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UNIVERSITY OF SAN DIEGO
Hahn School of Nursing and Health Science
DOCTOR OF PHILOSOPHY IN NURSING

SYMPTOM BURDEN AT END OF LIFE- IN PATIENTS WITH
TERMINAL AND LIFE-THREATENING ILLNESS IN INTENSIVE CARE UNITS

By

Peggy G. Kalowes RN, MSN, CNS

A dissertation presented to the
FACULTY OF THE HAHN SCHOOL OF NURSING AND HEALTH SCIENCE
UNIVERSITY OF SAN DIEGO

In partial fulfillment of the
requirements for the degree of
DOCTOR OF PHILOSOPHY IN NURSING

April 2007

Dissertation Committee

Cynthia D. Connelly PhD, RN, FAAN, Chair

Jane Georges PhD, RN

Linda Urden DNSc, RN, CNA-BC, FAAN

Abstract

The purpose of this study was to examine the symptom burden and severity of symptom distress reported by ICU patients at high-risk for death and to compare patient-rated symptoms and distress for concordance with symptoms reported by a family member.

A prospective, correlational design with two data-points was used to study a convenience sample of 80 patients and 53 family members. The Condensed Memorial Symptom Assessment Scale (CMSAS) was used to gain patient/proxy report of symptoms on the first and third day after admission to the ICU.

The majority of patients were symptomatic (98%), reporting an average of 10.23 symptoms. Most common symptoms reported on Day-1, were lack of energy (fatigue) and difficulty concentrating, with a mean symptom distress score of 2.96 (SD = 0.70) and 2.79 (SD = 0.84), scored on a scale of 1 = low symptom distress to 4 = high symptom distress, respectively. The CMSAS Total Distress Score was 2.24 (SD=0.66). The Physiological Symptom Distress Subscale (CMSAS-PHYS) score was 2.19 (SD=0.71). Approximately 97.9% of patients reported psychologic symptoms (sadness, worry, nervousness) with a mean symptom distress score of 2.45 (SD=0.66), measured by the Psychological Symptom Distress Subscale (CMSAS-PSYCH). On Day-3, 65 of the patients were still in the ICU. The most prevalent symptom reported was difficulty sleeping (90.8%), with a medium intensity distress score of 3.79 (SD=1.06). Eighty percent of patients reported additional symptoms: lack of energy, lack of appetite, pain, dry mouth, feeling drowsy, shortness of breath, and difficulty concentrating, with a moderate intensity mean score of 3.42. Overall distress increased among all symptoms, as

measured by the CMSAS-Total Distress Score of 3.17 (SD=0.44), and the two distress subscales: CMSAS-PHYS mean score of 3.07 (SD=0.46) and CMSAS-PSYCH means score of 3.46 (SD=0.52). Hospital mortality was 17 (21%) during initial hospitalization and 16 (25%) at 3-months follow-up. Family members correctly estimated the presence and absence of symptoms 85.5% of the time, yet rated the patients' physiologic symptoms higher than psychological distress.

This study identified ICU patients *near death* experience a significant burden of multiple symptoms, yet receive limited treatment for significant symptom distress. A need for widespread institution of symptom management strategies with proven effectiveness is indicated. Further research is needed to develop and test new evidence-based interventions to serve as a practice standards in the delivery of consistent, high quality care for all dying patients.

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Dedication

This educational journey has been supported and encouraged by those nearest and dearest to me. I would like to dedicate this work to my husband, family and friends who have been there through every step of the way, as I have endeavored to complete this study and advanced degree.

Bob Kalowes, my husband whose *never ending* encouragement and support at just the right times, has helped me to achieve this life-long goal. My children, Jeff, Chris, and Cyndi and her husband Jonathan, who have been incredibly patient, supportive and always interested in my work.

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Jane Georges PhD, RN
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Chapter 1

Introduction

Overview of Problem

Improvements in medical science and healthcare have gradually changed the nature of dying (National Institutes of Health [NIH], 1999). Death is no longer most likely to be the sudden result of infection or injury, but is now more likely to occur slowly, in old age, and at the end of a period of life-limiting or chronic illness (Field & Cassel, 1997). As a result, a demographic shift is beginning to occur that will include an increase in the number of seriously ill and dying people requiring end-of-life care (EOLC), while the number of caregivers decreases. Faced with this challenge, the best evidence that science can offer must be applied to guarantee the quality of care provided to dying individuals and their surviving loved ones (National Institutes of Health, 1999).

Many end-of-life care (EOLC), experts as well as patients and families, consider effective symptom management along with the psychosocial and spiritual aspects of dying, as the essential components of excellent EOLC. Despite these goals, current evidence suggests the care that patients with cancer and terminal illness, receive at end-of-life (EOL) is sub-optimal. For example, recent studies indicate that care is often fragmented among providers and provider settings, leading to a lack of continuity of care

and impeding the ability to provide high-quality, multi-professional care (Clarke, Curtis, Luce, Levy, & Danis, 2003; Emanuel, 2006; Tranmer *et al.*, 2003; Treece, 2006; von Gunten, 2005; Walke, Byers, Gallo, Endrass, & Fried, 2007). Symptoms such as pain, nausea, and dyspnea are inadequately treated, while depression and delirium are often underdiagnosed; and conversations with patients and families about advance care planning occur late in the course of life-prolonging treatments, if discussed at all (Field & Cassel, 1997; Iwashyna, 2004; Jablonski, 2007; James, 2005). Although these problems were initially noted in the care of cancer patients, anecdotal evidence is beginning to emerge documenting similar problems in the care of patients for a number of chronic life-limiting illnesses, such as renal failure, heart failure, dementia, cirrhosis, and obstructive lung diseases (Barnes *et al.*, 2006; Jablonski, 2007; Kris & Dodd, 2004; Solano, Gomes, & Higginson, 2006; Weisbord *et al.*, 2003).

While there is a growing body of scientific inquiry addressing end-of-life care, covering a range of issues, the research is still in its infancy in terms of rigorous testing and evaluation of models of care, in terms of patient and family outcomes, resource utilization and measurement with respect to distressing symptoms other than pain (Nelson & Danis, 2001). To date, our current understanding of the symptom burden at EOL is derived primarily from studies recruiting individuals with cancer, with a paucity of research in critically ill patients with life-threatening illness, in intensive care units (ICUs). The symptom burden during critical illness has not been prospectively studied in a systematic way in any large cohort, despite the recommendations by NIH, National Institute of Nursing Research (NINR), and the Institute of Medicine (IOM). (Nelson & Danis, 2001; NIH Panel Final Statement: February 2005; Steinhauser, 2005; Tranmer *et*

al., 2003).

There is a need and desire to know the diverse and subjective symptom experiences of patients as it relates to their health, and the effects of treatment. The current study attempts to add to the body of knowledge of symptom management, as well as to close the scientific gap in understanding the symptom prevalence and burden among critically ill patients, from the real-time perspective of the patient through self-report. Only one such study of symptoms self-reported “in real time” by ICU patients, has been conducted by Nelson and colleagues (2001). Their empirical study of 100 cancer patients revealed a 56% mortality and multiple, unrelieved symptoms were common at significant levels of severity among survivors and non-survivors. Data of this type is particularly limited in ICUs, as it is commonly thought that critically ill patients cannot report their symptoms. This is surprising since the comfort needs of patients dying in other settings have received much attention. Yet, with respect to ICU, where mortality among patients with and without malignancy is typically high (20% to 40%), research relating to symptom prevalence and management remains scant (Allen, Haley, Small, & McMillan, 2001; Baggs & Schmitt, 2000; Ciccarello, 2003; Desbiens & Wu, 2000). An explanation and major challenge in research into care at EOL in ICU, is the difficulty of obtaining views and experiences of representative samples of patients, due to their critical condition (Allen et al., 2001). Patients often lack capacity, or become too critical to continue in a study, hence, attrition is high either by death or inability to continue. An alternative approach that overcomes this problem is the reliance on surrogate raters, through either a prospective or retrospective (after death) approach (Lobchuk, Degner, Chateau, & Hewitt, 2006). Generally, next-of-kin or significant others have had more exposure

seeing the patient cope with illness in a variety of situations and during a longer period (Lobchuk, Degner, Chateau, & Hewitt, 2006; Nekolaichuk et al., 1999).

One of the problems noted by most researchers in gathering information indirectly from proxies at a later point in time, is the introduction of potential problems regarding the validity of reports (Sulmasy & McIlvane, 2002; Teno, 2004). Validity in this context, refers to the degree to which proxy accounts accurately reflex the experiences of the individual they are representing (Heyland, Rocker, O'Callaghan, Dodek, & Cook, 2003.). At present, there are only limited studies regarding the accuracy of proxy responses, despite the fact that inaccuracy may compromise validity and lead to erroneous conclusions. According to Teno (2004), proxies are a significant source of information, and often the only sources for a large proportion of dying patients. Therefore, it is crucial to understand how and why their accounts might differ from those of the patient. Numerous authors have offered sound arguments for including a designated surrogate as proxy respondents on patients' illness experience (Coppolino & Ackerson, 2001; Desbiens & Mueller-Rizner, 2000; Hayes, 2003; Hickman, Tilden, & Tolle, 2001; Kane *et al.*, 2005; Kutner, Bryant, Beaty, & Fairclough, 2006). Results from some studies indicate that on the whole, there is more agreement concerning the more overt symptoms and aspects of the patient's functioning, for example immobility, activities of daily living, and for some, symptoms such as fatigue, difficulty sleeping, dyspnea, and vomiting (Hayes, 2003; Kane et al., 2005; Kutner et al., 2006; Lobchuk & Voraaurer, 2003). Others suggest that agreement seems to be poorest for subjective aspects of the patient's experience, such as pain, anxiety and depression (Addington-Hall & McPherson, 2001; Hickman et al., 2001), which are often some of the most distressing symptoms that

patients experience.

According to (Steinhauser, 2005; Steinhauser, Christakis, Clipp, McNeilly, & McIntyre, 2000), and Teno (2004) there are methodological challenges that plague both prospective and retrospective EOL data collection among terminal and acutely ill patients. Teno posits, that “An argument claiming that one method is superior is wrong. Rather, multiple methods, either combined or in sequence, are needed to examine a complex, multi-dimensional phenomenon such as end-of-life care” (p. 44). Prospective studies are primarily limited to diseases such as cancer that have an identifiable terminal phase, and where patients are likely to be known to relevant services and care, thus, there continues to be a gap in studies in real time among critically ill patients (McPherson & Addington-Hall, 2003). This is in part because of the inability of ICU clinicians to be able to accurately identify critically ill patients who will not survive, although numerous prognostic systems are available.

Clinical research involving critically ill patients is necessary to reduce the extreme morbidity and mortality encountered in the ICU setting. The most comprehensive approach to understanding the multiplicity of symptoms at the end-of-life, as noted previously, is to take into consideration information from multiple sources, including patients, family members and providers. Within such a framework, the present study included evaluation of the concordance and quality of proxy reporting (family respondent), since it varies by rater relationship, by EOL domain, and over time (Steinhauser, 2005). Proxy data will provide a more comprehensive approach to understanding the multidimensional nature of symptoms at EOL and their impact on different aspects of quality of life.

Current reports on the way people die indicate that the majority of older and seriously ill persons—one in five (~500,000) Americans— die in hospitals following treatment in the ICUs each year (Nelson *et al.*, 2006; Walke *et al.*, 2007; Wood & Ely, 2003). Unfortunately, data suggests that despite resource-intensive treatment, outcomes for many patients remain poor with high rates of mortality (15-40%), high symptom distress, and extreme functional dependence among survivors (Squires *et al.*, 2004). The frequency of death following ICU care is also high and has been reported to range from 6.1 to 27% (Azoulay *et al.*, 2003; Friedrich, Wilson, & Chant, 2006). Studies indicate that death after ICU discharge can be related to factors occurring before or after the ICU stay, and is usually associated with advanced age, poor chronic health status, severe comorbidities and often sepsis-related organ failure (Azoulay *et al.*, 2003; Laupland, Kirkpatrick, Kortbeek, & Zuege, 2006) The morbidity and mortality of critical illness underscores the need for effective clinical research.

Although the burden of critical illness is immense today, this trend will most likely accelerate, because according to the projections by the U.S. Census Bureau (2000), the population aged 85 years > is likely to grow from about 4 million in 2000 to 19 million by 2050. Changes in the way Americans die are mirrored in health care cost patterns. The overwhelming preponderance of U.S. health care costs now takes place in the final years of life (Berge, Maiers, & Schreiner, 2005). For example, in 2000, ICU expenditures represented 13.3% of hospital costs, 4.2% of national health expenditures, and 0.56% of the U.S. gross domestic product (GPD). According to a study generated by the Centers for Medicare and Medicaid Services, real inpatient expenditures for the Medicare fee-for-service population increased by 60 percent from \$58 billion in 1985 to

\$90 billion in 1999, one quarter of which were accrued by elderly decedents (Barnato & Angus, 2004). Furthermore, inpatient admissions to ICUs increased from 30.5 percent to 35.0 percent among decedents, along with a ten percent increase in the use of one or more intensive care procedures. Although Barnato & Angus findings indicate that the majority of patients who received intensive care procedures were survivors, it was noted in the analysis that in 1999, 50% of feeding tube placements, 60 % of intubations / tracheostomies, and 75% of cardiopulmonary resuscitations were in patients who died. These ICU procedures are somewhat emblematic of end-of-life care, and known to cause distress and suffering during critical illness.

Other studies have also provided anecdotal evidence that ICU patients are at risk for suffering considerable amount of pain and distress from their diseases, traumatic injuries, invasive ICU procedures, blood draws, and other routine care such as suctioning, turning, positioning, drain and catheter removal, and wound care (Nelson, Meier, Oei, Nierman, & Senzel, 2001; Novaes *et al.*, 2001; Puntillo, 2001). Additionally, data from studies conducted by (Rotondi, Lakshmipathi, & Sirio, 2002; Schelling, Richter, & Roozendall, 2003; Thomas, 2003) have further documented the physiological and psychological distress of ICU patients' unrelieved pain during their ICU stay.

According to the Medicare data presented by (Barnato, Mcclellan, Kagay, & Garber, 2004), one of the most frequent diseases noted in ICU patients is respiratory failure, (Diagnosis Related Group-DRG 475), which by definition is > 96 hours of prolonged mechanical ventilation in critically ill patients. Prolonged mechanical

Table 1

*Challenges of unrelieved pain***Physical suffering**

- ★ 40% of 80 post-ICU Acute Respiratory Distress Syndrome (ARDS) patients recalled having pain while in ICU
- ★ 40% higher frequency of chronic pain than in the controls'
- ★ 87% of 97 post-ventilation patients remembered being moderately to extremely bothered by pain

Psychic suffering

- ★ Significantly higher Post-Traumatic Stress Disorder (PTSD) scores in post-ICU ARDS patients than in controls (28% vs 12%)
- ★ Traumatic memories associated with pain after cardiac surgery (81.6% of 184 patients)
- ★ Dyspnea, anxiety fear, and pain perceived by mechanically ventilated patients causing a stressful experience 42%-56%

Modified and reprinted with permission from K. Puntillo, UCSF, School of Nursing, March 2007.

ventilation and subsequent ARDS are contributing factors causing increased length of stay (LOS), increased costs and increased suffering and distress, as noted in Table 1. This further highlights the disparity of care in the prospective management of individuals with multiple co-morbidities throughout their illness trajectory; and flaws inherent in a system that cannot even provide comfort and pain relief in society's most vulnerable subjects, according to the domains of quality end-of-life care (Wolff, Starfield, & Anderson, 2002).

Domains of Quality Care at End of Life

Advancing the science of end-of-life care requires knowledge and a foundation of clear domains and variables to guide research and clinical practice (Ferrell, 2005).

Numerous researchers, organizations, and expert clinicians—including the professions of nursing, medicine, social work, psychology, and clergy—have collaborated together to conceptualize the important domains that should be addressed by high-quality care at

EOL and hence by measures of quality. While experts do not agree on a single best conception, most domains and variables overlap considerably to provide uniformity for quality clinical care and services and shared measures of quality care (Clarke et al., 2003; Ferrell, 2005). Table 2 provides an overview of the various organizations and expert groups which have identified key domains of quality EOL care, through a rigorous, scientific and consensus process.

Although, the extent of activity in developing and testing quality measures is encouraging, much more is needed to assess and improve the EOL care received by the elderly and those with advanced life-limiting illness, known to spend their last days and hours in ICUs. These domains of end-of-life care were used as a framework to explore the variables and concepts relevant to symptom burden in critically ill patients/and families, where death may be near. The broad domains addressed in the current study can be seen in Table 3.

Table 2

Comparison of Quality Indicators for End-of-Life Care (EOLC) Domains Identified Across Select Sources

<i>NCP Domains¹</i>	<i>NHPCO²</i>	<i>Emanuel and Emanuel³</i>	<i>AGS⁴</i>	<i>NCCN⁵</i>	<i>Institute of Medicine (IOM)⁶</i>	<i>RWJF Critical Care End-of-Life Peer Work Group⁷</i>
Structure and Processes of Care			Patient and family expectations; Survival time; Provider continuity & skill	Palliative care assessment; Early referral for palliative care	Improve environment and structure; provider continuity & skill;	Continuity of care Communication within team and with patients and families
Physical Aspects of Care	Safe and comfortable dying	Physical symptoms	Physical and symptoms	Management of key symptoms pain; dyspnea; anorexia/cachexia; fatigue	Physical well-being and functioning	Symptom management and comfort care Standardize & follow best clinical practices for symptom management
Psychological and Psychiatric Aspects of Care	Self-determined life closure; Effective grieving	Psychological and cognitive symptoms	Psychosocial/Emotional symptoms Global QOL	Management of delirium; After-death care / bereavement	Psychosocial well-being and functioning	Emotional and practical support for patients and families Emotional & organizational support for ICU clinic
Social Aspects of Care	Safe and comfortable dying	Economic demands and care-giving needs; Social relationships and support	Support of function and autonomy; family burden	Resource management, social support	Psychosocial well-being and functioning	
Spiritual, Religious, and Existential Aspects		Spiritual and existential beliefs			Spiritual and Cultural well-being	Spiritual support for patients and families
Cultural Aspects						
Care of the Imminently Dying			Lack of aggressive care near death	Imminently dying	Relieve symptoms	Provide comprehensive comfort care to patient /family
Ethical and Legal Aspects of Care		Hopes and expectations	Advance care planning	Advance care planning; "Special" palliative care (PC) interventions	Advance care planning; PC interventions	Patient and family-centered decision making

1) National Consensus Project (National Consensus, 2004); 2) National Hospice and Palliative Care Organization (National Hospice and Palliative Care, 2002); 3) (Emanuel & Emanuel, 1998); 4) American Geriatrics Society (AGS) (American Geriatrics Society, 1997); 5) IOM (Institute of Medicine, 1997); 6) Robert Wood Johnson Foundation (RWJF) Critical Care End-of-Life Peer Work Group (Clarke et al., 2003)

Table 3

Domains of Quality End-of-Life Care

Broad Domains Used In Study
<ul style="list-style-type: none"> • Structure and Processes of Care / Continuity of Care / Communication within Team and with Patients/ Families • Symptom Management / Physical Aspects of Care • Psychological and Psychiatric Aspects of Care • Emotional / Social Aspects of Care • Cultural Aspects of Care • Care of the Imminently Dying Patient • Ethical and Legal Aspects of Care/Patient & Family Centered Decision Making
National Consensus Guidelines, 2004; (Clarke et al., 2003)

Conceptual Framework—Symptom Management Model

In order to explore the scope of the multidimensional nature of the symptom experience among critically ill patients, a broad-based theoretical framework is necessary. The University of California, San Francisco (UCSF) School of Nursing, Symptom Management Conceptual Model (see Figure 1) guided this study (Dodd *et al.*, 2001). In this model, a *symptom* is defined as “a subjective experience reflecting changes in the biopsychosocial functioning, sensations, or cognition of an individual” (Dodd *et al.*, 2001, p.669). Three interrelated dimensions, the symptom experience, symptom management strategies, and symptom outcomes, characterize the model.

Two important components of the symptom experience are symptom evaluation and response (Dodd et al., 2001; Larson, Uchinuno, Izumi, Kawano, & Takemoto, 1999; Larson, Carrieri-Kohlman, & Dodd, 1994). Symptom evaluation refers to how individuals describe their symptoms, for example, in terms of frequency, duration, intensity and distress. Symptom response includes physiological, emotional, and/or behavioral reactions to a symptom, such as physical, cognitive, and affective alterations.

Viewed in the context of the model, the symptom experience influences both symptom management and symptom outcomes.

Successful management of a troubling symptom usually requires a partnership between the patient and the healthcare provider (Dodd et al., 2001; Larson et al., 1999). Self-management strategies are those practices initiated or maintained by the patient to control the symptom experience and outcomes and may include recommendations from the healthcare provider and family. Self-management strategies may or may not be based on scientific evidence and are often derived from experience with trial and error and suggestions of family and friends. Symptom management strategies on the other hand, influence both the symptom experience and symptom outcomes (Larson et al., 1999).

Symptom outcomes are the third dimension of the symptom management model (Dodd et al., 2001). Symptom outcomes are assumed to influence both the symptom experience and self-management strategies.

In the current study, the three components of the symptom experience were assessed via a self-report method, using the Condensed Memorial Symptom Assessment Survey (CMSAS) (Chang, Hwang, Kasimis, & Thaler, 2004). The identification of symptoms is determined by the patient's identification of the presence or absence of symptoms. The evaluation of prevalence, intensity, and distress are assessed to characterize the symptom experience. Although degree of distress is not clearly specified in the SMCM, in this study the degree of distress caused by symptoms is considered a psychological response to symptoms. Symptom distress has been defined as patient reported discomfort in relation to their perception of the symptom experience (McCorkle & Young, 1978) and has been characterized as the physical or mental suffering that

results from the symptom experience and/or the perception of feeling states (Rhodes & Watson, 1987). In the critical care setting, there are numerous procedures/treatments, including nursing care commonly performed on critically ill patients. Yet, little is known about the patient's pain perception and distress, nor their responsiveness across procedures in ICU, despite the high use of procedures in dying patients (Barnato et al., 2004; Nelson et al., 2001; Puntillo, 2001; Puntillo, 1990). In order to capture patients distress related to their ICU care, patients in the current study were also asked to complete a Treatment and Procedure Survey (TPS) on day-3 of their ICU stay, in order gain a more comprehensive assessment of patients suffering and distress, related to ICU treatments and environmental risks.

Figure 1 provides a schematic presentation of the UCSF's Symptom Management Conceptual Model (SMCM). Symptom status is considered the central outcome of the model.

Patients' Responses to Symptoms

Figure 1. University of California, San Francisco, School of Nursing Symptom Management Conceptual Model

Significance of the Study

The huge human and financial costs of critical illness creates a pressing need for a sound research base on the epidemiology of various diseases among critically ill patients, during their dying trajectory, so that care can be customized based on age, co-morbidities, anticipated outcomes and patient/family preferences (Wolff et al., 2002; Wood & Marik, 2004; Wu, 1995; Wu *et al.*, 2002). While the symptom profile and experience for patients with cancer has garnered much attention in the literature, characterization of the symptom experience of patients with chronic, critical illnesses at EOL has received minimal attention. Care of the dying has become a focus of intense attention both inside and outside the medical and nursing profession. According to the IOM 1997 report, the rights of elderly and dying individuals to have autonomy, integrity, safety, quality of care and freedom of choice, in their medical care has never been greater (Field & Cassel, 1997). Prospective research studies are needed to examine the symptom experience and distress, as reported by the ICU patients, given the high morbidity associated with ICUs (Cook, Giacomini, Johnson, & Willms, 1999; Cook, Rocker, & Heyland, 2004).

The current study is one of the first to extend the work of Nelson and colleagues (2001) who first examined the symptom experience of cancer patients in ICU (2001), and most recently examined the symptom burden, ventilator outcomes and functional status at discharge, in a small, cohort of chronic critically ill (CCI) patients in a respiratory ICU (Nelson *et al.*, 2004). In the later study, results indicated that seventy-two percent (36 of 50) of patients were able to self-report symptoms during the period of respiratory care unit treatment. Results indicated that approximately 90% were symptomatic. Forty-four

percent of patients reported having pain at the highest levels, while more than 60% reported psychological symptoms at these levels; and 90% of patients reported severe distress due to communication difficulties (2004).

Finally, the current research adds to the science of end-of-life research by enhancing the body of literature of earlier empirical studies on symptom burden (Klinkenberg, Willems, Wal, & Deeg, 2004; Kris & Dodd, 2004; Tilden, Tolle, Drach, & Hickman, 2002; Tranmer et al., 2003).

Purpose of the Study

The purpose of this exploratory study was to explore the symptom burden at end-of-life in critically ill patients with life-limiting illness in ICUs; and to examine the relationships among variables related to patient (age, gender, physiologic acuity, previous health status), symptom distress and overall mortality.

Study Aims

***Aim #1:** Examine the perceived symptom burden (prevalence, intensity, frequency), and overall distress, as reported by ICU patients with complex disease states, at high-risk for dying.*

***Aim #2:** Examine the relationships between the independent variables of demographic characteristics, antecedent conditions, and the dependent variable of symptom burden and overall distress using the (CMSAS-PSYCH and CMSAS-SUM Subscales).*

***Aim #3:** Explore the relationship between symptom distress and overall patient mortality.*

***Aim #4:** To compare the critically-ill patient-rated symptoms (prevalence, intensity, frequency) and distress scores for concordance, with those rated by designated surrogate-responders. This will provide a more comprehensive approach to understanding the differences in various raters, regarding the multidimensional nature of symptoms at EOL and their impact on different aspects of quality of life. (Dependent Variable)*

Nursing Implications

The proposed research study is an essential first step towards informing nursing science by filling in the gaps of our knowledge surrounding the multidimensional nature of the symptom burden of critically ill patients with multiple diagnoses. Quite often, patients are admitted to the ICUs to receive treatment aimed at prolonging life, yet, because of the patients advanced disease state these treatments may only prolong dying, while patients experience pain and other distressing symptoms. The SMCM guided this study, and was characterized in this review to present how the symptom experience / burden was studied to achieve the aims of the research protocol. Previous research has indicated that EOL research is still in its infancy, therefore, there is a need to understand, interpret and measure the symptom experience in frail and vulnerable populations, who are at risk for extreme suffering and stress, or death. Knowledge of symptom prevalence and burden can enable interdisciplinary teams to help in the identification of patients' needs in terms of interventions to relieve symptoms' and service provision to patients/families so that strategies can be targeted to achieve the desired outcome of increased quality of life at end of life.

Chapter 2

Review of the Literature

The purpose of this chapter was to review and critique literature focused on the symptom experience for critically ill patients and families at end-of-life. It gives a comprehensive overview of the current state-of-the-science research on EOL and symptom measurement among patients with cancer and non-cancer disease states, particularly those cared for across care settings. The explanation of the method used for the literature review is presented in the first section. While the second section examines the historical context of end-of-life research, gaps in science related to symptom research in non-cancer patients, particularly those cared for in intensive care units and the impetus for reform in end-of-life care. In the third section, the UCSF Symptom Management Conceptual Model (SMCM) is portrayed to illuminate factors such as disease, demographic information, physiologic acuity, and the risk for dying; thought to influence the symptom experience. The final section analyzes and synthesizes the literature on the variables specific to this study, including symptom burden (prevalence, intensity, frequency) and distress; antecedent conditions, morbidity and mortality, age, gender and symptom experience perceived by patient and proxy assessment.

Method of Literature Review

To establish a thorough review of the extant literature the following steps were taken. An electronic search was conducted among the following databases of MEDLINE, EMBASE, CINAHL, ERIC, Ageline, PsychInfo, and Sociological Abstracts for published articles that reported on symptom burden, individual symptoms, symptom clusters, end-of-life experience in cancer and non-cancer diseases and critical illness, that went beyond mortality data. The key words used for the article search strategy included key words, title, or abstract, such as symptoms, symptom experience, symptom assessment, symptom distress, death, dying, measurement, end-of-life care, intensive care unit, intensive care, critical care, critical illness, critical care medicine, critical care nursing, mortality rate, palliative care, pain, pain measures, mechanical ventilation, cancer, dyspnea, quality of life, prognostication models, self-report, and symptom instruments. In addition, author searches were done, which yielded further research articles.

The list was then limited to English-language articles relevant to symptom experience, symptom distress, pain, suffering, dying and hospitalized acutely ill and terminal patients, and the intensive care units, reduced the number to 524. Limiting the search further to articles to exclude children and adolescents eliminated 152 studies, yielding 372 studies for review.

After the initial electronic database searches, hand searches were also conducted of the citations in the reference lists of relevant articles. Electronically searchable meeting abstracts (e.g. Society for Critical Care Medicine, American Association of Critical Care Nurses, Trauma Nurses Society, American Society of Clinical Oncology,

Oncology Nursing Society, Hospice and Palliative Care Association, Medical-Surgical Nurses Association, American Society for Pain Management, Chest Society), and printed proceedings (e.g., University of California, San Francisco, Symptom Management Symposia; Western Institute of Nursing Assemblies; Sigma Theta Tau International), also were examined. Book chapters, editorials, and presentations that did not report research were excluded. Eliminating dissertations and theses in which the operationalization of symptoms, critical care, dying, end-of-life could not be determined from the abstract further reduced the list. The research articles included instrument validation, descriptive and exploratory, intervention, and evaluation studies.

The literature synthesis highlights the many issues related to the care of chronic and critically ill patients with life-limiting illness-approaching end-of-life. Future research is necessary, in order to further develop a multiple interventional approach to reduce the symptom burden and improve the quality of care and the death experience, for a rapidly growing population of frail, high-risk patients receiving treatment in intensive care units.

Symptom Experience at End-of-Life

Although death is an inevitable fact of life, the experience of a peaceful death is not. The final days of life are frequently marked by needless physical, emotional, and spiritual suffering (Field & Cassel, 1997; Hanson, 1997). Despite the availability of effective management strategies across care settings, unrelieved symptoms continue to be a major source of distress for both patients and families throughout the illness trajectory. The fact that symptoms often go unrecognized, under-diagnosed, and under-treated has become a concern of healthcare professionals, researchers, policymakers, and the public

at large. This has resulted in a number of initiatives being launched in recent years aimed at improving the quality of EOL care, particularly in the area of symptom management (Last Acts, 2002; National Institutes of Health, 1999).

According to the literature, the quality of care and quality of life changes substantially for those with a serious chronic illness and nearing the end of their lives (Field & Cassel, 1997; Teno, Byock, & Field, 1999; Teno, Field, & Byock, 2001). As one dies, life takes on new shape—values change and things once ignored become more important. Existing quality of care measures do not attend to the changes in priorities or to dimensions that acquire new significance (e.g., spirituality and transcendence) for patients and families. An important barrier to addressing the inadequacies in the evidence base for palliative care, improving shortcomings of care, and holding institutions or health care systems accountable for the quality of care at EOL, is the lack of valid and reliable measurement tools, and the lack of inclusion of critically ill patients in empirical studies (Tonelli, 2005). Inclusion of acute and critically ill patients is of particular importance, since there is wide recognition that the principles of palliative care should be applied as early as possible in the course of any chronic, ultimately fatal illness.

Understanding the patient's symptom burden in critical illness will allow clinicians to understand the dying experience and offer palliative care throughout the hospitalization. According to the World Health Organization (WHO), *palliative care* can be defined as:

Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable

assessment and treatment of pain and other problems, physical, psychosocial and spiritual (WHO, 2002).

Definitions of palliative care and descriptions of a good death would suggest great sensitivity to the physiological, psychosocial, existential, and spiritual aspects of patient well-being. Yet, in spite of this, there are aspects of EOL distress that are not routinely assessed, let alone effectively treated or managed, particularly in ICUs (Chang, Thaler, Polyak, Lepore, & Portenoy, 1998; Chochinov, 2006). Few studies have addressed the gaps in understanding the suffering at EOL, nor other antecedent conditions, that may influence a patients' perception of suffering, particularly in patients with life-limiting illness in ICUs. Anecdotal studies, such as a recent report by Abraham, Kutner, & Beaty (2006), have shown that factors other than physical symptom distress, such as diagnosis, age, and quality of life (QOL) appear to affect the perception of suffering. While study findings are extremely important and contribute to our understanding of the dying experience, the study population was drawn from a large population-based hospice program, thus, it is limited to primarily cancer patients (Abraham, Kutner, & Beaty, 2006).

According to the WHO, end-of-life care is defined as "the active, total care of patients whose disease is not responsive to curative treatment. The philosophy of this care is to attain maximal QOL through control of the myriad physical, psychological, social, and spiritual distress of the patient and family" (World Health Organization, 1998). Although the imperative of care is providing optimal symptom relief and alleviation of suffering, there is clear evidence in the current medical literature that we are failing to do this. For example, despite wide dissemination of pain management guidelines, many

patients with lung cancer and other diseases continue to suffer not only from pain, but also from other troubling symptoms and interpersonal scenarios in their final days (Desbiens, Mueller-Rizner, Connors, Wenger, & Lynn, 1999; Doorenbos, Given, Given, & Verbitsky, 2006; Walsh, Donnelly, & Rybicki, 2000; Wolff, Dy, Frick, & Kasper, 2007).

Although the symptom experience is complex and multifaceted, knowledge of it has been limited by a paradigm that has been mostly directed toward studying a limited number of symptoms, such as pain or fatigue, rather than total symptom burden in this patient population (Beck, 2004; Becker, 2006; Dodd et al., 2001). Thus, gaps in knowledge exist concerning *symptom burden*, which includes the prevalence and severity of physical and psychological symptoms and their relationship to interference of life in patients, with chronic and life-limiting illnesses. Large well-designed, well-controlled prospective studies in non-cancer patients, particularly those hospitalized and in the ICUs, have not been performed to date (Kirkova *et al.*, 2006; von Gunten, 2005). In fact, most of the existing evidence regarding symptom burden for this review has been gleaned from high-quality studies among ambulatory care, hospice and palliative care populations (Bowman, Martin, & Singer, 2000; Bradley, Fried, Kasl, & Idler, 2000; Chang et al., 1998; Cleeland *et al.*, 2000; Degner & Sloan, 1995; Doorenbos *et al.*, 2005; Gift, Stommel, Jablonski, & Given, 2003). While some progress has been made in studying hospitalized patients with non-cancer conditions, the lack of evidence base is disturbing, given that over 1 million Americans die in hospitals today. Thus, definitive studies are needed to study the epidemiology of the symptom experience at EOL, in order to implement measures to relieve symptoms in terminally ill and improve the dying

experience for patients and families (von Gunten, 2005; Wood & Ely, 2003; Wood & Marik, 2004; Zimmerman, Kramer, McNair, & Malila, 2006).

Theories of symptom experiences and symptom management in nursing describe and explain clinical phenomena and serve as a foundation for planning, implementing, or evaluating effective management protocols (Hegyvary, 1993; Lenz, Pugh, Milligan, Gift, & Suppe, 1997). Understanding the interaction of the components of the symptom experience is essential, along with critical measurement of outcomes of symptom distress, as the suffering experienced by dying patients extends beyond just the physical distress, but also includes the emotional, social and spiritual dimensions (Lobchuk & Degner, 2002). The symptom experience is the individual's perception of the symptom, evaluation of its meaning and subsequent response. Because the SMCM is broad and extensive, it provides a framework by linkage of the concepts, to guide the assessment of the symptom experience (see Figure 1). This model also facilitates understanding the impact of any of the antecedent conditions influencing a persons' response or distress, thus, the outcomes as well (Armstrong, 2003). For the purposes of this study, the *antecedents* to the production of the symptoms experience in critically ill patients have been broadly classified as demographic characteristics (age, gender) disease characteristics (disease type, co-morbid conditions, severity of illness) and individual characteristics (previous health status).

Organizing the findings of previous research within the context of the symptom management model provided a lens to elucidate the gaps in our current knowledge regarding the symptom experience of critically ill patients at end-of-life.

Symptom Prevalence

Discussion of symptoms, and the accompanying distress experienced at end-of-life, are often confined to physical symptoms (Teno, Weitzen, & et al, 2001; Yennurajalingam, Braith, & et al, 2005). However, psychological symptoms and distress may also be present (Ahlberg, Ekman, Wallgren, & Johansson-Gaston, 2004; Andenaes, Kalfoss, & Wahl, 2004). Also, suffering can arise from social and spiritual problems (Chochinov, 2006; McMillan, 1996; Steinhauser & et al., 2000).

Symptom assessment is important because the prevalence of symptoms influence a patient's distress, QOL, and survival. Yet, symptom assessment is challenging because of the evolving course of cancer, and other progressive, chronic diseases. Symptoms are disease related, treatment related, related to concurrent comorbid illnesses, or a combination of all three (Oi-Ling, Man-Wah, & Hung-Kam, 2005). Although there are a number of existing valid instruments to assess the symptom experience in cancer patients, few instruments have been tested in prevalent non-cancer conditions or among ICU patients (Bergner, Bobbitt, & Carter, 1981; Bruera, Kuehn, Miller, Selmser, & Macmillan, 1991; Emanuel, Fairclough, Slutsman, & Emanuel, 2000; Portenoy *et al.*, 1994; Rhodes, McDaniel, Homan, Johnson, & Madsen, 2000). Related methodological issues include assessing patients with dementia or acute cognitive impairment and better understanding of the opportunities, yet limitations of proxy response (Steinhauser, Clipp, & Tulsky, 2002). Another barrier in measurement of symptoms in critically ill patients is that most existing valid, self-report, instruments have a range of 16 to 50 questions, and take between 15 to 45 minutes to complete, which may cause extreme fatigue and harm in critically ill patients. Hence, this is in part an explanation for the lack of research using

self-report instruments among ICU patients to date. Most measures need to be refined, validated for dying elderly patients with non-cancer, and tested for responsiveness to changes in the items being measured (Emanuel, 2000).

Symptoms have been relatively well-characterized in cancer, with most studies revealing a high symptom burden (Adenaes, Kalfoss, & Wahl, 2004; Ahlberg et al., 2004; Allen et al., 2001; Arnold & Liao, 2006; Barnes et al., 2006; Doorenbos et al., 2006; Ellershaw & Ward, 2003; Walke et al., 2007; Walsh et al., 2000). However, high quality studies of the incidence, epidemiology of pain and other symptoms, including the relationship among symptoms, and the clinical significance of symptoms remain sparse, among other life-limiting illnesses, such as congestive heart failure (CHF), end-stage renal disease (ESRD), chronic obstructive pulmonary disease (COPD), liver failure, and dementia, particularly in the intensive care units.

Recently, (Kirkova et al., 2006), conducted a systematic review for cancer symptom assessment instruments, where twenty-eight prevalence/incidence (severity and/or symptom burden) studies were identified. Among these studies, symptom prevalence and severity were the main determinants of symptom burden (2006). Twenty-one of the studies were prospective studies, nine were longitudinal, and one was a randomized, controlled trial (RCT). Seven studies included cancer and noncancer patients, one was particular to hospice patients. Out of the 21, only eight used validated symptom assessment instruments, three were original, and the rest modified (Kirkova et al., 2006). The remaining 21 studies used nonvalidated symptom checklists containing 4 to 38 symptoms (2006). Only one study in this review, involved consecutive patients in a prospective design with a modified validated instrument. According to Kirkova and

colleagues (2006), “Symptom lists varied among the surveys, however, anorexia, dry mouth, fatigue, lack of energy, pain, shortness of breath, and weight loss, were included consistently. The mean number of symptoms reported per patient ranged from ($\pm$ two) to ($\pm$ six)” (p. 1461). Findings noted in this systematic review suggest that symptom prevalence and burden among cancer and non-cancer patients is very high, and that designs of symptom prevalence studies need to be improved, because of the methodological disparities in symptom assessment and designs.

In another study, Potter, Hami, Bryan & Quigley (2003), examined the demographics and prevalence of symptoms in patients ($n=400$) referred to various palliative care services, in London. In this study, ninety five percent (380/400) had cancer. Moreover, the five most prevalent symptoms overall were pain (64%), anorexia (34%), constipation (32%), weakness (32%) and dyspnea (31%), which is similar to other published reports among hospice/palliative care services including out-patient and in-hospital. Overall, the range of symptoms was from (± 3) to (± 7.21). Among this cohort significant differences in symptom prevalence occurred, most likely because there were marked differences across the sub-groups and settings, however, most interestingly, the majority of patients did not have advanced disease. Differences in symptom prevalence may also have been related to the lack of use of a valid symptom-rated instrument, since a standardized profoma (checklist) was used, along with qualitative notes in each setting Potter et al., (2003). While study findings suggest high symptom burden among cancer patients, more rigorous research is needed among palliative care teams, to glean more generalizable results, and to aid in providing appropriate interventions and planning of services (Potter, Hami, Bryan, & Quigley, 2003).

