatic Symptoms.

Symptom checklist: a checklist of 12 symptoms reported by at least 10% of patients (Field & Cassel, 1997).

Memorial Pain Assessment Card (Fishman, et al., 1987) consists of 3 visual analog scales that measure pain intensity, pain relief, and distress level, and a set of pain severity descriptors.

Caregiver strain indicators

Physical health. A visual analog scale will be used to assess self-reported general health monthly. Major medical conditions will be recorded.

Chalder fatigue scale (Chalder et al., 1993): 7 item self-report physical fatigue

Caregiver burden: 6 items from the Zarit Caregiver Burden Scale (Zarit et al., 1980) and Folkman's (Folkman et al., 1994) 4-item measure of finding positive meaning in caregiving.

Resources (Patient and caregiver except where noted)

Holland Schedule of Beliefs Inventory (Holland et al., 1998): 15-item self-report measure with a 4-point response format asking about spiritual beliefs..

Perceived caregiver/patient support: 14 self-report items from Manne et al (1999) including 7 negative and 7 positive support items.

Appraisal and coping (patient and caregiver) will be assessed with respect to a recent illness-related event that the participant will be asked to describe in narrative form. (Audio taped.)

Appraisal: Appraisal of controllability will be assessed with one Likert-scaled item (Folkman, Lazarus, Gruen, & DeLongis, 1986).

Coping:

Ways of Coping: Four 3-item scales from the short form (Folkman et al, 1987) will assess distancing, positive reappraisal, escape-avoidance, and problem-focused coping.

Positive coping will be assessed with 5 items selected from the Positive Coping Inventory (Billings & Folkman, 1999).

Spiritual coping will be assessed with a structured interview about spiritual resources that the person used in the stressful situation. Spiritual or religious beliefs, practices or experiences

that influenced the stressful situation will be queried. Additionally, the interview guide will be used to probe for the meaning or interpretation of the event in relation to the person’s life, his or her illness, and his or her relationship to others, including God or a higher power.

Attitudes about euthanasia and physician-assisted suicide: (patients and caregivers)

Three questions from Emanuel et al’s (2000) national survey ask about general attitudes toward euthanasia, whether the respondent has seriously thought about taking his/her life or asking the doctor (or someone else [our addition]) to do so, and about goals (palliative or curative) for one’s medical care. (If respondent endorse the questions, “have you seriously thought about taking you life...?” in the affirmative, there are 2 or 3 subsequent probes about reasons, and communication of such desire to others). This survey was conducted by telephone with over 900 terminally ill patients and were found to be informative.

Assessment Schedule

Note: After baseline, bi-weekly and monthly assessments repeat for six months or until patient dies if sooner. Please note that many measures Are only given on alternate visits The caregiver will be interviewed once more one month after the death.

Procedures

Data will be collected using standardized instruments, and pre-coded questionnaires. In the initial interview, cognitive status will be assessed at the outset. If the patient is unable to participate in the interview because of cognitive impairment, compensation will be provided but the dyad will not be entered in the longitudinal study.

Patients and caregivers will be seen in their homes biweekly throughout the study. At the first visit, two interviewers will go together, and interview the participants separately. The initial interviews will take 60 minutes as feasible for patients, and slightly longer for caregivers. Subsequent home visits may be made by one interviewer who will see the participants successively. If the participants are able and would prefer to be seen in our

offices, this will be arranged instead. The semi-structured interview will be followed by self-report scales (which will be read aloud if literacy, energy or eyesight are problems). In the event that the

MEASURE	PATIENT			CAREGIVER		
	En-try	Wks 2,6, 10...	Wks 4,8, 12..	En-try	Wks 2,6, 10..	Wks 4,8, 12..
<u>CLINICIAN ADMINISTERED</u>						
MMSE*/delirium**	x	x	x			
Somatic symptoms	x	x	x			
Services checklist	x	x	x	x	x	x
SCID Screen/Patient Health Q.	x		x	x	x	x
Stressful event		x			x	
Katz ADL**						
Karnofsky Perf. Index	x	x	x			
Manne support/conflict	x		x	x		x
Demo/financial	x			x		
<u>SELF-REPORT</u>						
Beck Depression Inv.*	x	x	x	x	x	x
Memorial Pain	x	x	x			
Lawton IADL	x	x	x			
Beck Hoplessness	x		x	x		x
Endicott Qual of life	x		x	x		x
End of life query	x		x	x		x
Visual analog scales	x	x	x	x	x	x
Appraisal/coping		x			x	
Holland Beliefs		x			x	
Brad. pos/neg affect		x			x	
Chalder fatigue				x	x	x
Caregiver burden				x	x	x
* Short form used after baseline visit						
** Administered only when clinically indicated						

