The Pennsylvania State University

The Graduate School

School of Nursing

BURDEN, UNCERTAINTY, AND PATIENT SYMPTOMATOLOGY IN FAMILY CAREGIVERS OF HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS: A PROSPECTIVE STUDY

A Dissertation in
Nursing

by

Margaret Davitt Harris

Submitted in Partial Fulfillment
of the Requirements
for the Degree of

Doctor of Philosophy

August 2008

The dissertation of Margaret Davitt Harris was reviewed and approved* by the following:

Carol A. Smith
Associate Professor of Nursing
Dissertation Advisor
Chair of Committee

Sharon K. Falkenstern
Assistant Professor of Nursing

Vernon M. Chinchilli
Distinguished Professor of Biostatistics and Statistics
and Chair of Health Evaluation Services

James O. Ballard
Professor of Pathology, Medicine, and Humanities

Ian M. Paul
Associate Professor of Pediatrics

Paula F. Milone-Nuzzo
Acting Professor-in-Charge, Graduate Program
Professor and Dean of Nursing

*Signatures are on file in the Graduate School.

Abstract

This descriptive study examined the experience of family caregivers of Hematopoietic Stem Cell Transplantation (HSCT) patients to identify stress-related factors that could impact the effectiveness of their caregiver role in the current atmosphere of early discharge of bone marrow transplant recipients from hospital care.

A conceptual framework that integrated caregiver burden, uncertainty, and patient symptom pattern assessment served as a basis for this prospective repeated measures study design, whereby several instruments were administered to the study participants at two sites.

Data were collected from 46 patient-caregiver dyads at four points in the acute transplant treatment process: (a) pre-transplant, (b) immediately after transplant, (3) one week after discharge from the hospital, and (d) one month after discharge. The data collection was conducted by the principal investigator at the Penn State Milton S. Hershey Medical Center in central Pennsylvania in 2004 and by the co-investigator at the Stanford University Hospital in Los Angeles in 2008. The data analysis was conducted using descriptive statistics, ANCOVA, and Pearson Partial Correlation.

The following were the principal findings: caregiver burden and uncertainty were most evident at Interview 1 and 2 (pre-transplant and immediately post-transplant); levels of burden and levels of uncertainty in this population were at or above levels reported for caregivers of patients with chronic diseases; burden was at a level associated with diagnosis of depression in other research; and times of highest stress were associated with

the greatest difference in caregiver and patient assessment of symptoms (e.g., pain, fatigue, and other psychological and physical symptoms).

The findings of this study support the need for focused support for caregivers early in the HSCT treatment process, monitoring of caregivers for signs of clinical depression, and recognition that their stress level may alter the accuracy of their assessment of patient symptoms. The lack of increase in burden and uncertainty scores post discharge suggests that the caregivers in this study may not have found care of the patient at home to be more stressful than during hospitalization, and may have considered it to be an acceptable treatment model. Limitations related to the convenience sampling in this study support the need for additional research to confirm these findings and improve generalization to other HSCT caregiver populations. The contribution to the literature of an understanding of the family caregiver experience revealed in this study provides new insights into potential areas for the development of healthcare intervention.

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Acknowledgments

I am deeply appreciative of the guidance and support I received from the members of my dissertation committee: Carol A. Smith, DSN; J. O. Ballard, MD; Vernon M. Chinchilli, PhD; Sharon K. Falkenstern, PhD; and Ian M. Paul, MD. In particular I would like to thank Dr. Smith for her encouragement, guidance, and persistence in supporting my completion of this dissertation. I would also like to acknowledge the thoroughness and skill of my editor, Hazel Hunley, who helped pull all the materials together in an organized fashion.

I am also indebted to Dr. D. Katherine Tierney, who coordinated the study at Stanford University Hospital.

Finally, I am grateful to my husband, Ed, for his support and understanding throughout the many years it took me to complete this dissertation. I would also like to thank my mother, Sheila, and my siblings, Martin, Andy, Sheila, and Patty for their patience throughout this long journey.