Doorenbos, Given, Given, & Verbitsky (2006) examined study subjects ($n=174$), by secondary analysis of data from three prospective, descriptive, longitudinal studies of individuals with cancer (Doorenbos et al., 2006). “The purpose of this study was to examine the symptom burden during the last year of life, and to determine if symptom experiences change with proximity to death, or differs by depressive, symptomatology, sex, site of cancer, or age” (p. 403). Fatigue, weakness, pain, shortness of breath, and cough were the most prevalent symptoms (2006). In addition, data revealed that the symptom experience in the last year of life was significantly associated with site of cancer, depression, dependencies in activities of daily living (ADL) and functional independence (Doorenbos et al., 2006). The SMCM guided this inquiry, examining the *person* domain (age, sex) (Doorenbos et al., 2006). Characteristics from the *health/illness* domain included depressive symptomatology, site of cancer and ADL and functional independence (2006). Insights from this exploration study provide clinicians with a greater understanding of the multiplicity of symptoms and related symptom burden, throughout the dying trajectory, and as death approaches. With a greater understanding of the symptom experience, intervention strategies reflected in the SMCM as the domain of symptom management, can be targeted to achieve the desired outcome of the increased QOL at end-of-life. A limitation of this study is that while data analysis is pooled from three longitudinal descriptive studies, the sample size ($n=174$) remains small, and limited to cancer patients. Most likely increasing the sample size would allow greater differentiation between the various cancer diagnoses.

While research among cancer patients is robust, only a few recent studies have addressed the symptom management needs of patients with other life-threatening

diseases, even though these cause three of four deaths in developing countries. Some studies suggest that people with noncancer conditions experience a similar degree of symptom distress as cancer patients, and would benefit from a more holistic, inclusive, and supportive care network (Dudgeon, Kristjanson, Sloan, Lertzman, & Clement, 2001; Dudgeon & Lertzman, 1998; Dudgeon, Lertzman, & Askew, 2001; Mancini & Body, 1999; Soares *et al.*, 2006; Solano *et al.*, 2006; Stromgren *et al.*, 2006; Tranmer *et al.*, 2003).

For example, recently Solano, Gomes & Higginson (2005) conducted a systematic review of medical databases, to determine to what extent patients with progressive chronic diseases have similar symptom profiles. The review yielded 64 original studies reporting the prevalence of 11 common symptoms among end-stage patients with cancer, acquired immunodeficiency syndrome (AIDS), heart disease, chronic obstructive pulmonary disease, or renal disease. Data was extracted into a comparative table, where analysis revealed the prevalence of 11 symptoms, which were often widely but homogeneously spread across the five diseases (2005). Three symptoms—pain, breathlessness, and fatigue—were found among more than 50% of patients, for all five diseases, which is consistent within the current literature review. There appears to be a common pathway toward death for malignant and nonmalignant diseases, which creates the need for introduction of palliative care early in the disease trajectory (Solano *et al.*, 2006).

Although variable evidence is emerging, which recognizes that persons with chronic disease experience a large number of symptoms (Tranmer *et al.*, 2003), most of these studies have examined the association of a limited number of symptoms, including

pain, fatigue, and dyspnea, with a single health outcome (Adenaes et al., 2004; Ahlberg et al., 2004; Hewitt, Smeeth, Bulpitt, Tulloch, & Fletcher, 2005; Heyland, Rocker, & Dodek, 2002). Developing a targeted approach to symptom management based on evidence, is the best means of addressing this challenge. If symptoms are considered as potentially modifiable risk factors for a range of health-related outcomes, strategies could be directed to decrease symptoms morbidity and thereby enhance their quality of life (Walke et al., (2007).

The study done by Walke and colleagues (2007), attempted to determine the association of a range of symptoms with quality of life, self-rated health, and functional status among chronically-ill, community-dwelling adults ($n=226$), and to assess methods for evaluating the independent associations of symptoms that may be interrelated. Seven symptoms (physical discomfort, pain, fatigue, problems with appetite, feelings of depression, anxiety, and shortness of breath) were assessed, using the Edmonton Symptom Assessment Scale (Bruera et al., 1991), and were examined for their association with self-rated quality of life, self-rated health, and functional status (Walke et al., 2007) .

Principal component analysis and logistic regression revealed similar results. The latter demonstrated that physical discomfort was associated with lower self-rated health and functional disability. Feelings of depression were associated with poorer quality of life, and shortness of breath was associated with lower self-rated health. The association between a range of symptoms and quality of life, self-rated health, and functional status differed across outcomes, but only three symptoms—physical discomfort, feelings of depression, and shortness of

breath—maintained their associations when multiple symptoms were examined concurrently. These findings suggest that interventions targeting these symptoms could improve several health-related outcomes (p. 58).

Pain, which has been the focus of much investigation (Arbour, 2000; Bonham, 2001; Ellershaw, 2001; Feldt, 2004), has also been shown to be associated with poor quality of life, low self-rated health and disability. The results of Walke et al., (2007) study in contrast, showed that when compared to pain, physical discomfort had a *higher prevalence* and *stronger associations* with quality of life, self-rated health, and functional status. In addition, feelings of depression were associated with poorer quality of life in chronically ill adults. Further studies are needed, particularly randomized clinical trials (RCTs); clinical controlled trials (CCTs), and intervention studies, to rigorously test symptom management strategies to improve the QOL among patients with advanced diseases. An overarching goal, would be to prevent frequent hospitalizations for patients with advanced, life-limiting diseases, through rigorous symptom management, and reduce suffering and mortality among a rapidly, growing number of aging adults (Casarett, 2005; Desbiens & Mueller-Rizner, 2000; Desbiens & Wu, 2000).

As noted, evidence continues to suggest that we are not rigorously managing patients' symptoms to reduce pain and suffering in any healthcare setting. Data reflects that patients have a high symptom burden in most palliative care settings, and in the acute care hospital, where evidence-based therapies are prescribed and available (Paice, Muir & Shott, 2004). For example, in a quantitative study ($n=134$) conducted by Kris & Dodd (2004), data showed that hospitalized medical-surgical patients reported multiple symptoms (average of 9.3) and had high levels of symptom distress. The most commonly

reported symptoms in this study included pain ($n=242$, 74.0%) and dryness of the mouth ($n=218$, 66.5%). The next most commonly reported symptoms appear to be somewhat interrelated: lack of energy ($n=193$, 58.3%), difficulty sleeping ($n=181$, 55.4%) and feeling drowsy ($n=162$, 49.7%) (Kris & Dodd, 2004). Another important aspect of this study, interestingly, was that pain was the only symptom that ranked consistently high in frequency, severity and distress. While standards issued by the Joint Commission on the Accreditation of Healthcare Organizations have required assessment and intervention to alleviate pain since 2001, pain management continues to be inadequate (2004). These findings suggest poor management of pain, despite available therapies (Kutner et al., 2006; Tranmer et al., 2003). Most authorities believe that by using medications that are readily available, the American health care system has the means at hand to decrease the pain and suffering of patients in hospitals and nursing homes. What has been lacking is sensitivity to the issue and determination to solve it. The failure of our health care system to address pain and suffering seriously is a major ethical issue for our times (Desbiens & Wu, 2000). The public and the legal profession are quickly becoming aware of the failure of medicine to pay adequate attention to its traditional nemeses—pain and suffering (Rocker & Curtis, 2003).

Specific Symptoms

Dyspnea

Dyspnea is a source of distress for 21-70% of dying patients in the days and weeks prior to death (Burdon, Pain, Rubinfeld, & Nana, 1994; Desbiens, Riznera, Connorsb, & Wengerc, 1997; Desbiens & Wu, 2000; Paice, 2004), particularly in patients with advanced cancer. A complex physiological and psychological sensation, its causes

are often multifactorial, including the underlying disease, cachexia, and deconditioning (Bruera, Schmitz B, J., Neumann, & Hanson, 2000; Hall, 2004; Mosenthal & Lee, 2002). Dyspnea can be caused by chemical (oxygen and carbon dioxide levels in the blood), mechanical (airway obstruction), or emotional (increased anxiety or panic) factors (Tanaka, Akechi, Okuyama, Nishiwaki, & Uchitomi, 2002; Tarzian, 2000). Dyspnea presents multiple challenges to the clinician, due to its poorly understood pathophysiology, subjective nature and lack of correlation between its severity and objective measurements such as oxygen saturation and pulmonary function tests. Furthermore, multiple psychological, spiritual, social and emotional factors may impact the patient's perception and expression of dyspnea (Bruera et al., 2000; Campbell, 2004; Mancini & Body, 1999).

Among critically ill patients, existing literature suggests that dyspnea, anxiety, sleep disturbance, depression, and distress due to inability to communicate, are common among patients requiring mechanical ventilation, especially for prolonged periods (Nelson *et al.*, 2004; Rao & Gray, 2003; Stein-Parbury & McKinley, 2000). Although dyspnea during ventilator weaning might be expected, there is evidence that dyspnea may also be prevalent when patients are receiving full ventilator support (Knebel, Janson-Bjerklie, Malley, & et al, 1994; Nelson et al., 2001). For example, Knebel et al., (1994), found that patients ventilated for at least 3 days in an ICU experienced significant levels of dyspnea and anxiety during the baseline period of ventilator support, before weaning was initiated, as well as during weaning using either intermittent mandatory or pressure support ventilation. Several other studies have found that among ICU survivors, approximately half who could recall the experience, claimed to have felt anxiety, and/or

fear while ventilated, and 30% described feelings of agony and/or panic (Curtis & Patrick, 2001; Desbiens & Wu, 2000; Dudgeon et al., 2001). These symptoms highlight the multidimensional nature of dyspnea, and warrant further research.

Despite the fact that dyspnea is the most common and distressing symptom for people with cancer and end-stage disease, the evidence base regarding adequate management of this symptom remains controversial, compared to pain management (Bruera et al., 2000; Desbiens & Wu, 2000). Yet, despite the lack of congruence on treatment of dyspnea, there is still robust research available, according to a recent evidence-based report on End-of-Life and Outcomes, by the (Agency for Healthcare Research and Quality (AHRQ), 2004). For example five systematic reviews were identified in the AHRQ report, addressing the topic of dyspnea in the context of end of-life care (see Table 4). One of the reviews focused specifically on dyspnea in cancer patients, one on patients with COPD, and three on mixed disease. Two additional studies were randomized controlled studies, two were qualitative, and one was observational. The sample sizes ranged from 34 to 207 patients and two of the studies focused specifically on dyspnea in a patient population with lung cancer. Interventions included a nurse clinical intervention, complementary alternative methods (CAM) provide by an APN; home care with a focus on dyspnea treatment, palliative care services, and one with an unclear intervention. Four of the five intervention studies, demonstrated beneficial results by reducing the symptoms of dyspnea and/or the anxiety associated with dyspnea. While these studies generated knowledge regarding various interventions to relieve dyspnea among practice settings, only one study (Jennings & et al., 2003) reviewed any pharmacologic (opioids) or other interventions to manage acute dyspnea, which is needed

to relieve the dyspnea patients experience at EOL. Most of the systematic reviews on dyspnea lacked inclusion of acute and critically ill patients.

The AHRQ review (2004) also reviewed twenty-seven randomized clinical trials (RCTs) / Clinical Controlled Trials (CCTs) on pain and dyspnea. Furthermore, only two of the RCTs were in the hospital (non-ICU) setting. According to the recommendations by AHRQ to improve EOL outcomes, high-quality studies are needed to characterize symptoms at EOL in non-cancer conditions. In addition, because of the lack of scientific congruence on the effectiveness of interventions to alleviate dyspnea, larger intervention studies are needed, among hospitalized patients, to decrease patient suffering, when death is near. Table 4 provides an overview of the key studies on pain, dyspnea, depression and anxiety, included in the AHRQ systematic review.

Table 4

Systematic reviews for symptoms: pain, dyspnea, depression /anxiety

Study	Symptoms Addressed
Higginson, (Draft). Systematic Review (March 2003 Unpublished)	Pain, dyspnea, depression, anxiety
Booth, S., Anderson, H., Swannick, M., et al. (2004). The use of oxygen in the palliation of breathlessness. A report of the expert working group of the Scientific Committee of the Association of Palliative Medicine. <i>Respir Med.</i> , 98(1), 66 -77.	Dyspnea
Wilson, K.G., Graham, I.D., Viola, R.A., Chater, S, & Faye de, B.J., & et al. (2004). Structured interview assessment of symptoms and concerns in palliative care. <i>Can J. Psychiatry</i> , 49(6), 350-358	Pain
Carr D., Goudas, L., Lawrence, D., et. al. (2002). Management of cancer symptoms: pain, depression, and fatigue. Evidence report/technology assessment No. 61 AHRQ Publication No. 02-E032. Rockville, MD: Agency for Health Care Research and Quality.	Pain, Depression
Jennings, A. L., Davies, A. N., Higgins, J. P., et al. (2002). A systematic review of the use of opioids in the management of	Dyspnea

Study	Symptoms Addressed
dyspnoea. <i>Thorax</i> , 57(11), 939-44.	
Salman, G. F., Mosier, M. C., Beasley, B. W., et al. (2003) Rehabilitation for patients with chronic obstructive pulmonary disease: meta-analysis of randomized controlled trials. <i>J Gen Intern Med</i> , 18(3), 213-21.	Dyspnea
Higginson, I. J., Finlay, I. G., Goodwin, D. M., et al. (2003). Is there evidence that palliative care teams alter end-of-life experiences of patients and their caregivers? <i>J Pain Symptom Management</i> , 25(2), 150-68.	Pain
Pan C. X., Morrison, R. S., Ness, J., et al. (2000). Complementary and alternative medicine in the management of pain, dyspnea, and nausea and vomiting near the end of life. A systematic review. <i>J Pain Symptom Manage</i> , 20(5), 374-87.	Pain, Dyspnea

While dyspnea is a frequent symptom in patients with advanced cancer, it is also highly associated across other chronic diseases, such as chronic obstructive lung disease (COPD), and congestive heart failure (CHF) (Barnes et al., 2006; Claessens *et al.*, 2000), yet less studied. Furthermore, this is particularly evident in dying patients in the ICUs, because often patients/families choose to withdraw mechanical ventilation and other life-prolonging therapies; yet despite the fact there are national guidelines for withholding or withdrawal of life-sustaining therapies (Truog et al., 2001), patients often experience dyspnea and severe anxiety following removal of the breathing tube. Furthermore, little research through descriptive studies or RCTs is available, which test interventions such as morphine, and other sedative medications to ease the pain and suffering during the patients final hours (Clarke et al., 2003; Costello, 2006; Dunn, Otten, & Stephens, 2005; Harwood, 2004).

Barnes and colleagues (2006), explored the prevalence and burden of symptoms in a community-based sample of patients aged >60 with symptomatic congestive heart

failure ($n=542$). Compared to previous research into the symptoms of heart failure, other studies have mainly relied on retrospective data gathered from hospital records. This large, community-based study provided self-reported data as perceived by the subjects, as well as perspectives from primary health care professionals (2006). Older people are more likely to attribute symptoms such as fatigue and sleeplessness to normal aging rather than heart failure. Hence, treatment seeking is delayed until symptoms become acute and very distressing (Evangelista, Dracup, & Doering, 2000; Friedman, 1997). Findings from Barnes et al. (2006) study indicate high physiological distress (breathlessness), fatigue, chest pain, nausea, sleep disruption, and confusion. Symptom prevalence and burden was high in this population, with depression being a strong predictor of short-term decline in patients with CHF (Barnes et al., 2006).

Another study by (Levenson, McCarthy, Lynn, Davis, & Phillip, 2000), attempted to characterize the experiences of patients with CHF, particularly dyspnea, during their last 6 months of life. The study design was a retrospective analysis of data from a prospective cohort study, which included several data collection points. Out of 1404 patients enrolled, 539 patients died within one year of their index hospitalization. The results of this study showed that EOL with CHF may be marked by increasing symptoms and disability for most patients (depending on stage of CHF). For example, a number of functional impairments, median depression scores and percent of patients reporting severe pain or dyspnea increased as death approached, with 41% of patient surrogates reporting that the patient was in severe pain and 63% reporting that the patient was severely short of breath during the three days before death (Levenson et al., 2000). Perceived quality of life did not change appreciably, with 29 to 58% of patients reporting

good to excellent quality of life in all intervals before death (2000). The place of death for 40% for this cohort was the ICU, where most patients have a high prevalence of distressing symptoms related to their progressive disease(s) or sudden life-threatening illness. Prospective assessment and more aggressive symptom management in this population, will reduce the end-points of a death in the ICU, which is known to be associated with physical and psychological distress, and poor QOL (Levenson et al., 2000; Levy & McBride, 2006).

Symptom Severity / Pain

One of the first prospective studies to examine end-of-life care in the United States, was the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment (SUPPORT) (Desbiens et al., 1999). The SUPPORT study evaluated the prevalence of pain in cancer and noncancer patient, which included over 9,105 patients, in a two phase study, at five teaching hospitals across the country, from 1989-1991 (Desbiens et al., 1999). The results of this study changed the entire landscape on EOLC in America. Findings revealed that 80% of Americans are dying in institutional settings, and are receiving end-of-life care incongruent with their wishes (Knaus & Lynn, 1997). Moreover, hospitalized patients were found to experience one or more symptoms, such as pain, at least moderate to extreme severity, gravely interfering with their quality of life (QOL); while 10% of the patients in the study died after spending four weeks in the intensive care unit. Worse yet, many patients received mechanical ventilation and life-sustaining measures, despite the documentation of patients' advance directives (Desbiens et al., 1999; SUPPPORT & Investigators, 1995; Teno *et al.*, 2000).

The SUPPORT data, revealed that pain is one of the most common, yet

distressing symptoms in hospitalized patients, as not only does pain interfere with daily activities, it causes emotional distress, and decreases overall quality of life. Pain is one of the most studied symptom in general, yet patients continue to rate their pain as moderate to severe in intensity (Puntillo, 1990; 1997; 2002; 2004). Pain research has been examined through patient recollections of the symptom experience, and the effectiveness of clinical interventions, yet findings reveal an ongoing, unethical amount of distress and suffering among hospitalized patients (Ardery, Titler, Schmitt, Herr, & Sorofman, 2003) Carroll, 1999; Feldt, 2004; Niv & Kfeitler, 2001; Yorke, 2004 #22}). Researchers have also examined through comprehensive studies, descriptions of pain perceptions, including responses to common procedures in critical care, which uncovered a myriad of factors that influence the painfulness of common procedures (Arbour, 2000; Carroll *et al.*, 1999; Easley & Elliott, 2001; Gibson & Helme, 2000; Max, 2003; Puntillo, 2001; Puntillo *et al.*, 1997; Puntillo, Morris, Thompson, Hutt-Stanik, & White, 2004; Puntillo *et al.*, 2002; Steinhauser & et al., 2000; SUPPPORT & Investigators, 1995; van de Leur *et al.*, 2004)

Pain and symptom management is often the first component identified by patients, families, and healthcare professionals as integral to a “good death” (Steinhauser & et al., 2000). This is illustrated, in a qualitative study by Singer, Martin, & Kelner (1999), who used in-depth, open-ended, face-to-face interviews to examine and describe elements of quality EOLC from the patient's perspective (Singer, Martin, & Kelner, 1999). A total of 126 participants from three patient groups: dialysis patients (n = 48), people with human immunodeficiency virus infection (n = 40), and residents of a long-term care facility (n = 38), were included in the study. “Participants identified 5 domains of quality end-of-life care: receiving adequate pain and symptom management, avoiding inappropriate

prolongation of dying, achieving a sense of control, relieving burden, and strengthening relationships with loved ones” (p.163). These findings are extremely important, as they characterize important domains of end-of-life care, from a patients' perspective, which can serve as focal points for improving the quality of end-of-life care. Yet, unfortunately evidence continues to accrue, which reflects we are failing to meet these needs among patients with terminal and life-limiting illnesses.

Symptom Assessment / Role of Proxy Reports

While assessment of symptom distress is most accurate through the perception of the patient, this limits our understanding of an individuals dying trajectory, as often patients in the final stages of death, often become cognitively impaired, or even lose consciousness. Therefore, family members can provide insight into this valuable phase across the trajectory of illness and its impact on quality of life. For example, family members from the SUPPORT(1995) and Hospitalized Elderly Longitudinal Project (HELP) (Teno *et al.*, 2000) studies reported that during the last three days of their lives, almost 40% of patients had severe pain, more than 50% of patients had severe dyspnea (excluding patients with colon cancer), and approximately 25% of patients had severe confusion. These findings illuminate the need to improve the care of people nearing life's end, and as patients lose the ability to provide “self-report” regarding their symptom experience, clinicians must seek alternative approaches to gain an integrated symptom assessment, by using multiple sources, such as proxy reports (professional/family surrogate). In another study, family members reported that 34% of dying patients were in moderate to severe pain during the last week of life (Tolle, 2000). More specific data from this study demonstrates that more hospitalized patients experienced moderate to

severe pain during the final week of life (44%), as compared to individuals dying at home (34%) or dying in a nursing home (27%). At times, proxies may be the only method to gain an estimate of the patients symptom burden, in order to provide the scope of quality care that patients and families desire, according to the domains of quality care at EOL (Higginson, Priest, & McCarthy, 1994; Kane et al., 2005; Kutner et al., 2006; Lobchuk & Degner, 2002; McPherson & Addington-Hall, 2003; McPherson & Hall-Addington, 2004; Nekolaichuk et al., 1999).

Symptom Distress in Critically Ill Patients

Among the extant studies available in critical care, Nelson and colleagues (2001) found that 55 to 75 percent cancer patients being treated in the ICU, had moderate to severe pain, discomfort, anxiety, sleep disturbance or unsatisfied hunger or thirst (Nelson et al., 2001). Other studies suggest retrospective patient recall of ICU is often very unpleasant and painfully distressing, as noted in the study by (Jones, Griffiths, Humphris, & Skirrow, 2001). Jones and colleagues examined prospectively, the relationship between memories of ICU and levels of anxiety after ICU discharge, the stability of these memories with time, and their relationship to the development of acute posttraumatic stress disorder (PTSD)-related symptoms (2001). Results revealed that the only predictors of possible acute PTSD-related symptoms at the 8-week assessment were trait anxiety ($p = .006$) and having delusional memories without recall of factual events in the ICU at 2 wks ($p < .0001$) (2001). Only delusional memories were retained over time, whereas, the recall of factual events in the ICU declined. The findings here suggest that even relatively unpleasant memories for real events during critical illness may give some protection from anxiety and the later development of PTSD-related symptoms when

memories of delusions are prominent. However, more importantly this study illuminates that accurate patient recall is present in a number of patients, however, inclusion of proxy report, would most likely have provided another dimension of a patient's symptom experience (Nekolaichuk et al., 1999; Nolan, 2005; Oi-Ling et al., 2005).

Although detailed prospective studies of the epidemiology of pain and other symptoms in ICUs are limited, it is recognized that multiple symptoms have an impact on the quality of life (QOL) for patients in ICUs, approaching end-of-life (Mularski & Osborne, 2003). For example, in a study of critically ill post-operative patients by (Puntillo, 2002), pain was often times so crippling; it triggered a range of problems that included depression, social isolation, disturbed sleep, decreased mobility, falls, difficulty in thinking clearly, and loss of appetite. Unfortunately, medical experts agree that at least 90 to 95 percent of all serious pain can be safely and effectively treated, yet at least half of dying patients report being in pain (Puntillo, 2003).

Among ICU patients, there are also other contributing factors, such as the advanced technology and treatment modalities, that place these frail patients at the risk of undue suffering and pain from multiple sources, aside from their underlying disease state (see Table 5). Risks may be related to tissue injury from prolonged immobilization, repeated exposure to a wide variety of treatment procedures, continuous instrumentation of sensitive tissues and, pre-existing or new pain syndromes associated with surgery, trauma, burns, or other medical illnesses such as cancer. Factors such as these could indeed serve as an antecedent condition-initiating the mediators of pain and a further cascade of physical and psychological distress in critically ill patients, with a cumulative impact of chronic illness, and prolonged treatment (Granja, Lopes, Moreira, Dias, &

Costa-Pereira, 2005; Green, Anderson, & al., 2003; Groeger, Lemeshow, & Price, 1998; Klinkenberg et al., 2004; Morrison, Ahronheim, Morrison, Darling, & Shari, 1998; Nelson, 2002; Novaes et al., 2001; Puntillo, 2001).

Table 5

Sources of Suffering and Stress in the Intensive Care Unit

Underlying diseases/Co-morbidities

- Hematological disorders; respiratory failure, massive hemorrhage, cardiovascular /vascular disorders, cancer. gastrointestinal (GI) [hepatic failure; GI bleeding], neurologic /neuromuscular, renal; multiple organ failure

Treatments

- Endotracheal/enteric intubation, mechanical ventilation, suction, intravascular/urethral catheterizations, arterial blood gases, phlebotomy, mechanical restraints, other procedures

Clinical interventions

- Administration of oral medications, intramuscular/subcutaneous injections, vital signs being taken, movement from side to side; or bed to chair, transfer to a procedure by stretcher/wheelchair, portable chest x-rays
 - Environmental stressors
 - Noise, temperature, lights, odors, sleep deprivation, alteration of biological rhythms; fatigue
 - Psychological stressors
 - Fear, helplessness, depersonalization, isolation, limited visiting, inability to communicate
-

Adapted from Nelson et al., 2002, with permission.

Recollective studies in patients who had been recently discharged from ICU provide insight, regarding various complaints of discomfort, pain and anxiety, which in several studies, seem to be the most commonly remembered experiences (Puntillo, 2001; Puntillo et al., 1997; Stein-Parbury & McKinley, 2000; Thomas, 2003). Lack of rest, placement of the endotracheal tubes, and application of face masks were some of the primary events most frequently associated with pain and anxiety. Patients also reported that they used eye signals, facial expressions, and hand and leg motions to alert ICU staff that they were in pain (Puntillo, 2001; Puntillo, 1990; Puntillo et al., 1997). According to (LaDuke, 2002) it is unethical practice not to provide pain management and comfort care, which is calculated, purposeful and requires collaboration with patients and families.

These studies however, further reflect the antithesis of poor quality basic nursing care, while patients are being provided advanced treatment modalities. Although pain and anxiety are often undertreated in this population because of the difficulties in assessment and patient self-report, this further underscores the need for prospective research in critically ill patients, to assess the patients perception—including proxy reports—regarding the prevalence and severity of all common symptoms, known to occur in seriously ill patients at end-of-life (Carter, MacLeod, & McPherson, 2004; Cook et al., 2004; Todd, Deaton, & D'Adamo, 2000; Volker, 2003)

Fatigue

Fatigue is one of the most frequently reported symptom in patients with cancer, however, recent data suggests that fatigue is also prevalent among patients with chronic illnesses, such as COPD, CHF, and Chronic Renal Failure (CRF) at end-of-life (von Gunten, 2005). The term fatigue is a subjectively experienced symptom and can be described in terms of perceived energy, mental capacity and psychological status (Ahlberg et al., 2004). In Sweden, fatigue was studied among sixty women with uterine cancer, who were scheduled to receive external radiation therapy. Patients were asked to describe their experience of fatigue, psychological distress, coping resources and quality of life (Ahlberg et al., 2004). Findings in this study showed that patients experienced a low grade of fatigue and psychological distress, but their functional status and global QOL was high. Significant correlations were found between general fatigue and anxiety and also between general fatigue and depression. There was a significant negative correlation between general fatigue and coping resources. Depression explained 44% of the variance in general fatigue (2004). Another study on fatigue was done with 910

cancer patients from five data collection sources (Ferrell, Grant, Dean, Funk & Ly, 1996).

The results of this large quantitative study revealed fatigue was not just a physical symptom, but had an effect on all domains of quality of life.

Delirium

Preservation of the ability to think clearly, and in comfort, is a goal of EOL.

Delirium is a cognitive disorder characterized by acute onset and impairment in perception, cognition, and behavior (Truman, 2004). Traditionally in the ICU, this syndrome has been called “ICU psychosis” and has been considered an expected, temporary, and minor consequence (Truman, 2004). This point of view has changed in recent years, and the Society of Critical Care Medicines (SCCM) 2002 Clinical Practice Guidelines, now consider the identification and treatment of delirium an important measure of patient comfort in addition to pain control and adequate sedation (Jacobi, 2002).

Unfortunately, delirium is often misunderstood and underrecognized, particularly in patients who are near death. In fact, although up to 80% of patients in the ICU develop delirium, it remains unrecognized in 66-84% of patients (Ely, Shintani, Truman, Speroff, & Gordon, 2004; Greenberg, 2003). Furthermore, the incidence of delirium is likely to increase in the future, as older person with multiple co-morbidities more frequently receive aggressive life-prolonging care. According to Ely and colleagues (2004), delirium in the acute care setting has repeatedly been associated with prolonged hospital stay (21 vs 11 days), higher costs (\$22,000 vs \$13,000 in ICU costs), increased mortality, greater dependency of care on discharge, and higher nursing home disposition rates (Ely, Shintani, Bernard, & et al., 2002). Risk factors for delirium in the hospital/ICU setting

include immobility, medications, iatrogenic events, intercurrent illness, sensory deprivation and social isolation (McCusker *et al.*, 2001).

Since delirium often has an emotional component, early delirium may appear to be a problem in mood or anxiety (Greenberg, 2003). The patient at EOL has many reasons to be fearful, anxious, or sad, so the mood may be attributed to the stress of illness. What appears to be anxiety about the situation at first may actually be panic, terror, and paranoia. According to Greenberg (2003), “The ICU patient may have fluctuating consciousness and is in a dreamlike state, delusions may be unspoken and unrecognized, so the patient may be frightened that what he or she “dreamed” is happening” (p. 63).

Approximately half of patients are able to recall the delirious episode (Breitbart, Gibson, & Tremblay, 2002). Delirium is an important symptom to assess, particularly in patients with a high-severity of illness index. For the patient with pain who is treated at EOL, pain relief often requires opiates, yet pain is difficult to assess when the patient appears confused, or is moaning and grimacing. All critically ill patients should be monitored for delirium as part of the routine assessment. The first step is to assess a patient’s level of consciousness/sedation using an objective sedation assessment scale (Jacobi, 2002). The Glasgow Coma Scale (GCS) and Richmond Agitation-Sedation Scale (RASS) (Ely, 2003; Sessler *et al.*, 2002) are the most common and reliable methods to assess for confusion and sedation. The RASS was used to assess patients’ mentation in the current study, to assure that those patients receiving sedation medications were awake and had capacity to provide informed consent. The RASS was used in conjunction with the Confusion Assessment Method for Intensive Care Unit (CAM-ICU), which is the first

delirium assessment tool designed and validated specifically to measure cognitive status in non-verbal ICU patients (Ely, Margolin, Francis, May, & Truman, 2001). The CAM-ICU was adapted for use in nonverbal ICU patients from the CAM, a well-validated delirium assessment scale that is widely used and is easy to administer (Inouye, van Dyck, Alessi, & et al., 1990).

The best way to prevent or reverse delirium at the end-of-life is to regularly monitor for cognitive deficits with focused attention to short-term memory loss. Care needs to be taken to recognize, and eliminate this very distressing symptom for patients/families, and reduce the risk factor for prolonged length of stay and increase morbidity and mortality often associated with delirium (Ely et al., 2001; Nowels, Bublitz, Kassner, & Kutner, 2002; Truman & Ely, 2003).

Measurement of Symptoms

Although substantial progress has been made in the past decade on the psychometric measurement of variables central to end-of-life care, demand is intense for better indicators of quality of care and quality at end-of-life. The need for valid and reliable measures is heightened by the demand to demonstrate objectively, as evidenced by the pressure of numerous quality-indicators projects nationally (Tilden, Drach, Tolle, Rosenfeld, & Hickman, 2002). A key development in recent years has been the recognition that symptoms are multidimensional and that accurate interpretation of symptom outcomes hinges on assessment of these dimensions. The measurable dimensions of symptoms may include prevalence, severity, frequency, and distress (Chang & Ingham, 2003). The impact of each symptom on a variety of family, social, financial, spiritual, and existential issues and on global constructs such as quality of life

(QOL) can be evaluated as another “dimension” of symptoms (Kroenke, Stump, Clark, Callahan, & McDonald, 1999).

The problem of symptom assessment is particularly challenging among critically ill patients, because impairments of cognition and communication often may preclude direct, real time reports from the patients themselves, which is the gold standard of symptom information (Nelson & Danis, 2001). No satisfactory “patient–passive” method of assessing pain or discomfort has yet been found according to Nelson & Danis (2001) and (Tilden et al., 2002). Physical indicators of distress are known to lack sensitivity and specificity; distress may be experienced in the absence of such signs, and their presence may be the manifestation of another condition. Furthermore, measurement is especially intense with elderly persons, where frailty, dementias, and diminished vision and hearing, among other factors, affect validity, reliability, and utility of measures (de Rooij & Hanna, 2005).

Complex challenges complicate psychometric measurement particularly at EOL whether for research or quality improvement. According to (Tilden et al., 2002), some of these challenges include “difficulties in defining end-of-life time periods to delineate the denominator for statistical analyses; controlling for extraneous influences or other interactions on the variability of construct; minimizing subject burden while maximizing robustness of a scale; and using proxies as respondents for a patient population that is largely incapacitated at the final stage” (p. 71). Research on agreement between patients and families have produced conflicting reports (Desbiens & Mueller-Rizner, 2000; Engelberg, Patrick, & Curtis, 2005; Nekolaichuk et al., 1999; Oi-Ling et al., 2005). Research surrounding agreements between patients and families have primarily been in

the area of treatment preferences (Fried, Bradley, Towle, & Allore, 2002; Hanson, Tulskey, & Danis, 1997; Shalowitz, Garrett-Mayer, & Wendler, 2006). In their review of the literature, (McPherson & Addington-Hall, 2003) suggest that, while proxies are valid reporters for some aspects of the patient's experience at the end of life, their reports are prone to bias, especially in domains concerning a patient's subjective experiences.

(Steinhauser et al., 2000) have examined attributes of a "good death" using a cross-sectional sample of four types of respondents: patients, bereaved family members, physicians, and other clinicians. Although they found a number of attributes that were defined as important for a good death by all respondents, they examined similarities *across* groups, rather than concordance between paired respondents (2000). For example in a study by (Lobchuk & Degner, 2002), patients and caregiver achieved better levels of agreement on physical versus psychological symptoms. While the evidence-based is growing in the area of surrogate reports, further research is needed to assess the reliability of these reports related to their concordance regarding the symptom experience and why their accounts might differ from those of the patients (Kutner, Kassner, & Nowels, 2001).

This literature review found no prospective, studies examining the symptom experience concurrently with patients and designated proxies, among critically ill patients in the ICU. A more comprehensive approach to understanding the multifactorial nature of symptoms at the end of life is to take into consideration information from multiple sources, including patients, family members and providers (Lobchuk, 2003). The current study examined the surrogate assessment of the patients' symptom experience concurrently, probing for congruence of the various rater(s). The symptom assessment instrument used for both patient/designated respondent was the Condensed Memorial

Symptom Assessment Scale (CMSAS) (Chang et al., 2004), which is a valid and reliable instrument utilized in cancer patients, and most recently among non-cancer patients with critical illness (Nelson et al., 2004).

Measurement bridges the conceptual and operational levels of scientific research, clinical care, and quality improvement (Tilden et al., 2002). There is a large array of psychometric instruments used in the past ten years to assess single symptoms; and multiple symptoms in one or more dimensions, at end-of-life for a variety of populations (Portenoy et al., 1994). However, the final choice for an instrument, should be guided by the conceptualization of the research variables, and based on the congruence between the purpose for which the researcher will use an instrument and the purpose for which the instrument was originally developed. Overall, if the setting and the sample of the investigation do not match those for which the instrument was developed, the reliability and validity of the data collected will be compromised (Frank-Stromborg & Olsen, 2004). Hence, this has been one of the noted barriers in the conduct of research among critically ill patients, as most symptom instruments were developed specifically to measure the multiple aspects of cancer, and the related effect on individuals. It is only until recently, that these multi-dimensional instruments have been appropriately adapted and shortened to extend their utility in non-cancer patients, particularly for ease of use in chronic and critically ill patients (Chang et al., 2004; George, 2002; Tranmer et al., 2003).

A full description and discussion of the extensive array of symptom instruments is beyond the scope of this review. However, seven validated instruments which assess a broad spectrum of physical and psychological symptoms described widely in the literature were reviewed extensively for use in data collection for this study. Table 6

provides a list of these instruments designed to measure symptom burden and distress in cancer and chronically ill patients (eg CHF; COPD; CRF; and AIDS). A full discussion of the instruments utilized in this study, including the CMSAS, the primary instrument used, to assess the patients' symptom burden, will be discussed in detail in Chapter 3.

Table 6

Symptom Assessment Instruments Reviewed for Study

Measure Name	Instrument Brief Description	Validity Testing Reliability Data	Sample
Adapted Symptom Distress Scale-2 (ASDS-2) (Rhodes et al., 2000; Rhodes & Watson, 1987)	Patient Self-Report. Measures symptom experience. Modified ASDS-1; added symptoms & identified subscales. Adapted from the McCorkle & Yung Distress Scale, 31-item, 5-point	Content Internal consistency (Cronbach's α)	N=257(175) oncology, 82 medical surgical; 97 healthy volunteers
Edmonton Assessment Scale (ESAS) The Edmonton symptom assessment system, (ESAS): A simple method for the assessment of palliative care patients. (Bruera et al., 1991)	Patient Self-Report /Assisted Assessment. ESAS consists of nine 100 mm visual analog scales for pain, activity, nausea, depression, anxiety, drowsiness, appetite, shortness of breath and sensation of well-being.	Construct (convergent/divergent) Internal consistency was high for the psychological subscale (Cronbach's alpha coefficients of 0.85 for the cancer group and 0.77 for noncancer group and for the physical subscale groups, with coefficients ranging between 0.78 to 0.87. Sx scores were highly correlated with perceptions of fatigue.	N=135 palliative cancer patients N=282 medical oncology out-and-inpatients.
Memorial Symptom Assessment (MSAS) The Memorial Symptom Assessment Scale: An instrument for the evaluation of symptom prevalence, characteristics and distress. (Portenoy et al., 1994). Measuring the symptom experience of seriously ill cancer and noncancer hospitalized patients near the end of life with the MSAS. (Tranmer et al., 2003)	Patient Self-Report MSAS is a multi-dimensional, 32-scale which measures prevalence, severity and distress for 32 symptoms or conditions in the last week. Validation using the MSAS in non-cancer patients comparing to the Piper Fatigue Scale. Measures symptom experience of seriously ill cancer & noncancer hospitalized patients near the EOL	Content Construct (factor analysis) Tested in cancer patients, inpatient and outpatient. Cronbach's alpha coefficients for (MSAS-Short Form) Subscales range from 0.76 to 0.87, with test-retest correlation coefficients of 0.86-0.94 at one day in group of cancer patients	N=246 cancer in patients and outpatients
Memorial Symptom Assessment-Short Form (CMSAS-SF). The memorial symptom assessment scale short form (MSAS-SF). (Chang, Hwang, Feuerman, Kasimis, & Thaler, 2000)	Patient Self-Report Patients rated symptom distress associated with 26 physical symptoms and the frequency of 4 psychologic symptoms during the past 7 days.	All the MSAS subscales were reliable in the MSAS-SF. Cronbach's alpha coefficient was 0.80 for the GDI, 0.82 for the physical symptom distress (PHYS), 0.76 for the psychologic symptom distress (PSYCH), and 0.87 for the CMSAS. Criterion Validity The MSAS-SF subscale scores were assessed against	N=299 medical oncology; 45 medical oncology for test-retest

Measure Name	Instrument Brief Description	Validity Testing Reliability Data	Sample
		subscales of the Functional Assessment Cancer Therapy (FACT-G) with pairwise. Pearson correlation coefficients. Correlation coefficients were -0.74 ($P < 0.001$) for the PHYS and FACT-G PWB, -0.68 ($P < 0.001$) for the PSYCH and FACT-G EWB, and -0.70 ($P < 0.001$) for Global Distress Index (GDI) and FACT-G SUMQOL score.	
Condensed-Memorial Symptom Assessment Scale (CMSAS) Shorter symptom assessment instruments: The condensed memorial symptom assessment scale (CMSAS). (Chang et al., 2004).	Patient Self-Report Shortened version of the MSAS, rates nine physical symptoms and three emotional symptoms, which combine survival and QOL. Three sub-scales are physical symptom distress (CMSAS PHYS) 10 questions; psychological distress subscale (CMSAS PSYCH) worrying, feeling sad, and feeling nervous; total SD- 14 symptoms (CMSAS SUM)	Content Construct (canonical analysis) Construct (convergent/ Karnofsky performance scale (KPS) Concurrent (MSAS-SF); Functional Assessment Cancer Therapy (FACT-G)	N=479 medical oncology patients
M. D. Anderson Symptom Inventory (MDASI) Assessing symptom distress in cancer patients. (Cleeland et al., 2000)	Patient Self-Report 19 Items, Physical and Psychological. Measures function, symptom presence, severity and interference with life	Content Construct –Physical (factor analysis) Construct – Psychological - Convergent/divergent with Eastern Cooperative Oncology Group (ECOG) (Grosvenor, Bulcavage, & Chlebowski, 1989) Construct – Presence/Severity (discriminative)	N=660 cancer out-and-inpatients
Rotterdam Symptom Checklist Measuring psychological and physical distress in cancer patients: Structure and application of the Rotterdam symptom checklist. (de Haes, van Knippenberg, & Neijt, 1990; (de Haes, van Knippenberg, & Neijt, 1990)	Patient Self-Report 34 –item instrument designed to assess symptom experience of cancer patients.	Content and construct validity have been established. Cronbach's alpha for the physical (.71-.88) and psychological (.88-.94) subscales support the internal consistency of subscales	(n = 86), patients undergoing chemotherapy for advanced ovarian cancer (n = 56); third cancer patients under treatment, disease-free 'patients', and 'normal' controls (n = 611).