interview cannot be completed, the self-report questionnaires will be left with the participant along with a self-addressed pre-stamped envelope for their return to our offices. Note will be made in the data base if this was necessary.

If the patient moves to an institutional setting, he/she will be interviewed on the same schedule at that site and the caregiver also will be followed separately. All interviews will be audio taped. Dyads will be considered to have completed the study if they complete three assessment occasions. The last participants will be enrolled six months prior to the conclusion of data collection.

Compensation. At the conclusion of each interview, each participant will be compensated with \$25.

Analysis

Specific Aims 1 to 3: Feasibility

Of the three aims that address feasibility – prognosis, recruitment, and retention -- we assign the greatest weight to recruitment. We will not pursue the full-scale study if we do not have evidence that recruitment is feasible. Success with recruitment, but failure to achieve feasibility with the other two criteria will lead to modifications of the full-scale study.

Aim 1: Feasibility of predicting how long patients will live.

The ability to predict death within a specified period was more critical in our original submission, in which location of death was a key dependent variable, than it is in this revised proposal, in which the emphasis is on congruence between patients' and caregivers' preferences and actual type and site of care. Further, in the present study we will follow patients for up to six months, whereas in the full-scale study we will be able to follow patients for up to 1 year. In light of these considerations, we will consider a 50% 1-to-6 month mortality rate evidence of feasibility. Evidence of lack of feasibility with respect to predicting mortality will lead to further modification of the full-scale study.

Aim 2: Feasibility of recruiting terminally ill patients and their primary family caregiver.

We plan to recruit 3 to 4 dyads a month at each site. We believe that a recruitment rate that falls below 2.5 dyads/month at each site would make it unfeasible to conduct the full-scale study within a reasonable amount of time.

Aim 3: Feasibility of retaining terminally ill patient/caregiver dyads until the patient dies or through six months, while interviewing them bi-weekly. The specific aims of the full-scale study require multiple assessments in order to assess change (and predictors of mood and preferences for treatment and site of care). The condition of terminally ill patients can change dramatically within very short periods of time. We determined that a bi-weekly schedule will allow us to monitor such change while not overburdening participants.

Our goal in the full-scale study is to have <20% attrition. For the preliminary study, we would consider 30% attrition evidence of feasibility, on the assumption that observations by interviewers and feedback from participants can be used in the full-scale study to improve retention without significantly altering the design of the study. Lack of feasibility with respect to retention would lead to a redesign of the full-scale study.

Specific Aim 4: Refine the interview protocol for the full-scale study.

A number of measures include an alternative Visual Analogue Scale (VAS). It will be important to determine the correlation of the VAS measures with their long forms. For those variables that have VAS forms, we will administer both the long form and its VAS to all patients who are able to complete the long forms. These correlations will provide the basis for determining which short (VAS) forms can be substituted for long forms in the full-scale study. We will also use correlational analysis to examine overlap among measures within categories to determine redundancy. We will also identify, and replace measures that fail to discriminate among respondents. This will further guide measure selection for the full-scale study.

Secondary aim: We will examine the data to obtain preliminary estimates of effects associated with disease (AIDS, cancer), site (New York, San Francisco), and ethnicity. This information will guide the design of the subsequent full-scale study.

An index of congruence between treatment preferences and actualities will be developed during the preliminary study.

Qualitative analysis

The goal during the preliminary study is to develop codes that will be applied to the full-scale study data. Codes will be developed from two sets of narratives:

Stressful event narratives: Participants will be asked to describe a recent stressful event related to the patient's illness. Based on stress and coping theory, interview probes are designed to elicit goals and expectations that were violated, the reasons the event was stressful, the emotions the participant experienced, and what it was that caused them to feel the emotion. Codes will be developed for these themes

Spirituality: Narrative data will be elicited in the interviews in response to questions about spiritual resources and coping. Codes will be developed to distinguish beliefs, practices and experiences that support positive meaning from those that do not.

Our qualitative analysts will develop coding schemes through a dynamic process that involves both the underlying theoretical coping model and themes that emerge from the narratives. Procedures for establishing inter-rater reliability are established, and coding schemes are applied to the data, using a qualitative program (Ethnograph®).

Interviewer training, supervision, and support

Training will be developed collaboratively but conducted separately at each site because interviewers will be hired at a staggered schedule based on anticipated subject flow. For each, training will entail: 1) overview of study objectives, 2) review of current knowledge about the issues being studied; 3) training on elicitation and assessment of psychosocial resources, appraisal and coping 4) training on assessment of clinical depression, cognitive impairment, delirium, and functional status; 5) review skills for interviewing technique, establishing rapport, interviewing very sick patients, determining whether and when the interview should be interrupted and deferred because of fatigue or other reasons; 6) obtaining medical history; management of issues associated with discussions of hastened death and role of psychiatrist (site psychiatrist); 7) review procedures for protecting confidentiality, especially between caregiver and patient.

Supervision. Audio tapes will be exchanged so that Dr. Folkman can monitor interview portions concerning elicitation of stressful events, spirituality, and hastened death, and Drs. Rabkin and Albert can review assessment of cognitive, functional, and psychiatric status. The first 5 interviews of each interviewer will be monitored in this way; thereafter, every tenth will be selected for monitoring by the site project directors, with back-up from both Drs. Folkman and Rabkin. The PIs and the project directors will meet with interviewers weekly as a group and individually as needed.

Support. The interviews are likely to be psychologically taxing. Dr. Rabkin in NY and Dr. Folkman in San Francisco and their project directors will devote a portion of the weekly meetings to support needs of the interviewers as appropriate. The site psychiatrists will also attend as needed.

Data management

Data will be collected on paper and by audio tape. Questionnaires will be visually inspected for missing data at each site. Missing items asked orally during the interview will be reviewed by audio tape to determine the correct answer. Data will be double entered locally, and the New York data will be sent electronically to Ms. Dizon, the data manager at the San Francisco site, who will clean and transmit them to Dr. Acree for entry into SAS and analysis.

Cross-site coordination

The successful completion of this study depends on close co-ordination across the two study sites (New York and San Francisco) to ensure standardization in each aspect of the research. Our organizational structure is designed to facilitate this close coordination.

1. Executive Committee (Principal Investigators, Project Directors, and Senior Biostatistician.)
Responsibilities: scientific oversight, including quality assurance within each site, consistency of methodology across the two sites, review of questionnaires and interview protocol.
Meetings: Weekly one-hour conference calls throughout. Weekly group e-mails including other co-investigators and staff as needed. During the first year, the PIs and project directors will meet in person three times for 2-day meetings to ensure tight coordination on all details of the study. During the succeeding years, there will be two in-person meetings/year.
2. Project Directors' Committee (New York and San Francisco project directors)
Responsibilities: implement recommendations from the Executive Committee for maintaining scientific consistency across studies; develop and maintain common guidelines for hiring and training personnel, recruiting participants, and conducting interviews.
Meetings: Bi-weekly by conference call during the planning phase of the study and monthly thereafter. E-mail throughout.
3. Data Committee (Senior Biostatistician (Dr. Acree), data managers/programmers, and qualitative analysts. Dr. Acree will chair)
Responsibilities: maintain consistent and high quality data collection and data management at each site and develop common protocols for preparing and transmitting data. (Qualitative data and most quantitative data will be analyzed centrally at San Francisco.)
Meetings: E-mail on a bi-weekly basis, and as needed, and conference calls as needed.