Research Variables and Related Conceptual Framework

Managing adverse health symptoms is a core focus of nursing research and clinical practice. Symptom management is essential for those with acute and chronic health problems for which there may be no cure, for patients who elect a conservative therapeutic approach, for patients on wait-lists for organ transplants, and for others whose disease has advanced and the risk of complications of more definitive treatments are deemed to outweigh possible benefits (Larson et al., 1994; Dodd et al., 2001; Nelson et al., 2004). More than one million Americans have chronic health problems and many will require treatment and care in ICUs (Wolff et al., 2002). Symptom management addresses these experiences to be consistent with the patient-centeredness of critical care nursing: to impede or prevent disability, palliate physical and emotional suffering, improve the quality of living and dying, involve patients in their care, and uphold the dignity of each individual (Carter et al., 2004; Ferrell, Virani, Grant, & Uman, 2000).

Correlates of the Symptom Experience

The concept of symptom experience consists of how the patient perceives the symptoms, evaluates and responds to symptoms (Larson et al., 1994). In the SMCM, the metaparadigm domains of nursing science (person, environment, and health/illness) are three, contextual variables that provide a lens which affect how the patient perceives the symptoms (Larson et al., 1994; Dodd et al., 2001). Personal variables can be further subdivided into demographic, psychological, sociological, and physiological. According to Walker and Avant (1995), all of these factors may serve as *antecedents* conditions which may affect the experience of symptoms perceived by patients, and therefore, their quality of life (Walker & Avant, 1995). Personal variables can be further divided into

demographic (age/gender), psychological, sociological, and physiological (disease characteristics /comorbidities) all which can be *antecedents* to the production of the *symptom experience* among critically ill patients with life-threatening illness.

Gender

A number of studies have reported gender differences for specific symptoms and total number of symptoms for a wide variety of medical conditions. Yet, a quick review of virtually any research topic documents the pervasiveness of sex and gender bias throughout all of science. A large portion of both animal and human research has been, and continues to be, done primarily with male subjects (NIH Panel Final Statement: February 2005). This gender bias influences research results and often leads to inappropriate and questionable generalizations of research findings, usually from studies done with male participants to females. This bias exists in symptom management research on pain, fatigue, and depression in patients with cancer, although, they are minimal in number (Miakowski, 2004). Anecdotal studies reviewed, are restricted to research on the differences in prevalence rates and severity scores, and for the most part have yielded inconsistent results. According to Miakowski (2004) and others (Desbiens et al., 1999; O'Neill & Morrow, 2003; Skaug, Eide, & Gulsvik, 2007; Wachterman & Sommers, 2006; Walsh et al., 2000), additional investigations are warranted to determine whether the gender differences in prevalence rates and severity of these symptoms represent clinically meaningful differences among variable conditions, other than cancer.

Nonetheless, a few studies do provide further insight into the gender differences among non-cancer conditions. For example, (Bulpitt, Palmer, Battersby, & Fletcher, 1998) found that in diabetic patients, the total number of symptoms were related to body

mass index, fasting plasma glucose level, and female gender. Furthermore, women and less educated patients with diabetes were found to be at greater risk for developing depression and anxiety (Goldney, Phillips, Fisher, & Wilson, 2004). More recently, Chen, Woods, Wilkie, & Puntillo (2005), conducted a study to compare the symptom experiences between men and women with acute coronary syndromes (ACS), among a sample of 112 subjects, with a final diagnosis of ACS in four hospitals. (Chen, Woods, Wilkie, & Puntillo, 2005) found that after adjusting for cardiac diagnosis, diabetes, and age, women were more likely than men to experience chest discomfort rather than chest pain; pain/discomfort only in areas of the body other than the chest; pain/discomfort that started first either in the arm(s) or in areas of the body other than the chest; and unexplained anxiety. In addition, women were less likely than men to experience chest pain/discomfort, pain/discomfort in the left side of the chest, and chest pain/discomfort as the most worrisome symptom. Significant gender differences were observed in the reports of several symptoms associated with ACS. This study is the first to identify different pain/discomfort referral patterns between men and women that require further validation (Chen et al., 2005). Further research in this area is needed, as heart disease in women has become a major health issues, unrecognized by providers and patients themselves.

Further studies regarding gender differences are particularly important, among critically ill patients, since scant studies exist, which address gender differences. Findings will guide the design of studies to elucidate the underlying mechanisms for these differences, as well as the development and testing of gender specific interventions to the array of symptoms known to occur in patients with variable diagnoses such as heart

disease, COPD, chronic renal failure (CRF), liver disease and diabetes.

Age

Research on the relationship between age and symptoms has not yielded steady findings. Older age has been associated with specific symptoms and higher symptom scores in some studies (Hamel, Davis, Teno, Knaus, & Lynn, 1999; Wood & Ely, 2003). These variables are particularly crucial in critically ill patients, especially age for example, since the mean age of ICU patients is around ≥ 80 years old (Chelluri, 2001; Chelluri & Grenvik, 1995). Since the elderly do not have the physiologic reserves of all organ function as younger individuals, with stress whether it be secondary injury or acute illness, the older patient cannot respond well to the increased needs because of decreased reserve.

A specific search of the literature was conducted to examine the symptom experience and risk of mortality with increased age (see Table 7), since current studies glean inconsistent results. In fact, some studies suggest that functional status prior to the illness, dementia, severity of acute illness, may have a greater influence on mortality during the ICU stay, and after discharge than age (Ellershaw, 2001; Hamel et al., 1999). Nonetheless, the relationship to age to long-term mortality is not well studied (Chelluri, 2001; Nelson, 2002).

In the current research study, *gender and age were independent variables* and may be considered *antecedent* factors that influence the patients' perception of their symptom experience and distress. These variables were recorded on the principal investigator's (PIs) demographic log, and included with the descriptive analysis.

Table 7

Studies Concerning Intensive Care Outcome and Age

Study	Sample	Study Type	Age	Main Findings
(Chelluri, Pinsky, Donahoe, & Grenvik, 1993)	97 ICU patients	Prospective chart investigation	65–74 years ($n = 43$) and ≥ 75 years ($n = 54$)	Age itself was not an adequate predictor of long-term survival and quality of life, but severity of illness was
(Dardaine, Constans, Lasfargues, Perrotin, & Ginies, 1995)	110 ICU patients on mechanical ventilation (MV)	Prospective cohort study	> 70 years	ICU mortality was 31% and 6-month mortality was 52%; outcome predictors were shock on admission and previous health status
(Cohen & Lambrinos, 1995)	14,848 ICU patients on MV	Retrospective cohort study	>18 years	In-hospital mortality, in patients receiving mechanical ventilation aged ≥ 85 years, was 70% versus 32% in patients aged ≤ 29 years
(Dewar, Kurek, Lambrinos, Cohen, & Zhong, 1999)	37,573 patients on prolonged MV	Retrospective database analysis	> 18 years	Inverse relation between age and survival; older survivors were often discharged to residential health care facilities
(Ely, Evans, & Haponik, 1999)	300 ICU patients	Prospective cohort study	<75 years versus >75 years	No difference in duration of mechanical ventilation
(Montuclard <i>et al.</i> , 2000)	75 ICU patients	Prospective cohort study	> 70 years	ICU mortality was 60% in elderly patients receiving ICU treatment
(Ely <i>et al.</i> , 2002)	902 Patients with acute lung injury or ARDS	Prospective cohort study	<70 years ($n = 729$) and >70 years ($n = 173$)	Patients aged 70 years and older were twice as likely to die than were younger patients, and had greater difficulty achieving liberation from the ventilator
(Rosenthal, Kaboli, Barnett, & Sirio, 2002)	156,136 Consecutive admissions to medical, surgical, neurological, and mixed medical /surgical ICUs	Retrospective cohort study	18–100 years	The adjusted odds of death increased with each 5-year age increment
(Djaiani & Ridley, 1997)	474 ICU patients	Prospective cohort study	>70 years	The 1-year survival of patients aged <85 years was 56%, which was significantly better than that of patients aged >85 years (27%)
(Bo <i>et al.</i> , 2003)	659 Medical ICU patients	Prospective cohort study	≥ 65 years	Independent predictors of mortality were functional dependence & cognitive impairment before admission, high APACHE II score & low body

Study	Sample	Study Type	Age	Main Findings
				mass index
(Tang, Hsu, Lam, & Pang, 2003)	365 ICU patients on MV	Prospective cohort study	≥ 65 years ($n = 206$) and <65 years ($n = 159$)	Severity of acute illness and chronic comorbidities, but not age, were predictors of medical ICU and hospital mortality in elderly ventilated patients
(Chelluri <i>et al.</i> , 2004)	817 ICU patients on mechanical ventilation	Prospective cohort study	Mean age 65 years	Long-term mortality rate was associated with old age and poor pre-hospitalization functional status
(Esteban, 2004)	5,183 ICU patients on MV	International prospective cohort study	>70 years ($n = 1612$)	Patients older than 70 years had higher in-hospital mortality (55%) but similar duration of mechanical ventilation & length of stay
(Boumendil <i>et al.</i> , 2004)	233 ICU patients aged 80 years and older	Prospective cohort study	>80 years	Long-term survival after ICU stay was mainly related to the underlying condition and preadmission functional status
(Vosylius, Sipylaite, & Ivaskevicius, 2005)	2067 ICU patients	Prospective observational cohort study	>75 years ($n = 477$)	Mortality in elderly patients was higher than in younger patients; importantly risk factors were severity of illness, impaired level of consciousness and infection.

*MV = mechanical ventilation

Among the other domains of nursing science that relate to the SMCM, is the *division of the environment*, which refers to the aggregate of conditions or the context within which a symptom occurs, such as: physical, social, ethnic, and cultural variables (Dodd *et al.*, 2001). The physical environment may encompass work, home and hospital. Within the physical environment of the ICU (see Table 5), studies support that patients have increased pain and discomfort related to the environment and other extraneous sources (Kwekkeboom & Herr, 2001; Lasch, 2000; Morrison *et al.*, 1998; Nelson *et al.*, 2004), which in turn increases their perception of symptom distress. The social context includes one's social support network and interpersonal relationships. While there is only scant data available regarding the relationship of symptom distress and social support, a recent study by (Kris & Dodd, 2004) found that patients who were partnered had

significantly lower levels of symptom distress ($M=1.71$, $SD=0.81$), than those who were not partnered with ($M=1.87$, $SD=0.84$). Further assessment of the role of social support is needed, particularly because the ICU is an extremely stressful and frightening experience, and patients often report feeling lonely and isolated (Desbiens et al., 1999; Nelson et al., 2001; Tranmer et al., 2003).

Chronic Health (Comorbidities)

The final category among the symptom management model is the health and illness domain, which is comprised of variables unique to the health or illness state of an individual, and includes risk factors, health status, and signs of illness, disease or injury (Larson et al, 1994). Functional status, including physical, cognitive and social functioning, has also been shown to be an important predictor of the hospital outcomes, particularly in older patients (Klinkenberg et al., 2004; Knight, 2000; Patrick, Kinne, Engelberg, & Pearlman, 2000; Walke et al., 2007; Wu, 1995).

In the current study, *the patients' health status was deduced through the Acute Physiology and Chronic Health Evaluation (APACHE) III Scores and through patient and surrogate reports, using the Condensed Memorial Symptom Assessment Scale*. Health data was obtained from patient/surrogates perception, based on the symptom assessment on the CMSAS collected on day one of admission, which requires patients to rate the prevalence and distress of various symptoms experienced in the previous seven days, prior to hospital admission. Additionally, the patients' medical record was reviewed for any additional health problems or risk factors, which may not have been entered into the APACHE III prognostic system. This data was recorded on the principal investigator's (PIs) demographic log, and entered into the data management system for the study.

Symptom Evaluation /Assessment

The evaluation of symptoms reflects factors which patients evaluate and characterize the symptom experience and include its intensity, location, temporal nature, frequency, the associated pattern of disability, and an evaluation of the threat posed by a symptom (Armstrong, 2003). Responses to symptoms include physiological, psychological, and behavioral components (Larson et al., 1994; Dodd et al., 2001).

In the current study, *the three components of the symptom experience* was assessed using the CMSAS, which is a modified, shortened version of the Memorial Symptom Assessment Scale, which is a validated, multidimensional symptom instrument that captures patient rated severity, frequency, and distress associated with 32 highly prevalent symptoms (Portenoy et al., 1994). The shortened version is the CMSAS, developed by (Chang *et al.*, 2004; Chang et al., 2000; Chang et al., 2004), which rates eleven physical symptoms in terms of frequency from 0 (not present) to 4 (almost constant). The prevalence of symptoms is determined by the patient's identification of the presence or absence of symptoms. The evaluation of prevalence, intensity, and distress are assessed to characterize the symptom distress and overall experience.

Symptom Distress

Symptoms are multidimensional in nature and include the dimensions of duration, severity or intensity, frequency, and associated distress. Although symptom distress is not directly referred to in the SMCM, it can be inferred indirectly as the awareness by the individual of the extent of the physical or mental suffering, discomfort or bother reported by individuals, in relation to their perception to a symptom occurrence. The degree of symptom distress perceived by an individual is an influential factor that determines the

initiation, continuation, or discontinuation of the actions intended to bring relief or prevent the symptoms (Fu, Lemone, & McDaniel, 2004; Rhodes & Watson, 1987).

According to (Carlet *et al.*, 2004; Chang *et al.*, 1998) symptom distress has effect on the quality of life and survival. Factors noted to influence an individual's perception of symptom distress are age, gender, culture, family role, education, health knowledge, type of treatment, values, beliefs and past experiences (Abraham *et al.*, 2006; Hickman *et al.*, 2001; Kutner *et al.*, 2006; Oi-Ling *et al.*, 2005; Rhodes *et al.*, 2000).

Researchers in the field of oncology nursing have continued to produce the major body of work in the area of symptom distress, although, there is no congruence regarding conceptual definitions of distress among the extant literature. Table 8 illuminates the wide interpretation and operationalization of distress in the literature.

Table 8

Operationalization of Symptom Distress in the Literature

Operationalization of Symptom Distress	Source
Bother is equal to distress and distinct from pain intensity	(Johnson, 1973)
Distress is synonymous with discomfort. Distress from treatment and disease are similar. Distress is equal to the intensity and frequency of symptoms	McCorkle, 1987; (McCorkle & Young, 1978)
Distress is physical or mental upset, anguish, or suffering. Distress and frequency of occurrence are two fundamental symptom attributes.	(Rhodes <i>et al.</i> , 2000; Rhodes & Watson, 1987)
Distress, intensity, and frequency are three fundamental symptom attributes.	(Portenoy <i>et al.</i> , 1994)
Distress is equal to bother and one of four symptom attributes (the others are quality, timing, and intensity.	(Lenz <i>et al.</i> , 1997; Lenz, Suppe, Gift, Pugh, & Milligan, 1995)
Distress equals symptom interference with life activities or emotional upset.	(Cleeland <i>et al.</i> , 2000)

Operationalization of Symptom Distress	Source
Distress is psychological, emotional, social, or spiritual concern caused by physical symptoms or other sources.	(National Comprehensive Cancer Network., 2004)

McCorkle and Young (1978) were the first to attempt development of an instrument to measure symptom distress in oncology patients receiving chemotherapy and/or radiation therapy looking at the effects on the gastrointestinal system such as nausea, vomiting and retching and later in myocardial patients (Dodd et al., 2001; Dodd, Miaskowski, & Lee, 2004). Quality of life also is a measure of symptom management. Research findings show that an increase in the number and distress of symptoms is associated with decreased quality of life (Adenaes et al., 2004; Ahlberg et al., 2004; Chang, Hwang, Feuerman, & Kasimis, 2000; Chang et al., 1998; Granja et al., 2005; Kassa, 2000; Mitchella & Kempa, 2000; Wennman-Larsen, Tishelman, Wengstrom, & Gustavsson, 2007).

Using the CMSAS instrument, the degree of distress was measured by the mean total of the Physiologic (CMSAS-PHYS) and Psychologic (CMSAS-PSYCH) sub-scales. A CMSAS-SUM sub scale is the calculated average of all symptoms (physiologic / psychologic). *The CMSAS-SUM sub-scale is considered to be a measure of overall symptom distress and is correlated to quality of life* (Chang et al., 2000).

Symptom Management

Symptom management is an important component of nursing practice across care settings, client populations, and types of practice, and begins with the assessment of the symptom experience from the patient's perspective (Larson et al., 1994). This is followed by the identification of focused interventions, along with actual implementation of interventions, and concludes with the evaluation of outcomes and the symptom

management process itself. The goal of symptom management is to avoid or delay a negative outcome through biomedical, provider and self-care strategies. In the SMCM model, symptom management strategies can be initiated by patients, family members, providers, and the larger health care system.

The overarching goal of this current research was to determine the symptom burden reported by patients in ICU, understand the value of the meaning of that experience, and gain insight into the possible correlates among patient variables (antecedents and consequences), that may mediate the level of symptom distress by the patient. In this study, socio-demographic variables (*age/gender*), *chronic health status*, *APACHE III Score*, *functional outcomes (death) or (discharge)* are all considered potential correlates of the symptom experience. Ultimately, findings from this study will lead to a greater understanding of the multi-faceted nature of the symptom experience and lay the framework to guide more comprehensive assessments among critical care patients who are actively dying in the ICU. Data will also be used to develop and test interventions through clinical trials, in order to affect the overall symptom occurrence, distress and quality of life in critically ill patients.

Outcomes of Symptom Management

Symptom status is considered the primary outcome of interest when examining the effects of symptom management strategies. The concept of symptom outcomes includes eight components of the patient's biopsychosocial status: morbidity & co-morbidity, and mortality outcomes functional status, emotional status, self-care ability; financial status; and QOL (Larsen et al., 1994).

In the present study, the primary outcomes of interest were the symptom

experience and symptom status and its relationship to patient outcome (eg LOS, mortality). A patient's health status, or severity of illness, is considered as the most influential patient characteristic related to length of hospital stay while age, gender, race, and type of insurance have also shown to be correlates of lengthy of stay (Barnato et al., 2004; Garland, Shaman, Baron, & Connors, 2006; Volker, 2005; Wood & Marik, 2004). Determining the severity of (co-morbidities) and (mortality) outcomes were addressed in the present study by extraction of clinical variables from the APACHE III Prognostic System (note background on the APACHE III Systems is discussed separately). Upon admission to the ICU, all patient data is entered into the APACHE III national data set, which calculates the severity of illness score (Acute Physiologic is based on four groups (age, co-morbidities, physiologic abnormalities, and acute diagnosis). The APACHE III Prognostic Model provided risk stratification for severely ill hospitalized patients; along with risk estimates for hospital mortality (Knaus et al, 1991), which is calculated using a logistic regression equation that estimates the risk of death. Mortality was evaluated at three time intervals, during hospitalization, at 30-days post-discharge; and at 3-months.

Mortality Outcome Prediction Models

Acute Physiology and Chronic Health Evaluation (APACHE III) Prognostic System

The high-complexity features of ICU services and the clinical situation of patients themselves render correct prognosis fundamentally important not just for, their families and physicians, but also for hospital administrators, fund-providers and controllers. Although it is difficult to predict how long a patient will live, estimating prognosis is an important component of effective EOL discussions, both with patients and their families, and is essential for planning of care. Prognostic scoring systems such as the Acute

Physiology and Chronic Health Evaluation (APACHE III) System, the Mortality Prediction Model II (MPM II) and the Simplified Acute Physiology Score (SAPS II), were developed to estimate the probability of hospital mortality rates for adult ICU admissions (Knaus, Wagner, Draper, Zimmerman, & Bergner, 1991; Le Gall, Lemeshow, & Saulnier, 1993; Lemeshow & Le Gall, 1994). In general, these systems are based on logistic regression models that use a set of clinical and physiological variables-evaluated and registered on admission or on the first day of intensive care-to predict hospital mortality (Rocker, 2004). These models differ considerably in the number and types of variables used, as well as the time frame for data collection. For example, the APACHE III system consists of two options: 1) an APACHE III Acute Physiologic Score (APS), which can provide initial risk stratification for severely ill hospitalized patients within independently defined patient groups. This is based on 17 physiological variables, age, and chronic health status and; 2) the *predictive APACHE III equation* which uses the APS, using a series of predicted equations, linked to ICU admission diagnosis, patient selection criteria, and the APACHE III database (Pronovost *et al.*, 2004).

Developers of the models have used either a theoretical approach or an empirical approach in deciding which physiologic variables and constructs to include in their models. The theoretical approach involves the selection and weighing of variables based on past studies and expert opinion; the developers of the APACHE I-IV use this approach (Knaus *et al.*, 1991; Knaus, Wagner, Zimmerman, & Draper, 1993; Zimmerman *et al.*, 2006). The empirical approach of the MPM II and SAPS II involves collecting information on groups of patients and then contrasting the physiologic patterns of survivors and non-survivors (Arabi, Shirawi, Memish, Venkatesh, & Al-Shimemeri,

2003; Le Gall et al., 1993). Multiple regression techniques are used to reduce a large number of potential outcome predictors to a smaller set. The APACHE system, constructed in 1981 is the most familiar (Arabi et al., 2003; Knaus et al., 1991; Le Gall et al., 1993), and has undergone four revisions, most recently by (Zimmerman et al., 2006).

The usefulness of predictive models that estimates prognosis has been an important dimension of critical care, as patients and their families seek a prediction of duration and outcome of illness ((Markgraf, Deutschinoff, Pienka, Scholten, & Lorenz, 2001); Nelson & Danis, 2001). Historically, prognostication has been based on data obtained from studies of risk factors (smoking, age, diet, activity, and current disease), complications of diseases, and experience of a physician (Langendoen-Faber & Lanken, 2000). The result is a subjective prediction that may not be sensitive to an individual's severity of illness. Health care reform initiatives are being put in place to control costs, as it is estimated that end-of- life care consumes 10% to 12% of all healthcare costs and 27% of Medicare cost (Moran, 2003) The number of those enrolled in Medicare will grow considerably in the next 20 years, raising concerns of the costs to provide care to the increasing elderly population (Arabi, Venkatesh, Haddad, Shimemeri, & Malik, 2002). Similarly, predicting resource use is important to hospital administrators and ICU directors who manage critical care services with limited resources and budgets (Tilden *et al.*, 2002). Mortality prediction models can supply knowledge that provides an empirical basis for quality assurance and utilization services, and serve as one of many indices in making decisions at end of life, to assure the quality of the patients' death in the ICU.

Symptom Assessment and the APACHE III Model

The APACHE III Predictive Model is the most widely used system, particularly among academic affiliated medical centers, which value the ability to objectively estimate patient risk for mortality or other important outcomes, such as clinical research. The APACHE IV Model is currently being released and hospitals are gradually migrating to updated model, to have greater discrimination and calibration, which will be useful for benchmarking performance in the U.S. ICUs (Zimmerman et al., 2004).

The clinical site used for data collection for this study, utilized the APACHE III prognostic system, which currently provides 95% confidence intervals for the day of ICU admission, with updated predictions for subsequent ICU days (Zimmerman, Wagner, Draper, Wright, & Alzola, 1998). The purpose of this study did not include predicting mortality, whereas, the APACHE III Score and risk of death prediction (r), served as a clinical reference point to identify patients for study enrollment, who were at high-risk for death, as well as it will generated data daily, to measure the independent variables delineated.

Utilization of the UCSF (SMCM) is a goodness-of-fit model to help illuminate the symptom experience (occurrence, intensity, timing, distress level, and quality of symptoms) as a framework for this study (Dodd et al., 2001). The demographic data, physiologic factors, psychological factors, and situational factors all are potential correlates to the patient's symptom burden and end-of-life experience in the ICU (2001). These factors overlap and affect the patient and family. Physiological derangements are reflected in, and may be diagnosed by the presence of unpleasant symptoms. The aspects

of physiologic factors may be related to body function, pathology, trauma or surgery (Lenz et al., 1997). Physiological factors are measured and weighed by prognostication models and are used to predict mortality. Critical care nurses and other members of the ICU team need to monitor and treat derangements to promote the wellbeing of the patient with aggressive care in the ICU and if needed, facilitate an early transition from aggressive curative care to palliative care.

The *psychological component of the SMCM* includes the individual's mental state, reaction to illness, and degree of uncertainty and knowledge about the symptoms and their meanings (Larson et al, 1994; Dodd et al, 2001). Nurses must be aware of the psychological component in the ICU. Nelson and Danis (2001) show that the patient and family desire accurate prognostication of outcomes. They also acknowledge that the patient and family will have mood changes, feelings of anger and loss of control. To help the patient and family feel empowered the nurse, along with the entire health care team, must include the patient and/or family in decisions made about treatment with clear options, including the patient's preference (Steinhauser et al., 2000). Situational factors include aspects of the social and physical environment that may affect the individual's experience. Potentially relevant social situational considerations include employment status, marital and family status, social support and access to health care resources, and lifestyle behaviors. In a study of dying patients in the ICU, patients and families voiced the need for preparation of wills, obituaries, and funeral services. Death affects a wide social network, thus it's important for the ICU patient to receive religious offerings of their choice, reflect and conduct a life review, and be around family and friends in the time of death (Steinhauser et al., 2000).

The average daily cost in the ICU is about \$3,000/day (Garland et al., 2006). Data from the SUPPORT study (1995), report that 20% of families had to quit work or make major life changes. One third of reported a loss of most or all of the family savings, especially in younger, poor, or functionally dependent ICU patients (Curtis, Cook, Wall, Angus, & Bion, 2006). Critical care nurses must be aware of how physiologic, psychological, and situational factors overlap to provide optimal care for the patient and family in the ICU. Clinical research is needed to stratify improved utilization of the prognostic severity-of-illness systems, to include outcomes other than survival, e.g., functional outcomes and quality of life.

Limitations of Logistic Regression Models

Mortality prediction models based on linear regression have limitations (Clermont, 2002). According to Clermont and colleagues, a logistic function does not accommodate nonlinear relationships between predictor and outcome variables. Second, important interactions between predictor variables may be present. These interactions may complicate interpreting the odds ratio and require an explanation of their presence. Third, these models cannot directly accommodate missing data, and finally Clermont states these models require large samples to model outcomes with a large number of predictor variables (Clermont et al., 2002).

Gaps in the Literature/Future of Prognostication

A shortcoming in this literature review regarding prognostic models is that no articles were used from nursing specific journals. The journals providing the greatest amount of information were: Chest, Journal of American Medical Association (JAMA), and Critical Care Medicine. This demonstrates the need for nursing to take a leadership

role in research and the development of comprehensive EOL care planning in ICUs. Advanced Practice Nurses have the background and knowledge to participate in such planning when utilized in the intensive care unit. Rosenberg (2002) posits that a potential use of prognostication models is using them to detect the overall response to a treatment and the expected benefits gained by using a certain strategy.

Nursing Implications

Mortality prediction models can serve as a useful tool for the nurses in the ICU setting. Modeling draws on the experience of several thousand patients, and may be helpful in sorting patients out by providing objective estimates of the risk of death for the patient. Prediction models also provide objective estimates of survival, and can prove useful in understanding the likely outcome of a patient and be useful in staffing appropriate number of nurses, and triaging patient care. Prediction tools also help reduce errors stemming from bias and overestimating or underestimating the importance of a variable. However, continued research is needed, to explicate the value of predictive models and patient indicators, in order to guide clinicians to provide the highest quality end-of-life care, for those patients at risk for hospital death.

Chapter Summary

A comprehensive analysis of the empirical literature relevant to the symptom burden and degree of distress among patients with terminal and critical illness was presented. The research literature was critiqued on the variables pertinent to this study, which include patient characteristics (age, gender, ethnicity), antecedent conditions, comorbidities, and severity of illness, which may be correlates associated with the perceived symptom experience of patients with life-threatening illness, in ICUs. Results

of this review revealed a robust amount of research among terminally ill cancer patients, who are continuously burdened by distressing symptoms at end-of-life. However, with respect to other life-limiting illnesses, such as CHF, COPD, ESRD and elderly patients admitted with sepsis research is scant. Moreover, with respect to ICUs, where mortality among patients with and without underlying malignancy is typically high, research related to symptom prevalence and management remains surprisingly limited. Existing anecdotal evidence suggests that the ICU can be a difficult and painful place to die. The present study contributes to the knowledge base of symptom management by documenting the relationship that exists between specific physiologic (disease severity and pre-morbid conditions), and situational/demographic (age, gender), factors, including increased ICU length of stay, and overall symptom burden in patients who have high rates of mortality.

This research is also one of the first to examine the multidimensional nature of symptoms reported in real-time by critically ill patients, which also included a concurrent symptom assessment of a designated family respondent (proxy), regarding the patients symptom burden. Study findings reveal a high level of symptom burden and distress among critically ill patients, which is known to be associated with decreased quality of life (Bowman et al., 2000; Chang & Ingham, 2003; Clarke et al., 2003). Factors associated with diminished QOL among critically ill patients/families were also identified in the current study. Findings will be helpful to guide future interventions to improve symptom relief (physiological and psychological) and other strategies to improve the lives of patients with advanced diseases.

Finally, this study ultimately, responds to an appeal from the National Institutes of

Health (NIH); National Institute of Nursing Research (NINR), and findings from the 1997 publication of the Institute of Medicine report “Approach Death: Improving Care at the End of Life, to increase activities and research to improve the quality of care and the quality of life at the EOL for seriously ill and dying people (National Institutes of Health, 1999; NIH Panel Final Statement: February 2005; Steinhauser et al., 2000; Teno et al., 1999).

Accepting this challenge, this investigation seeks to characterize the symptom experience of critically ill patients/families, in order to improve the scientific gaps noted in this literature review, which will also help further to identify future directions in research related to the domains central to end-of-life care, among critically ill patient and their families.

Chapter 3

Methodology

The purpose of this study was to explore the symptom burden at end-of-life in patients with terminal and life-threatening illness in ICUs; and to examine the relationships among variables related to the patient (age, gender, physiologic acuity, previous health status), symptom distress, and overall mortality. This chapter outlines the research design, methods, and procedures applied in this study. The sample, settings, power computation, data, statistical analysis, limitations and ethical considerations are also described.

Design

A descriptive, correlational repeated measure design was used in this study to explore the following research questions:

1. What is the perceived symptom burden (prevalence, intensity, frequency) and overall distress, as reported by critically ill ICU patients at high-risk for dying?
 - A. Is there a relationship between age and gender in the reported symptom burden (prevalence, intensity, frequency), and overall distress experienced by subjects?

2. What is the incidence of other sources (treatments / procedures) of pain and the degree of discomfort, reported by patients during their ICU stay?
3. What is the relationship between demographic characteristics, antecedent conditions, symptom distress and overall predicted hospital mortality experienced by critically ill subjects?
4. What is the relationship between overall symptom burden and distress (CMSAS PHYS/PSYCH and CMSAS SUM Subscale Scores) and patient mortality?
5. Is there concordance between critically-ill patient-rated symptom prevalence, intensity and distress scores, with those rated by designated surrogate responders, using the Condensed Memorial Symptom Assessment Survey (CMSAS)?

This design provided several scientific benefits, such as helping to understand the relationship between the variables of interest in an attempt to identify key variables for the future development and evaluation of targeted interventions. This design also permitted the recruitment of a wide variety of patients with varying ages and disease severity, resulting in a description of the symptom burden of a diverse and underrepresented population of patients during their dying trajectory. It was the intent of this study to provide a real-time snapshot of the symptom experience among terminal and critically ill patients.

Sample and Sampling

A nonprobability convenience sampling method was used to screen/enroll participants. A convenience sample was drawn from all adult patients admitted,

consecutively to the ICUs, at a university-affiliated, tertiary-care, urban medical center, from January, 2006 – December 2006.

Eligibility Criteria

Inclusion criteria included (1) 18 years or older, (2) ability to speak, read and understand English or Spanish, (3) ability to complete self-report instrument by written or alternative method (e.g. if questionnaire read to patient by Primary Investigator [PI]), (4) considered to have normal mental status, assessed by the Richmond Agitation-Sedation Scale (RASS) and the Confusion Assessment Method for the ICU (CAMU-ICU) and, (5) probability factor of 60-80 % risk for hospital death, using the first 24-hour APACHE III predicted mortality score.

Exclusion Criteria

Patients were excluded from study enrollment if: (1) diagnosis of cancer and receiving related treatments; (2) patients with a principal diagnosis of dementia with altered cognitive status; or (3) patients with altered level of consciousness.

Recruitment

The study hospital has 3 ICUs which vary in size from 15 beds to 35 beds each, with an average daily occupancy ranging from 85 to 98%, and an average nurse ratio of 1:1 approximately 85% of the nursing time. On a monthly basis, approximately 197 to 240 patients are admitted with a mix of trauma, surgical and medical diagnoses. To help recruit patients for the current study, the nurses, attending physicians, residents were all provided with a study brochure and pocket guide. These were also posted in the ICU and in the family waiting room, to inform patients/families regarding the study opportunity. Interested patients/and families could contact the principal investigator (PI) by signing

the recruitment flyer and giving their phone number on how to contact them to discuss potential eligibility for the study, or they could call the PI directly on the phone number(s) listed on the brochure. Each ICU had a symptom study “box” in a visible location for placement of referrals.

The physicians/and nurses assisted as much as possible in the screening for potential study subjects during daily ICU rounds, by discussing briefly the purpose of the study with potential subjects. If the patients expressed an interest in learning more about the study, the PI was then introduced to the patient/and family to discuss the purpose of the research and study information. Because eligible subjects needed to be screened and interviewed within 24 hours of admission/and upon availability of the patient’s first 24-hour APACHE III risk mortality score, it was necessary to obtain a Health Insurance Portability and Accountability Act (HIPPA) Waiver (Appendix K) thru the Institutional Review Board (IRB). This allowed the PI to review the daily census sheets and APACHE III scores within the prognostic system, for each newly admitted patient, to boost study enrollment and to assure adherence to the study protocol.

Following a patient’s stated interest in being a volunteer for the study, the investigator then reviewed each patient’s record for inclusion eligibility. Patients were then provided informed consent, and those who wished to participate signed two consent forms.

Sample Size

To determine the minimum sample size required for this study, it was necessary to select the desired power and effect size. Cohen (1987) recommended a power of .80 for behavioral sciences and behavioral science research generally utilizes a moderate effect

size (.50). Munroe (2005) suggests that effect size should be based upon previous studies, if possible. There were six variables in this study: 1) gender, 2) age, 3) chronic health state (co-morbid conditions), 4) admission source, 5) outcomes [LOS; ICU mortality (%); hospital LOS / hospital mortality (%), and 6) severity of illness (odds ratio-death) [APACHE III predicted mortality risk (.60-.80) for hospital death and the APS Score [physiology; age and chronic health] for risk stratification. Thus, for the purposes of this research, computations were based on a 0.05 level of significance with a moderate effect size (.50) and an estimate power of .80 (80%) to yield a sample size of 127 SOLO Power Analysis Software, (Hintze, 1991).

Procedures and Measurement

Definition of Terms

The following section provides the conceptual and operational definitions for key terms used in this research.

Antecedent Condition

Conceptual definition: (Walker & Avant, 1995) define antecedents as the events or incidents that occur prior to the occurrence of a concept. Antecedents affecting the experience of symptoms include gender, age, ethnicity, disease characteristics such as type and stage; type of treatment; co-morbid medical and clinical conditions; individual characteristics (health knowledge, values, past experiences, and sense of coherence) (Dodd et al., 2001; Dodd, Miaskowski, & Paul, 2001; Ferris, von Gunten, & Emanuel, 2002; Rhodes & Watson, 1987; Walker & Avant, 1995).

Operational definition: Antecedent conditions identified above, will be measured by looking at the occurrence of the departure, beyond normal function, as calculated by

the APACHE III score, generated by the Acute Physiology and Chronic Health Evaluation Prognostic System. The APACHE III score is based on 17 potential physiologic variables, age, and chronic health status, and through logistic regression, the APACHE III Score is generated from the national data base.

Acute Physiology and Chronic Health Evaluation (APACHE) III Model

Conceptual definition: (APACHE) III is an outcome prediction model, which provides predictions of risk of hospital or ICU mortality. The APACHE III consists of two options: (1) an APACHE III score, which can provide initial risk stratification for severely ill hospitalized patients within independently defined patient groups; and (2) an APACHE III predictive equation, which uses APACHE III score and reference data on major disease categories and treatment location immediately prior to ICU admission to provide risk estimates for hospital mortality for individual ICU patients (Knaus et al., 1991).

Operational definition: To produce an equation for predicting hospital mortality after the first day of ICU treatment, the model will combine the disease and patient location coefficients with the relative weights assigned to the first day values of the three groups of variables of the APACHE III score (physiology, age, chronic health). The APACHE III score is a cardinal number with scores that range from (0 to 299) described above (Knaus et al., 1991). The final acute physiology score (APS score is determined by adding the weights for the individual variables to determine the APS. The APS is then placed into an equation that includes variables and coefficients for age, chronic health conditions, pre-ICU length, location admitted from, reason for ICU admission, and whether the patient had emergency surgery or not to determine the predicted risk of

mortality. Risk estimates for death are calculated on the patient's initial data, and thereafter, reflected by the patients' response to treatment.

Risk Estimates Equations for Hospital Mortality: An equation combining the explanatory power of the APACHE III score with major disease category and prior patient location permits the calculation of hospital death risk estimates for ICU patients (Knaus et al., 1991). The explanatory power of estimates calculated from the data obtained during the first day of ICU admission is demonstrated by the (total $r^2 = 0.41$ and Receiver Operator Characteristics [ROC] of 0.90). The explanatory power of the APACHE III compares well to the previous versions of APACHE I, II. Overall classification on the first day at a 0.50 predicted risk was 88.2 percent in the validation study for improving the risk stratification for APACHE III (Knaus et al., 1991). The current study used a 0.60 predicted risk of hospital death, as the indices to consider subjects for enrollment into this study.

Arousal and Agitation

Conceptual definition: Distress is common among critically ill patients, particularly if they are intubated or unable to communicate easily with their caregivers. Patient distress may result in untoward physiologic changes, including increases in sympathetic tone, protein catabolism, and plasma levels of circulating catecholamines. Critical physiologic changes can also lead to neurohormonal changes and imbalances, causing agitation and delirium. *Agitation* refers to an unpleasant state of extreme arousal, increased tension, and irritability. Extreme agitation can lead to confusion, hyperactivity, hostility and injury to self. Agitation can come on suddenly or gradually. It can last for just a few minutes or for weeks and even months. Pain, stress, and fever can

all increase agitation. Agitation by itself may not have much clinical significance; but, if viewed with other symptoms, it can be a good indicator of a acute disease state (Ely et al., 2001).

Arousal can be further defined as hyperactivity, or a state of excessive muscular activity. Sedative medications are widely used in intensive care units, to treat agitated behavior and relax patients so they may benefit more efficaciously from advanced treatments, such as endotracheal tubes and prolonged mechanical ventilation, along with other invasive therapies. Structured assessment of sedation and agitation is necessary to titrate sedative medications and evaluate agitated behaviors.

Operational definition: Arousal is measured using the Richmond Agitation-Sedation Scale (RASS), which is a 10-point scale, with four levels of anxiety or agitation (+1 to +4) [combative], one level to describe a calm and alert state (0), and five levels of sedation (-1 to -5) culminating in unarousable (-5). The RASS is a reliable and valid sedation tool to assess the routine arousal and agitation level of intensive care patients receiving sedative medication (Sessler et al., 2002). RASS is also used in the assessment of delirium in critically ill patients. The RASS will be used as a baseline, prior to completing the CAM-ICU for delirium and cognitive assessment.

Cognitive Impairment

Conceptual definition: Cognition comprises perception, memory and thinking, the recognition, registration, storage, and use of information processing. The loss of the ability to take care of one's daily living needs due to a deficiency in the ability to think, perceive, reason or remember is referred to as cognitive impairment. Altered thought processes with cognitive impairment can be manifested as confusion/delirium or

simultaneous disturbances in consciousness, attention, perception, memory, thinking, orientation, and psychomotor behavior that develop abruptly and fluctuate diurnally (Truman & Ely, 2003).

Concordance

Conceptual definition: Concordance is defined as the patient and family surrogate/caregiver giving the exact same answer to a question on the symptom assessment instrument (CMSAS).

Death

Conceptual definition: “A widely accepted statement defines death for legal purposes as the irreversible cessation of circulatory and respiratory function or the irreversible cessation of all functions of the entire brain, including the brain stem” (Field & Cassel, 1997, p.27).

Operational definition: Actual death during ICU stay or at (30-day Outcome) end-point, will be compared with APACHE III predicted death score (Graham & Cook, 2004) for potential correlation to symptom burden.

Delirium

Conceptual definition: Delirium is defined as an acute, reversible organic mental syndrome, characterized by the rapid onset with disorder of attention and cognitive function, increased or decreased psychomotor activity, and a disordered sleep-wake cycle. The essential features of delirium include disturbances of consciousness, attention, cognition, and perception. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day (Roberts, 2001).

According to the fourth edition of the Diagnostic and Statistical Manual of Mental

Disorders (DSM-IV), the essential feature of a delirium is a disturbance in consciousness that is accompanied by a change in cognition that cannot be better accounted for by a preexisting or evolving dementia (American Psychologic Association, 1994).

Operational definition: In order for patients to consent for participation in the study, the patient's neurologic status will be assessed for acute delirium and alterations in cognitive function. Delirium is measured using the Confusion Assessment Method for the ICU (CAM-ICU), which is a behavioral assessment scale. The CAM-ICU has four questions (features), and delirium is considered present if there is the presence of acute onset of changes or fluctuation in the course of the mental status (feature1) and inattention (feature 2) and either disorganized thinking (feature 3) or an altered level of consciousness (feature 4) (Ely et al., 2001; Truman & Ely, 2003).

Dying

Conceptual definition: Dying is not a precise medical or diagnostic term. It is difficult to predict exactly when a person is within six months of death (Copp, 1998). For the purpose of this study, dying refers to those within days or months of death (unexpected & anticipated). Risk for dying will be assessed using the APACHE III predicted mortality score of $> (0.60)$ risk for hospital death.

Dying Trajectories

Conceptual definition: A trajectory is essentially the time course of care needs and patient experiences from the onset of serious illness to the end of life (Teno et al., 2001). Currently, clinicians are embracing the concept of “*dying trajectories*”, as being more useful in designing reliable and effective care arrangements surrounding end of life, than strategies that rely upon diagnoses, procedures, or settings of care. Lunney and

colleagues (2003), builds the case for a relatively small set of trajectories that could warrant separate planning for care needs. They propose one trajectory for a short course of rapidly progressive disability in the last two months of life (often seen with solid cancers), one for a longer course of slow decline with intermittent life-threatening exacerbations and usually a sudden death (often seen with chronic lung or heart failure), and one for a very long course of slow decline with self-care disability arising from dementia or frailty (Lunney, Lynn, & Foley, 2003).

Family

A family is defined as a basic human social system that involves commitment and interaction between its members. Current definitions of families have been expanded to include those that are biologically related, and those who are not, but are living as a unified family unit. The family commitment includes a responsibility for the physical and emotional well-being and successful development of the children in that family. A healthy family is not necessarily a family where all members are at optimal health. A healthy family is one that can successfully adapt to crises, challenges, and changes during the life cycle. The role of the nurse is to help families adapt to these changes across the life-span (Leifer & Harston, 2004).

Palliative Care

Conceptual definition: The World Health Organization defines palliative care as the active total care of patients whose disease is not responsive to curative treatment, including control of pain, other symptoms, and psychological, social, and spiritual problems (WHO, 1998).

Quality of Life (QOL)

Conceptual definition: Quality of life is defined as ‘the gap between the expectations and the present situation of the individual (Lynn, 1997).

Conceptual definition: According to Rhodes & Watson (1987), signs are described as alterations ascertained by the sense of the observer and symptoms as changes in the functions of the parts affected.

Symptoms

Conceptual definition: “A symptom is defined as a subjective experience reflecting changes in the biopsychosocial functioning, sensations, or cognition of an individual. Change in normal functioning as experienced and verified “ Dodd et al., 2001, p.669).

Symptom Burden

Conceptual definition: According to (Haubrich, 1997), a symptom is the subjective evidence of disease or physical disturbance observed by a patient. Self-perceived symptom burden (one-six symptoms) is described as “a multidimensional construct arising from the patients’ subjective interpretation of the prevalence of physical and psychological distress. Symptoms can be the subjective expression of the disease itself, or the products of disease treatment (e.g. life-prolonging therapies, such as mechanical ventilation), or a patients response may be side effects and toxicities.

Symptom burden can be thought of as the subjective counterpart of summary expressions of disease such as tumor burden.

Patients typically experience multiple concurrent symptoms, due either to the disease or its treatment, thus, it is proposed that a measure of symptom burden be a

summative indicator of: 1) The severity of the symptoms that are most associated with a disease or treatment 2) A summary of the patient's perception of the impact of these symptoms on daily living, including activity, mood, ability to work, and ability to relate to others (Cleeland & Reyes-Gibby, 2002).

Operational definition: Symptom burden is correlated with quality of life (QOL), and many QOL measures (Functional Assessment of Cancer Therapy [FACT]) (Cella, et al., &, 1993); Symptom Distress Scale (McCorkle & Young, 1978); Rotterdam Symptom Checklist (de Haes et al., 1990); Memorial Symptom Assessment Scale (Portenoy et al., 1994); and CMSAS (Chang et al., 2004), have components that measure symptoms and their related severity. Symptom severity is a strong predictor of scores on QOL measures, suggesting the potential of symptom- burden measures as an immediate indicator of deteriorating quality of life. The current study utilized the CMSAS instrument, which is correlated to quality of life in the validation studies, and is evidenced by the increased score ≥ 1 on the CMSAS-PSYCH and CMSAS-SUM Subscales.

Symptom Experience

Conceptual definition: The symptom experience is dynamic, and involves the interactions between three components: the patient's perception (frequency, intensity, distress) and evaluation of the meaning and response to symptoms (Dodd et al., 2001). The perception of symptoms refers to an individual conscious recognition of perceived changes in the way one usually feels or behaves and can be conceived as an individual's identification of symptoms.

Operational definition: The occurrence of a departure from normal function as measured on a symptom scale which lists 11 physiologic symptoms and 3 psychologic

symptoms, rated present (Yes) or not present (No), rated on the Condensed Memorial Symptom Assessment Scale (CMSAS) (Chan et al. 2004). The mean is calculated for the number of symptoms, the most commonly reported symptoms, degree of distress and frequency.

Symptom Frequency

Conceptual definition: Frequency refers to how often a symptom occurs as perceived by the patient (Dodd & et al., 2001).

Operational definition: The frequency of a departure from normal function as measured on a scale from zero for N, 1 (a little bit) to 4 (very much) = “almost constantly.” Symptom frequency will be measured using the CMSAS psychological symptoms (worrying, feeling sad, feeling nervous) (Chan et al., 2004). Means for each symptom and frequencies will be calculated.

Symptom Distress

Conceptual definition: The extent of physical or mental suffering attributed to the attributed to the occurrence of a symptom (Dodd et al., 2001).

Operational definition: The distress rating is derived from nine physiologic symptoms, and is comprised of the following: (lack of energy, lack of appetite, pain, dry mouth, weight loss, feeling drowsy, shortness of breath, difficulty sleeping and difficulty concentrating). The symptoms are given a rating of 0 if symptom not present, 0.8 if it was present, but caused no distress, 1.6 for a little bit, 2.4 if symptom present and caused Somewhat of distress, 3.2 if symptom present and caused quite a bit of distress, and 4.0 if symptom present and caused very much distress. A mean symptom distress among the sample of patients will be calculated using the nine-items from the physiological

symptoms (Chang, Hwang, & Feuerman, 2000; Chang et al., 2004).

Symptom Severity

Conceptual definition: The dimensions of a symptom that refers to the strength, and is often associated with timing (duration and frequency)

Operational definition: Symptom severity on the CMSAS is measured in one-dimension (CMSAS-PHYS), unlike the three-dimensions captured on the original MSAS 32-Item instrument (Portenoy et al., 1994). The CMSAS symptom severity is measured on of overall symptom distress of nine-weighted symptoms (Chang et al., 2000; Chang et al., 2004).

Physiological Symptom Distress (PHYS)

Conceptual definition: The CMSAS has a total of eleven physical symptoms which are ranked by the patient to specify the frequency and degree of bother or distress (intensity) of each physical symptom. The physical (PHYS) symptoms are rated by the patient, summed and averaged, to produce a (PHYS) subscale score. The CMSAS-PHYS score indicates the degree of suffering or distress associated with the patients perception the intensity and occurrence (Kris & Dodd, 2004).

Operational definition: The (CMSAS-PHYS) subscale average is derived from the distress rating of nine (*) physiologic symptoms, comprised of the following: (lack of energy, lack of appetite, pain, dry mouth, weight loss, feeling drowsy, shortness of breath, difficulty sleeping and difficulty concentrating (Chang et al., 2004; Chang et al., 2000). The physical symptoms are given a rating of 0 if symptom not present, 0.8 if it was present, but caused no distress, 1.6 for a little bit, 2.4 if symptom present and caused Somewhat of distress, 3.2 if symptom present and caused quite a bit of distress, and 4.0 if

symptom present and caused very much distress.

Psychological Symptom Distress (PSYCH)

Conceptual definition: The CMSAS has three psychologic symptoms, which may be marker for predicting quality of life and decreased survival in patients with terminal diseases (Chang et al., 1998; Desbiens & Wu, 2000; Feldt, Ryden, & Miles, 1998; Hwang, Chang, & Fairclough, 2003; Rushton, 2004; Truog, Cist, & Brackett, 2001). The patient rates the frequency of each psychological symptom, and a CMSAS-PSYCH subscale score is derived by determining the average frequency rating associated with 3 psychological symptoms (Chang et al., 2000; Chang et al., 2004).

Operational definition: The CMSAS-PSYCH subscale average is derived from the average frequency rating associated with 3 psychological symptoms (worrying, feeling sad, feeling nervous). The psychological symptoms are given a rating on a scale from zero for N, 1 (a little bit) to 4 (very much) = “almost constantly.”

Measurement

Instruments were selected based on their brevity and simplicity of use, as well as their conceptualizations and psychometric properties. The relationship between the conceptual framework, instruments, and their timing of administration is presented in Table 9. The schedule of instrument administration was chosen after consideration of the following factors: (a) respondent burden (b) frequency required to gain a temporal trend of perceived symptom burden during ICU care (c) projected survival of the patients.

Instrument Translation

Collecting accurate health data on the growing number of ethnic minorities in the United States has increased in policy relevance in recent years. Hence, a number of valid

and reliable instruments used in the general population, require translation into Spanish and often other languages as well. The technique of translation-backtranslation, was used to translate the survey used in this study into Spanish, (versions for patient and family), attempting to achieve an equivalent version of the instrument that is culturally appropriate. The translation procedure attempted to achieve: translation equivalence (translation process should be appropriate) linguistic equivalence (each item retains same meaning) conceptual equivalence (instrument measures the same concept in different cultures) and lastly measurement equivalence (similar scores on instrument mean the same thing) (Hambleton & Patsula, 1998).

Efforts were made to select appropriate, yet varied translators, in order to assure that the final survey instrument(s) were culturally appropriate for Latinos in the United States. The forward translation of the instrument(s) for this study was done by two Mexican Americans, with Spanish as their first language. The reverse-translation was then conducted by two other Mexican Americans with English as their first language. All translators held certification credentials. The back-translation process produced Spanish-language versions of the survey instruments that were adequate for least educated respondents, to assure that all study participants were able to understand and respond to survey items accurately. In the future, researchers may also be required to modify the English versions of instruments as well as subjecting Spanish-language instruments to more rigorous testing that includes cognitive testing, pretesting, and an evaluation of the reading level by a literacy expert (Hambleton & Patsula, 1998)

Instrumentation

Investigator Demographic Data Log

Demographic information was collected through chart review, and included the following: age, sex, and ethnicity of each patient; insurance, diagnosis, admission location, specific treatments (mechanical ventilation; medications, particularly analgesics and sedatives that may alter the patients' level of consciousness or sedation level). The APACHE III Acute Physiologic Score (APS) and Predicted Mortality (r) for hospital death, was extracted from the APACHE III data system daily, as this was a key indices for enrollment into the study. Demographics and APACHE III data were recorded on the investigator's data log, along with any other pertinent anecdotal notes (Appendix A).

Acute Physiology and Chronic Health Evaluation Prognostic Model (APACHE III)

On a daily basis, the APACHE nurse generated a unit report with APACHE Data for each patient. This form was used to screen all ICU patients by examining the severity of illness, using the APS Score and APACHE III predicted mortality risk (r) (Knaus et al., 1991). If patients had a $> .60\%$ mortality risk in the first 24 hours, they were considered for study enrollment. APACHE III Scores were recorded and monitored on Day-1-Day-3.

Richmond Agitation-Sedation Scale (RASS)

To assess for evidence of mental confusion, agitation and any signs of cognitive impairment, the RASS and the Confusion Assessment Method for ICU (CAM-ICU) instruments were used, as noted on the diagnostic algorithm (Appendix B). The RASS is a 10-point scale, with four levels of anxiety or agitation (+1 to +4) [combative], one level to describe a calm and alert state (0), and 5 levels of sedation (-1 to -5) culminating in unarousable (-5). It was chosen for its completeness, ease of use, and psychometric

properties. The RASS is a reliable and valid sedation tool to assess the routine arousal and agitation level of intensive care patients, who may be receiving sedative medication (Sessler et al., 2002).

The RASS was tested for validity and interrater reliability in two phases. Phase 1 demonstrated excellent ($r = 0.956$, lower 90% confidence limit-0.948; $\alpha=0.73$, 95% confidence interval = 0.71, 0.75) inter-rater reliability among five investigators. Robust inter-rater reliability ($r = 0.922-0.983$) ($\alpha = 0.64-0.83$). In validity testing, the RASS highly correlated ($r=0.93$) with a visual analog scale anchored by “combative” and “unresponsive”. Correlations between the RASS and the Ramsay Sedation Scale ($r = 0.78$) and the Sedation Agitation Scale ($r = 0.78$) supported validity (Ely, 2003; Sessler et al., 2002). The RASS and CAM-ICU was used prior to each data collection point.

Confusion Assessment Method-Intensive Care Unit (CAM-ICU)

The CAM-ICU is a well validated, behavior observation scale used for the assessment of delirium or acute mental status changes in special populations such as ICU patients, or difficult populations (e.g., non-verbal patients, patients with dementia >65years old, and patients with very high severity of illness (Truman & Ely, 2003). CAM-ICU was tested using a total of 471 daily paired evaluations. Study nurses, an intensivist who used the CAM-ICU were compared to reference standard, a delirium expert who used DSM-IV delirium criteria. Strong interrater reliability for CAM-ICU ratings with kappa statistics of 0.84 to 0.79 and 0.95 respectively ($p < .001$). Two nurses and the intensivist reference standard was 95%, 96%, and 100% respectively (Ely et al., 2001). The CAM-ICU was designed to be a serial assessment tool for use by bedside

clinicians (nurses and physicians). Thus, it is easy to use; it takes only 2 minutes to complete and requires minimal training.

The CAM-ICU assessment was considered positive if patients demonstrated an acute change or fluctuation in the course of their mental status, plus inattention and either disorganized thinking or an altered level of consciousness (LOC) (Ely et al., 2001; Ely et al., 2004; Truman & Ely, 2003). The RASS and CAM-ICU were available in English and Spanish, depending upon patient language preference.

Symptom Assessment Instruments

Condensed Memorial Symptom Assessment Scale (CMSAS)

The CMSAS is a shortened version of the Memorial Symptom Assessment Scale (MSAS), which is a valid cancer instrument which assesses multiple dimensions (severity, frequency, and distress) of 32 physical and emotional symptoms (Portenoy, Thaler, Kornblith, Lepore, & Friedlander-Klar, 1994). The CMSAS rates eleven physical symptoms in terms of distress from 0 (none) to 4 (very much), and three emotional symptoms in terms of frequency from 0 (not present) to 4 (almost constant) (Chang et al., 2004). In the first description of the reliability and validity of the original MSAS, Portenoy (1994) observed that assessment of a shortened list of symptoms provided a valid measure of overall symptom distress. The CMSAS was developed by (Chang et al., 2004) by combining items and dimensions that, in the longer instrument's (MSAS) validation study, showed the strongest association to quality of life and survival. The CMSAS was modified so that at the bottom of the form, patients had the option to describe the prevalence and rate the severity of any symptoms they perceived to bother them, which weren't listed on the survey

Validation of the CMSAS. In order to test for the total amount of symptoms needed to measure quality of life to validate the CMSAS, Chang and colleagues (2000) performed canonical correlation analyses, which identified a five-dimensional QOL factor structure. Symptoms important for QOL also correlated significantly with survival and provided the basis for the CMSAS with 14 symptoms and 3-subscales The Global Distress Index (GDI), the physical symptom distress score (PHYS), and the psychological distress score (PSYCH). In multivariate analyses, the CMSAS PSYCH predicted survival independently of stage of disease (Chang et al., 2004). Reliability, Cronbach's alpha coefficient was 0.82 for CMSAS PHYS, 0.72 for CMSAS PSYCH, and 0.85 for CMSAS SUM (global distress). The mean CMSAS PHYS was 1.13 (range, 0-3.36) standard deviation (SD) 0.86. Mean CMSAS PSYCH was 0.83 (range, 0-4, SD 0.97); and mean CMSAS SUM was 1.04 (range, 0-23, SD 0.77).

The importance of the symptoms identified in Chang's study is strengthened by the fact that they have also appeared in other widely used clinical symptom assessment instruments, such as the Edmonton Symptom Assessment Scale (Bruera et al., 1991), Rotterdam Symptom Checklist (de Haes et al., 1990) and the Symptom Distress Scale (McCorkle & Young, 1978). The utility of the CMSAS use has been extended to patients, with non-cancer conditions, whereas, studies have shown a high symptom burden at EOL among these populations (Abraham et al., 2006; Chang et al., 2000; Kris & Dodd, 2004; Kutner et al., 2006; Kutner et al., 2001; Nelson, 2002)

The advantages of the CMSAS is that it captures distress and frequency dimensions of the symptom experience, and includes symptoms and dimensions that have been correlated to quality of life. In this study, separate reliabilities were computed for

the CMSAS physical subscale, CMSAS psychological subscale, and CMSAS global scale for the patient and family member on both days 1 and 3. The reliabilities for the patient CMSAS physical subscale on day 1 and day 3 were .76 and .43 respectively. The reliabilities for the patient CMSAS psychological subscale on day 1 and day 3 were .73 and .70 respectively. The reliabilities for the patient CMSAS global scale on day 1 and day 3 were .82 and .60 respectively. The reliabilities for the family member CMSAS physical subscale on day 1 and day 3 were .75 and .54 respectively. The reliabilities for the family member CMSAS psychological subscale on day 1 and day 3 were .77 and .75 respectively. The reliabilities for the family member CMSAS global scale on day 1 and day 3 were .82 and .70 respectively.

Treatment & Procedure Survey (TPS)

In the ICU, there are many necessary treatments and procedures performed on patients, to help monitor and improve their condition. The aim of this study was to identify the symptom burden in critically ill patients, which included asking patients to quantify how painful or bothersome the various treatments or procedures they have received during their care. This instrument was adapted from a recent study, which examined symptom burden in Chronic Critically Ill Patients in a step-down respiratory unit, using the CMSAS and a procedure survey to associate frequently performed procedures and patient pain (Nelson et al., 2001). This data will help us plan comfort measures prior to procedures and evaluate efficacy vs burden of treatment intervention (see Appendix D).

Family Respondent Instruments

Family Demographic Form: Family respondents were asked to complete this demographic form, which included broad information such as: relationship to patient; age; ethnicity; religion and whether they were primary care providers for the patient.

CMSAS- Family Respondent Survey

Family respondents completed the CMSAS symptom survey, which was modified to state “Which of these symptoms bothered your loved ones in the last seven days” and “Which of these symptoms bothered your loved ones in the past two days”. Data points are day 1 and day 3 of the patients ICU stay. Families also had the option to write down and rate the severity of any symptoms they perceived to bother the patient. The utility of the CMSAS has been recently used to advance the understanding of the relationships among proxy and patient reports of symptom distress and quality of life (Kutner et al., 2006; Lobchuk & Degner, 2002; Lobchuk, 2003; Lobchuk & Degner, 2002) The CMSAS-Family Respondent form was available in English/Spanish, depending on surrogate preference.

Data Collection Procedure

The data collection procedures are presented in Table 9. Once the subject agreed to participate, a preliminary mental status examination was conducted to detect gross cognitive abnormalities and capacity, and the ability to verbalize or complete the written questionnaire. Written informed consent was obtained (Appendix I) from the patient in the presence of a witness. If patients’ family or significant other was present, the study was explained to them, and they were invited to participate in the study at that time.

Surrogate informed consent and completion of a demographic questionnaire and study instrument, were done in another location away from the patient to minimize potential bias during patient assessment. Study instruments were available in English or Spanish, depending on subject preference.

Patients were given specific directions on how to use the CMSAS form to rate their symptom experience. If patients were awake and alert, but unable to verbalize secondary to (intubation/tubes); or were unable to record answers on the data form because of intravenous and monitoring lines or soft restraints on wrists, the investigator read the study questions and rating scale options to patients. Many patients were alert but non-verbal, yet were able to respond by head nods, eye blinking, holding up fingers, or squeezing the researcher hand in response to the question(s).

There were several methods of data collection used for this prospective study. An investigator developed demographic (Appendix A), RASS and CAM-ICU, (Appendix B). Patient instruments included the symptom assessment survey, the Condensed Form of the MSAS (CMSAS) (Appendix E) (day 1, 3), and the Treatment and Procedure Survey (TPS) (day 3) (Appendix D). Family respondents (FR) completed a FR demographic form (day 1) (Appendix C); and the CMSAS-FR version (day 1, 3) (Appendix G).

Data Collection Points

Time 1 Data Point

Within the first 24-hours of admission, patients were asked to complete the symptom assessment instrument, to quantify their perception of their symptoms in the previous 7-days. The first 24-hour APACHE III Physiologic Score and Predicted Mortality (r) for hospital death, was retrieved from the APACHE data system. Predicted

mortality risk(s) are calculated initially within 24-hours and every 12-hours, thereafter, as long as the patient remains in the ICU.

Table 9

Data Collection Procedure / Study Variables / Data Source

6 Independent Variables	Baseline Admission Time-1 Data Point	Time-2 Data Point Day 3 ICU	Data Source	Outcome
Sociodemographic Factors (IVs) Variables* (2) (*age, gender) Race, Religion, Martial Status, Culture	*		MR /IV Researcher Demographic Log	
Sedation Level Pre-screen patient for sedation level (Sedation/Pain Medications)	*	*	RASS /IV	
Cognitive Status-Assess for capacity Delirium Evaluation Glasgow Coma Scale (GCS)	*	*	IV / CAM-ICU; GCS Scale	
Clinical Variables (IV) Chronic Health (co-morbid conditions/disease)* (1)	*		DB – APACHE III MR	
Admitting Source (IV) ER, OR, hospital ward, ICUs, other hospitals* (1)	*		MR/IV	
Severity of Illness (IV) (APACHE III Predicted Mortality >.60% Risk; and Acute Physiologic Score *(1)	*	*	DB – APACHE III MR	
Outcomes (IV) (1) Hospital (LOS) / % Mortality; ICU LOS / % Mortality	*	*	MR /DB – APACHE III	MR/ for IPDC
Mortality (Outcome) Predicted / Observed (DV) ICU / Hospital Death (IPEXP)	*	*	MR * check hospital for IPDC / IPEXP	MR / 30-Day Outcome / and 3-months
Symptom Burden (DV) Assess. of Symptoms (14) -Items	*	*	CMSAS Questionnaire	
• Symptom prevalence	*	*	CMSAS	
• Symptom intensity	*	*	CMSAS	
• Frequency/Distress	*	*		
Symptom Burden (DV) ICU Sources of Pain & Suffering		*	TPS/IV	

IV = Independent variable; DV = Dependent variable; IPEXP= Inpatient Expiration; IPDC= Inpatient discharge (alive at discharge).

Data sources are: medical record abstraction (MR); interview of patients, surrogates and staff (I/V); and existing databases (DB). APACHE III-APS = Acute Physiologic Score of APACHE III severity of illness scoring system (Knaus et al., 1991); CAM-ICU = Confusion Assessment Method for the Intensive Care Unit (Ely et al., 2001; Truman

& Ely, 2003); CMSAS= Condensed Memorial Symptom Assessment Scale (Chang et al., 2004); RASS =Richmond Agitation and Sedation Scale (Sessler et al., 2002); TPS = Treatment and Procedure Survey (Nelson et al., 2001).

Time 2 Data Point

Subjects were approached two days later (day 3) of ICU care, and assessed for changes in their condition and capacity. If no cognitive deficits were noted on CAM-ICU, patients completed the same instrument (CMSAS), which measured their perception of symptom burden during the first 3-days of ICU treatment and care. At this time, patients were also asked to complete the TPS instrument, which measured their perception of pain and distress related to common ICU treatments and procedures.

Data Analysis

Data analysis using descriptive and multivariable statistics were conducted on data collected from January 2006 to December 2006. The statistical package for Social Sciences (SPSS Version 14.0) was used to perform the analysis of data. All subjects who met the delimitations of the study sample were included in the analysis of data. Descriptive statistics were used to summarize the demographic variables of age, gender, ethnicity, religion, marital status and health insurance. Correlations were analyzed using Pearson's Product Moment Correlations and Spearman's Non-Parametric correlations. All correlations were compared to the statistical significance level of $p < .05$.

***Aim #1:** Examine the perceived symptom burden (prevalence, intensity, frequency), and overall distress, as reported by ICU patients with complex disease states, at high-risk for hospital death.*

The null hypothesis is that overall symptom burden would not be independently associated with disease type/number of co-morbidities, severity of illness (APACHE III Mortality Risk) and significant distress, as reported by critically ill patients in ICUs.

In this study, the CMSAS was used, which has high correlations with clinical status and quality of life measures (Chang et al., 2004; Chang et al., 1998; Portenoy et al., 1994). The CMSAS instrument focuses on distress related to the most prevalent symptoms among patients at end-of-life. CMSAS assesses a single dimension for each of the 11 physiologic symptoms: the dimension of distress (how much does it bother you)? (Five response options ranging from not at all to very much). The dimension of frequency (how often do you experience this?), had five response options ranging from (never to almost constantly) for three psychologic symptoms. The CMSAS yields several validated subscale scores, including (CMSAS-PHYS) score, which measures the average intensity of the 9/11 physical symptoms; the CMSAS-PSYCH score, which measures the degree of psychological distress of three symptoms (worrying, feeling sad, and feeling nervous); and (CMSAS SUM), the total symptom distress score. In the validation studies, the CMSAS PSYCH subscale was an independent predictive of survival in multivariate analysis (Chang et al., 2004). According to Chang and colleagues (2000), CMSAS subscale scores greater than 1.0, suggest the presence of significant symptom distress.

Descriptive statistics were conducted to delineate the prevalence, distress and frequency of patient symptom ratings on day 1 and day 3 (Table 12). A repeated measures analysis of variance for each symptom was done, to determine whether or not there were any significant differences, between the symptom dimensions on day 1 and day 3. The statistical significance level was set at $\leq .05$. Cronbach's alpha.

T-tests were conducted to determine whether the amount of symptom distress for each day (i.e., 1 and 3) varied between males and females. The t test is a useful statistical method for comparing differences between two groups. The test requires a continuous

dependent variable on which the groups are being compared. The test assumes that the variable is normally distributed in the populations from which the samples are drawn and that the samples have equivalent variances (Munro, 2005). If the two groups being compared are matched or paired on some basis, the scores are likely to be similar. The change difference between the two groups will not be as large as when they are drawn independently. Correlations were conducted to determine whether age was associated with the prevalence and degree of distress of each symptom.

A second instrument, the Treatment & Procedure Survey (TPS), was used to measure the interventions that may cause pain, discomfort and suffering among ICU patients, which often are caused by the life-prolonging treatments themselves, the environment and nursing procedures. Descriptive statistics were computed to analyze the treatment and procedure survey (TPS), which will provide us with an expanded understanding of other sources of suffering, that patients' experience, in addition to their physiologic and psychological symptom experience at end-of-life.

***Aim #2:** Examine the relationships between the independent variables of demographic characteristics, antecedent conditions, and the dependent variable of symptom burden (prevalence, intensity, frequency) and overall distress using the (CMSAS-PSYCH and CMSAS-SUM Subscales).*

Pearson correlations were conducted to assess the relationships between gender and the CMSAS symptom burden (prevalence, intensity, frequency) and CMSAS subscales; the relationships between age and the chronic health conditions, CMSAS symptom prevalence. Spearman's non-parametric correlations were conducted to evaluate the relationships between gender and chronic health conditions; gender and

CMSAS prevalence; and chronic health conditions and overall distress CMSAS total subscale.

Aim #3: Explore the relationship between symptom distress and overall patient mortality.

Pearson correlations were conducted to examine the relationship of CMSAS symptom distress and subscales with overall patient mortality. In an attempt to keep the sample size as large as possible, pairwise deletion was used instead of listwise deletion, because it allowed the most amount of people per correlation to be included. Pairwise deletion was considered acceptable because the nature of the study questions did not require that everyone answer each question; rather, it was only necessary for a patient to respond to a question if it pertained to them. So, the symptoms and treatment procedures that did not have responses were not so much missing, as they were not relevant to certain respondents.

Aim #4: To compare critically-ill patient-rated symptoms (prevalence, intensity, frequency), and distress scores for concordance, with those rated by designated surrogate-responders.

Crosstabs with a chi-square statistic were used to evaluate the agreement between patients and their surrogate responders on CMSAS symptom prevalence and distress. Descriptive statistics were used to obtain the frequencies of symptom ratings and means for both patient/surrogates for day 1 and day 3. This data provides clinicians with a greater understanding in the differences in various raters; and the multidimensional nature of symptoms at EOL and their impact on different aspects of quality of life.

Protection of Human Subjects

The research study was explained to each patient/and family member available. This included (a) study purpose, (b) review of the inclusion/exclusion criteria, (c) overview of the data collection procedure and the data instruments and recording process involved in the study, (d) confidentiality of identity of information (e) risks and benefits, (f) voluntary participation, (g) freedom to refuse to answer any questions, and (h) freedom to withdraw from the study at any time. The researcher asked potential subjects to state their understanding (or use some other form of communication, such as nodding head, squeezing researchers hand), of the purpose and procedures involved in participating in the study, to determine their understanding for consent purposes. The researcher screened patients for capacity and potential cognitive deficits, using the RASS and CAM-ICU, prior to obtaining written consent (in the presence of a witness). Subjects/legal surrogate signed two forms, whereas, one was given to the patient and the other retained by the investigator. Following patient consent, family respondents were invited to be a volunteer in the study, and provided informed consent, which included the study information, as noted above, and included signing two consent forms.

Procedures to Protect Confidentiality

Confidentiality of both the written questionnaires and participant identification was of utmost concern. The collected data were for the sole purpose of the research project. Participants received verbal and written information about the purpose of the study, potential risk, and benefits of the study. Study surveys were separated from consent forms, coded, and access was limited to only those directly active in the research

process, including the investigator, a research assistant, and the faculty dissertation chair. Data were analyzed using SPSS Version 14 (2006) and codes without names were used in the database.

Consent forms were written in accordance with HIPPA regulations, the University of San Diego's Internal Review Board (Appendix Q), and other participating ethics committee regulations (Appendix H). No participant names appeared on any of the data collection tools. All data will be kept in a locked file for a minimum of 5 years before being destroyed.

Potential Benefits of Proposed Research and the Safety Ratio

The findings from this research will contribute to the scientific base of nursing through a greater understanding of the multifactorial nature of symptom burden in terminal and critically ill patients, who may be nearing end-of-life. Data will enable clinicians to generate potential interventions to be tested through clinical trials, in an effort to generate new evidence-based therapies, which will reduce a patient's emotional and physical symptoms during their dying trajectory. The risk of harm was assessed to be minimal, since this was a casual interactive experience, while subjects complete a questionnaire. Subjects are free not to participate and free to refuse any questions stated on the questionnaire(s) and instrument. However, given the potential critical condition of study participants and age, there was always the risk for fatigue overall, which would be found in this population generally. If the subject became fatigued/or was unable to complete the questionnaire due to changing condition, arrangements were made for the PI to reassess the patient at a later time, to allow for completion of the self-report survey. The CMSAS instrument was purposefully selected because it only takes 2-3 minutes to

complete (compared to other symptom instruments which take 30-45 minutes), which minimized the potential risk of extreme fatigue in this fragile population.

There was a minimal risk for *psychological harm* through responding to the CMSAS, primarily because the questionnaire is short, and only takes a couple of minutes to complete. However, if patients did exhibit anxiety or fear, a psych mental health nurse practitioner was available for patient referral. During data collection, no patient exhibited associated anxiety, fear or pain related to study procedures. This instrument has been used in previous research with similar populations without report of psychological harm (Nelson et al., 2001). If subjects experienced distress, they also had a right to discontinue participation in the study.

Chapter 4

Results

The purpose of this exploratory study was to (1) examine the symptom burden at end-of-life in critically ill patients with life-limiting illness in ICUs, and (2) examine the relationships among variables related to patients (age, gender, physiologic acuity, chronic health status), symptom distress and overall mortality. In this chapter, a discussion of the findings is presented in three sections. In the first section, a description of the sample will be presented, the second section presents the analysis of the study variables and finally study results specific to the research questions are presented in section three.

Characteristics of the Sample

The demographic questionnaire (Appendix A) was used to collect demographic and personal data from participants. This questionnaire was designed to obtain information from which a sample profile could be developed. These data included age, gender, chronic health status (co-morbidities), admission source, LOS (ICU/Hospital), severity of illness (APACHE III predicted mortality), and observed mortality.

The sample included 244 patients admitted to two intensive care units of a large teaching hospital during January 2006 – December 2006, with an APACHE III mortality

risk of $\geq 60\%$ - 100%, of those 170 were eligible for the current study. Eighty patients were enrolled and able to respond to symptom assessments on day-1 while only 66 (80%) were able to complete the study instruments on day-3. Reasons for study attrition were as follows; the patient expired (10%), the patient was discharged (5%), or the patient lacked capacity (5%), following a deterioration of critical illness (see Figure 2). Overall, there was no significant difference in age, gender, ethnicity, and ICU admission source among those who did or did not complete day-3 symptom assessments.

MR = Mortality Risk

Figure 2. Patient / Family Respondent Recruitment Trends

Once a patient was enrolled in the study, family proxies were invited to participate in the study in order to provide a broader perspective of the patients symptom burden, thus a total of 53 designated family respondents were enrolled. A descriptive profile of the patient sample is presented in Table 10 and family respondent characteristics are presented in Table 11. Each group characteristics will be discussed separately.

Patient Characteristics

Patient participants ranged in age from 35 to 97 years, mean age was $70.5 \pm$ and was predominately male (62.5%). Racial/ethnic composition of the group was diverse

with 48.8% White, 22.5% Black, 15% Hispanic, 11.3% Asian and 2.5% other. The marital status was mixed with 35% married, 30% single, 23.8% widowed and 11.3% divorced. Religious affiliation included Protestant (66.3%), Roman Catholic (27.5%), Jewish (1.3%), not religious (3.8%) and other (1.3%). Participants were predominately English speaking (81.3%), 12.5% of the participants completed the symptom survey in Spanish.

Three quarters of the patients originated from the emergency department, 1.3% from the operating room, 21.3% transfers from medical floors and 2.5% from other hospitals. Upon ICU admission the four most common diagnostic categories among the cohort included respiratory (35%), gastrointestinal (13.8%), sepsis/other (12.5%), cardiovascular (10%) (see Table 10). Chronic health conditions (comorbidities) among the patients were distributed as follows: one-comorbidity (37.5%), two comorbidities (36.3%) three (16.3%), four (6.3%) and five (1.3%) comorbidities.

Patients included in the study were among the “*most critical*” patients treated in the ICU for ≥ 3 days. By definition, the most critical patients were those with the first-ICU-day APACHE III-predicted hospital mortality rate $\geq 60\%$ - 100%. Among the cohort, the first-ICU-day mean (%) predicted hospital mortality rate was 69%, as noted in Table 10. The mean first-ICU-day APACHE III score was 97 ± 23 . The mean ICU length of stay (LOS) was 10, with a range of 1-49 days and mean hospital LOS was 15, (range = 1.5-73) days. Following discharge from the ICU approximately 16% of the patients had to be readmitted to the ICU from the discharge unit for further treatment. The observed ICU and hospital mortality rates were 19% and 2% respectively. Thirty percent of the patients who died in the ICU, were as a result of the decision to withhold or withdraw

life-sustaining treatments while in the ICU. Of the 63 patients who survived to hospital discharge, 16 (25%) died within three months following discharge.

Table 10

Patient Profile and Study Characteristics

Characteristic	M (sd)	N (%)
Age		
<50 years		8 (10)
50-59 years		12 (15)
60-69 years		14 (18)
70-79 years		23 (29)
80-89 years		18 (23)
90-97 years		3 (6)
	70.05 ± 14.6	
Gender		
Male	50	62.5
Female	30	37.5
Ethnicity		
White	39	48.8
Black	18	22.5
Hispanic	12	15
Asian	9	11.3
Other	2	2.5
Marital Status		
Married	28	35
Single	24	30
Divorced	9	11.3
Widowed	19	23.8
Single	24	30
Religion		
Roman Catholic	22	27.5
Protestant	53	66.3
Jewish	1	1.3
Other	1	1.3
None, not religious	3	3.8
Insurance		
Medicare	48	60
Medicaid	11	13.8
HMO	14	17.5
No Insurance	2	2.5
Private/Other	5	6
Admission Source		
Emergency department	60	75
Floor	17	21.3
Operating room	1	1.3
Other hospital	2	2.5

Characteristic	M (sd)	N (%)
Primary ICU Admitting Diagnosis		
Respiratory	28	35
Gastrointestinal	11	13.8
Sepsis/Other	10	12.5
Cardiovascular	8	10
Renal	5	6.3
Neurological	5	6.3
Trauma	4	5.0
UTI Sepsis	4	5.0
Re-Admission to ICU from Discharge Units	13	16.3
APACHE III Chronic Health – Top Five		
Heart Problems	78	97.5
Respiratory Disease	59	73.8
Gastrointestinal Disease	58	72.5
Sepsis/Other	47	58.8
Renal Disease	45	56
Co-morbid Conditions		
1	30	37.5
2	29	36.3
3	13	16.3
4	5	6.3
5	1	1.3
APACHE III Predicted Mortality	Mean	± SD
First Day Hospital	69	± .09
Third Day Hospital	66	± .18
First ICU Day	49	± .14
Third ICU Day	45	± .21
APACHE III Score		
First ICU Day	97	± 23
Third ICU Day	81.9	± 33
Outcomes Mean ± SD		
ICU LOS	10	± 8.83
Hospital LOS	15.85	± 11.97
ICU Mortality	15	19%
Hospital mortality	2	3%
3-Month Follow-Up	16	25%

*Data are presented as mean ± SD or No. (%).