Overview of Subsequent Full Scale Study

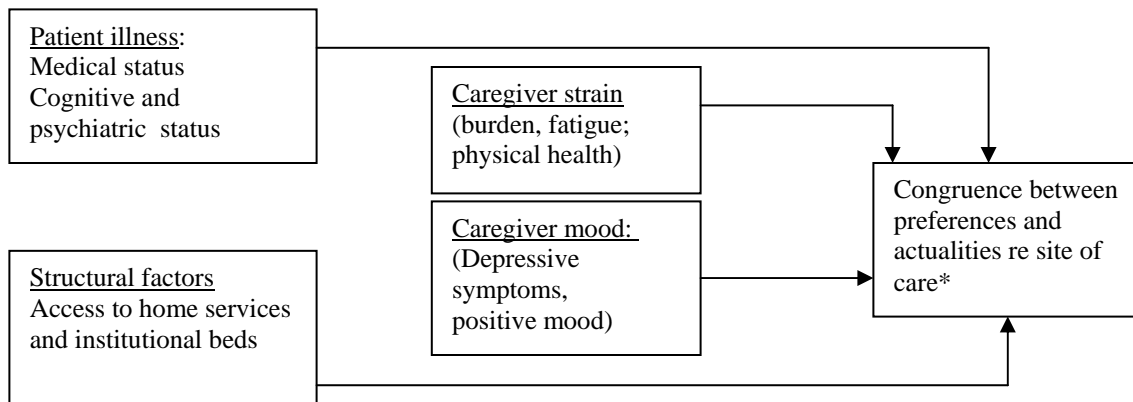
The full-scale study will be a prospective, observational cohort study of 220 patient-caregiver dyads who will be interviewed bi-weekly until the patient's death in New York and San Francisco. The

surviving caregiver will be interviewed once after the patient’s death. The aims are to describe and explain congruence between preferences and outcomes in patients and caregivers regarding and type and site of care during terminal illness; assess prevalence and course of depressive disorders and symptoms in patients and caregivers; identify patient and caregiver characteristics that influence their psychological well-being; and examine the relationship between degree of congruence and level of well-being in patients and caregivers. The eventual goal is to develop useful interventions to improve end of life care and quality of dying. The analytic models that explain congruence and well-being are described below. The models explaining well-being are based on stress and coping theory (Lazarus & Folkman, 1984; Folkman, 1987). Details of the Analysis plans will be described in the subsequent proposal for the full-scale study.

Explaining Congruence between Preferences and Actualities of Site of Terminal Care

This analytic model explaining congruence between preferences and actualities regarding site includes structural factors, patient illness indicators, and caregiver strain and mood.

Figure 1: Congruence of Preferences and Actualities re Site (and Type) of Terminal Care

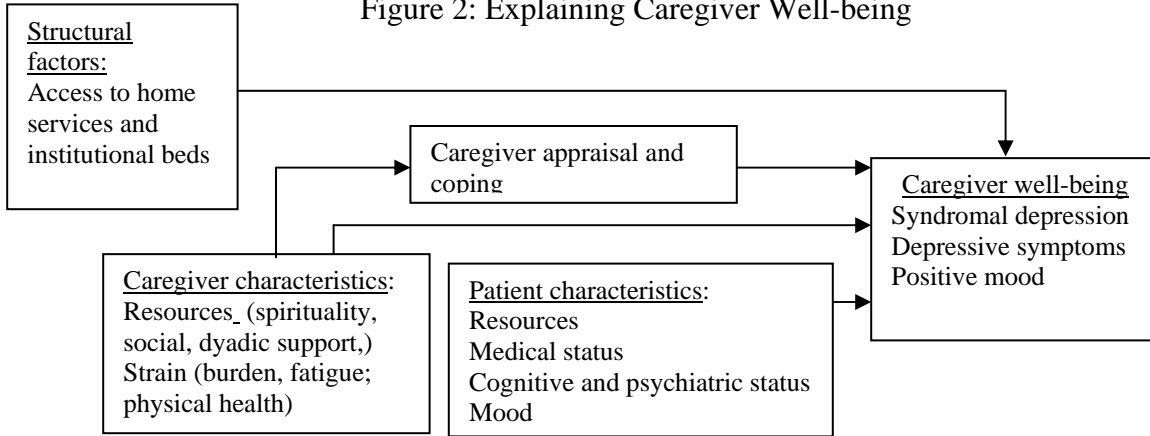


*The model predicting congruence regarding type of treatment differs from this model only in that it does not include caregiver variables.