APACHE III = Acute Physiology and Chronic Health Evaluation III - Prognostic System

ICU = Intensive Care Unit; LOS = Length of Stay

For patients discharged alive from the hospital, follow-up information about their survival status was obtained from computerized medical records and a national obituary data-base. While the overall combined mortality among the cohort (n=80) was 46%, the post-discharge mortality figure may actually be higher since the data systems available may not have located some patients who may have died outside the immediate area or

whose obituaries were never posted in newspapers.

Family Respondent Profile

Table 11 presents a profile of the family respondents. In this study, family respondents (FRs) were any close family member or significant other, designated by the patient. There was no attempt to create a matching dyad of patient with a specific family member. A voluntary convenience sample of family respondents was recruited and obtained once families were informed of study opportunity. Of the 80 patients who agreed to participate in the study, 16 did not have family or a designated family respondent. Although 64 FRs were identified, 11 were unavailable/or declined to participate. The mean age of the FRs was 59 years (25-92) and over two thirds (69.8%) were female. Racial/ethnic composition was diverse: White (43.4%), Black (17%), Hispanic (20.8%), Asian (15.1%) and other (3.8%). The relationship of the FRs to the patient included spouse (43.4%), patient's child (41.5%), patient's sibling (5.7%), patient's parent (3.8%) and significant partner (5.7%). The majority of FRs were married (84.9%), with 5.7% single, 3.8% widowed and 5.7% divorced. Religious affiliation included Protestant (51.9%), Catholic (51.9%), Jewish (3.8%), other Christians (7.5%), and other (1.9%). Three quarters were English speaking, 9.4% Spanish speaking and 13.2% other languages. Approximately 70% identified themselves as the primary caregivers. While the majority of patients lived at home 64.2%, 16% of FRs reported that their loved ones were receiving care in long-term facilities because caregiving needs were beyond what they could provide, particularly for those patients with dementia, advanced chronic illnesses and the frail elderly. Patients who were residing at home with limited functionality and complex care needs received home health services (11.3%). Finally,

86.8% of family respondents reported they were the legal surrogate should the patient become incapacitated and unable to make their own decisions regarding life-prolonging treatments and advance care planning.

Table 11

Family Respondent Profile

Characteristics	M (sd)	%
Age		
Mean age $\pm$ SD	59.32	14.27
Years (range)	25-92	
Gender		
Male	16	30.2
Female	37	69.8
Ethnicity		
White	23	43.4
Black	9	17
Hispanic	11	20.8
Asian	8	15.1
Other	2	3.8
Marital Status		
Married	45	84.9
Single	3	5.7
Divorced	3	5.7
Widowed	2	3.8
Religion		
Roman Catholic	18	34.6
Protestant	27	51.9
Jewish	2	3.8
Other	1	1.9
None	4	7.7
Relationship to Patient		
Spouse	23	43.4
Patient's Child	22	41.5
Patient's Sibling	3	5.7
Patient's Parent	2	3.8
Partner	3	5.7
Legal Surrogate for Patient		
Yes	46	86.8
No	7	13.2
Primary Care Giver for Patient		
Yes	37	69.8
No	16	30.2
Patient's Residence		
Home	34	64.2
Long Term Care	13	16

Characteristics	M (sd)	%
Other Family Member/Friends Home	7	13.2
Patient Receiving Home Health Care at Home	6	11.3

Descriptive Findings

***Aim #1:** Examine the perceived symptom burden (prevalence, intensity, frequency), and overall distress as reported by ICU patients with complex disease states, at high-risk for dying.*

Symptoms / Symptom Distress

The CMSAS instrument was originally designed to measure a patients perception of their symptoms (physiologic/psychologic) occurring in the previous seven days only. In this study the CMSAS was administered on day-1 ICU admission, in which patients reported symptoms that were most bothersome in the previous 7-days (previous health status) and on day-3, to report their symptoms and distress following 3-days of ICU care. Table 12 presents the patient report of symptom distress (prevalence, intensity, frequency) experienced at Day-1 and Day-3.

Among patients responding to symptom assessment, approximately 98% were symptomatic. Overall, patients reported an average of 10.23 out of 11 physical symptoms assessed. The two most common physiologic symptoms reported on day-1 by 98.8% of patients, were lack of energy (fatigue) and difficulty concentrating, with a mean symptom distress rating of 2.96 (SD = 0.70) and 2.79 (SD = 0.84) respectively on a scale of 1 = no distress to 4 = great distress. The next most common symptoms were feeling drowsy (97.5%), feeling pain (95%), shortness of breath (95%), dry mouth (95%), and difficulty sleeping reported by 93.8% with a mean distress level scores (with standard deviations in

parentheses) of 2.66 (0.84), 2.52 (1.21), 3.05 (0.88), 1.18 (1.22) and 1.84 (1.42) respectively. The least bothersome symptoms reported on day-1 constipation (87.5%), and nausea (87.5%) with a mean distress level scores (with standard deviations in parentheses) of 2.30 (1.14), 1.07 (1.10), and 1.62 (1.28) respectively.

Nearly all of the critically ill patients (97.9%) reported psychologic symptoms (sadness, worry, and nervousness) with a mean distress score of 2.45 (SD=0.67) with a 2.45 at the highest levels of frequency. Overall patients reported an elevated level of symptom distress on day 1, with increasing severity and number of symptoms on day-3 ICU care, as presented in the analytic comparisons of subscale means in Table 14. CMSAS-PHYS, CMSAS PSYH and CMSAS-Total Distress Subscales showed increased mean levels of distress (standard deviations in parentheses) of 3.07 (0.46), 3.46 (0.52) and 3.17 (0.44).

Patients were also given the opportunity to report any other symptoms that may be bothering them that were not listed on the CMSAS instrument. Of the 24 additional symptoms reported by patients, 20% were physiological, three were psychological (4%) and 15% was related to noise, an added environmental stressor, which inhibits the healing environment for patients (Table 13).

Table 12

Means and Standard Deviations for Patient Reported Mean Symptom Distress Day 1 and Day 3

	Day 1		Day 3	
	Bother or Distress in Past 7 days		Bother or Distress since 2 Days Ago	
Physical Symptoms	n (%)	Mean Sx Distress Score (Std Dev)	n (%)	Mean Sx Distress Score (Std Dev)
Lack of energy (fatigue)*	79 (98.8)	2.96 (0.70)	65 (81.3)	3.80(0.44)
Lack of appetite*	76 (95.0)	2.30 (1.14)	64 (80.0)	3.18 (0.81)
Pain*	76 (95.0)	2.52 (1.21)	66 (82.5)	3.62 (0.66)
Dry mouth*	76 (95.0)	1.18 (1.22)	64 (80.0)	2.58 (0.88)
Weight Loss*	74 (92.5)	1.18 (1.31)	64 (67.5)	1.21(1.38)
Feeling drowsy*	78 (97.5)	2.66 (0.84)	64 (80.0)	3.60 (0.45)
Shortness of breath*	76 (95.0)	3.05 (0.88)	65 (81.3)	3.75 (0.66)
Constipation	70 (87.5)	1.07 (1.10)	58 (72.5)	0.99 (1.25)
Difficulty sleeping*	75 (93.8)	1.84 (1.42)	59 (90.8)	2.79 (1.06)
Difficulty concentrating*	79 (98.8)	2.79 (0.80)	64 (80.0)	3.40 (0.69)
Nausea	70 (87.5)	1.62 (1.28)	57 (71.3)	2.10 (1.26)
CMSAS-PHYS Subscale		2.19 (0.71)		3.07 (0.46)
CMSAS-PHYS Subscale is the average of the nine (*) Items				
Psychological Symptoms	Frequency of Symptom Occurrence in Past 7 days		Frequency of Occurrence Since 2 Days Ago	
	n (%)	Mean Sx Distress Std Dev	n(%)	Mean Sx Distress Score (Std. Dev.)
Worrying	79(98.8)	2.58(0.70)	66(82.5)	3.50 (0.58)
Feeling sad	77(96.3)	2.20(1.02)	66(82.5)	3.48 (.68)
Feeling nervous	80(98.7)	2.33(0.88)	66(82.5)	3.42 (.72)
CMSAS-PSYCH Subscale		2.45(0.67)		3.46 (0.52)
CMSAS Total Distress Score		2.24(0.66)		3.17 (0.44)
CMSAS-PSYCH Subscale is the average of the 3 Psychological Symptoms; CMSAS Total Distress Score is average of all symptoms.				

Table 13

Other Distressing Symptoms Identified by Patients

Other CMSAS Symptoms	Frequency	%
Leg spasms	1	1
Hand tremor	1	1
Sweaty	1	1
Numbness	1	1
Sore Lips (ETT bothersome)*	1	1
Blurry vision	1	1
Angry	1	1
Coughing	1	1
Hiccups	1	1
Hunger	1	1
Legs hurt bad	1	1
Numbness stump	1	1
Tongue hurts	1	1
Dry eyes	1	1
Feels helpless	1	1
Afraid/Scared	2	2
Bad taste	2	2
Tingling	2	2
Headache	5	5
Bloating	4	5
Itchy skin	4	5
Diarrhea	6	6
Noisy	12	15
Thirsty	27	34

*ETT = Endotracheal Tube

Table 14

Mean Comparison of CMSAS Scales – Day 1 and Day 3

Scale	Day 1 (N = 80)		Day 3 (N = 66)	
	Mean Sx Distress Score (Std Dev)	Range	Mean Sx Distress Score (Std Dev)	Range
CMSAS-PHYS Subscale	2.19 (0.71)	0.20 – 3.56	3.07 (0.46)	1.16 – 3.91
CMSAS-PSYCH Subscale	2.45 (0.67)	1 – 4	3.46 (0.52)	1.67 – 4.0
CMSAS TOTAL SCORE	2.24 (0.66)	0.44 – 0.51	3.17 (0.44)	1.28 – 3.93

Note: CMSAS= Condensed Memorial Symptom Assessment Scale; PHYS=Physical; PSYCH=Psychological; Std. Dev = Standard deviation

Aim #2: *Examine the relationships between the independent variables of age, gender, chronic health conditions, and the dependent variable of symptom burden (prevalence, intensity, frequency), and overall distress (CMSAS SUM subscale).*

A. Is there a relationship between age and gender in the reported symptom burden (prevalence, intensity, frequency) and overall symptom distress?

A correlation matrix was computed to identify relationships between gender, age, chronic health conditions and symptom burden (prevalence, intensity, frequency) and overall severity of symptom distress, using the CMSAS-PHYS/PSYCH and CMSAS-SUM subscales as indices.

Table 15

Significant Correlations of Gender and Age with Physiological and Psychological Symptom Prevalence on Day-1 and Day-3

	Gender			Age		
	<i>r</i>	p-value	n	<i>r</i>	p-value	n
<i>Day 1 Physiological Symptom</i>						
Lack of Appetite	.26	.02	80	-	-	-
Pain	-	-	-	-.27	.02	80
Dry Mouth	.26	.02	80	-	-	-
Feeling Drowsy	.22	.05	80	-	-	-
Constipation	-.39	.00	80	-	-	-
Difficulty Sleeping	-	-	-	-.26	.02	80
<i>Day 3 Physiological Symptom</i>						
Constipation	-.35	.00	66	-	-	-
Nausea	-	-	-	-.34	.01	65

Notes: Spearman's Correlations (significant $p < .05$); Gender coded: Male=1, Female=2

Table 15 presents the significant correlations of gender and age with physiologic prevalence; there were no significant correlations with the psychological symptoms. Data indicates some important gender and age-related differences among patient symptom reports. For example, on Day 1, females reported higher levels of distress for lack of

appetite ($r = .26, p=.02$), dry mouth ($r = .26, p=.02$), and feeling drowsy ($r = .22, p=.05$). In contrast, males reported higher levels of distress related to constipation ($r = -.36, p=.05$) on day 1 and day 3 ($r = -.32, p=.01$). Age was negatively correlated with pain ($r = -.27, p=.02$) and difficulty sleeping ($r = -.26, p=.02$) on Day-1 and with nausea ($r = .34, p=.01$) on Day 3.

Table 16

Significant Correlations of Gender and Age with Day 1 and Day 3 Physiological and Psychological Symptom Distress

	Gender			Age		
	<i>r</i>	p-value	n	<i>r</i>	p-value	n
<i>Day 1 Physiological Symptom</i>						
Lack of Appetite	.29	.01	76	-	-	-
Pain	-	-	-	-.33	.00	76
Dry Mouth	.33	.00	76	-	-	-
Constipation	-.36	.00	70	-	-	-
Difficulty Sleeping	-	-	-	-.32	.00	75
Nausea	-	-	-	-.30	.01	70
CMSAS-PHYS Subscale	-	-	-	-	-	-
<i>Day 1 Psychological Symptom</i>						
Worrying	-	-	-	-.43	.00	79
Feeling Nervous	-	-	-	-.39	.00	80
CMSAS-PSYCH Subscale	-	-	-	-.41	.00	80
CMSAS—SUM Subscale	-	-	-	-.22	.05	80
<i>Day 3 Physiological Symptom</i>						
Lack of Appetite	.27	.03	64	-	-	-
Pain	-.26	.04	66	-	-	-
Constipation	-.32	.01	58	-	-	-
CMSAS-PHYS Subscale	-	-	-	-	-	-
<i>Day 3 Psychological Symptom</i>						
Worrying	-	-	-	-.32	.01	66
Feeling Nervous	-	-	-	-.25	.05	66
CMSAS-PSYCH Subscale	-	-	-	-.25	.04	66

Notes: Pearson's correlations. (Significant $p < .05$); Gender coded: Male=1, Female=2

Table 16 presents correlations of gender and age with the physiological and psychological symptom distress on day 1 and day 3. There was continued distress

reported by females on both day 1 and 3 regarding lack of appetite ($r = .29, p=.01$) and ($r = .27, p=.03$) respectively. Males reported significant amounts of distress related to constipation on both day 1 ($r = -.32, p=.05$) and day 3 ($r = -.26, p=.01$), while they reported pain ($r = -.26, p=.04$) on day-3. When correlations were computed for age, there was a significant negative correlation to the overall CMSAS Total Score Distress ($r = -.22, p=.05$), the physiologic symptoms of pain, difficulty sleeping and nausea, the CMSAS PSYCH Subscale ($r = -.41, p<=.05$), and the psychological symptoms of worrying ($r = -.43, p=.01$) and feeling nervous ($r = -.39, p=.05$), at Day 1. At day 3 significant negative correlations were again found for the psychological symptoms of worrying and feeling nervous as well as for the overall CMSAS-PSYCH subscale.

Pearson correlations were next computed to examine the relationship of CMSAS symptom distress and chronic health conditions. In an attempt to keep the sample size as large as possible pairwise deletion was used instead of listwise deletion, because it allowed the most amount of people per correlation to be included. Table 17 and Table 18 present the correlations of the physiological symptom distress and chronic health conditions Day 1 and Day 3 respectively. Findings from the analysis reveal that there are a number of chronic health conditions are significantly correlated with the symptom burden among the study cohort,

Symptom distress was significantly correlated with several of the top five admitting diagnoses to the ICU. Respiratory disease was the most frequent admitting diagnosis to the ICU. Patients with respiratory failure experienced multiple distressing symptoms on Day 1: lack of energy ($r = 0.24, p = .03$), feeling drowsy ($r = .30, p = .01$), shortness of breath ($r = .30, p = .01$), difficulty concentrating ($r = .38, p=.05$) and a

CMSAS PHYS distress score of ($r = .25, p = .03$). Trauma had a significant negative correlation with lack of energy ($r = -0.68, p = 0.05$, feeling drowsy ($r = -0.36, p \leq .05$) and CMSAS-PHSY subscale ($r = -0.39, p \leq .05$). Hematological disease is significantly positively correlated with feeling drowsy ($r = 0.26, p = 0.03$) and nausea ($r = 0.37, p \leq .05$); muscular skeletal disease has a significant negative correlation with shortness of breath ($r = -0.23, p = .05$) and difficulty concentrating ($r = -0.24, p = .05$). GI disease is significantly positively correlated with dry mouth ($r = 0.23, p = .04$) and CMSAS-PHYS Subscale ($r = 0.24, p = .03$). Cerebral vascular accident has a significant negative correlation with difficulty sleeping ($r = 0.28, p = .01$) and is significantly positively correlated with difficulty concentrating ($r = 0.22, p = .05$). Neurological conditions is significantly positively correlated with weight loss ($r = 0.30, p = .01$). Disease severity, mortality risk and a patients' chronic health status, would appear to be an independent factors associated with higher symptom burden and decreased quality of life.

Table 17

Correlations of Physiological Symptom Distress and Chronic Health Conditions Day 1

	Cardiac	DM	Endocr.	GI	Neurol.	CVA	Renal	Liver	Muscul.	Hemat.	Resp.	Sepsis	Trauma	Vascul.
Lack of Energy	0.04	-0.04	-0.10	0.16	0.09	0.08	0.08	0.02	0.03	0.21	0.24*	0.14	-0.68*	-0.01
Lack of Appetite	-0.01	-0.03	-0.11	0.14	0.06	0.02	0.18	-0.06	0.13	-0.03	0.03	0.16	-0.10	-0.17
Pain	-0.15	0.04	0.08	-0.04	-0.01	-0.03	0.04	0.00	-0.06	0.19	0.08	0.10	-0.18	0.07
Dry Mouth	0.05	-0.02	-0.04	0.23*	0.01	-0.04	0.17	0.03	-0.02	0.16	0.05	0.08	-0.16	-0.10
Weight Loss	-0.10	-0.22	-0.15	0.22	0.30*	0.19	-0.12	-0.18	-0.03	0.07	0.07	0.15	0.04	-0.11
Feeling Drowsy	-0.03	0.07	-0.05	0.05	0.11	0.16	-0.01	-0.06	-0.09	0.26*	0.30*	-0.09	-0.36*	0.11
Shortness of Breath	-0.12	0.16	-0.16	0.02	-0.09	0.02	0.11	-0.11	-0.23*	0.05	0.30*	0.01	0.02	-0.09
Constipation	-0.15	-0.01	0.13	-0.02	0.14	-0.09	-0.18	0.03	-0.13	-0.07	0.03	0.08	0.00	0.10
Difficulty Sleeping	-0.11	0.05	-0.09	-0.03	0.08	-0.28*	0.09	-0.02	-0.15	0.08	0.14	-0.07	0.04	0.23
Difficulty Concentrating	0.00	0.06	-0.06	0.12	0.21	0.22*	0.05	-0.07	-0.10	0.16	0.38*	0.07	-0.16	0.01
Nausea	-0.10	-0.15	-0.05	0.19	0.03	-0.19	0.09	0.20	-0.24*	0.37*	-0.15	0.00	-0.06	0.18
CMSAS PHYS Total	-0.03	0.00	-0.09	0.24*	0.11	0.05	0.10	-0.05	0.01	0.19	0.25*	0.12	-0.39*	0.04

*Significant $p < .05$; n range 56-80. Note: DM = Diabetes Mellitus; Endocr. = Endocrine; Neurol. = Neurological; CVA = Cerebral Vascular Accident; Muscul. = Musculoskeletal; Hemat. = Hematological; Resp. = Respiratory; Vascul. = Vascular Diseases

Table 18

Correlations of Physiological Symptom Distress and Chronic Health Conditions Day 3

	Cardiac	DM	Endocr.	GI	Neurol.	CVA	Renal	Liver	Muscul.	Hemat.	Resp.	Sepsis	Trauma	Vascul.
Lack of Energy	-0.08	-0.02	0.12	-0.06	0.10	0.13	-0.02	-0.22	0.11	-0.16	0.13	-0.01	-0.30*	-0.03
Lack of Appetite	-0.09	0.14	-0.02	-0.01	0.08	-0.06	-0.19	-0.17	0.06	-0.18	-0.14	0.15	-0.22	-0.26
Pain	-0.10	0.20	-0.02	-0.07	-0.09	-0.10	-0.07	-0.02	-0.34*	-0.02	-0.10	0.16	0.04	-0.00
Dry Mouth	-0.04	-0.09	-0.11	0.06	-0.05	0.06	0.21	-0.12	-0.08	0.13	0.05	0.19	-0.05	-0.28*
Weight Loss	-0.06	-0.22	-0.12	0.18	0.22	0.25	-0.08	-0.18	0.07	0.27	0.05	0.22	-0.21	-0.25
Feeling Drowsy	-0.16	0.06	-0.24	-0.03	0.03	0.09	-0.20	-0.08	-0.17	-0.07	0.06	-0.09	-0.07	-0.04
Shortness of Breath	-0.07	0.25*	-0.16	-0.16	-0.13	0.11	-0.15	-0.12	-0.30*	-0.21	0.28*	-0.07	-0.01	-0.11
Constipation	-0.09	0.16	0.04	-0.09	0.02	-0.09	-0.16	0.02	-0.06	-0.13	0.12	-0.09	-0.15	0.10
Difficulty Sleeping	-0.00	0.25*	-0.05	0.13	0.00	-0.10	-0.00	0.02	-0.14	-0.12	-0.10	0.01	0.09	0.33*
Difficulty Concentrating	-0.16	0.15	0.00	-0.01	0.09	0.10	0.01	-0.11	-0.20	0.04	0.08	0.16	-0.06	-0.07
Nausea	-0.12	-0.04	0.15	-0.13	-0.24	-0.32*	0.00	0.23	-0.02	-0.02	-0.38*	-0.20	0.11	-0.04
CMSAS	-0.13	0.13	-0.08	0.04	0.07	0.08	-0.08	-0.22	-0.16	-0.03	0.01	0.16	-0.12	-0.12
PHYS Total	0.13													

*Significant $p < .05$; n range 40-66. Note: DM = Diabetes Mellitus; Endocr. = Endocrine; Neurol. = Neurological; CVA = Cerebral Vascular Accident; Muscul. = Musculoskeletal; Hemat. = Hematological; Resp. = Respiratory; Vascul. = Vascular Diseases

Relationship Analysis of the Data Related to the Research Questions

Research Question 1: *Is there a relationship between age and gender in the reported symptom burden (prevalence, intensity, frequency), and overall distress experienced by subjects?*

Independent samples t-tests were performed to examine differences in symptom distress across males and females are presented in Table 19. Overall there was a significant difference with females reporting higher levels of symptom distress across various symptoms. Females reported a lack of energy ($t = 2.079$, $df 75.04$, $p = .04$), lack of appetite ($t = 2.937$, $df 73.97$, $p < .05$), and dry mouth ($t = -3.009$, $df 74$, $p \leq .05$) while males reported increased symptoms of constipation ($t = 3.228$, $df 68$, $p < .05$). On day 3, males again reported higher symptom ratings than women for constipation. In contrast women reported lack of energy and lack of appetite. Overall these findings have some limitations, as males represent (63%) of study cohort versus (38%) women. Men and women differ with respect to the prevalence of diseases such as cardiovascular and autoimmune diseases, the sensory perception of pain, symptom report, illness behavior health care use, and treatment response (van Middendorp et al., 2005). The effect of age is unidirectional, whereas, there are some gender differences in the symptom experience as noted above. The most important results clinically from this research, is that persons with advanced, multiple-chronic diseases are polysymptomatic, and that symptom prevalence is multifactorial (Husain et al., 2007; van Middendorp, 2005). Multiple and interrelated determinants of gender and age differences in objective and subjective health characteristics need further study.

Table 19

Significant T-Tests Comparing Symptom Distress (Days 1 & 3) for Males and Females.

		<i>N</i>	<i>M</i>	<i>SD</i>	<i>t</i>	<i>df</i>	p-value
<i>Day 1 Symptoms</i>							
Lack of Energy	Males	49	2.85	0.82	-2.079	75.04	p = .04
	Females	30	3.14	0.42			
Lack of appetite	Males	47	2.04	1.26	2.937	73.97	p < .05
	Females	29	2.73	-.79			
Constipation	Males	44	1.38	1.04	3.228	68.00	p < .05
	Females	26	.554	1.03			
Dry Mouth	Males	48	.883	1.11	-3.009	74.00	p < .05
	Females	28	1.714	1.25			
<i>Day 3 Symptoms</i>							
Lack of Energy	Males	42	3.73	.74	-1.920	59.82	p = .06
	Females	23	3.93	.51			
Lack of appetite	Males	42	3.03	.88	-2.229	62.00	p = .03
	Females	22	3.49	.58			
Constipation	Males	37	1.30	1.30	2.756	50.80	p < .05
	Females	21	.46	1.00			

Research Question 2: *What is the incidence of other sources (treatments / procedures) of pain and the degree of discomfort, reported by patients during their ICU stay?*

Although patients experience a multiplicity of symptoms related to their disease state while in the ICU, there are also a number of interventions that cause patients additional pain and suffering related to the ICU environment/routine. Patients were given the Treatment and Procedure Survey (TPS) to complete on day 3 of their care. Data was analyzed using descriptive statistics to delineate how the respondents rated their pain and discomfort (Tables 20-21).

In examining the findings from procedure-related symptoms, seventy to eighty percent of patients reported six of the major procedures as severely painful and severely uncomfortable (arterial blood gas puncture; ETT, ETT suctioning, central line placement and moving from bed

to gurney for transport, and turning in bed) which are nursing and interdisciplinary elements of care. Other procedures rated as moderately and severely painful or severely uncomfortable respectively, included arterial catheter insertion (18.8%) / (31.3%); and (20%) / (28.8%),, bladder catheters (27.5%) / (53.8%); and (46.3%) / (35%), nasogastric tube (NGT) in place (20%) / (30%); and (32.5%) / (47.5) , and mechanical ventilation (23.8%) / (50%); and (31.3%) / (42.5%). Only eight percent of the patients undergoing these invasive procedures and other interventions were pre-medicated with sedatives and/or opioids, to reduce anxiety and pain prior to the procedure. The three least uncomfortable procedures included medications given by intramuscular (IM) and subcutaneous (SQ) routes, peripheral intravenous catheter (PIC) insertion and vital signs (VS) being taken. A possible explanation for these low ratings is that IMs and SQ medications are rarely given in ICU rather most medications are delivered intravenously or thru enteral methods (e.g. NGTs, gastrostomy tubes). PIC insertion is also less frequent, since most peripheral lines are initiated in the emergency or operating rooms. Moreover, 80% of all ICU patients require central venous lines for delivery of large volumes of fluid/blood products and many medications which require central lines, to avoid injury to peripheral vessels because of the chemical composition and actions of the medication itself. Finally, vital signs do not seem to be too painful or uncomfortable, most likely because of the non-invasive blood pressure cuffs used and the electrocardiographic monitoring, both of which provide continuous information on the monitors without disturbance to the patient. The procedures identified as severely painful and uncomfortable are very common interventions used to treat and monitor critically ill patients, yet, these therapies designated to improve overall condition were causing additional pain and suffering to over seventy percent of critically ill patients. Studies indicate that variation in pain

intensity and distress can depend on how patients are prepared for ICU procedure and on the different stimuli that may occur with various procedures, thus, anticipatory preparation that includes information about expected sensations may prepare patients better for the experience (Puntillo et al., 2001). Because of the frequency with which procedures are done on critically ill patients, more directed individualized attention to preparation for and control of procedure pain is necessary. Further research is warranted to test interventions that would maximize comfort prior to the initiation of these therapies, and basic nursing procedures.

Table 20

Prevalence of Symptoms of Most Distressing Intensive Care Unit Interventions – (TPS Survey N=66)

Patients Experiencing Procedure as Moderately or Severely Painful or Uncomfortable (%)						
Procedure	No. Rating Procedure	Painful		No. Rating Procedure	Uncomfortable	
		Moderate	Severe		Moderate	Severe
Arterial blood gas puncture	66	9 (11.3%)	57 (71.3%)	66	18 (22.5%)	48 (60%)
Arterial catheter insertion	40	15 (18.8%)	25 (31.3%)	39	16 (20%)	23 (28.8%)
Endotracheal breathing tube in place	64	1 (1.3%)	58 (72.5%)	59	6 (7.5%)	53 (66.3%)
Endotracheal suctioning (Airway)	60	3 (3.8%)	57 (71.3%)	60	12 (15%)	48 (60%)
Catheter in the bladder	65	22 (27.5%)	43 (53.8%)	65	37 (46.3%)	28 (35%)
Mechanical ventilation (Breathing) machine	59	19 (23.8%)	40 (50%)	59	25 (31.3%)	34 (42.5%)
Medications being given, Intramuscular, Subcutaneous	60	45 (56.3%)	15 (18.8%)	60	45 (56.3%)	15 (18.8%)
Moving from bed to gurney to transport to special procedures	66	2 (2.5%)	64 (80%)	66	14 (17.5%)	52 (65%)
Nasogastric tube in place (nose or mouth)	64	16 (20%)	48 (60%)	64	26 (32.5%)	38 (47.5%)
Peripheral IV catheter insertion	66	42 (52.5%)	24 (30%)	66	45 (56.3%)	21 (26.3%)
Central line insertion	60	3 (3.8%)	57 (71.3%)	66	10 (12.5%)	50 (62.5%)
Turning in bed (bath, positioning, upright for x-ray)	66	7 (8.8%)	59 (73.8%)	66	17 (21.3%)	49 (61.3%)
Blood being drawn for lab specimens	65	24 (30%)	41 (51.3%)	65	31 (38.8%)	34 (42.5%)
Vital Signs being taken	65	45 (56.3%)	20 (25.0%)	65	43 (53.8%)	22 (27.5%)

Adapted from Nelson et al., 2001.

Table 21

Means and Standard Deviations for TPS Survey Day 3-ICU Care

	Painful Score	Mean	Std Dev.	Min.	Max.	Uncomfortable Score	Mean	Std Dev.	Min.	Max.
Arterial blood gas puncture		1.86	.346	1	2		1.73	.449	1	2
Arterial catheter insertion		.98	.886	0	2		.94	.875	0	2
Endotracheal breathing tube in place		1.77	.627	0	2		1.70	.656	0	4
Endotracheal suctioning (Airway)		1.77	.602	0	2		1.64	.648	0	2
Catheter in the bladder		1.64	.515	0	2		1.41	.526	0	4
Mechanical ventilation (Breathing) machine		1.50	.685	0	2		1.41	.679	0	2
Medications being given, Intramuscular, Subcutaneous		1.14	.552	0	2		1.14	.552	0	2
Moving from bed to gurney to transport to special procedures		1.97	.173	1	2		1.79	.412	1	2
Nasogastric tube in place (nose or mouth)		1.70	.525	0	2		1.55	.560	0	2
Peripheral IV catheter insertion		1.36	.485	1	2		1.32	.469	1	2
Central line insertion		1.77	.602	0	2		1.67	.641	0	2
Turning in bed (bath, positioning, upright for x-ray)		1.89	.310	1	2		1.74	.441	1	2
Blood being drawn for lab specimens		1.61	.523	0	2		1.50	.533	0	2
Vital Signs being taken		1.29	.489	0	2		1.32	.501	0	2

Std. Dev. = Standard Deviation; Min. = Minimum; Max. = Maximum; Scoring Moderate = 1; Severe = 2

Aim #3: *Explore the relationship between symptom distress and overall patient mortality.*

Research Question 3: *What is the relationship between overall symptom burden and degree of bother/distress (CMSAS PHYS/PSYCH and CMSAS SUM Subscale Scores) and patient mortality?*

Age is thought to be strongly associated with intensive care outcomes (e.g. mortality), however, this relationship is confounded by many clinical variables (Vosylius et al., 2005). Pearson correlations (2-tailed) and nonparametric correlations (Spearman's rho) were used to examine the relationship of CMSAS symptom distress with overall patient mortality.

The presence of severe chronic diseases was more common among elderly patients, however, age was not found to have a significant relationship to overall mortality (Table 22), nor was it significantly correlated with symptom distress (Table 23). In general, elderly patients have poorer outcomes than do younger patients, but prognosis and mortality is more dependent on severity of illness and functional status before admission than on high age itself (de Rooij & Hanna, 2005).

Table 22

Age and Relationship to Mortality

		Age of subject	In-patient Expiration
Age of subject	Pearson Correlation	1.00	-.143
	Sig. (2-tailed)		.205
In-Patient Expiration	Pearson	-.143	1.00
	Correlation Sig. (2-tailed)	.205	

Table 23

Correlation of Symptom Distress and Overall Mortality Day 1 and Day 3

<i>Physiological Symptoms</i>	Day 1		Day 3	
	<i>r</i>	p-value	<i>r</i>	p-value
Lack of energy (fatigue)*	.93	0.77	-.22	0.07
Lack of appetite*	.18	0.12	.10	0.45
Pain*	.16	0.17	.17	0.16
Dry mouth*	.15	0.21	.21	0.10
Weight Loss*	.04	0.76	-.13	0.36
Feeling drowsy*	.07	0.55	-.12	0.34
Shortness of breath*	.17	0.13	.04	0.74
Constipation	.08	0.51	.06	0.64
Difficulty sleeping*	.12	0.29	-.08	0.64
Difficulty concentrating*	.02	0.87	-.01	0.92
Nausea	.14	0.24	.16	0.22
CMSAS-PHYS Subscale	.08	0.49	.07	0.57
No significant correlations				

<i>Psychological Symptoms</i>	Day 1		Day 3	
	<i>r</i>	p-value	<i>r</i>	p-value
Worrying	-.01	0.90	.04	0.76
Feeling sad	-.17	0.14	.11	0.40
Feeling nervous	-.02	0.87	.07	0.56
CMSAS-PSYCH Subscale	.09	0.40	.09	0.46
CMSAS Total Distress	.03	0.81	-.03	0.81
No significant correlations				

Aim #4: *To compare the critically-ill patient-rated symptoms (prevalence, intensity, frequency) and distress scores for concordance, with those rated by designated surrogate-responders. This will provide a more comprehensive approach to understanding the differences in various raters, regarding the multidimensional nature of symptoms at EOL and their impact on different aspects of quality of life.*

Research Question 5: What is the level of concordance between critically-ill patient-rated symptom prevalence, intensity and distress scores, with those rated by designated surrogate responders using the Condensed Memorial Symptom Assessment Survey (CMSAS)?

Although comparisons of patient symptom ratings and those of significant others have been the focus of numerous studies during the past decade, no studies exist among the critical care literature, which examines the concurrent, “real time” examination of a patient’s perception of their symptom burden, taken at the same time as a surrogate rater. In this exploratory study, attempts were made to include family respondents in order to determine the utility and accuracy of proxy ratings of patients’ symptoms, and different explanatory factors for patterns of disagreement between the two groups. Levels of agreement among patient and family raters were analyzed using crosstabs with chi-square to test for concordance and the Kappa Statistic. Studies that measure the agreement between two or more observers should include a statistic that takes into account the fact that observers will sometimes agree or disagree simply by chance. The kappa statistic (or kappa coefficient) is the most commonly used statistic for this purpose (Vierra & Garrett, 2005). A general rule of thumb for significance for the Kappa statistic is any value that is greater than .6 indicates significant agreement between the two groups, while a kappa of 1 indicates perfect agreement, and a kappa of 0 indicates agreement equivalent to chance (Sim & Wright, 2005).

Overall family raters reported an average of 9.75 out of 11 physical symptoms assessed. The most common and distressful symptoms reported (98.1%), by family raters on day-1 was pain and shortness of breath, with a symptom distress score mean of 2.73

(SD=1.10) and 3.03 (SD=.900) respectively. Three other physiologic symptoms reported by 96.2% of FRs were lack of energy (fatigue), lack of appetite, and feeling drowsy, with the symptom distress score mean (standard deviation in parentheses) of 3.32 (.53), 2.44 (0.30), and 2.85 (.83). The next most common symptoms were difficulty concentrating, difficulty sleeping, nausea, and weight loss. The least bothersome symptoms reported on day-1 were constipation (69.9%) and dry mouth (56.6%).

Psychological symptoms reported most frequently by the FR were worrying (98.1%), feeling sad (94.3%) and feeling nervous and (94.3). Symptom distress score means for the psychological symptoms (standard deviations in parentheses) were 2.65 (.81), 2.54 (.83), and 2.66 (.77) respectively. Table 24 provides an overview of family ratings on day 1 and day 3.

Table 24

Means and Standard Deviations for Mean Symptom Distress Day 1 and Day 3-Family Raters

	Day 1		Day 3	
	Bother or Distress in Past 7 days		Bother or Distress since 2 Days Ago	
Physical Symptoms	n (%)	Mean Sx Distress Score (Std Dev)	n (%)	Mean Sx Distress Score (Std Dev)
Lack of energy (fatigue)*	51(96.2)	3.32(.539)	46(86.8)	3.94(.199)
Lack of appetite*	51(96.2)	2.44(1.30)	45(84.9)	3.30(.629)
Pain*	52(98.1)	2.73(1.10)	46(86.8)	3.72(.420)
Dry mouth*	30(56.6)	1.36(1.31)	45(84.9)	2.72(.807)
Weight Loss*	44(83)	1.70(1.53)	26(49.1)	1.93(1.57)
Feeling drowsy*	51(96.2)	2.85(.835)	45(84.9)	3.59(.500)
Shortness of breath*	52(98.1)	3.03(.900)	45(84.9)	3.80(.423)
Constipation	37(69.8)	.864(1.05)	37(69.8)	1.05(1.22)
Difficulty sleeping*	47(88.7)	1.83(1.36)	42(79.2)	2.59(1.15)
Difficulty concentrating*	49(92.5)	3.05(.705)	46(86.8)	3.65(.400)
Nausea	45(84.9)	1.67(1.42)	45(84.9)	2.38(1.21)
CMSAS-PHYS Subscale		2.54(.540)		3.33(.321)
Day-1 (mean/Std. Dev.)				
CMSAS-PHYS Subscale is the average of the nine (*) Items				
	Frequency of Symptom Occurrence in Past 7 days		Frequency of Occurrence Since 2 Days Ago	
	n (%)	Mean Sx Distress (Std Dev)	n (%)	Mean Sx Distress Score (Std. Dev.)
Psychological Symptoms				
Worrying	52(98.1)	2.65(.814)	48(90.6)	3.58(.498)
Feeling sad	50(94.3)	2.54(.838)	48(90.6)	3.71(.504)
Feeling nervous	50(94.3)	2.66(.772)	48(90.6)	3.54(.582)
CMSAS-PSYCH Subscale		2.58(.706)		3.61(.431)
CMSAS Total Distress Score		2.56(.502)		3.40(.298)
CMSAS-PSYCH Subscale is the average of the 3 Psychological Symptoms; CMSAS Total Distress Score is average of all symptoms.				

Patient and Family Member Concordance

Crosstabs with the Pearson Chi-Square and Cohen's Kappa statistics were computed to assess the concordance between patients and family members on ratings of CMSAS symptom presence. These results can be found in Table 25. Only a subset of the symptoms are presented in the tables because some of the symptoms had a constant reported value of yes for at least one of the reports (i.e., patient, family member) and, therefore, the Chi-Square and Kappa statistics could not be computed. The p-value associated with the Chi-Square statistic indicates whether the null hypothesis, that the patient and family member ratings are independent or unrelated, should be accepted. If the p-value is less than .05 then the null hypothesis is rejected indicating that the patient and family ratings are related. Cohen's Kappa statistic was included to measure the agreement between the patient and family member ratings of symptom presence.

The Chi-Square results indicated that on Day-1 there was significant relatedness between the patients and family members for the physiological symptoms, but not for the psychological symptoms. The Kappa statistic for Day-1 symptoms was not as clear in which there was significant agreement between patients and family members for lack of energy, lack of appetite, weight loss, drowsy, difficulty sleeping, difficulty concentrating, and nausea while there was no significant agreement between pain, dry mouth, shortness of breath, and constipation.

The Chi-Square results indicated that on Day 3 there was significant relatedness between the patients and family members for some of the physiological symptoms (weight loss, constipation, and nausea) while none of the psychological symptoms were evaluated due to constant values (see Table 25). The Kappa statistic for Day-3 symptoms

indicated that there was significant agreement between patients and family members for weight loss and nausea, but not for constipation.

Table 25

Concordance between Patient and Family Raters on Day 1 and Day 3 CMSAS Symptom Prevalence

	<i>df</i>	<i>n</i>	<i>X</i> ² (p-value)	<i>Kappa</i>
<i>CMSAS Symptom Day 1</i>				
Lack of Energy	1	53	25.99 (<i>p</i> <.05)	.66
Lack of Appetite	1	53	22.80 (<i>p</i> <.05)	.66
Pain	1	53	18.15 (<i>p</i> <.05)	.57
Dry Mouth	1	38	9.89 (<i>p</i> <.05)	.49
Weight Loss	1	49	25.42 (<i>p</i> <.05)	.72
Drowsy	1	52	21.72 (<i>p</i> <.05)	.65
Shortness of Breath	1	52	5.24 (<i>p</i> =.02)	.30
Constipation	1	41	9.90 (<i>p</i> <.05)	.49
Difficulty Sleeping	1	52	23.22 (<i>p</i> <.05)	.67
Difficulty Concentrating	1	53	22.16 (<i>p</i> <.05)	.65
Nausea	1	51	26.51 (<i>p</i> <.05)	.72
Sad	1	51	0.37 (<i>p</i> =.54)	-.09
Nervous	1	52	0.09 (<i>p</i> =.77)	-.03
<i>CMSAS Symptom Day 3</i>				
Lack of Appetite	1	44	0.50 (<i>p</i> =.83)	-.03
Dry Mouth	1	43	0.14 (<i>p</i> =.71)	-.04
Weight Loss	1	27	12.71 (<i>p</i> <.05)	.64
Constipation	1	39	14.45 (<i>p</i> <.05)	.58
Difficulty Sleeping	1	42	0.72 (<i>p</i> =.40)	.13
Nausea	1	45	29.01 (<i>p</i> <.05)	.78

Overall, these results point to some agreement between patients and family members regarding the presence of CMSAS physiological symptoms, with higher agreement on Day-1 than Day-3. There was no significant agreement found between patients and family members regarding the presence of CMSAS psychological symptoms. Figure 3 provides an overview of the concordance between symptom ratings by patients and families.

Figure 3. Correlation of Symptom Prevalence: Patient/Family Comparisons (Day-1)

Prevalence of physical and psychological symptom prevalence reported by patients and families. The figure shows the percentage of patients (n=80) and family respondents (n=53) providing self-reports, who responded that the symptom was present.

Figure 4. Correlation of Symptom Prevalence: Patient/Family Comparisons (Day-3)

Prevalence of physical and psychological symptom prevalence reported by patients and families on day-3 of ICU Care. The figure shows the percentage of patients (n=66) and family respondents (n=48) providing self-reports, who responded that the symptom was present.

Chapter Summary

This chapter presented the results of the data analysis in three sections—a description of the sample and the demographic data; analysis of study aims, and data analysis related to each research question. The *null hypothesis* was only partially supported, as there were some correlations noted regarding age, gender and symptom distress, yet no correlation between age, severity of illness and overall mortality were found. Significant correlations were found in relationship to symptom distress and the number of chronic health conditions.

Comparisons were done to measure critically-ill patient-rated symptoms and distress scores for concordance, with those rated by designated surrogate-responders. Overall, results point to some agreement between patients and family members regarding the presence of CMSAS physiological symptoms, with higher agreement on Day-1 than Day-3. There was no significant agreement found between patients and family members regarding the presence of CMSAS psychological symptoms.

Chapter 5

Summary, Conclusions, Implications, and Recommendations

Overview

In this study, symptom burden (prevalence, intensity, frequency) and overall distress among (N=80) critically ill patients at end-of-life was investigated, using the University of San Francisco, Symptom Management Conceptual Model (Dodd et al., 2001; Larson et al., 1994) as a theoretical framework and the Condensed Memorial Symptom Assessment Scale (Chang et al., 2004), as the multidimensional instrument to measure the symptom experience. Proxy assessment (N=53) was also obtained, to provide a greater understanding of a patients' symptom burden, and to investigate the accuracy and utility of observer rated assessment. Symptom assessment is important because symptoms directly influence patient distress, quality of life, survival, and family experiences during the dying trajectory. Although the goal of patient comfort is embraced almost universally, deficiencies in the symptom database and inadequate instrument development have hampered research and the achievement of this goal in the ICU. This chapter will present the meaning and the significance of the study findings, along with correlates in the literature. The strengths and limitations of this study are also reviewed.

Finally, the implications of the study findings and directions for future research are outlined.

Symptom Burden Findings

This is one of the first studies among *non-cancer* populations in critical care, which focused on the symptom burden during critical illness and the first systematic examination of symptoms reported in real time by a cohort of ICU patients. The study provided strong evidence that among the patients providing self-report, multiple physical and psychological symptoms were prevalent, causing substantial patient distress.

Overall patients reported an average of 10.23 out of 11 physical symptoms assessed. The two most common physiologic symptoms reported on day-1 by 98.8% of patients, were lack of energy (fatigue) and difficulty concentrating, with a mean symptom distress rating of 2.96 (SD = 0.70) and 2.79 (SD = 0.80) respectively on a scale of 1 = least bothersome to 4 = most bothersome. The next most common symptoms were feeling drowsy (97.5%), feeling pain (95%), shortness of breath (95%), dry mouth (95%), and difficulty sleeping reported by 93.8% with a mean distress level scores (with standard deviations in parentheses) of 2.66 (0.84), 2.52 (1.21), 3.05 (0.88), 1.18 (1.22) and 1.84 (1.42) respectively. The least bothersome symptoms reported on day-1 were constipation (87.5%), and nausea (87.5%) with a mean distress level scores (with standard deviations in parentheses) of 1.07 (1.10), and 1.62 (1.28) respectively.

On Day-3 of data collection, 66 patients remained in the study. Attrition was related to death (10%), patient discharges (5%), and failed capacity (5%) to complete study instrument (s). Overall, there was no significant difference in age, gender, ethnicity, and ICU admission source among those who did complete day-3 symptom assessments.

The most prevalent symptom reported was difficulty sleeping (90.8%), with medium intensity 2.79 (SD=1.06). This finding is alarming, since many of the patients were receiving intravenous agents to reduce anxiety and improve overall relaxation, therefore, sleep should be enhanced. Approximately 80% of patients continued to have symptom distress related to lack of energy, lack of appetite, pain, dry mouth, feeling drowsy, shortness of breath, and difficulty concentrating, with moderate intensity mean of 3.42. Improved and scientifically tested symptom management strategies need to be considered in order to improve the comfort and well-being of ICU patients near death.

The least bothersome symptoms on day-3 were constipation (72.5%), nausea (71.3%) and weight loss (67.5%). The CMSAS-PHYS Subscale mean of 3.07 (SD =0.46), compared to a mean of 2.19 (SD=0.71) on day 1. Patients continued to report psychological distress (worrying, feeling sad, feeling nervous), with a CMSAS-PSYCH Subscale 3.46, SD=0.52 on Day 3, compared to 2.45 (SD=.67) on day 1 of ICU care.

The symptom burden (prevalence, intensity, frequency,) and high distress (see Figure 4) found among ICU patients at risk for dying, is supported by prior research among cancer and a few non-cancer studies (Arnold & Liao, 2006; Caroci & Lareau, 2004; Chang et al., 2000; Chang et al., 2004; Chochinov, 2006; Desbiens et al., 1999; Desbiens & Wu, 2000; Ellershaw & Ward, 2003; Friedrich et al., 2006; Kutner et al., 2001; Nelson et al., 2004; Nelson et al., 2001; Solano et al., 2006).

Other sources (procedure-related interventions) of potential pain and suffering were examined among the study cohort. A number of frequently used procedures and nursing measures were found to be another source of distressing symptoms for patients (Table 20). The majority of patients reported procedures as severely painful and

uncomfortable. These findings are similar to those reported by (Puntillo, 2001) who conducted a multisite study to examine the painfulness of procedures commonly performed in critical care and (Morrison et al., 1998) who examined rankings of pain and discomfort resulting from hospital procedures encountered by advanced dementia patients. These findings illuminate added stress and suffering for ICU patients all of which can be prevented with opioid and non-opioid agents along with other palliative measures to promote comfort. Other environmental/routine stressors reported by patients in this study included noise, inability to communicate (attributable to laryngeal intubation) and sleep disruptions and are consistent with other studies on discomfort and factual recollections in intensive care units (Puntillo, 2001; Puntillo *et al.*, 1997; Rotondi, Chelluri, Sirio, Mendelsohn, & Schulz, 2002; van de Leur *et al.*, 2004; van de Leur, Zwaveling, Loef, & Van der Schans, 2003).

Nearly all of the critically ill patients (97.9%) reported psychologic symptoms (worrying, feeling sad, and feeling nervous) with a mean distress score of 2.58 (SD=0.70) as the highest levels of frequency on day-1 and 3.50 (SD=0.58) on day-3. Overall patients reported a high level of symptom distress on day 1, with increasing severity and number of symptoms on day-3 of ICU care. These findings provide important data that suggests that increased severity of physiological symptoms, along with growing psychological distress, are important correlates for diminished quality of life and predictors of survival in patients with terminal illness and life-limiting illness (Chang et al., 2000; Chang et al., 2004; Chang et al., 2000; Chang et al., 1998; Finlayson, Moyer, & Sonnad, 2004; Granja et al., 2005; Jordhoy, 2001; Kutner et al., 2006; Webb & Norton, 2004).

Correlational Findings Related to Hypothesis

Correlational analysis was conducted to examine the relationships between the independent variables of demographic characteristics, antecedent conditions (patient variables), and symptom burden. Age was also examined as a potential correlate of overall mortality. The influence of demographic factors (age, gender) on symptom scores was examined first. The correlations among these predictor variables were significant among age with physiologic symptoms ($r = -.34, .05$; $r = -.33, p < .05$; $r = -.32, p < .05$; $r = -.30, p < .05$; and psychologic symptom distress day-1 ($r = -.43, p < .05$; $r = -.22, p < .05$ and day-3 ($r = -.32, p = .01$; $r = -.25, p = .05$; $r = -.25, p = .04$).

T-tests were computed to examine gender differences among symptom prevalence and distress. Females reported higher levels of distress for lack of appetite ($r = .26, p = .02$), dry mouth ($r = .26, p = .02$), and feeling drowsy ($r = .22, p = .05$). In contrast, males reported higher levels of distress related to constipation ($r = -.36, p = .05$) on day 1 and day 3 ($r = -.32, p = .01$). Age was negatively correlated with pain ($r = -.27, p = .02$) and difficulty sleeping ($r = -.26, p = .02$) on Day-1 and with nausea ($r = .34, p = .01$) on Day 3. Overall these findings have some limitations/bias, as males represent (63%) of study cohort versus (38%) women. In addition, men and women differ with respect to the prevalence of diseases such as cardiovascular and autoimmune diseases, the sensory perception of pain, symptom report, illness behavior health care use, and treatment response (Middendorp; & et al, 2005). Recent research shows (Chen et al., 2005) that women are less likely than males to experience typical chest pain/discomfort, pain/discomfort in the left side of the chest, and chest pain/discomfort as the most worrisome symptom among men and women with acute coronary syndromes (ACS).

Further studies are needed which include more women, to eliminate research bias and to extend our knowledge base regarding the gender differences, in some of the most crucial health conditions (e.g. heart disease; pulmonary) which are leading causes of death nationally (CDC, 2000).

Pearson correlations were computed to examine the relationship of CMSAS symptom distress and chronic health conditions. Findings indicate there are a number of chronic health conditions that contribute significantly to the symptom burden among the study cohort, with eight of fifteen co-morbidities correlating to significant symptom distress. Symptom distress was correlated with several of the top five admitting diagnoses to the ICU. Respiratory disease was the #2 top admitting diagnosis to the ICU. Patients with respiratory failure had multiple distressing symptoms on Day 1—lack of energy ($r=0.24$ $p=.03$); feeling drowsy ($r=.30$ $p=.01$); shortness of breath ($r=.30$ $p=.01$); difficulty concentrating ($r=.38$ $p=.05$) and a CMSAS PHYS distress score of ($r=.25$ $p=.03$). Trauma had a significant negative correlation with lack of energy ($r=-0.68$, $p=0.05$, feeling drowsy ($r=-0.36$, $p<.05$) and CMSAS-PHSY subscale ($r=-0.39$, $p<.05$). Hematological disease is significantly positively correlated with feeling drowsy ($r=0.26$, $p=0.03$) and nausea ($r=0.37$, $p<.05$); muscular skeletal disease has a significant negative correlation with shortness of breath ($r=-0.24$, $p=.05$) and difficulty concentrating ($r=0.24$, $p=.05$). GI disease is significantly positively correlated with dry mouth ($r=0.23$, $p=.04$), and CMSAS-PHYS Subscale ($r=0.24$ $p=.03$). Cerebral vascular accident has a significant negative correlation with difficulty sleeping ($r=0.28$, $p=.01$) and is significantly positively correlated with difficulty concentrating ($r=0.22$, $p=.05$). Neurological conditions is significantly positively correlated with weight loss ($r=$

0.30, $p = .01$). Disease severity (using APACHE III risk estimates for mortality risk) and a patients' chronic health status (comorbidities), would appear to be a more important factor associated with higher symptom burden and decreased quality of life. The most important results clinically from this research, is that persons with advanced, multiple-chronic diseases are polysymptomatic, and that symptom prevalence is multifactorial (Husain et al., 2007; van Middendorp, 2005).

Age and Relationship to Mortality

Age is thought to be strongly associated with intensive care outcomes, however, this relationship is confounded by many clinical variables (Vosylius et al., 2005). Age was not found to have a *significant* relationship to overall mortality ($r = -.143$, $p = .205$) and ($r = -.143$, $p = 1.00$) in this study, despite the high mortality (21%), nor was it a correlate of severe symptom distress. However, the *presence* of severe chronic diseases was more common among elderly patients. Studies support mortality rates are higher in elderly ICU patients than in younger patients (de Rooij & Hanna, 2005), however, it is not age *per se* but associated factors such as severity of illness and premorbid function status, that appear to be responsible for the poorer prognosis (Angus et al., 2004; Arabi et al., 2002; Chelluri & Grenvik, 1995; Chelluri et al., 1993; Esteban, 2004; Hamel et al., 1999). Some studies indicate that hospital mortality for patients aged 80-84 years, can be as high as 85% for those with infection as their reason for admission, as compared with 58% for those with diagnoses of GI disorders (de Rooij et al., 2005). In another study (van Den, Vogelaers, Afshrift, & Colardyn, 1999) found in-hospital mortality in elderly patients on mechanical ventilation due to pneumonia was 62%, in comparison to 40% in ventilated trauma patients. Outcome after brain injury in geriatric trauma patients is notoriously

poor with mortality and functional disability rates twice those in younger patients (van Den et al., 1999). In a general population of all ages it was shown that 13.6% of the predictive power of the Acute Physiology and Chronic Health Evaluation (APACHE) III model was due to admitting diagnosis. Studies also support, as this study did (25%), that mortality after ICU discharge occurred predominantly during the first 3 months, and was found to be higher among the elderly (de Rooij et al., 2005). Research also indicates that mortality among the elderly is also related to pre-hospital functional independence (Arabi et al., 2002), although this was not assessed in the current study.

Assessment of Proxy Symptom Report

The use of an integrated symptom assessment approach, involving patient and proxy ratings, would be of great value across the spectrum of critically ill patients. For cognitively intact patients, a consensus of patient and proxy assessments would be an ideal outcome. Even with discordant assessments, the use of such an integrated approach could help address apparent differences in symptom assessment among patients, and various raters. For cognitively impaired patients, the selection of individuals who may best understand and represent the patient's symptom experience would also be an ideal outcome. Hence, it would then be important to determine the degree of consistency of ratings across patients and surrogates.

The current study is the first attempt, to examine the reliability of patient and proxy symptom ratings concurrently among critically ill patients and families, using the Condensed Memorial Symptom Assessment Survey (CMSAS). Every effort was made to include family respondents, in order to determine the utility and accuracy of proxy ratings of patient symptoms, and different explanatory factors for patterns of disagreement

between the two groups. Levels of agreement among patient and family raters were analyzed using crosstabs with chi-square to test for concordance and the Kappa Statistic.

Overall, family raters reported an average of 9.75 out of 11 physical symptoms assessed. The most common and distressful symptoms reported (98.1%), by family raters on day-1 was pain and shortness of breath with mean symptom distress scores of a 2.73 (SD=1.10) and 3.03 (SD=.90). Three other physiologic symptoms rated at 96.2% were lack of energy (fatigue), lack of appetite, and feeling drowsy. Other symptoms were difficulty concentrating, difficulty sleeping, nausea and weight loss. The least bothersome symptoms reported on day-1 were constipation and dry mouth. Figures 5- 6 illustrate the comparison of average symptom distress means, reported by patients and families on day 1 and day 3.

Psychological symptoms reported most frequently were worrying, feeling sad, and feeling nervous. The levels of agreement between patients and significant others regarding symptoms indicated that on Day1 there was significant relatedness between the patients and family members for the physiological symptoms, but not for the psychological symptoms.

For Day 3 there was a significant relationship between the patients and family members for some of the physiological symptoms (weight loss, constipation, and nausea). None of the psychological symptoms were evaluated due to constant values. The Kappa statistic for Day 3 symptoms indicated that there was significant agreement between patients and family members for weight loss and nausea, but not for constipation. Overall, these results point to some agreement between patients and family members regarding the presence of CMSAS physiological symptoms, with higher agreement on

Day 1 than Day 3. There was no significant agreement found between patients and family members regarding the presence of CMSAS psychological symptoms.

This study sought to advance our understanding of the relationships among proxy and patient reports of symptom distress. A number of studies that compare patient and proxy symptom ratings have been conducted, however, many of these have focused on a single symptom, such as pain (Desbiens & Mueller-Rizner, 2000; Dudgeon & Lertzman, 1998; Fraser, 2000.; Gift et al., 2003), using physicians, nurses, and/or primary family caregivers as proxy raters. More recently, a number of studies have focused on the role of proxy assessment in palliative care (Kristjanson, Nikoletti, & Porock, 1998; Kutner et al., 2006; Lobchuk et al., 2006; McPherson & Addington-Hall, 2003; McPherson & Hall-Addington, 2004; Nekolaichuk et al., 1999). Although research findings remain inconsistent across studies, there are also notable trends. Both health care providers and significant caregivers tend to underestimate quality of life and performance status of patients, while overestimating physiological symptoms. Within the realm of quality of life, family proxy most often under-estimate the psychological symptoms and well-being of patients.

In contrast, other studies have shown no differences across rater groups. For example, results from a study comparing patient and proxy assessments, using the Memorial Symptom Assessment Scale (MSAS), revealed that professional assessments were comparable to patient and family assessments (Higginson *et al.*, 2003). Similarly (Sneew, Aaronson, & Sprangers, 1997) concluded that proxy ratings of quality of life were reasonably consistent with patient ratings, although there were greater discrepancies in patient-proxy scores in physically and cognitively impaired patients.

Despite these inconsistent findings, proxy raters play an important role in symptom assessment in advanced cancer patients and patients with terminal and life-threatening illness. There are a number of key reasons why proxy assessments may be helpful or necessary: (1) to provide an additional perspective when patients overreport or underreport their symptoms (Coppolino & Ackerson, 2001). (2) to minimize the impact of inaccurate assessments of healthcare providers on symptom management (Cleeland et al., 2000). (3) to increase the reliability of symptom assessment measures (Nekolaichuk et al., 1999), and (4) to reduce the loss of missing data in longitudinal studies (Kutner et al., 2006; Mularski & Osborne, 2003; Oi-Ling et al., 2005).

The current study adds to the scientific knowledge of symptom management and can serve as a framework to use for regular symptom assessments within various clinical settings. Through the development of a reliable integrated symptom assessment approach that incorporates multiple raters and multidimensional profiles, effective interventions will ultimately enhance patients' comfort and quality of life can be made. Further research is needed in critical care, to study the trajectory of symptoms across their illness and to explore individual differences among raters (Coppolino & Ackerson, 2001; Desbiens & Mueller-Rizner, 2000; Engelberg et al., 2005; Hayes, 2003; Levenson et al., 2000; Shalowitz et al., 2006)

Figure 5. Symptom Distress Means: Patient-Family Comparison (Day-1)

Average distress experienced for each symptom, reported by patients (n=80) and families (n=53) on day-1. The left vertical axis represents the distress rating scale of 0 to 4.

Figure 6. Symptom Distress Means: Patient-Family Comparison (Day-3)

Average distress experienced for each symptom, reported by patients (n=66) and families (n=48) on day-3. The left vertical axis represents the distress rating scale of 0 to 4.

Research Strengths and Limitations

Although researchers have begun to investigate the symptom burden at end-of-life in patients with cancer, scant research has been conducted among critically ill patients and their families. This has been one of the first studies to systematically examine the symptom burden and quality of life in real time, as reported by patients and designated proxies, among critically ill patients. This study was important in advancing the science of understanding the symptom experience of patients at EOL in intensive care units. The symptom management model described by Larson and colleagues (1994), provided a strong conceptual framework for the study. Utilizing the symptom management model assisted the researcher in building a theoretical framework for exploring symptom management in patient with complex diseases, receiving life-prolonging therapies. Extending the utilization of the CMSAS instrument to other important populations, was an important in bridging the gap of measurement issues in patients at EOL.

Limitations

When interpreting the results of this study, important limitations need to be considered. First, this cohort study was conducted as a single-center study. Although this yielded a therapeutically homogeneous, and ethnically diverse study population, it may preclude wide generalization of the results to other health care centers, because of institution-based differences in treatment, patient population, and admission policies. Another potential limitation is that APACHE III prognostic model predictions are exclusively based on data obtained during the first 24 hours after ICU admission and that they do not take into account complications that may develop during treatment. It has also been shown that the accuracy of prognostic models based on data from the first 24

hours after ICU admission is maintained at an acceptable level only in patients who stay in the ICU for a short period of time. Finally, although the research instrument was designed to be read and completed by patients, many patients were too ill to read the CMSAS/and record their responses, thus the researcher read the questionnaire to patients, and often recorded their response. This occurred on many occasions, since many ICU patients were not free of physical restraints in their hands/wrists due to IVs and monitoring devices. This process may have decreased the internal validity of the questionnaire responses.

Conclusions

There is limited research addressing the end-of-life needs of critically ill patients with life-limiting illness. According to the literature, this is the first study focusing specifically on the symptom burden during critical illness, and the first systematic examination reported in real time by a cohort of ICU patients in medical/surgical and trauma units. This study found that hospitalized ICU patients at high-risk for hospital death (APACHE Mortality Risk .60-.80), experience a high prevalence of physical and psychological symptoms with only limited treatment of significant distress. These findings were supported by proxy raters overall. Given the level of symptom distress found, and the high mortality rate, that this research and others have observed, there is an urgent need for critical care clinicians to pay greater attention to the dying patients overall symptom distress, and provide evidence-based relief of pain and other distressing symptoms in this population. Furthermore, given the high probability of death and severe functional impairment following critical illness, the critical care team should maximize palliative care therapies, while initiating discussions with patients and their surrogates

about achievable goals for medical care and to establish treatment plans consistent with these goals to minimize preventable pain and discomfort and improve their quality of life.

Implications for Nursing Practice

The routine self-assessment of symptoms is beneficial for patients as it give patients the opportunity to voice their health-related concerns and provides the most valid and reliable method for capturing symptom data. Routine assessments are essential for nursing because nurses are responsible for monitoring and managing patient symptoms, particularly among vulnerable populations such as ICU patients. Nurses must test and use valid instruments to assess their patients more systematically, and identify changes over time. Interventions need to be developed and tested through clinical research trials, to assure that critically ill patients near end of life receive maximum relief for both physiological and psychological symptom distress.

Future Research

Research on the natural trajectory of symptoms for both chronic and critical illness is necessary, in order to understand the multi-dimensional nature of the symptom experience of diverse patients and to enhance patient care. Further studies should also include more formal evaluation of the efficacy of these interventions to help point the way to consistent and high quality care for all dying patients. Researchers must continue to examine patterns of proxy reporting, because as dying patients become unable to communicate, proxy respondents become the primary source of data, whereas investigators can contribute to our body of knowledge in multiple ways.

Clinicians must also conduct research developing and testing theoretical conceptual models of the experience of dying. This may occur at the level of the study

section, in which investigators are encouraged to link variable and measurement selection to testing specified theoretical constructions. Large scale efforts to improve measurement uniformity is currently underway by NHPCO and its advisors, who have identified the domains of end of life care, to be further tested among patients and families with a variety of illnesses.

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Appendix A

PI Log and Monitoring Record

Investigator: _____ Subject Study ID # _____		
Date: _____		
Patient Enrollment	Yes	No
		Date of Patient/Family Interview _____ Phone: _____
Patient must meet ALL of the following Inclusion Criteria		
1) age >18;		
(2) mental capacity to consent, assessed using the Richmond Agitation Sedation Scale (RASS) and Cognitive Assessment Method-ICU (CAM-ICU)		
(3) ability to speak, read and understand English or Spanish;		
(4) ability to complete the self-report instrument through written, verbal or alternative methods, e.g., if questionnaire read to patient by Primary Investigator (PI) or Research Assistant (RA);		
(5) a first-day (within 24-h of ICU Admission) Acute Physiology & Chronic Health Evaluation (APACHE III) risk estimate for hospital death (.60 –.80).		
Other notes: EXCLUDE: Reason _____		
Exclusion Criteria (1) <18 years of age; (2) diagnosis of cancer and receiving related treatments; (3) patients with a principal diagnosis of dementia or patients with altered level of consciousness.		
Demographic Information	Gender ☐ Male ☐ Female	Language Spoken ☐ English ☐ Spanish Other _____
Healthcare Insurance ☐ Private/Commercial ☐ Medicare ☐ Medicaid ☐ HMO ☐ None /Self-pay	Age _____ DOB _____ Race ☐ White ☐ Black ☐ Hispanic ☐ Asian ☐ Native American ☐ Other _____	Religion ☐ Jewish ☐ None, Not Religious ☐ Roman Catholic ☐ Jehov. Wit. ☐ Christian Scientist ☐ Seventh Day Adventist ☐ Protestant
Hospital Admit Date	Admission Diagnostic Category (Location prior to ICU Admission)	
ICU Admit _____ RM # _____ Readmission from: _____ ICU MD Team(s): _____ Medical/Intensivist/ Trauma/	☐ ER ☐ OR: Scheduled ☐ OR Non-Scheduled ☐ Other Hospital _____ ☐ Special Procedure Area ☐ Medical Floor _____ ☐ Other ICU _____	

Investigator: _____ Subject Study ID # _____ Date: _____						
Family Information ☐ Married ☐ Single ☐ Widow ☐ Divorced Adv. Directive at Admission ☐ Yes ☐ No Surrogate: _____ Designated Fam. Respondent Spouse ☐ Patient's Child ☐ Pts Parent ☐ Pts Sibling ☐ Friend ☐ Partner ☐ Other Phone: _____ Was this person Pts caregiver? Yes ☐ No ☐	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td colspan="2" style="padding: 5px;"> Patient's Primary Medical Doctor _____ </td> </tr> <tr> <td style="width: 50%; vertical-align: top; padding: 5px;"> APACHE III Predicted Risk for Hospital Death Day 1 _____ Day 2 _____ Day _____ APACHE III Predicted Risk for ICU Death Day 1 _____ Day 2 _____ Day 3 _____ If no APACHE III Data on Day 3 Why _____ If patient withdrawn from study indicate why. _____ </td> <td style="width: 50%; vertical-align: top; padding: 5px;"> APACHE III Score (0-299) Day 1 (Admission) _____ Day 2 _____ Day 3 _____ RASS Score Day 1 _____ Day 3 _____ CAM-ICU Day 1 ☐ Negative ☐ Positive Day 3 ☐ Negative ☐ Positive Cognitive Changes _____ _____ </td> </tr> </table>		Patient's Primary Medical Doctor _____		APACHE III Predicted Risk for Hospital Death Day 1 _____ Day 2 _____ Day _____ APACHE III Predicted Risk for ICU Death Day 1 _____ Day 2 _____ Day 3 _____ If no APACHE III Data on Day 3 Why _____ If patient withdrawn from study indicate why. _____	APACHE III Score (0-299) Day 1 (Admission) _____ Day 2 _____ Day 3 _____ RASS Score Day 1 _____ Day 3 _____ CAM-ICU Day 1 ☐ Negative ☐ Positive Day 3 ☐ Negative ☐ Positive Cognitive Changes _____ _____
Patient's Primary Medical Doctor _____						
APACHE III Predicted Risk for Hospital Death Day 1 _____ Day 2 _____ Day _____ APACHE III Predicted Risk for ICU Death Day 1 _____ Day 2 _____ Day 3 _____ If no APACHE III Data on Day 3 Why _____ If patient withdrawn from study indicate why. _____	APACHE III Score (0-299) Day 1 (Admission) _____ Day 2 _____ Day 3 _____ RASS Score Day 1 _____ Day 3 _____ CAM-ICU Day 1 ☐ Negative ☐ Positive Day 3 ☐ Negative ☐ Positive Cognitive Changes _____ _____					

| **Patients Admitting Diagnosis:** **Please check all Chronic Health Conditions that apply** ☐ History of cardiac disease, congestive heart failure, or angina (specify) _____ ☐ Endocrine (specify other disorders) _____ ☐ Diabetes, type I ☐ Diabetes, type II _____ ☐ Gastrointestinal (GI) Disease (specify) _____ ☐ Neurologic conditions (specify) _____ ☐ Cerebral Vascular Accident _____ ☐ Renal Disease (specify) _____ ☐ Liver Disease (specify) _____ ☐ Musculoskeletal Disease (specify) _____ ☐ Hematological disease (specify) _____ ☐ Respiratory Disease (specify) _____ ☐ Sepsis (specify) _____ | | |

Investigator: _____ Subject Study ID # _____	
Date: _____	
☐ Trauma (specify) _____ ☐ Vascular _____ ☐ Other (please specify) _____	
<u>Outcome Data</u>	
Hospital Admit: _____	Admit to ICU: _____
Discharge from ICU - Date: _____	Discharge Location _____
Readmitted to ICU from discharge unit: _____	
LOS: ICU: _____	Discharge Date _____
Hospital: _____	LOS: _____
<u>Alive -Inpatient Discharge(IPDC):</u>	
Was Patient made a DNR before transfer from ICU to other unit/or IPD from hospital?	
☐ yes ☐ no IPDC Location: ☐ Home ☐ Home Health ☐ LTC ☐ Hospice ☐ MWR	
In-Patient Expiration (IPE) Date: _____	
Was patient DNR at time of death? ☐ yes, If yes, date written _____ ☐ No _____	
Was Treatment Withheld or Withdrawn before death? _____	
30-Day Outcome / Location / Patient Status _____	
Predicted Mortality: _____	Observed Mortality: _____
Standardized Mortality Ratio (SMR) _____	
<u>Financial Outcomes:</u>	
Primary DRG _____ (\$)	Total Hospital Costs(\$): _____

Appendix B

Richmond Agitation and Sedation Scale (RASS) and Cognitive Instrument CAMU-ICU

(English/Spanish)

**Linking Sedation and Delirium Monitoring
A Two Step Approach to Assess Consciousness**

Step One: Sedation Assessment**The Richmond Agitation and Sedation Scale: The RASS**

Score	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
+2	Agitated	Frequent non-purposeful movement, patient fights ventilator
+1	Restless	Anxious but movements not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye-contact) to <i>voice</i> (≥ 10 seconds)
-2	Light sedation	Briefly awakens with eye contact to <i>voice</i> (≤ 10 seconds)
-3	Moderate sedation	Movement or eye opening to <i>voice</i> (but no eye contact)
-4	Deep sedation	No response to voice, but movement or eye opening to <i>physical</i> stimulation
-5	Unarousable	No response to <i>voice</i> or <i>physical</i> stimulation

IF RASS IS -4 or -5, then **Stop** and **Reassess** patient at later timeIF RASS is above -4 (-3 through +4) then **Proceed to Step 2***Sessler, & et al., (2002). *Am J Respir Crit Care Med*, 166, 1338-1344.*Ely, et al., (2003). *JAMA*, 289, 2983-2991.**Step Two: Delirium Assessment**

CAM-ICU Worksheet

Feature 1: Acute Onset or Fluctuating Course Positive if you answer 'yes' to either 1A or 1B.	Positive	Negative
1 A: Is the pt different than his/her baseline mental status? Or 1 B: Has the patient had any fluctuation in mental status in the past 24 hours as evidenced by fluctuation on a sedation scale (e.g. RASS), GCS, or previous delirium assessment?	Yes	No
Feature 2: Inattention Positive if either score for 2A or 2B is less than 8. Attempt the ASE letters first. If pt is able to perform this test and the score is clear, record this score and move to Feature 3. If pt is unable to perform this test or the score is unclear, then perform the ASE Pictures. If you perform both tests, use the ASE Pictures' results to score the Feature.	Positive	Negative
2A: ASE Letters: record score (enter NT for not tested) Directions: Say to the patient, "I am going to read you a series of 10 letters. Whenever you hear the letter 'A' indicate by squeezing my hand." Read letters from the following letter list in a normal tone. SAVE A HAART Scoring: Errors are counted when patient fails to squeeze on the letter "A" and when the patient squeezes on any letter other than "A."	Score (out of 10): _____	
2B: ASE Pictures: record score (enter NT for not tested) Directions are included on the picture packets.	Score (out of 10): _____	
Feature 3: Disorganized Thinking Positive if the combined score is less than 4	Positive	Negative
3A: Yes/No Questions (Use either Set A or Set B, alternate on consecutive days if necessary): Set A 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does one pound weigh more than two pounds? 4. Can you use a hammer to pound a nail? Score _____ (Patient earns 1 point for each correct answer out of 4) 3B: Command Say to patient: "Hold up this many fingers" (Examiner holds two fingers in front of patient) "Now do the same thing with the other hand" (Not repeating the number of fingers). *If pt is unable to move both arms, for the second part of the command ask patient "Add one more finger" Score _____ (Patient gets 1 point if able to successfully complete the entire command)	Combined Score (3A+3B): (out of 5) _____	
Feature 4: Altered Level of Consciousness Positive if the Actual RASS score is anything other than "0" (zero)	Positive	Negative
Overall CAM-ICU (Features 1 and 2 and either Feature 3 or 4):	Positive	Negative

Enlazando la Monitoria de la Sedación y del Delirio: Un Enfoque en Dos Pasos para Valorar el Estado de Conciencia

Primer paso: Evaluación de la Sedación

Escala de Agitación y Sedación de Richmond: RASS*

Puntaje	Término	Descripción	
+ 4	Combativo	Combativo, violento, peligro inmediato para el grupo	
+ 3	Muy agitado	Se jala o retira los tubos ó catéteres; agresivo	
+ 2	Agitado	Movimiento frecuentes y sin propósito, lucha con el ventilador	
+ 1	Inquieto	Ansioso, pero sin movimientos agresivos o vigorosos	
0	Alerta y calmado		
-1	Somnoliento	No está plenamente alerta, pero se mantiene despierto (apertura y contacto ocular) al llamado verbal (≥ 10 segundos)	Verbal Stimulation
-2	Sedación leve	Despierta brevemente al llamado verbal con contacto ocular (< 10 segundos)	
-3	Sedación moderada	Movimiento o apertura ocular al llamado verbal (pero sin contacto visual)	Physical Stimulation
-4	Sedación profunda	Sin respuesta al llamado verbal, pero hay movimiento o apertura ocular al estímulo físico	
-5	Sin respuesta	Sin respuesta a la voz o estímulo físico	

Si RASS es -4 or -5, **Deténgase y Reevalúe** el paciente posteriormente
Si RASS es mayor a -4 (-3 a +4), entonces **Proceda con el Segundo paso**

Segundo paso: Evaluación del Delirio

1er Criterio: Inicio agudo de la alteración del estado mental o curso fluctuante

Criterios y Descripción del CAM-ICU				
1. Inicio agudo o curso fluctuante	Ausente	Presente		
<p>A. Hay evidencia de un cambio agudo en el estado mental sobre el estado basal?</p> <p style="text-align: center;">O</p> <p>B. Ha fluctuado el comportamiento (anormal) en las últimas 24 horas, es decir, tiende a aparecer y desaparecer, o aumenta y disminuye en severidad evidenciado por la fluctuación en una escala de sedación (p.e., RASS), Escala de Glasgow, o evaluación previa del Delirio?</p>				
2. Inatención	Ausente	Presente		
<p>¿Tuvo el paciente dificultad para fijar la atención, evidenciada por puntajes menores a 8 en cualquiera de los componentes visual o auditivo del Examen de Tamizaje para la Atención (ASE)? (Instrucciones en la página siguiente).</p>				
3. Pensamiento desorganizado	Ausente	Presente		
<p>¿Hay evidencia de pensamiento desorganizado o incoherente evidenciado por respuestas incorrectas a 2 o más de las 4 preguntas, y/o incapacidad para obedecer órdenes?</p> <p>Preguntas (Alternar grupo A y grupo B):</p> <table border="0" style="width: 100%;"> <tr> <td style="vertical-align: top;"> <p>Grupo A</p> <p>1. ¿Podría flotar una piedra en el agua?</p> <p>2. ¿Existen peces en el mar?</p> <p>3. ¿Pesa más una libra que dos libras?</p> <p>4. ¿Se puede usar un martillo para pegarle a un clavo?</p> </td> <td style="vertical-align: top;"> <p>Grupo B</p> <p>1. ¿Podría flotar una hoja en el agua?</p> <p>2. ¿Existen elefantes en el mar?</p> <p>3. ¿Pesaran más dos libras que una libra?</p> <p>4. ¿Se puede usar un martillo para cortar madera?</p> </td> </tr> </table> <p>Otros:</p> <p>1. ¿Tiene usted algún pensamiento confuso o poco claro?</p> <p>2. Muestre esta cantidad de dedos. (El examinador muestra dos dedos en frente del paciente).</p> <p>3. Ahora repita lo mismo con la otra mano. (Sin repetir el mismo número de dedos).</p>			<p>Grupo A</p> <p>1. ¿Podría flotar una piedra en el agua?</p> <p>2. ¿Existen peces en el mar?</p> <p>3. ¿Pesa más una libra que dos libras?</p> <p>4. ¿Se puede usar un martillo para pegarle a un clavo?</p>	<p>Grupo B</p> <p>1. ¿Podría flotar una hoja en el agua?</p> <p>2. ¿Existen elefantes en el mar?</p> <p>3. ¿Pesaran más dos libras que una libra?</p> <p>4. ¿Se puede usar un martillo para cortar madera?</p>
<p>Grupo A</p> <p>1. ¿Podría flotar una piedra en el agua?</p> <p>2. ¿Existen peces en el mar?</p> <p>3. ¿Pesa más una libra que dos libras?</p> <p>4. ¿Se puede usar un martillo para pegarle a un clavo?</p>	<p>Grupo B</p> <p>1. ¿Podría flotar una hoja en el agua?</p> <p>2. ¿Existen elefantes en el mar?</p> <p>3. ¿Pesaran más dos libras que una libra?</p> <p>4. ¿Se puede usar un martillo para cortar madera?</p>			
4. Nivel de Conciencia alterado				
<p>Ausente Presente</p> <p>¿Tiene el paciente un nivel de conciencia diferente al estado de <i>alerta</i>, tales como vigilante, letárgico, o estupor?</p> <p>(p.e., RASS diferente a "0" al momento de la evaluación)</p> <table border="0" style="width: 100%;"> <tr> <td style="vertical-align: top;"> <p>Alerta:</p> <p>Vigilante:</p> <p>Letárgico:</p> <p>Estupor:</p> </td> <td style="vertical-align: top;"> <p>espontánea y plenamente conciente del medio ambiente e interactúa apropiadamente</p> <p>hiperalerta</p> <p>somnoliento pero fácil de despertar, no conciente de algunos elementos del medio ambiente, o no interactúa de manera apropiada y espontánea con el entrevistador; llega a estar plenamente conciente e interactúa apropiadamente con estímulos mínimos</p> <p>Incompletamente conciente cuando es estimulado fuertemente; puede ser despertado únicamente con estímulos vigorosos y repetidos, y tan pronto como el estímulo cesa, vuelve al estado de no respuesta</p> </td> </tr> </table>			<p>Alerta:</p> <p>Vigilante:</p> <p>Letárgico:</p> <p>Estupor:</p>	<p>espontánea y plenamente conciente del medio ambiente e interactúa apropiadamente</p> <p>hiperalerta</p> <p>somnoliento pero fácil de despertar, no conciente de algunos elementos del medio ambiente, o no interactúa de manera apropiada y espontánea con el entrevistador; llega a estar plenamente conciente e interactúa apropiadamente con estímulos mínimos</p> <p>Incompletamente conciente cuando es estimulado fuertemente; puede ser despertado únicamente con estímulos vigorosos y repetidos, y tan pronto como el estímulo cesa, vuelve al estado de no respuesta</p>
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<p>CAM-ICU general (Criterios 1 y 2 y cualquiera de los criterios 3 ó 4):</p>				
		<p>Sí No</p>		

Appendix C

Family Respondent Demographic Form (English/Spanish)

Primary Investigator: Peggy Kalowes RN, PhD

Study: Symptom Burden in Patients with Life Threatening Illness in ICU Respondent ID Code: _____ Date: _____ Study Instruments: ☐ Demographic Form Condensed Memorial Symptom Assessment Scale (MSAS): Day 1 ☐ Yes ☐ No Day 3 ☐ Yes ☐ No (In person ☐ Telephone Interview ☐ If Day 3 is no, Why _____
--

Please complete the following questions. This information will be kept strictly confidential.