Explaining Caregiver Well-being

The analytic model explaining caregiver well-being (syndromal depression, depressive symptoms, positive mood) includes structural variables (availability of hospital beds, funds for wanted services) and caregiver characteristics (strain, psychosocial resources); and appraisal and coping. The model also allows for examination of the effects of patient characteristics (resources, illness indicators, depressive symptoms) on caregiver well-being.

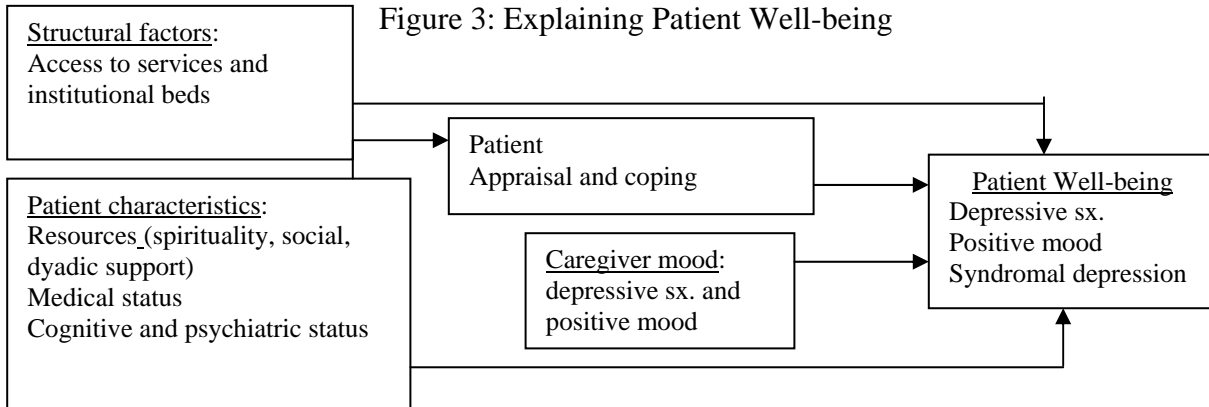
Figure 2: Explaining Caregiver Well-being



Explaining Patient Well-being

The analytic model explaining patient well-being includes structural variables, patient characteristics, appraisal and coping, and caregiver mood.

Figure 3: Explaining Patient Well-being



The analysis plan for each of these models will be described for each specific aim in the subsequent proposal for the full-scale study.

Limitations

1. Generalizability to other terminally ill patients is limited by the study requirement that all patients have a family caregiver.
2. By providing attention and listening, interviewers may have a therapeutic effect on patients and caregivers, and thereby may affect the outcomes.
3. Because of our concern about participant burden, we are not using state-of-the-art psychiatric assessments such as the SCID or comprehensive neuropsychological tests; and we have omitted several potentially significant areas of inquiry including the doctor-patient communications and relationships or social relationships outside of the dyad under study.
4. We will not assess the adequacy of, or satisfaction with formal care (e.g., hospice service), which could have a major impact on decisions regarding location of death.

Despite these limitations, we expect to generate significant information about influences on patient and caregiver mood during end of life care, and psychosocial determinants of where patients receive their terminal care, beyond those accounted for by structural variables.

E. Human Subjects

1. Participant characteristics

During the first two years, we expect to recruit 44 patient-caregiver dyads at the San Francisco site and 44 at the New York site. Potential participants are adult patients who have a life expectancy of 6-12 months, who are receiving their care in their home at time of entry into the study, and who have an identified informal caregiver who is a family member or significant other, and the identified caregiver.

We will exclude patients with dementia (Alzheimer's and other) because these patients will not be able to give informed consent and would not be able to respond sufficiently to the interview queries. Health status of caregiver is unrestricted unless their health status precludes their providing assistance to the patient, in which case they would not be eligible.

Inclusion criteria for the patient:

- a. >Age 21
- b. English speaking
- c. Receives his/her care at home at study entry (may receive temporary care, e.g., treatments, in institutional setting from time to time)
- d. Has an identified caregiver who is a family member or a significant other
- e. Has a survival prognosis of 6 – 12 months, according to the patient's physician
- f. Able and willing to give informed consent

Exclusion criterion for the patient:

- a. Alzheimer's diagnosis or other dementia

Note: Patients identified at the outset by referral sources as having dementia or delirium will not be contacted. If, during the initial home visit, the patient scores <18 on the MiniMental Status Exam, is unable to respond meaningfully to the interview questions, or is in the process of being institutionalized, the patient and caregiver will receive compensation for this visit but will not be followed. The interviewer will explain to both the patient and the caregiver that their time is appreciated, but in the interviewer's opinion the study is too burdensome and demanding.