FAMILY RESPONDENT DEMOGRAPHIC FORM	
Your Demographic Information: Age: _____ Phone Number: _____	
Gender: ☐ Male ☐ Female Language Spoken: ☐ English ☐ Spanish ☐ Other _____	
Race ☐ White ☐ Black ☐ Hispanic ☐ Asian ☐ Native American ☐ Other _____	Religion ☐ Jewish ☐ Roman Catholic ☐ Jehovah's Witness ☐ Christian Scientist ☐ Seventh Day Adventist ☐ Protestant (all other Christian) ☐ None, Not Religious
Family Information ☐ Married ☐ Single ☐ Widow ☐ Divorced	
1. Please identify your relationship with the patient. ☐ Spouse ☐ Patients Child ☐ Patient's Sibling ☐ Patient's Parent ☐ Friend ☐ Partner ☐ Other _____	
2. Are you the legal Surrogate to make decisions, if the patient is unable to? ☐ Yes ☐ No	
3. Was the patient living at home prior to this hospitalization? ☐ Don't know ☐ Yes ☐ No If no, please identify ☐ Living alone at home ☐ Home with family or friends ☐ Assisted living facility ☐ Nursing home	
4. Were you providing care for your loved one during his/her course of illness? ☐ Yes ☐ No	
5. To your knowledge was the patient receiving any home health services, prior to admission?	

FAMILY RESPONDENT DEMOGRAPHIC FORM

Your Demographic Information: Age: _____ Phone
Number: _____

Gender: ☐ Male ☐ Female **Language Spoken:** ☐ English ☐ Spanish
☐ Other _____

Race

☐ White ☐ Black ☐ Hispanic ☐ Asian
☐ Native American ☐ Other _____

Religion

☐ Jewish ☐ Roman Catholic ☐
Jehovah's Witness
☐ Christian Scientist ☐ Seventh Day
Adventist
☐ Protestant (all other Christian)
☐ None, Not Religious

Family Information

☐ Married ☐ Single ☐ Widow ☐ Divorced

☐ Yes ☐ No ☐ Don't know If yes, please identify below

☐ Home health nurse/aid ☐ Visiting nurse ☐ Hospice ☐ Respiratory Care, such as
Oxygen ☐ Church based ministries ☐ Other, please specify

Forma demográfica para el respondedor familiar
Investigadora primaria: Peggy Kalowes RN, PhD

Estudio: Carga del síntoma en pacientes con enfermedades peligrosos para la vida en el cuidado intensivo
 ID Código del respondedor: _____ Fecha: _____
 Instrumentos del estudio: ☐ Forma demográfica
 Escala Memorial Condensada de Evaluación de los Síntomas (CMSAS): Día 1 ☐ Sí ☐ No
 Día 3 ☐ Sí ☐ No (En persona ☐ Entrevista por teléfono ☐ Si por Día 3 responde "No", ¿por qué? _____

Por favor conteste las siguientes preguntas. Esta información será mantenida confidencial.

FORMA DEMOGRÁFICA PARA EL RESPONDEDOR FAMILIAL	
Información demográfica de usted: Edad: _____ Número de teléfono: _____	
Género: ☐ Varón ☐ Hembra Idioma hablada: ☐ Inglés ☐ Español ☐ Otro _____	
Raza ☐ blanco ☐ negro ☐ hispano ☐ asiático ☐ indio nativo americano ☐ Otro _____	Religión ☐ Judío ☐ Católico ☐ Testigo de Jehová ☐ Científico cristiano ☐ Adventista del séptimo día ☐ Protestante (otros cristianos) ☐ Ningunos, No religioso
Información familiar ☐ Casado(a) ☐ Soltero(a) ☐ Viudo(a) ☐ Divorciado(a)	
1. Por favor identifique su relación con el paciente. ☐ Esposo/a ☐ Niño/a del paciente ☐ Hermano/a del paciente ☐ Padre del paciente ☐ Amigo/a ☐ Socio/a ☐ Otro _____	
2. ¿Está usted el sustituto legal para tomar decisiones, si el paciente no pueda? ☐ Sí ☐ No	
3. ¿Estaba viviendo el paciente en casa antes de esta hospitalización? ☐ No sé ☐ Sí ☐ No <u>Si no, identifique por favor</u> ☐ Vive solo en casa ☐ Vive en casa con familia y/o amigos ☐ Facilidad de vida asistida ☐ Residencia de ancianos	
4. ¿Estaba usted cuidando del paciente durante el curso de la enfermedad? ☐ Sí ☐ No	
5. Que usted sepa, ¿estaba recibiendo el paciente algunos servicios de salud en casa antes de su ingreso? ☐ Sí ☐ No ☐ No Sé <u>Si sí, identifique abajo</u> ☐ Enfermera en casa ☐ Enfermera visitante ☐ Residencia para enfermos desahuciados ☐ Cuidado respiratorio, como oxígeno ☐ Ministros de la Iglesia ☐ Otro, especifique por favor	

FORMA DEMOGRÁFICA PARA EL RESPONDEDOR FAMILIAL

Información demográfica de usted: Edad: _____ Número de teléfono: _____

Género: ☐ Varón ☐ Hembra **Idioma hablada:** ☐ Inglés ☐ Español ☐ Otro

Raza

☐ blanco ☐ negro ☐ hispánico
☐ asiático
☐ indio nativo americano ☐ Otro

Religión

☐ Judío ☐ Católico ☐ Testigo de Jehová
☐ Científico cristiano ☐ Adventista del séptimo día
☐ Protestante (otros cristianos)
☐ Ningunos, No religioso

Información familiar

☐ Casado(a) ☐ Soltero(a) ☐ Viudo(a)
☐ Divorciado(a)

Appendix D

Patient Treatment and Procedure Survey (TPS)

Symptom Burden Study ICU

Study: Respondent ID Code: _____ Date: _____ Patient Self-Report Instruments: ☐ MSAS: Day 1 ☐ Yes ☐ No Day 3 ☐ Yes ☐ No Treatment & Procedure Survey (Patient) Day 3 ☐ Yes ☐ No If no, Why _____
--

Procedure	<u>Painful</u>			<u>Uncomfortable</u>		
	Moderate	Severe	Total	Moderate	Severe	Total
Arterial blood gas puncture	1	2		1	2	
Arterial catheter insertion	1	2		1	2	
Endotracheal breathing tube in place	1	2		1	2	
Endotracheal suctioning (Airway)	1	2		1	2	
Catheter in the bladder	1	2		1	2	
Mechanical ventilation (Breathing) machine	1	2		1	2	
Medications being given, Intramuscular, subcutaneous	1	2		1	2	
Moving from bed to gurney to transport to special procedures	1	2		1	2	
Nasogastric tube in place (nose or mouth)	1	2		1	2	
Peripheral IV catheter insertion	1	2		1	2	
Central line insertion	1	2		1	2	
Turning in bed (bath, positioning, upright for x-ray)	1	2		1	2	
Blood being drawn for lab specimens	1	2		1	2	
Vital Signs being taken						

Adapted from Nelson et al., 2001.

Encuesta del tratamiento y procedimiento
Estudio del carga del síntoma

Estudio: ID Código del respondedor: _____ Fecha: _____
Instrumentos del paciente (reportado por sí mismo): ☐ MSAS: Día 1 ☐ Sí ☐ No Día 3 ☐ Sí ☐ No
Encuesta del tratamiento y procedimiento (Paciente) Día 3 ☐ Sí ☐ No Si no, ¿Por qué? _____

	<u>Doloroso</u>			<u>Incómodo</u>		
	Moderado	Severo	Total	Moderado	Severo	Total
Perforación Gases en la Sangre Arterial	1	2		1	2	
Inserción del Catéter arterial	1	2		1	2	
El tubo endotraqueal para respirar (en lugar)	1	2		1	2	
La succión endotraqueal (vía aérea)	1	2		1	2	
Catéter en vejiga	1	2		1	2	
Máquina de ventilación mecánica (respirar)	1	2		1	2	
Dar medicamentos, Intramuscular	1	2		1	2	
Mover de la cama a la camilla para transportar a procedimientos especiales	1	2		1	2	
Sonda (tubo) naso gástrica en su lugar (nariz o boca)	1	2		1	2	
Inserción del suero periférico	1	2		1	2	
Inserción de la línea central del Catéter	1	2		1	2	
Voltearse en la cama (baños, posiciones, rayos x en posición vertical)	1	2		1	2	
Sacando sangre para los especímenes del laboratorio	1	2		1	2	
Tomando los vitales						

Adaptado por Nelson et al., 2001.

Appendix E

Condensed Memorial Symptom Assessment Scale (CMSAS) Patient Version (English/Spanish)

Interviewer ID: _____ Subject Code: _____

How much did this symptom bother or distress you during the past 7 days?

Symptom	Present	Not at all	A little Bit	Somewhat	Quite a bit	Very much
Lack of energy*	Y N	0	1	2	3	4
Lack of appetite*	Y N	0	1	2	3	4
Pain*	Y N	0	1	2	3	4
Dry mouth*	Y N	0	1	2	3	4
Weight Loss*	Y N	0	1	2	3	4
Feeling drowsy*	Y N	0	1	2	3	4
Shortness of breath*	Y N	0	1	2	3	4
Constipation	Y N	0	1	2	3	4
Difficulty sleeping*	Y N	0	1	2	3	4
Difficulty concentrating	Y N	0	1	2	3	4
Nausea*	Y N	0	1	2	3	4

How frequently did you experience these symptoms during the last week?

Symptom	Present	Rarely	Occasionally	Frequently	Almost constantly
Worrying	Y N	1	2	3	4
Feeling sad	Y N	1	2	3	4
Feeling nervous	Y N	1	2	3	4

OTHER SYMPTOMS

Identify any other symptoms that you believe bothered you during the past week. List them below & identify how distressful they were.	Not at all	A little Bit	Some what	Quite a bit	Very much
	0	1	2	3	4
	0	1	2	3	4
	0	1	2	3	4
	0	1	2	3	4

Condensed Memorial Symptom Assessment Scale (CMSAS)

How much did this symptom bother or distress you since I saw you 2 days ago?

Symptom	Present	Not at all	A little Bit	Somewhat	Quite a bit	Very much
Lack of energy*	Y N	0	1	2	3	4
Lack of appetite*	Y N	0	1	2	3	4
Pain*	Y N	0	1	2	3	4
Dry mouth*	Y N	0	1	2	3	4
Weight Loss*	Y N	0	1	2	3	4
Feeling drowsy*	Y N	0	1	2	3	4
Shortness of breath*	Y N	0	1	2	3	4
Constipation	Y N	0	1	2	3	4
Difficulty sleeping*	Y N	0	1	2	3	4
Difficulty concentrating*	Y N	0	1	2	3	4
Nausea	Y N	0	1	2	3	4

How frequently did you experience these symptoms since I saw you 2 days ago?

Symptom	Present	Rarely	Occasionally	Frequently	Almost constantly
Worrying	Y N	1	2	3	4
Feeling sad	Y N	1	2	3	4
Feeling nervous	Y N	1	2	3	4

OTHER SYMPTOMS

Identify any other symptoms that may have bothered you in the past 2 days. List them below & identify how distressful they were.	Not at all	A little Bit	Somewhat	Quite a bit	Very much
	0	1	2	3	4
	0	1	2	3	4
	0	1	2	3	4
	0	1	2	3	4

Appendix F

CMSAS Scoring Sheet

The scoring for the Condensed Memorial Symptom Assessment Scale (CMSAS) is similar to that for the MSAS Short Form

For the top box (physical symptoms), weights of zero for N, 0.8 for not at all, 1.6 for a little bit, 2.4 for somewhat, 3.2 for quite a bit, and 4.0 for very much. The average of the starred symptoms would be the PHYS subscale.

For the bottom box (psychological symptoms), weights of zero for N, 1 for rarely, 2 for occasionally, 3 for frequently, 4 for almost constantly. The average of the 3 symptoms would be the PSYCH subscale. The average of all symptoms would be the CMSAS-SUM subscale. Chang, Hwang, Kasimis & Thaler, (2004). Shorter symptom assessment instruments: The condensed memorial symptom assessment scale (CMSAS). *Cancer Investigation* 22, 526-536.

Memorial Symptom Assessment Scale (MSAS)

A 10 item MSAS Global Distress Index (MSAS-GDI) is considered to be a measure of overall symptom distress. The GDI is the average of the frequency of 4 prevalent psychological symptoms (feeling sad, worrying, feeling irritable, and feeling nervous) and the distress associated with 6 prevalent physical symptoms (lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth). Portenoy, Thaler, Kornblith, Lepore, Friedlander-Klar, Kiyasu E, et al (1994). The Memorial Symptom Assessment Scale: An instrument for the evaluation of symptom prevalence, characteristics and distress. *Eur J Cancer* 30(9), 1226-1336.

The Physical Symptom Subscale score (MSAS-PHYS) is the average of the distress associated with 12 prevalent physical symptoms: lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth, nausea, vomiting, change in taste, weight loss, feeling bloated, and dizziness. Note that the scaling is in increments of 0.8, with zero for no symptom, 0.8 for symptom present but no distress, and upwards for increasing levels of distress.

The Psychological Symptom Subscale score (MSAS-PSYCH) is the average of the frequency associated with 6 prevalent psychological symptoms: worrying, feeling sad, feeling nervous, difficulty sleeping, feeling irritable, and difficulty concentrating. Scoring is in increments of one, with zero for no symptom to 4 for "almost constantly". Total MSAS score (TMSAS) is the average of the symptom scores of all 32 symptoms in the MSAS instrument.

Memorial Symptom Assessment Scale Short Form Subscales

In the short form, there is only one dimension for each symptom, distress for physical symptoms and frequency for psychological symptoms. The sequence of symptoms in the short form is different from that in the long form. 1. Chang VT, Hwang S, Feuerman M, Kasimis BS, Thaler HT. The memorial symptom assessment scale short form (MSAS-SF). *Cancer* 2000b;89:1162-1171.

Scoring of physical symptoms in the MSAS-SF is as follows:**Zero if the symptom is not present**

- 0.8 if the symptom is present but causes no distress
- 1.6 if the symptom is present and causes a little bit of distress
- 2.4 if the symptom is present and causes somewhat of distress
- 3.2 if the symptom is present and causes quite a bit of distress
- 4.0 if the symptom is present and causes very much distress

Scoring of psychological symptoms is

- 0 if the symptom is absent
- 1 if the symptom is present and occurs rarely
- 2 if the symptom is present and occurs occasionally
- 3 if the symptom is present and occurs frequently
- 4 if the symptom is present and occurs almost constantly

Appendix G

Condensed Memorial Symptom Assessment Survey (CMSAS)—Family Respondent Version (English/Spanish)

Condensed Memorial Symptom Assessment Scale (CMSAS) - Family Respondent (English)

Interviewer ID: _____ Subject Code: _____

How much did this symptom bother or distress your loved one in the past 7 days?

Symptom	Present	Not at all	A little Bit	Some what	Quite a bit	Very much	Not Applicable (N/A)	Don't Know (D/K)
Lack of energy	Y N	0	1	2	3	4		
Lack of appetite	Y N	0	1	2	3	4		
Pain	Y N	0	1	2	3	4		
Dry mouth	Y N	0	1	2	3	4		
Weight Loss	Y N	0	1	2	3	4		
Feeling drowsy	Y N	0	1	2	3	4		
Shortness of breath	Y N	0	1	2	3	4		
Constipation	Y N	0	1	2	3	4		
Difficulty sleeping	Y N	0	1	2	3	4		
Difficulty concentrating	Y N	0	1	2	3	4		
Nausea	Y N	0	1	2	3	4		

How frequently did your loved one experience these symptoms during the last week?

Symptom	Present	Rarely	Occasionally	Frequently	Almost constantly	Not Applicable (N/A)	Don't Know (D/K)
Worrying	Y N	1	2	3	4		
Feeling sad	Y N	1	2	3	4		
Feeling nervous	Y N	1	2	3	4		

OTHER SYMPTOMS

Identify any other symptoms that you believe bothered your loved one in the last week. List them below & identify how distressful they were.	Not at all	A little Bit	Some What	Quite a bit	Very much
	0	1	2	3	4
	0	1	2	3	4
	0	1	2	3	4
	0	1	2	3	4
	0	1	2	3	4

Condensed Memorial Symptom Assessment Scale (CMSAS)- Family Respondent

Interviewer ID: _____ Subject Code _____

How much did this symptom bother or distress your loved one in the past 2 days?

Symptom	Present	Not at all	A little Bit	Some what	Quite a Bit	Very much	Not Aplicable (N/A)	Don't Know (D/K)
Lack of energy	Y N	0	1	2	3	4		
Lack of appetite	Y N	0	1	2	3	4		
Pain	Y N	0	1	2	3	4		
Dry mouth	Y N	0	1	2	3	4		
Weight Loss	Y N	0	1	2	3	4		
Feeling drowsy	Y N	0	1	2	3	4		
Shortness of breath	Y N	0	1	2	3	4		
Constipation	Y N	0	1	2	3	4		
Difficulty sleeping	Y N	0	1	2	3	4		
Difficulty concentrating	Y N	0	1	2	3	4		
Nausea	Y N	0	1	2	3	4		

How frequently did your loved one experience these symptoms during the last 2 days?

Symptom	Present	Rarely	Occasionally	Frequently	Almost constantly	Not Aplicable (N/A)	Don't Know (D/K)
Worrying	Y N	1	2	3	4		
Feeling sad	Y N	1	2	3	4		
Feeling nervous	Y N	1	2	3	4		

OTHER SYMPTOMS

Identify any other symptoms that you believe bothered your loved one. List them below & identify how distressful they were	Not at all	A little Bit	Some What	Quite a bit	Very much
	0	1	2	3	4
	0	1	2	3	4
	0	1	2	3	4
	0	1	2	3	4

Condensed Memorial Symptom Assessment Scale (CMSAS)—Respondedor de la Familia

Entrevistador ID: _____ Código sujeto: _____

¿En qué medida ha molestado al miembro de su familia este síntoma en los últimos 7 días?

Síntoma	Presente	En absoluto (no)	Un Poquito	Un Poco	Bastante	Mucho	No Aplicable (NA)	No Sé (N/S)
Falta de energía	S N	0	1	2	3	4		
Pérdida de apetito	S N	0	1	2	3	4		
Dolor	S N	0	1	2	3	4		
Boca Seca	S N	0	1	2	3	4		
Pérdida de peso	S N	0	1	2	3	4		
Amodorramiento	S N	0	1	2	3	4		
Dificultad de respirar	S N	0	1	2	3	4		
Estreñimiento	S N	0	1	2	3	4		
Dificultad de dormir	S N	0	1	2	3	4		
Dificultad de concentrar	S N	0	1	2	3	4		
Náusea	S N	0	1	2	3	4		

¿Con qué frecuencia ha experimentado estos síntomas durante la semana pasada?

Síntoma	Presente	Raramente	De vez en cuando	Con frecuencia	Casi constantemente	No Aplicable (NA)	No Sé (N/S)
Preocupación	S N	1	2	3	4		
Tristeza	S N	1	2	3	4		
Nerviosismo	S N	1	2	3	4		

OTROS SÍNTOMAS

Identifique cualquier otro síntoma que le incomodó al miembro de su familia durante los 7 días pasados. Enumerelos abajo y identifique el nivel de aflicción.	Presente	Un Poquito	Un Poco	Bastante	Mucho
	S N	1	2	3	4
	S N	1	2	3	4
	S N	1	2	3	4
	S N	1	2	3	4

Entrevistador ID: _____ Código sujeto _____

Appendix G

Condensed Memorial Symptom Assessment Scale(CMSAS)— Respondedor de la Familia
¿En qué medida ha molestado al miembro de su familia este síntoma desde la última vez que le ví (hace dos dias)?

Síntoma	Presente	En absoluto (no)	Un Poquito	Un Poco	Bastante	Mucho	No Aplicable (NA)	No Sé (N/S)
Falta de energía	S N	0	1	2	3	4		
Pérdida de apetito	S N	0	1	2	3	4		
Dolor	S N	0	1	2	3	4		
Boca Seca	S N	0	1	2	3	4		
Pérdida de peso	S N	0	1	2	3	4		
Amodorramiento	S N	0	1	2	3	4		
Dificultad de respirar	S N	0	1	2	3	4		
Estreñimiento	S N	0	1	2	3	4		
Dificultad de dormir	S N	0	1	2	3	4		
Dificultad de concentrar	S N	0	1	2	3	4		
Náusea	S N	0	1	2	3	4		

¿Con qué frecuencia ha experimentado el miembro de su familia estos síntomas desde la última vez que le ví (hace dos dias)?

Síntomas	Presente	Raramente	De vez en cuando	Con Frecuencia	Casi constantemente	No Aplicable (NA)	No Sé (N/S)
Preocupación	S N	1	2	3	4		
Tristeza	S N	1	2	3	4		
Nerviosismo	S N	1	2	3	4		

OTROS SÍNTOMAS

Identifique cualquier otro síntoma que le incomodó al miembro de su familia durante los dos días pasados. Enumerelos abajo y identifique el nivel de aflicción.	Presente	Un Poquito	Un Poco	Bastante	Mucho
	S N	1	2	3	4
	S N	1	2	3	4
	S N	1	2	3	4

Appendix H

IRB Approval Memorial Health Services (MHS) Study (299-05)

MHS-RESEARCH COUNCIL (IRB) APPROVAL LETTER

P.I.: Leslie Kern, RN, PhD/Peggy Kalowes, RN, PhD(c)
Memorial Heart and Vascular Institute

Date: October 16, 2006

Project # and Title: #299-05 "Understanding the Symptom Burden in Patients with Terminal and Life Threatening Illness in Intensive Care Units."

Extension Approval Date: October 16, 2006

Expiration Date: October 15, 2007

☒ Regular Review

☐ Direct Review

A request for an extension to the above project was reviewed and approved at the October 16, 2006 MHS Research Council meeting for a period of 1 year. The Memorial Health Services Research Council serves as the Institutional Review Board for Long Beach Memorial Medical Center. Enclosed please find an official stamped copy of the Informed Consent Form for the above named project. The previously approved Authorization form for use and disclosure of Protected Health Information should continue to be used.

- In compliance with FDA regulations and Memorial Health Services Research Council policies, a detailed progress report must be submitted to the Office of Research Administration before August 1, 2007.

MHS Research Council approvals are provided to Principal Investigators subject to the following conditions:

In accordance with MHS Policy and Procedures, the MHS Research Council may authorize staff to conduct spot checks or audits on their behalf. Please provide the information requested if an audit of your project occurs.

Per ICH guidelines, the MHS Research Council regards the Principal Investigator as responsible for the conduct of research trials at his/her site and all associated research facilities. Specific responsibilities of the Principal Investigator include ensuring:

- Supervision of all research at Long Beach Memorial Medical Center in accordance with Memorial Health Services policies and FDA regulations.
- Conduct of research according to the study protocol.
- Use of the most recently approved informed consent form.
- Provision of a MHS Research Council-approved consent form in the subject's first language to all non-English speaking subjects.
- Approval by the MHS Research Council for all changes in research activity including protocol amendments and/or consent form revisions prior to implementation.
- Prompt reporting (48 hours verbally and 5-10 days in writing) to the MHS Research

THE STANDARD OF EXCELLENCE IN HEALTH CARE

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Council of any significant changes in research activity including changes in Principal Investigator, changes in research site, addition of research facilities to a previously approved site, and study completion.

- Approval by the MHS Research Council of all advertisements and patient recruiting materials prior to use.
- Prompt reporting (48 hours verbally and 5-10 days in writing) to the MHS Research Council of serious and unexpected events related to study procedures as well as protocol deviations/violations.
- Timely submission of continuing review and progress reports.

Sincerely,

Harris R. Stutman, MD
Executive Director
Office of Research Administration
Approval letters/299-05 extension October 2006

Appendix I

IRB-MHS-Patient Informed Consent

Page 1 of 6
 PI: Leslie Kern RN, PhD/Peggy Kalowes RN
 Project No. 299-05

Memorial Health Services Research Council
 Institutional Review Board
 Long Beach Memorial Hospital

Informed Consent to Participate in a Research Study

Title: Understanding the Symptom Burden in Patients with Terminal and Life-Threatening Illness in Intensive Care Units

Principal Investigator:

Leslie Kern, RN, PhD, FAHA Phone Number: (562)933-3320

Principal Investigator:

Peggy Kalowes RN, MSN, CNS Phone Number: (562)225-2545

MHS Project Number: 299-05

You are being asked to participate in a research study conducted by Leslie Kern RN, PhD and Peggy Kalowes, RN, MSN, CNS, a doctoral student in nursing at the University of San Diego. Peggy is conducting a dissertation research study to gain a better understanding of the pain and suffering that various symptoms may cause you, related to your progressive disease and current life-threatening illness.

By participating in this research study, you will be adding to the body of nursing knowledge in symptom management, which will help us to improve the types of treatments to provide (or withhold) and the types of care and services needed by patients and families at different points in the course of their critical illness.

WHY YOU ARE ELIGIBLE

You were selected as a possible participant in this study because we have very little information/or research about the severity and frequency of symptoms reported by patients in intensive care units. These patients are known to have various illnesses such as heart, lung or liver disease, diabetes, stroke or acute traumatic injury. Most of the studies about symptoms in critical illness have been conducted on patients with advanced cancer, and the results of these studies may not be as helpful in understanding issues in the care of patients acutely ill with other diseases.

PURPOSE OF THE STUDY

The primary purpose of this study is to determine the frequency of various kinds of symptoms (example; pain, difficulty breathing, nausea), the frequency, severity and degree of distress, reported by patients, who have a progressive disease or a sudden life-threatening illness, being cared for in the intensive care units.

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Page 2 of 6
 PI: Leslie Kern RN, PhD/Peggy Kalowes RN
 Project No. 299-05

You can help us learn how to do a better job of caring for critically ill patients, by taking the time to answer questions on the attached questionnaire, which asks you to identify the symptoms that bother you and rate how frequently and severe they are. The information you provide may help identify any needs you currently have, and will also assist us to develop and further investigate new treatments and nursing interventions for various symptoms, because there are currently few therapies that may be available to provide relief.

PROCEDURES

If you volunteer to participate in this study, you will be asked to complete two questionnaires (**available in English and Spanish**):

- A 14-item questionnaire to assess your symptoms;
- A Treatment & Procedure Survey

On day 1, of your admission to the ICU, a research assistant will assess your ability to answer the questions and participate in the study. If you are eligible for the study, you will be asked to complete the symptom assessment questionnaire. This will tell us about your perception of your symptoms and health in the previous week. This will take about 2-4 minutes to complete. **Note:** *If you are unable to write, you may communicate your response in another way understandable to the interviewer, who can record your ratings on the questionnaire.*

On day 3 of your ICU care, the researcher will return, and again assess your ability to answer the questionnaires. You will be asked to complete the symptom assessment questionnaire again so we can see if your symptoms have changed after two days in the ICU. This will again take about 2-4 minutes to complete. In addition to the symptom questionnaire, at the same time we will have you complete a Treatment and Procedure Survey. Because we want to understand why some patients have additional pain and suffering, we would like you to take a moment to tell us how painful or bothersome the various treatments or procedures are to you. This will take 1-2 minutes to complete. This will complete your participation in the study.

POTENTIAL RISKS AND DISCOMFORTS

There is no foreseeable risk for physical injury for participating in this study, although, you may have the potential for fatigue while completing the questionnaire. This can be reduced or prevented by completing the questionnaire at your own pace, or asking the researcher to record your responses for you directly on the form.

The foreseeable risks are minimal for *psychological harm* through responding to the symptom questionnaire, primarily because it is very short, and should only take minutes to complete. Thus, there should be no associated anxiety, fear or pain. However, if any of the questions distress you or make you uncomfortable, an appropriate referral for further support will be available through pastoral care services.

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Page 3 of 6
 PI: Leslie Kern RN, PhD/Peggy Kalowes RN
 Project No. 299-05

This questionnaire has been used in previous research with similar populations without report of psychological harm. If you experience distress, you also have a right to discontinue participating in the study.

POTENTIAL BENEFITS TO SUBJECTS AND/OR TO SOCIETY

The first and most obvious benefit would be that the questionnaire used would identify the presence and intensity of multiple symptoms that you are able to describe through your own perception. This will help in identifying gaps in your current care, which we will try to improve.

There is also the greater benefit of adding to the scientific knowledge of nursing and the field of symptom management. The study results may help us develop new nursing therapies to reduce pain and suffering in patients during the course of their life-threatening illness.

ALTERNATIVES

There are no other alternatives, other than non-participation. You have been given the opportunity to ask questions which have been answered to your satisfaction. You understand your physician will answer any questions that you might have in the future.

PAYMENT FOR PARTICIPATION

Participants will receive no payments or other forms of an incentive to participate in this study.

VOLUNTARY PARTICIPATION/ RIGHT TO WITHDRAWAL

You can choose whether to be in this study or not. If you volunteer to be in this study, you may withdraw at any time without consequences of any kind. Participation or non-participation will not affect your current treatment and care, or any other personal consideration or right you usually expect. You may also refuse to answer any questions you don't want to answer and still remain in the study. The investigator may withdraw you from this research if circumstances arise, which in the opinion of the researcher warrant doing so.

CONFIDENTIALITY

You understand that any information that is obtained about you from this research will be kept confidential and your name will never be identified in any report or publication unless you sign a release. All data will be coded using numbers and not names, to assure confidentiality. The consent and the list matching the subject's name to the assigned code number will be kept separate from all research materials and will only be available to the principal investigator. All data and questionnaires you complete will be kept in a locked file cabinet in the researcher's office with access only by the Primary Investigator.

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Page 4 of 6
 PI: Leslie Kern RN, PhD/Peggy Kalowes RN
 Project No. 299-05

Information regarding your medical records, just like hospital records may be subpoenaed by court order. You consent to the publication of study results so long as the information is anonymous and/or disguised so that identification cannot be made. You also understand that authorized representatives of the Food and Drug Administration (FDA), and the MHS Institutional Review Board (MHS Research Council) may examine your records, and there will be no breach of confidentiality.

IRB CLAUSE

This proposal has been reviewed and approved by the Memorial Health Services Institutional Review Board (MHS Research Council), which serves as the IRB for Long Beach Memorial Medical Center, which is composed of physicians and lay persons. If you have any questions about your rights as a research subject, or regarding a treatment related injury, or desire further information concerning the availability of compensation or medical treatment, you may contact Harris R. Stutman, MD, the Executive Director, Office of Research Administration, Memorial Health Services, at (562) 490-3737.

The primary investigator(s) Leslie Kern RN, PhD and Peggy Kalowes, RN, MSN, CNS; or one of their Co-Investigators have discussed this study with you. If you have any questions you can reach them at (562) 933-3320; (562) 225-2545/ 985-1804.

I certify that I have read the preceding or it has been read to me, that I understand its contents, and that any question I have pertaining to the preceding have been, or will be answered by my doctor and that my permission is freely given. I have been given a copy of this consent form along with a copy of the "Rights of Human Subjects in Medical Research," and I consent to participate in this study.

 Patients Name

 Identifier Code Assigned

 Patient's Signature

 Date

 Time

 Witness to Patient's Signature

 Date

 Time

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Page 5 of 6

PI: Leslie Kern RN, PhD/Peggy Kalowes RN
Project No. 299-05

If the subject is a minor, or otherwise unable to sign, complete the following:

- a) Reason subject is unable to sign: _____

- b) _____
Name of Authorized Person Date

Signature of Authorized Person Time

Relationship and Basis of Authorization
To give Consent

Certificate of Person Obtaining Consent:

I have provided an explanation of the above research study, and have encouraged the patient to ask questions and request additional information regarding the study, its risks and complications and possible alternatives. A copy of this consent form has been given to the patient.

Signature of person obtaining consent Print name of person obtaining consent Date

Certificate of Investigator:

I certify that I am the Principal Investigator or Co-Investigator responsible for this study, for ensuring that the subject is fully informed in accordance with applicable regulations, and for advising the MHS Research Council (IRB) of any adverse reactions or unexpected events that may develop from this study.

Principal Investigator or Co-Investigator Date Time

NOT VALID WITHOUT IRB STAMP OF APPROVAL

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Page 6 of 6
 PI: Leslie Kern RN, PhD/Peggy Kalowes RN
 Project No. 299-05

RIGHTS OF HUMAN SUBJECTS IN MEDICAL RESEARCH

Any person who is requested to consent to participate as a subject involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.
2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.
3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
4. Be given an explanation of any benefits to the subjects reasonably to be expected from the experiment.
5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantages to the subject, and their relative risks and benefits.
6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
7. Be given an opportunity to ask any questions concerning the experiment of the procedure involved.
8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.
9. Be given a copy of any signed and dated written consent form used in relation to the experiment.
10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influences on the subject's decision.

PATIENT SIGNATURE: _____ DATE: _____

10-11-101 11/28/05 11/20/06

HIPAA AUTHORIZATION

Page 1 of 2

**Memorial Health Services Research Council
Institutional Review Board
Long Beach Memorial Medical Center**

Project Title: Understanding the Symptom Burden in Patients
with Terminal and Life Threatening Illness in
Intensive Care Units

Project Number: 299-05

**Authorization for the Use and Disclosure of Protected
Health Information**

How Will Your Confidentiality Be Protected?

You have rights regarding the privacy of your medical information collected prior to and in the course of this research. This medical information, called "protected health information" (PHI), includes demographic information, the results of physical exams, blood tests, x-rays and other diagnostic and medical procedures, as well as your medical history. You have the right to limit the use and sharing of your PHI, and you have the right to see your medical records and know who else is seeing them.

By signing this authorization form, you are allowing the research team to have access to your PHI for the purposes of conducting this study. The research team includes the investigators listed on the consent form and other personnel involved in this specific study at Long Beach Memorial Medical Center.

Your PHI will be used only for the purpose(s) described in the section of the informed consent entitled, "Purpose of the Study".

Your PHI will be shared, as necessary, with the MHS Research Council (also known as the Institutional Review Board (IRB) and with any person or agency required by law.

You are authorizing us to use and disclose your PHI until 12/31/2008

Last Revised: 06/15/2004

HIPAA AUTHORIZATION

Page 2 of 2

You may revoke this authorization to use and share your PHI at any time by contacting the principal investigator in writing. If you revoke this authorization, you will no longer participate in this research program. If you revoke this authorization, use or sharing of future PHI will be stopped. The PHI that has already been collected may still be used.

The results of clinical tests and therapy performed as part of this research may be included in your medical record. The information from this study may be published in scientific journals or presented at scientific meetings but your identity will be kept confidential and no information that may be personally identifiable, such as your name, picture, social security number or medical record number, will be published.

You will be given a copy of this authorization for your records.

_____ Patient Name	_____ Patient Signature	_____ Date and Time
_____ Witness Name	_____ Witness Signature	_____ Date and Time
_____ Name of Authorized Representative	_____ Relationship to Patient	
_____ Signature of Authorized Representative	_____ Date and Time

Last Revised: 06/15/2004

Appendix J

IRB-MHS-Informed Consent Family

Page 1 of 6

PI: Leslie Kern RN, PhD/Peggy Kalowes RN
Project No. 299-05Memorial Health Services Research Council
Institutional Review Board
Long Beach Memorial Hospital **Informed Consent to Participate in a Research Study
(Family Respondent)****Title: Understanding the Symptom Burden in Patients with Terminal and Life-Threatening Illness in Intensive Care Units****Principal Investigator:**

Leslie Kern, RN, PhD, FAHA

Phone Number: (562)933-3320

Principal Investigator:

Peggy Kalowes RN, MSN, CNS

Phone Number: (562)225-2545

MHS Project Number: 299-05

You are asked to participate in a research study conducted by Leslie Kern RN, PhD and Peggy Kalowes, RN, MSN, CNS, a doctoral student in nursing at the University of San Diego. Peggy is conducting a dissertation research study to gain a better understanding of the pain and suffering that various symptoms may cause patients with chronic disease or life-threatening illness, being cared for in the intensive care unit (ICU).

The information you provide will give us a valuable and "unique perspective" from a family's member's observation and perception, regarding a patient's symptoms and declining health, which often is different than the patient's assessment.

By participating in this research study, you will be adding to nursing knowledge in symptom management, which will help us to improve the types of treatments to provide (or withhold) and the types of care and services needed by patients and families at different points in the course of their critical illness.

WHY YOU ARE ELIGIBLE

You are being invited to participate in this study because your family member has agreed to participate in this research, by telling us about the severity and frequency of their disease-related symptoms. We currently have little information/or research, regarding the degree of distress and suffering that various symptoms may cause patients from their own or the family's perspective. Most of the studies about symptoms in terminal and critical illness have been conducted on patients with advanced cancer, and not other common disorders like heart, lung, liver disease, serious infections, diabetes, stroke and acute traumatic injury.

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PI: Leslie Kern RN, PhD/Peggy Kalowes RN
Project No. 299-05

PURPOSE OF THE STUDY

The primary purpose of this study is to determine the frequency of various kinds of symptoms (example; pain, difficulty breathing, nausea), the frequency, severity and degree of distress, reported by patients, who have a progressive disease or a sudden life-threatening illness. Little information is available from both patient's and family's perspective at the same time during the course of illness.

Families/friends often see how patients respond to their illness and symptoms from a totally different view than the patient. Because families/or friends often provide needed care to patients who are living at home, when they are very sick, you may be able to provide broader insight to the patients progressive illness.

Your input can help us learn how to do an even better job of caring for critically ill patients, by taking the time to answer questions on the attached questionnaire. The survey asks you to identify the various symptoms that may have bothered your loved one and rate how frequently they occurred and how severe you thought they were. The information you provide may help identify any current needs the patient may have, and the data will also assist us to develop and further investigate new treatments and nursing interventions for various symptoms, because there are currently few therapies that may be available to provide relief.

PROCEDURES

If you volunteer to participate in this study, you will be asked to complete two questionnaires (**available in English and Spanish**):

- A short information form that assesses family member characteristics (age, sex, ethnicity, occupation, role of care giving to patient)
- A 14-item questionnaire to assess your perception of the patient's symptoms;

On day 1, of the patient's admission to the ICU, you will be asked to complete the short information form and the symptom assessment questionnaire. The symptom questionnaire will tell us about your perception of the patient's symptoms and health in the previous week. This will take approximately 5-8 minute's total.

On day 3 of the patient's ICU care, you will be asked by the researcher to complete the symptom assessment questionnaire again. This will tell us about your perception of the patient's symptoms and quality of life, and whether this has changed while receiving treatment(s) for two days. This will take about 2-4 minutes to complete.

Note: If you cannot be physically present **on day 3**, a telephone interview can be scheduled and conducted at your convenience, so you may provide this very important information to complete the study.

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 PI: Leslie Kern RN, PhD/Peggy Kalowes RN
 Project No. 299-05

POTENTIAL RISKS AND DISCOMFORTS

There is no foreseeable risk of physical injury for participating in this study, although, you may have the potential for fatigue while completing the questionnaire. This can be reduced or prevented by completing the questionnaire at your own pace, or asking the researcher to record your responses for you directly on the form.

There is only a minimal risk for *psychological harm* through responding to the symptom questionnaire, primarily because it is very short, and should only take minutes to complete. Thus, there should be no associated anxiety, fear or pain. However, if emotional distress should occur, an appropriate referral for emotional support will be available through pastoral care services.

POTENTIAL BENEFITS TO SUBJECTS AND/OR TO SOCIETY

The first and most obvious benefit would be that the questionnaire used would identify the presence and intensity of multiple symptoms that you perceive the patient may be experiencing from your observations. This may help in identifying gaps in the patient's current care, which we will try to improve.

There is also the greater benefit of adding to the scientific knowledge of nursing and the field of symptom management. The study results will help us develop interventions to be further tested in clinical areas, which may prove to be far more effective therapies to reduce pain and suffering in patients during the course of their life-threatening illness.