Inclusion criteria for the caregiver

- a. Shares living quarters with the patient or visits frequently and regularly
- b. English speaking
- c. Is able and willing to take responsibility for patient's care
- d. Able and willing to give informed consent

Gender and Minority Inclusion

In San Francisco, the sample will be approximately 65% white, 25% African American, and 10% Latino. Approximately 40% of the patients will be female..

Children. This study does not include children because the object of inquiry is terminal care in the home for adult patients. There is a separate literature concerning parents as caregivers of their children which identifies separate challenges, issues and care arrangements.

2. Sources of research material

All data will be obtained by participant self-report and through clinical evaluations by interviewers during the course of the interview. The data will be obtained specifically for research purposes. No use will be made of existing specimens, records, or data.

3. Recruitment Plan and Consent Procedures

Susan Folkman and Anne Richards will be responsible for study recruitment in San Francisco and Judith Rabkin, Victor Grann, and Steven Albert in New York City. Because recruitment will be a challenge in terms of promptly identifying and enrolling eligible dyads, each site will employ a part time "recruiter" whose job will consist of recruiting from the several sites at each location. This includes weekly telephone calls and biweekly visits to each site. Recruitment will occur through clinics and home care programs.

Clinic recruitment will proceed as follows:

- 1) Each health care site will have a local clinical "point person" to identify patients who appear to meet eligibility criteria. This member of the clinic staff will identify patients who meet eligibility criteria. (These staff members or the service will be paid for their effort.)
- 2) The names of potential patient participants will be submitted to the treating physician for his/her review. Participants will be considered "approved" unless the physician notifies us otherwise within 1 week. **Note that this system does not depend on physicians to recruit or refer participants; it depends only on their reviewing the names of potentially qualified patients that staff members have identified.**
- 3) Patients who are considered approved will be contacted by the clinic staff member who will briefly describe the study and ask permission to have a research staff member contact him/her about possible participation.
- 4) The clinic staff person will provide the names of patients willing to be contacted to our research staff recruiter
- 5) The research staff recruiter will then telephone the patient and explain study goals and procedures. The patient will be asked to identify his/her primary family caregiver. The recruiter will speak with the caregiver and explain study goals and procedures and an initial interview will be scheduled. Both members of the dyad must consent to the initial interview. Patients and caregivers who refuse to participate will be asked their reasons for non-participation, which will be recorded, as well as basic sociodemographic information.

3. Consent Procedures.

The interviewer will meet with patient and caregiver together at their first home visit. First the interviewer will explain the purpose of the research, the procedures to be followed, the possible risks and benefits to the participant and to science. The voluntary, optional nature of participation is explained as well as the right to decline to answer particular questions or withdraw from the study without loss of any benefits to which they are otherwise entitled. The schedule of visits and methods to preserve confidentiality are described. The interviewer makes it clear that he/she will keep the reports of each member of the dyad entirely confidential and will not share any information with the

other. Finally, a consent form is presented for consideration, discussion and signature. By conducting this interview jointly, the two participants have the chance to fully explore their own and each other's concerns about participation.

4. Potential risks

There are three risk to participants. First, the interview may be tiring, especially for patients. Second, emotional distress may be triggered by questions about mood and end of life issues, including preferences regarding the circumstances of death. Patients and caregivers may find such questions uncomfortable, intrusive or stressful. Third, there is the risk of violation of confidentiality.

5. Risk Minimization Procedures

We are sensitive to the potentially tiring and distressing aspects of interviews about terminal illness and dying for people who are generally aware of their impending death. We have asked similar questions with ALS patients (Dr. Rabkin) and caregivers of AIDS patients (Dr. Folkman) and have found that they often welcome the opportunity to talk about these issues. We also ask about positive dimensions, which can be helpful for patients and caregivers to consider.

We have designed several steps to reduce the enumerated risks:

A. Trained clinicians. All interviewers will be mature RNs, MSWs, or master's level researchers with clinical experience. They will be directly supervised by Dr. Folkman and Ms. Richards in San Francisco, and Drs. Rabkin and Albert in New York. Weekly meetings will be held with interview staff to identify problems in administering interviews. The purpose of such meetings is to make sure that the staff is comfortable conducting the interviews, to identify interview questions that seem to be awkward or uncomfortable for respondents (and to revise them accordingly), and to serve as support for the interviewers themselves. If a need is indicated by interviewers in advance of the scheduled meeting, the study psychiatrist will be asked to attend as well.

B. Interviewer role defined. We will make it clear to the interviewers and the families that the interviewers are there to observe and gather information, not to intervene. The respondents may decline to answer a particular question or stop the interview at any point, without loss of benefits to which they are otherwise entitled and without necessarily ending their future participation. If the patient says he/she is too tired to continue, the interview will be terminated and resumed on another occasion.

C. Psychiatric support. We have included a psychiatrist as part of the research team at each site. He/she will be available for consultation with interviewers, and also for caregivers or patients who need or want consultation on a short-term basis, with subsequent referral as clinically indicated and financially feasible.

D. Alternative assessment techniques. We have designed "stepped-back" versions of interviews with patients as they get sicker, with priority given to measures of cognitive and physical functioning, depression, and positive mood. If patients or caregivers become tired or for other reasons wish to end the session, the interviewer will leave self-report scales to be returned by mail, and will either complete interview questions by telephone or subsequent visit within 48 hours.

E. Protection of Confidentiality. Standard measures to protect confidentiality of all research participants include coding all data and only entering study ID numbers, initials, and date of birth in computerized data bases. All records are kept in locked files in the investigators' offices with access limited to research staff. Only aggregate results are published.

In order to further protect confidentiality of patients, we will obtain a federal Certificate of Confidentiality:

6. Balance of risks and benefits

This study was not designed for the benefit of participants. However, the risk is minimal with the precautions we will have in place. The potential benefit to families and patients who confront the issues associated with terminal care at home and decisions regarding death and dying, will be considerable. To better understand death and dying, a significant issue in medical curricula and clinical practice these days, it is necessary to talk to persons who are dying and their caregiver relatives. In this study, we hope to gather essential information about this experience in order to increase the likelihood of "a good death ... one that is free of avoidable distress and suffering for patients, families and caregivers; in general accord with patients' and families' wishes; and reasonably consistent with clinical, cultural and ethical standards" as stated in the Institute of Medicine report entitled, "Approaching Death" (Field & Cassel, 1997).

F. Vertebrate Animals

Not applicable

G. Literature Cited

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H. Contractual/Consortium Agreement

The success of this study depends on our ability to recruit patients who are terminally ill with cancer or AIDS. To this end, Jeffrey Burack, MD, University of California, Berkeley, will be the liaison to the East Bay recruitment site, where he will oversee the local IRB processes, maintain relationship with the executive director, present to board of directors as needed, and work with the staff members who are responsible for coordinating recruitment for this study.

Collaboration plans between Dr. Folkman's and Dr. Rabkin's sites are described in the introduction to the Budget Justification Section on pg 9 and under the heading Cross Site Coordination in Section D pg 70 of this application. The text of these sections is identical in both applications.

I. Consultants and Shared Resources

1. Project specific consultants and collaborators: N/A.
2. IRPG interactions:

Description of interactive research activities

The description of interactive research activities is given on pp 64 of the Rabkin application and pp 70 of the Folkman application under the heading: Cross-site coordination. These descriptions are identical.

Program coordinator: Dr. Folkman is the program coordinator.

Shared resources: Resources are shared to the extent that most of the quantitative analyses and the development of the coding scheme for the qualitative analyses will be done at the San Francisco site, but the costs of these activities are borne by the San Francisco site alone. The two sites also share consultant resources. Dr. Breitbart (NY) will consult with the San Francisco site on

the identification delirium; Dr. Lo (SF) will provide advice to both sites on questions of medical ethics; and Dr. Wilson (SF) will be available to provide advice to both sites about structural characteristics of the health care system.