ALTERNATIVES

There are no other alternatives, other than non-participation.

You have been given the opportunity to ask questions which have been answered to your satisfaction.

PAYMENT FOR PARTICIPATION

Participants will receive no payments or other forms of an incentive to participate in this study.

VOLUNTARY PARTICIPATION/ RIGHT TO WITHDRAWAL

Participating in this study is strictly optional, as a family member. If you volunteer to be in this study, you may withdraw at any time without consequences of any kind. Participation or non-participation will not affect your family member's current treatment and care, or any other personal consideration or right you usually expect. You may also refuse to answer any questions you don't want to answer and still remain in the study. The investigator may withdraw you from this research if circumstances arise, which in the opinion of the researcher warrant doing so.

CONFIDENTIALITY

You understand that any information that is obtained about you from this research will be kept confidential and your name will never be identified in any report or publication unless you sign a release. All data will be coded using numbers and not names, to

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 PI: Leslie Kern RN, PhD/Peggy Kalowes RN
 Project No. 299-05

assure confidentiality. The consent and the list matching the subject's name to the assigned code number will be kept separate from all research materials and will only be available to the principal investigator. All data will be kept in a locked file cabinet in the researcher's office with access only by the Primary Investigator.

You consent to the publication of study results so long as the information is anonymous and/or disguised so that identification cannot be made.

IRB / FDA CLAUSE

This proposal has been reviewed and approved by the Memorial Health Services Institutional Review Board (MHS Research Council), which serves as the IRB for Long Beach Memorial Medical Center, which is composed of physicians and lay persons. If you have any questions about your rights as a research participant, or regarding a treatment related injury, or desire further information concerning the availability of compensation or medical treatment, you may contact Harris R. Stutman, MD, the Executive Director, Office of Research Administration, Memorial Health Services, at (562) 490-3737.

The primary investigator(s) Leslie Kern RN, PhD and Peggy Kalowes, RN, MSN, CNS; or one of their Co-Investigators have discussed this study with you. If you have any questions you can reach them at [(562) 933-3320; (562) 225-2545/ 985-1804].

I certify that I have read the preceding or it has been read to me, that I understand its contents, and that any question I have pertaining to the preceding have been, or will be answered by the investigators and that my permission is freely given. I have been given a copy of this consent form along with a copy of the "Rights of Human Subjects in Medical Research," and I consent to participate in this study.

 Family Respondents Name Identifier Code Assigned

 Family Respondents Signature Date Time

 Witness to Family Respondents Signature Date Time

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 PI: Leslie Kern RN, PhD/Peggy Kalowes RN
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If the subject is a minor, or otherwise unable to sign, complete the following:

a) Reason subject is unable to sign: _____

b) _____
 Name of Authorized Person Date

 Signature of Authorized Person Time

 Relationship and Basis of Authorization
 to give Consent

Certificate of Person Obtaining Consent:

I have provided an explanation of the above research study, and have encouraged the family respondent to ask questions and request additional information regarding the study, its risks and complications and possible alternatives. A copy of this consent form has been given to the family respondent.

 Signature of person obtaining consent

 Print name of person obtaining consent

 Date

Certificate of Investigator:

I certify that I am the Principal Investigator or Co-Investigator responsible for this study, for ensuring that the subject is fully informed in accordance with applicable regulations, and for advising the MHS Research Council (IRB) of any adverse reactions or unexpected events that may develop from this study.

 Principal Investigator or
 Co-Investigator

 Date

 Time

NOT VALID WITHOUT IRB STAMP OF APPROVAL

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PI: Leslie Kern RN, PhD/Peggy Kalowes RN
Project No. 299-05

RIGHTS OF HUMAN SUBJECTS IN MEDICAL RESEARCH

Any person who is requested to consent to participate as a subject involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.
2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.
3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
4. Be given an explanation of any benefits to the subjects reasonably to be expected from the experiment.
5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantages to the subject, and their relative risks and benefits.
6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
7. Be given an opportunity to ask any questions concerning the experiment of the procedure involved.
8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.
9. Be given a copy of any signed and dated written consent form used in relation to the experiment.
10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influences on the subject's decision.

PATIENT SIGNATURE: _____ DATE: _____

Appendix K

Request for HIPPA Waiver

WAIVER OF AUTHORIZATION

PAGE 1 OF 2

Memorial Health Services Research Council
Institutional Review Board
Long Beach Memorial Medical Center

**Request for Waiver of Authorization
For the Use and Disclosure of Protected Health Information in
Research**

INTRODUCTION

Patients have rights regarding the privacy of their medical information collected prior to and in the course of this research. This medical information, called "protected health information" (PHI), includes demographic information, the results of histories and physical exams, blood tests, x-rays and other diagnostic and medical procedures, as well as individually identifiable tissues or body fluids. Patients must authorize the use of PHI when used or disclosed for all purposes other than treatment, payment and healthcare operations. This includes the use and disclosure of PHI for research. In some cases, it is appropriate to seek a waiver of such authorization, such as for chart reviews and data registries.

REQUEST FOR WAIVER

I, Leslie Kern RN, PhD / Peggy Kalowes RN, PhD(c), Primary Investigator(s) and Louise DuBos RN, BSN, Co-Investigator, request a waiver of authorization for the use and disclosure of Symptom Burden in Patients with Terminal and Life-Threatening Illness in Intensive Care Units protected health information, consequent to a research project entitled, Understanding the Symptom Burden in Patients with Terminal and Life-Threatening Illness in Intensive Care Units

The waiver of authorization for use and disclosure of PHI is for 1-year from IRB Approval.

The specific information that will be used and disclosed includes the following: age, ethnicity, religion, health information, medications that may affect patient's level of consciousness, admission & discharge information (outcomes) and APPACHE III Mortality Risk & APS Score.

The members of the research team at Long Beach Memorial Medical Center, who will be using the described PHI include the following (persons or groups of persons): Leslie Kern RN, PhD / Peggy Kalowes RN, PhD(c), Louise DuBos RN, BSN.

I further certify the following (please initial box next to each statement):

The use or disclosure of PHI involves no more than minimal risk to the privacy of individuals, based on the presence of the following elements:

1. An adequate plan to protect the identifiers from improper use and disclosure.

Describe.

Patients/families will be informed verbally/and on the informed consent, that any information obtained from this research study, will be kept confidential. The subject name will never be identified in any report or publication unless a release is signed. All data will be coded using numbers and not names, to assure confidentiality. The

Revised: 10/13/2004

Long Beach Memorial Medical Center

WAIVER OF AUTHORIZATION

PAGE 2 OF 2

consent and the list matching the subject's name to the assigned code number will be kept separate from all research materials and will only be available to the principal investigator. All data and questionnaires you complete will be kept in a locked file cabinet in the researcher's office with access only by the Primary Investigator.

2. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a specific health or research justification for retaining the identifiers, or such retention is otherwise required by law; and
3. The PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of PHI may be subsequently permitted.

The research could not practicably be conducted without the waiver; and
The research could not practicably be conducted without access to and use of the PHI.

PRINCIPAL INVESTIGATOR NAME _____ SIGNATURE _____

DATE & TIME

PRINCIPAL INVESTIGATOR NAME / SIGNATURE

DATE & TIME

CO-INVESTIGATOR NAME	SIGNATURE
----------------------	-----------

DATE & TIME

FOR USE OF THE OFFICE OF RESEARCH ADMINISTRATION ONLY

MHS Research Council
Name of Institutional Review Board

3-20-06
Date of Approval of Waiver

Harris R. Stutman, MD
Research Council (IRB) Chair or
Designee

Signature _____

3/31/06 1300
Date & Time

Appendix L

IRB-MHS Approval Spanish Documents

February 17, 2006

Leslie Kern, RN, PhD/Peggy Kalowes, RN, MSN, CNS, PhD(c)

Subj: Spanish Informed Consent for project #299-05 "Understanding the Symptom Burden in Patients with Terminal and Life Threatening Illness in Intensive Care Units."

Dear Dr. Kern/Ms. Kalowes:

Enclosed please find a stamped copy of the approved Spanish version of the informed consents along with the Authorization for the Use and Disclosure of Protected Health Information for the above-mentioned project. This project was last reviewed and approved by the MHS Research Council (MHS-IRB) for activation on November 28, 2005 for a period of 1 year; these dates are reflected on attached consent and Authorization for the Use and Disclosure of Protected Health Information. Because the Spanish version of the consent was not directly reviewed by the MHS Research Council, the dates reflect the most currently reviewed and approved version of the English consent for the above mentioned study. It is the policy of the MHS Research Council (MHS-IRB) that the patient and the witness must also sign an approved English informed consent form.

The Office of Research Administration notes that a notarized letter of attestation was received from Cynthia D. Connelly, PhD, RN noting that Blanca Mancillas and Norma Talamantes, of the Child and Adolescent Services Research Center, Children's Hospital and Health Center, San Diego, Spanish Interpreters, were responsible for this Spanish translation of the MHS-IRB approved English version of the informed consents and Authorization for the Use and Disclosure of Protected Health Information.

If you need any further assistance, please contact me at (562) 490-3728.

Thank you,

Sharon Denham
Regulatory Compliance Coordinator
Office of Research Administration

Cover letters for misc consent form items/spanish consent cover letters/299-05 spanish consent cover letter
2-17-06

THE STANDARD OF EXCELLENCE IN HEALTH CARE
2801 ATLANTIC AVENUE • LONG BEACH, CA 90806 • PHONE: 562-490-3737 • FAX: 562-490-3738

Appendix M

IRB-MHS-Spanish Consent Patient

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PI: Leslie Kern RN, PhD/Peggy Kalowes RN, MSN
Project No. 299-05MHS RESEARCH COUNCIL
APPROVEDMemorial Health Services Council
Institutional Review Board
Long Beach Memorial Hospital

MAR 20 2006

EXPIRES 11-20-06
INITIALS _____**Consentimiento Informado para participar en un estudio de la investigación****Título:** La Comprensión de la carga del síntoma en los pacientes con enfermedades terminales, y enfermedades graves, en el cuidado intensivo.**Investigadora Principal:** Leslie Kern RN, PhD, FAHA **Número de Teléfono:** (562) 933-3320**Investigadora Principal:** Peggy Kalowes RN, MSN, CNS **Número de Teléfono:** (562) 225-2545**Asistente al Investigadora:** Louise DuBos RN, BSN **Número de Teléfono:** (562) 522-9893**Número del proyecto MHS:** 299-05

Se ha sido preguntado a usted para participar en un estudio de investigación conducido por Leslie Kern RN, PhD y Peggy Kalowes, RN, MSN, un estudiante doctoral en el programa de enfermeras en la Universidad de San Diego. Peggy está conduciendo una disertación en la forma de un estudio de investigación para comprender más el dolor y sufrimiento que presenta con varios síntomas, relacionados a la enfermedad progresivo y la enfermedad grave.

Al participar en este estudio de la investigación, se añadirá al conocimiento del oficio de enfermera en el manejo de los síntomas, lo que puede ayudarnos en mejorar los tipos de tratamientos que podemos proporcionar (o no dar) y los tipos de cuidado y servicios que se necesitan los pacientes y las familias en varios puntos durante el curso de la enfermedad crítica.

¿POR QUÉ ES USTED ELEGIBLE?

Se han sido seleccionado usted como candidato posible en este estudio porque tenemos poquito información/o investigación sobre la severidad y la frecuencia de los síntomas reportados por los pacientes en el cuidado intensivo. Estos pacientes puede tener varias enfermedades como las del corazón, pulmón, hígado, la diabetes, el ataque cerebral, o una lesión traumática aguda. Se conduce la mayoría de los estudios sobre los síntomas en los pacientes críticos con el cáncer avanzado. Estos estudios no son tan provechosos para mejorar el cuidado de los pacientes con otras enfermedades agudas.

PROPÓSITO DEL ESTUDIO

El propósito primario del estudio es determinarse el predominio de varios tipos de síntomas (por ejemplo: dolor, dificultad de respirar, náusea), la frecuencia, y la severidad de aflicción de los pacientes que tiene una enfermedad progresivo o una enfermedad repentina que es peligrosa para la vida, que se cuidan en el cuidado intensivo.

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 PI: Leslie Kern RN, PhD/Peggy Kalowes RN, MSN
 Project No. 299-05

Puede usted ayudarnos comprender como hacer aún mejor en el cuidado de los pacientes críticamente enfermos, por contestar las preguntas en el cuestionario adjunto, que le pregunta identificar los síntomas que le molesta, y clasificar la frecuencia y severidad de los síntomas. La información que proporciona usted puede ayudar en la identificación de las necesidades que tiene, y además ayudar en la desarrollo y la investigación de tratamientos nuevos y intervenciones del oficio de la enfermera por varios síntomas, porque actualmente hay pocas terapias disponibles que puede aliviar.

PROCEDIMIENTO

Si se presenta voluntario en el estudio, se preguntará completar dos cuestionarios (disponibles en inglés y español)

- Un cuestionario de 14 puntos para determinar sus síntomas;
- Una encuesta de tratamiento y procedimiento

En el primer día del ingreso al cuidado intensivo, un asistente de la investigación determinará su capacidad de contestar las preguntas y participar en el estudio. Si satisface usted los criterios, se preguntará terminar el cuestionario del gravamen del síntoma. Este cuestionario nos dirá su percepción de los síntomas y la salud en la semana anterior. Tomará 2 a 4 minutos para completar.

Nota: Si usted no puede escribir, puede comunicar las respuestas en otra manera que comprende el entrevistador, quien puede recordar las respuestas en el cuestionario.

En el tercer día del cuidado, el entrevistador regresará y determinará su capacidad de responder de las preguntas otra vez. Se preguntará completar el cuestionario del gravamen del síntoma otra vez para que podamos evaluar el estatus de sus síntomas después de dos días en el hospital. Tomará 2 a 4 minutos para completar. Adicionalmente, completará el cuestionario de tratamiento y procedimiento al mismo tiempo. Porque queremos comprender porque algunos pacientes tienen dolor y sufrimiento adicional, queremos que tome usted un momento para decirnos el dolor o el fastidio que experimenta durante los varios tratamientos y procedimientos. Tomará 2 a 4 minutos para completar. Esto completará su participación en el estudio.

APPROVED

MAR 20 2006

RIESGOS Y MALESTARES POTENCIALES

No hay riesgo previsible para lesión física cuando participe en el estudio, aunque, es posible tener fatiga cuando responde al cuestionario. Puede reducir o prevenir la fatiga por completar el cuestionario en su propio paso, o preguntar el investigador recordar las respuestas para usted directamente en la forma.

Los riesgos previsibles son mínimos para daño psicológico cuando responde al cuestionario de los síntomas, porque es muy corto y sólo debe tomar 2 a 4 minutos para completar. Entonces, no debe ser ansiedad, miedo o dolor asociado. Sin embargo, si el estrés ocurre, se esta disponible una remisión apropiada para ayuda adicional a través de los servicios del cuidado pastoral.

Este cuestionario había sido usado en investigaciones anteriores con poblaciones similares sin informe del daño psicológico. Si experimenta usted aflicción, tiene el derecho de discontinuar su participación en el estudio.

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VENTAJAS POTENCIALES PARA PARTICIPANTES Y/O LA SOCIEDAD

La primera ventaja y la más obvia sería que el cuestionario usado puede identificar la presencia e intensidad de varios síntomas que no puede usted describir a través de sus percepciones propias. Ayudará en la identificación de lagunas en su cuidado actualmente, lo que podríamos tratar de mejorar.

Además, hay la ventaja de añadir al conocimiento científico del oficio de las enfermeras y el campo del manejo del síntoma. Es posible que este estudio nos ayude en el desarrollo de nuevas terapias para reducir el dolor y sufrimiento en los pacientes durante el curso de su enfermedad peligrosa para la vida.

ALTERNATIVOS

No hay alternativas, fuera de no participar. Tuvo la oportunidad para preguntar a los investigadores, y ellos le respondieron a su satisfacción. Comprende usted que su médico contestará otras preguntas que pueda tener en el futuro.

RENUMERACIÓN POR LA PARTICIPACIÓN

Participantes no van a recibir remuneración ni otra forma de incentivo para participar en el estudio.

PARTICIPACION VOLUNTARIO/DERECHO DE RETIRARSE

Puede usted elegir si quiere participar en este estudio o no. Si se presenta voluntario en este estudio, se puede retirar en cualquier momento sin consecuencias. Participación o la falta de participación no va a afectar su tratamiento ni su cuidado, ni otras consideraciones personales que espera normalmente. Tiene el derecho rechazar a contestar las preguntas que no quiere contestar y puede quedarse en el estudio todavía. La investigadora puede removerle del estudio si presenta circunstancias que, en la opinión de la investigadora, constituya el retiro.

CONFIDENCIALIDAD

Comprende usted que la información obtenida sobre usted en esta investigación se queda confidencial y nunca se identifica su nombre en un informe o publicación a menos que firme usted un descargo. Se usa un código de números en vez de nombres para todos los datos para asegurarse confidencialidad. El consentimiento, y la lista que empareja el nombre del participante al código asignado serán mantenidos separados de todas las materiales de la investigación, y sólo las investigadoras principales podrán tener acceso. Todos los datos y cuestionarios que completa será mantenidos en un gabinete bloqueado en la oficina del investigador, y sólo los investigadores tendrán acceso.

La información sobre sus archivos médicos, como los archivos del hospital, se pueden obtener una citación por orden del juicio. Consiente usted a la publicación de los resultados del estudio mientras la información sea anónima y/o disfrazado de modo que no se pueda hacer una identificación. Además, comprende usted que los representantes autorizados de la Administración de drogas y alimentos (ADA), y el MHS Institutional Review Board (MHS Research Council), puede examinar sus archivos, y no hay una abertura de la confidencialidad.

MHS RESEARCH COUNCIL
APPROVED

MAR 20 2006

EXPIRES 11-20-06
 INITIALS _____

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 PI: Leslie Kern RN, PhD/Peggy Kalowes RN, MSN
 Project No. 299-05

Cláusula de IRB / FDA

Se repasa y aprueba esta propuesta por Memorial Health Services Institutional Review Board (MHS Research Council), que sirve para el IRB de **Long Beach Memorial Hospital**, que contiene ambos médicos y personas del gran público. Si tiene usted alguna pregunta sobre sus derechos como participante del estudio, o el tratamiento relacionado con la lesión, o quiere más información sobre la disponibilidad de remuneración o tratamientos médicos, puede contactar Harris R. Stutman, MD, director ejecutivo, el oficio de administración de la investigación, Memorial Health Services, al número (562) 490-3737.

La(s) investigadora(s) principal(es) Leslie Kern RN, PhD y Peggy Kalowes, RN, MSN, CNS; o uno de los asistentes de las investigadoras le han discutido este estudio. Si tiene algunas preguntas, puede contactarles a [(562) 933-3320; (562) 225-2545/ 985-1804].

Yo certifico que he leído el texto que precede o alguien me ha leído, y que comprendo el contenido, y que el médico ha respondido/responderá a cualquier pregunta que tengo que pertenece al texto que precede, y que doy el permiso libremente. Se me da una copia de esta forma de consentimiento junto con una copia de "*Rights of Human Subjects in Medical Research*", y consiento a la participación en el estudio.

Nombre del paciente _____ Código de identificación asignado _____

Firma del paciente _____ Fecha _____ Hora _____

Testigo a la firma del paciente _____ Fecha _____ Hora _____

Si el participante es menor de edad, o por alguna razón no puede firmar, complete al siguiente:

a) Razón que el participante no puede firmar: _____

b) _____
 Nombre de persona autorizada _____ Fecha _____

Firma de persona autorizada _____ Hora _____

Relación y base de la autorización para dar consentimiento _____

Certificado de la persona que obtiene consentimiento

He proporcionado un explicación del estudio de investigación arriba, y he animado al paciente a preguntar y pedir por información adicional sobre el estudio, sus riesgos y complicaciones y alternativos posibles. Se da una copia de esta forma de consentimientos al paciente.

MHS RESEARCH COUNCIL
APPROVED

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 Project No. 299-05

_____ Firma de persona que obtiene consentimiento	_____ Imprima nombre de la persona que obtiene el consentimiento	_____ Fecha
---	--	----------------

Certificado del investigador:

Yo certifico que estoy el investigador principal o el asistente del investigador responsable para el estudio. Me aseguro que el participante es completamente informado de acuerdo con regulaciones aplicables, y para el aviso del MHS Research Council (IRB) de algunas reacciones adversas o acontecimientos inesperados que puede desarrollar debido a este estudio.

_____ Investigador principal o Asistente al investigador	_____ Fecha	_____ Hora	_____ Código I.D. del investigador
--	----------------	---------------	---------------------------------------

INVÁLIDO SIN ESTAMPILLA DE LA APROBACION DE IRB

MHS RESEARCH COUNCIL
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DERECHOS DE SUJETOS HUMANOS EN LAS INVESTIGACIONES MÉDICALES.

Alguna persona que ha sido solicitado para participar cómo sujeto de un experimento medical o que ha sido solicitado para el consentimiento a favor de otro tiene el derecho:

1. Ser informado de THE NATURE y el propósito de la investigación.
2. Ser dado una explicación de los procedimientos seguidos en el experimento medical, y algunas drogas o aparatos usados.
3. Ser dado una descripción de algunas molestias y riesgos razonables para esperar durante el experimento
4. Ser dado una explicación de algunos beneficios para los SUJETOS razonables para esperar durante el experimento.
5. Ser dado una revelación de algunos procedimientos alternativos apropiados, drogas o aparatos que puede ser ventajoso al SUJETO, y sus riesgos y beneficios relativos.
6. Ser informado de las vías de tratamientos medical, si hay, disponibles al SUJETO después del experimento, si hay complicaciones.
7. Ser dado la oportunidad preguntar algo sobre el experimento del procedimiento implicado.
8. Ser mandado que se puede retirar el consentimiento para participar en el experimento en alguno momento y el SUJETO puede parar la participación en este experimento sin prejuicio.
9. Ser dado una copia de algún consentimiento que es firmado o escrito, usado con relación al experimento
10. Ser dado la oportunidad decidir al consentimiento, o no al consentimiento, al experimento medical sin la intervención de algún elemento de fuerza, fraude, engaño, compulsión, coerción o influencias indebidas en la decisión del SUJETO.

FIRMA DEL PACIENTE: _____ FECHA: _____

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[Faint signature]

HIPAA AUTHORIZATION

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**Memorial Health Services Research Council
Institutional Review Board**

(Long Beach Memorial Medical Center)

Título del proyecto: Comprendiendo la carga de los síntomas en los pacientes con enfermedades terminales, y con enfermedades que amenazan la vida, en las unidades del cuidado intensivo.

Número de autorización de uso y revelación de información de salud protegida

Autorización de uso y revelación de información de salud protegida

¿Cómo se protege su confidencialidad?

Tiene usted derechos relacionados a la privacidad de su información médica, que ha sido recogida antes de y durante el curso de esta investigación. Esta información médica se llama "información de la salud protegida" (PHI), y incluye información demográfica, resultados de los exámenes físicos, pruebas de sangre, radiografías y otros procedimientos diagnósticos y médicos, al igual que su historia médica. Tiene usted el derecho para limitar el uso y el compartimiento de su PHI, y tiene el derecho para ver los registros médicos y saber quien los ve.

Al firmar esta forma de autorización, le permite al equipo de investigación el acceso a su PHI para el propósito de llevar a cabo este estudio. El equipo de investigación incluye los investigadores mencionados en la forma de consentimiento y otro personal específico involucrado en la investigación en Long Beach Memorial Medical Center.

Se utilizará su PHI solo para los propósito(s) descritos en la sección del consentimiento informado llamado [Comprendiendo la carga de los síntomas en los pacientes con enfermedades terminales, y con enfermedades que amenazan la vida, en las unidades del cuidado intensivo.]

Se compartirá su PHI, cuantas veces sea necesario con el MHS Research Council (también conocido como el Comité de Revisión Institucional) y con alguna persona o agencia requerida por la ley.

Last Revised: 06/15/2004

Memorial Health Services Research Council

Appendix N

IRB-MHS-Spanish Informed Consent Family

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 PI: Leslie Kern RN, PhD/Peggy Kalowes RN, MSN
 Project No. 299-05

Memorial Health Services Council
 Institutional Review Board
 Long Beach Memorial Hospital

**Consentimiento Informado para participar en un estudio de la investigación
 (Respondedor Familiar)**

Título: *La Comprensión de la carga del síntoma en los pacientes con enfermedades terminales, y enfermedades graves, en el cuidado intensivo.*

Investigadora Principal: Leslie Kern RN, PhD

Número de Teléfono: (562) 933-3320

Investigadora Principal: Peggy Kalowes RN, MSN, CNS **Número de Teléfono:** (562) 225-2545

Asistente al Investigadora: Louise DuBos RN, BSN

Número de Teléfono: (562) 522-9893

Número del proyecto MHS: 299-05

Se ha sido preguntado a usted para participar en un estudio de investigación conducido por Leslie Kern RN, PhD y Peggy Kalowes, RN, MSN, un estudiante doctoral en el programa de enfermeras en la Universidad de San Diego. Peggy está conduciendo una disertación en la forma de un estudio de investigación para comprender más el dolor y sufrimiento que presenta con varios síntomas, relacionado a la enfermedad progresivo y enfermedad grave.

La información que proporciona usted nos dará una perspectiva valiosa y única de la percepción de un miembro de la familia, con respeto a los síntomas y salud del paciente, que varían con frecuencia con la del paciente.

Al participar en este estudio de la investigación, se añadirá al conocimiento del oficio de enfermera en el manejo de los síntomas, lo que puede ayudarnos en mejorar los tipos de tratamientos que podemos proporcionar (o no dar) y los tipos de cuidado y servicios que se necesitan los pacientes y las familias en varios puntos durante el curso de la enfermedad crítica.

¿PORQUÉ ES USTED ELEGIBLE?

Se ha sido seleccionado usted como candidato posible en este estudio porque un miembro de su familia ha acordado participar en la investigación, y decimos sobre la severidad y la frecuencia de sus síntomas relacionada a su enfermedad. Actualmente tenemos poquito información/o investigación sobre los grados de aflicción y sufrimiento de varios síntomas en el paciente de una perspectiva familiar. Se conduce la mayoría de los estudios sobre los síntomas en pacientes críticos con el cáncer avanzado, y otras desordenes comunes como las enfermedades del corazón, pulmón, hígado, la diabetes, el ataque cerebral, o una lesión traumática aguda. Estos estudios no son tan provechosos para mejorar el cuidado de los pacientes con otras enfermedades agudas.

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PI: Leslie Kern RN, PhD/Peggy Kalowes RN, MSN
Project No. 299-05

PROPÓSITO DEL ESTUDIO

El propósito primario del estudio es determinarse el predominio de varios tipos de síntomas (por ejemplo: dolor, dificultad de respirar, náusea), la frecuencia, y la severidad de aflicción de los pacientes que tiene una enfermedad progresivo o una enfermedad repentina que es peligroso para la

vida, que se cuidan en el cuidado intensivo. Hay poca información disponible de ambos los perspectivas de los pacientes y las familias durante el curso de la enfermedad.

Familias/amigos vean como los pacientes responde a sus enfermedades y síntomas en una manera completamente diferente de la percepción del paciente. Además, las familias o amigos a menudo proporcionan el cuidado necesario para los pacientes que viven en casa cuando están enfermas. Entonces, puede proporcionar una perspicacia más amplia a la enfermedad del paciente.

Entonces, puede usted ayudarnos comprender como hacer aún mejor en el cuidado de los pacientes críticamente enfermos, si contesta a las preguntas en el cuestionario adjunto, que le pregunta identificar los síntomas que le molesta el miembro de su familia, y clasificar la frecuencia y severidad de los síntomas (como aparece a usted). La información que proporciona usted puede ayudar en la identificación de las necesidades que tiene, y además ayudar en la desarrolla y la investigación de tratamientos nuevos y intervenciones del oficio de la enfermera por varios síntomas, porque actualmente hay pocas terapias disponibles que puede proporcionar el alivio.

PROCEDIMIENTO

Si se presenta voluntario en el estudio, se preguntará completar dos cuestionarios (disponible en inglés y español)

- Una forma corta en que puede evaluar las características del miembro de la familia (edad, sexo, etnicidad, ocupación, papel del cuidado al paciente)
- Una encuesta de 14 cosas para evaluar su percepción de los síntomas del paciente.
- En el primer día, del ingreso del paciente al cuidado intensivo, le preguntará terminar una forma demográfica; y un cuestionario del gravamen del síntoma. El cuestionario de síntomas nos dirá su percepción de los síntomas del paciente y la salud durante la semana anterior. Tomará aproximadamente 5 a 8 minutos en total.
- En el tercer día del cuida del paciente, los investigadores van a preguntarle terminar el cuestionario del gravamen del síntoma otra vez. Nos dirá su percepción de los síntomas del paciente y calidad de vida, y si esto ha cambiado, cuando recibe tratamiento(s) por varios días. Tomará aproximadamente 2 a 4 minutos para terminar.

Nota: Si no puede estar presente físicamente en el tercer día, se puede arreglar y conducir una entrevista por teléfono en su conveniencia, así que puede dar esta información muy importante para terminar el estudio.

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RIESGOS Y MALESTARES POTENCIALES

No hay riesgo previsible para lesión física cuando participe en el estudio, aunque, es posible tener la fatiga cuando responde al cuestionario. Puede reducir o prevenir la fatiga por completar el cuestionario en su propio paso, o preguntar al investigador recordar las respuestas para usted directamente en la forma.

Los riesgos previsibles son mínimos para daño psicológico cuando respondes al cuestionario de los síntomas, porque es muy corto y sólo debe tomar 2 a 4 minutos para completar. Así, no debe ser ansiedad, miedo o dolor asociado. Sin embargo, si el estrés ocurre, se esta disponible una remisión apropiada para ayuda adicional a través de los servicios del cuidado pastoral.

VENTAJAS POTENCIALES PARA PARTICIPANTES Y/O LA SOCIEDAD

La primera ventaja y la más obvia sería que el cuestionario usado puede identificar la presencia e intensidad de varios síntomas que no puede usted describir a través de sus percepciones propias. Ayudará en la identificación de boquetes en su cuidado actualmente, lo que podemos tratar de mejorar.

Además, hay la ventaja de añadir al conocimiento científico del oficio de las enfermeras y el campo del manejo del síntoma. Es posible que el estudio nos ayude en el desarrollo de nuevas terapias para reducir el dolor y sufrimiento en los pacientes durante el curso de su enfermedad peligroso para la vida.

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ALTERNATIVOS

No hay alternativas, fuera de no participar. Tuvo la oportunidad para preguntar a los investigadores, y ellos le respondieron a su satisfacción.

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RENUMERACIÓN POR LA PARTICIPACIÓN

Participantes no van a recibir renumeración ni otra forma de incentivo para participar en el estudio.

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PARTICIPACIÓN VOLUNTARIO/ DERECHO PARA RETIRARSE

Participación en el estudio es opcional como miembro de la familia. Si participa en el estudio, se podrá retirar en cualquier momento sin consecuencias. Participación o la falta de participación no va a afectar el tratamiento ni el cuidado del miembro de su familia. Tiene el derecho rechazar contestar las preguntas que no quiere contestar y puede quedarse en el estudio todavía. La investigadora puede removerle del estudio si presenta circunstancias que, en la opinión de la investigadora, autoriza un despido del estudio.

CONFIDENCIALIDAD

Comprende usted que la información obtenida sobre usted en esta investigación se queda confidencial y nunca se identifica su nombre en un informe o publicación a menos que firme usted un descargo. Se usa un código de números en vez de nombres para todos los datos para asegurarse confidencialidad. El consentimiento, y la lista que empareja el nombre de participante al código asignado serán mantenidos separados de todas las materiales de la investigación, y sólo las investigadoras principales podrán tener acceso. Todos los datos y cuestionarios que complete será

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PI: Leslie Kern RN, PhD/Peggy Kalowes RN, MSN

Project No. 299-05

mantenido en un gabinete bloqueado en la oficina del investigador, y sólo los investigadores tendrán acceso.

Consienta usted a la publicación de los resultados del estudio mientras la información sea anónima y/o disfrazada así que nadie se pueda hacer una identificación.

CLÁUSULA DE IRB / ADA

Se repasa y aprueba esta propuesta por Memorial Health Services Institutional Review Board (MHS Research Council), que sirve para el IRB de **Long Beach Memorial Hospital**, que contiene ambos médicos y personas del gran público. Si tiene usted alguna pregunta sobre sus derechos como participante del estudio, o el tratamiento relacionado con la lesión, o quiere más información sobre la disponibilidad de remuneración o tratamientos médicos, puede contactar Harris R. Stutman, MD, director ejecutivo, el oficio de administración de la investigación, Memorial Health Services, al número (562) 490-3737.

La(s) investigadora(s) principal(es) Leslie Kern RN, PhD y Peggy Kalowes, RN, MSN; o uno de los asistentes de las investigadoras le han discutido este estudio. Si tiene algunas preguntas, puede contactarles a [(562) 933-3320; (562) 225-2545/ 985-1804].

Yo certifico que he leído el texto que precede o alguien me ha leído, y que comprendo el contenido, y que el médico ha respondido/responderá a cualquier pregunta que tengo que pertenece al texto que precede, y que doy el permiso libremente. Se me da una copia de esta forma de consentimiento junto con una copia de "Rights of Human Subjects in Medical Research", y consiento a la participación en el estudio.

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Nombre del respondedor familiar

Código asignado

Firma de los respondedores familiares

Fecha

Hora

Testigo a la firma del respondedor familiar

Fecha

Hora

Si el participante es menor de edad, o por alguna razón no puede firmar, complete al siguiente:

a) Razón que el participante no puede firmar: _____

b)

Nombre de persona autorizada

Fecha

Firma de persona autorizada

Hora

Relación y base de la autorización para dar consentimiento

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 PI: Leslie Kern RN, PhD/Peggy Kalowes RN, MSN
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Certificado de la persona que obtiene consentimiento

He proporcionado una explicación del estudio de investigación arriba, y he animado al paciente a preguntar y pedir por información adicional sobre el estudio, sus riesgos y complicaciones y alternativas posibles. Se da una copia de esta forma de consentimientos al paciente.

_____	_____	_____
Firma de persona	Imprima nombre de la persona	Fecha
que obtiene consentimiento	que obtiene el consentimiento	

Certificado del investigador:

Yo certifico que estoy el investigador principal o el asistente del investigador responsable para el estudio. Me aseguro que el participante es completamente informado de acuerdo con regulaciones aplicables, y para el aviso del MHS Research Council (IRB) de algunas reacciones adversas o acontecimientos inesperados que puede desarrollar debido a este estudio.

_____	_____	_____	_____
Investigador principal o	Fecha	Hora	Código ID. del investigador
Asistente al investigador			

INVÁLIDO SIN ESTAMPILLA DE LA APROBACION DE IRB

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 Project No. 299-05

DERECHOS DE SUJETOS HUMANOS EN LAS INVESTIGACIONES MÉDICAS.

Alguna persona que ha sido solicitado para participar cómo sujeto de un experimento medical o que ha sido solicitado para el consentimiento a favor de otro tiene el derecho:

1. Ser informado de THE NATURE y el propósito de la investigación.
2. Ser dado una explicación de los procedimientos seguidos en el experimento medical, y algunas drogas o aparatos usados.
3. Ser dado una descripción de algunas molestias y riesgos razonables para esperar durante el experimento
4. Ser dado una explicación de algunos beneficios para los SUJETOS razonables para esperar durante el experimento.
5. Ser dado una revelación de algunos procedimientos alternativos apropiados, drogas o aparatos que puede ser ventajoso al SUJETO, y sus riesgos y beneficios relativos.
6. Ser informado de las vías de tratamientos medical, si hay, disponibles al SUJETO después del experimento, si hay complicaciones.
7. Ser dado la oportunidad preguntar algo sobre el experimento del procedimiento implicado.
8. Ser mandado que se puede retirar el consentimiento para participar en el experimento en alguno momento y el SUJETO puede parar la participación en este experimento sin prejuicio.
9. Ser dado una copia de algún consentimiento que es firmado o escrito, usado con relación al experimento
10. Ser dado la oportunidad decidir al consentimiento, o no al consentimiento, al experimento medical sin la intervención de algún elemento de fuerza, fraude, engaño, compulsión, coerción o influencias indebidas en la decisión del SUJETO.

FIRMA DEL PACIENTE: _____ FECHA: _____

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Appendix O

Letter of Translator Certification

Child & Adolescent Services Research Center

3020 Children's Way • MC 5033 • San Diego, California 92123-4282
(858) 966-7703 • FAX (858) 966-7704 • www.casrc.org

TO: Harris R. Stutman, MD, Executive Director
Memorial Health Services
Office of Research Administration
Long Beach Memorial Medical Center
2801 Atlantic Blvd
Long Beach, CA 90806

FROM: Cynthia D. Connelly, Ph.D.

DATE: 1/20/06

RE: Symptom Burden in Patients with Terminal and Life-Threatening
Illness in Intensive Care Units

Dear Dr. Stutman:

Attached please find copies of the English version of patient/family respondent consents forms, PHI form; family demographic questionnaire, and patient treatment & procedure survey for the above-named protocol and the corresponding Spanish translations. Ms. Blanca Mancillas and Norma Talamantes employed by the Child and Adolescent Services Research Center, Children's Hospital and Health Center, San Diego CA have reversed translated the consent and assent forms, and they are satisfied that they are accurate and comprehensible. Both Ms. Mancillas and Talamantes are native Spanish speakers with over 10 years of experience in translation and reverse translation with a particular focus on behavioral health research.

Thank you for your assistance with this protocol. Please do not hesitate to contact me if you have any questions.

Cynthia D. Connelly, Ph.D., RN
Research Scientist – Child and Adolescent Services Research Center
Associate Professor – Hahn School of Nursing and Health Science
University of San Diego, San Diego CA

*A National Institute of Mental Health funded Center
in collaboration with:*

- San Diego State University • The University of California, San Diego
- San Diego County Probation Department • San Diego Health and Human Services Agency

Appendix P

IRB-MHS- Continuation Approval

MHS-RESEARCH COUNCIL (IRB) APPROVAL LETTER

P.I.: Leslie Kern, RN, PhD/Peggy Kalowes, RN, PhD(c)
Memorial Heart and Vascular Institute

Date: October 16, 2006

Project # and Title: #299-05 "Understanding the Symptom Burden in Patients with Terminal and Life Threatening Illness in Intensive Care Units."

Extension Approval Date: October 16, 2006

Expiration Date: October 15, 2007

☒ Regular Review

☐ Direct Review

A request for an extension to the above project was reviewed and approved at the October 16, 2006 MHS Research Council meeting for a period of 1 year. The Memorial Health Services Research Council serves as the Institutional Review Board for Long Beach Memorial Medical Center. Enclosed please find an official stamped copy of the Informed Consent Form for the above named project. The previously approved Authorization form for use and disclosure of Protected Health Information should continue to be used.

- In compliance with FDA regulations and Memorial Health Services Research Council policies, a detailed progress report must be submitted to the Office of Research Administration before August 1, 2007.

MHS Research Council approvals are provided to Principal Investigators subject to the following conditions:

In accordance with MHS Policy and Procedures, the MHS Research Council may authorize staff to conduct spot checks or audits on their behalf. Please provide the information requested if an audit of your project occurs.

Per ICH guidelines, the MHS Research Council regards the Principal Investigator as responsible for the conduct of research trials at his/her site and all associated research facilities. Specific responsibilities of the Principal Investigator include ensuring:

- Supervision of all research at Long Beach Memorial Medical Center in accordance with Memorial Health Services policies and FDA regulations.
- Conduct of research according to the study protocol.
- Use of the most recently approved informed consent form.
- Provision of a MHS Research Council-approved consent form in the subject's first language to all non-English speaking subjects.
- Approval by the MHS Research Council for all changes in research activity including protocol amendments and/or consent form revisions prior to implementation.
- Prompt reporting (48 hours verbally and 5-10 days in writing) to the MHS Research

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Council of any significant changes in research activity including changes in Principal Investigator, changes in research site, addition of research facilities to a previously approved site, and study completion.

- Approval by the MHS Research Council of all advertisements and patient recruiting materials prior to use.
- Prompt reporting (48 hours verbally and 5-10 days in writing) to the MHS Research Council of serious and unexpected events related to study procedures as well as protocol deviations/violations.
- Timely submission of continuing review and progress reports.

Sincerely,

Harris R. Stutman, MD
Executive Director
Office of Research Administration
Approval letters/299-05 extension October 2006