Chapter 1

INTRODUCTION

Caregivers experience significant stress that can result in marked disruption in their lives. Investigations of caregiving have shed considerable light on the magnitude of lifestyle changes that are encountered when family members or significant others assume the responsibility of caring for another person. Caregiving experiences have been most extensively studied in the context of long-term chronic illnesses in populations with dementia and Alzheimer's disease (AD) (Hughes, Hope, Savulescu, & Ziebland, 2002; 1992; Zarit, Todd, & Zarit, 1986), in the elderly (Bedard et al., 2001; Dellasega, 1990a; Dellasega & Zerbe, 2002), and in cancer patients (Goldstein et al., 2004; M. E. Kurtz, J. C. Kurtz, C. W. Given, & B. A. Given, 1995; Miaskowski, Kragness, Dibble, & Wallhagen, 1997; Nijboer et al., 2000; Oberst, Thomas, Gass, & Ward, 1989). Very little is known about caregiver experiences with patients when the illness involves life-threatening, short-term intensive treatment episodes (Eilers, 1996). Developments in medical science and health care have made certain previously fatal illnesses, e.g., types of cancer, potentially curable, but the treatments can cause long-term negative effects. In fact, the new technology necessary to achieve a cure may be as devastating as the original disease itself, both to the patient and to the caregiver who loves, watches over, and provides day-to-day, hands-on-care for his or her loved one.

The role of family caregivers has recently increased in responsibility due to the patient's shorter hospital stay for Hematopoietic Stem Cell Transplantation (HSCT)

treatment and increased outpatient care. The continuing need to improve the cost effectiveness of all health care makes it likely that family caregivers will continue to assume increasing responsibility for the post-treatment care of HSCT patients. Therefore, more knowledge of the HSCT caregiver experience is needed to assure that they are provided adequate support during the post-treatment process.

Research studies show that there is growing attention to the burden of family caregiving in cancer care. However, the studies are very limited on the caregiver experience with patients during Bone Marrow Transplantation (BMT) or Peripheral Stem Cell Transplant (PSCT), now called Hematopoietic Stem Cell Transplantation, which can be an important part of the treatment of some types of cancer. HSCT involves high doses of chemotherapy and potentially other treatments to eliminate the cancer at the cost of the elimination of the patient's bone marrow, and related severe side effects. Bone marrow function is restored by infusing bone marrow or stem cells into the patient. The patient may be ill for an extended period of time and require extensive monitoring and support. A further description of the HSCT procedure is detailed in Chapter 2.

The purpose of this chapter is to provide background on HSCT family caregiver research, describe the problem and its significance to nursing, describe the details of this study, provide and define the theoretical framework for the study, define the concepts within the study framework, and indicate how these concepts interact in the HSCT family caregiving process.

Background

The experiences and consequences for individuals who care for others outside the hospital setting have historically been referred to in the contexts of caregiving, caregiver burden (Zarit et al., 1986), and caregiver stress (Pearlin, Mullan, Semple, & Skaff, 1990). Early definitions of caregiver burden associated caregiving with "fear or shame" (Thompson & Doll, 1982, p. 380) or some degree of cost to the family (Grad & Sainsbury, 1963). Initial measurements of caregiver burden were limited to counting the number of tasks or events during the caregiving. However, Montgomery, Gonyea, and Hooyman (1985) further delineated the caregiving burden as being objective and subjective, with the former referring to concrete measurable events and the latter to feelings or reactions to the caregiving role. Other authors have used these subjective and objective categories, but the characterizations of caregiving have not been applied consistently across studies (Forssen, Carlstedt, & Mortberg, 2005).

Caregiver issues in cancer treatment, when declining patient health status and performance are common, are usually associated with a poor quality of life for the caregiver (Weitzner, Jacobsen, Wagner, Friedland, & Cox, 1999). Spouses who are caregivers were shown to receive greater support from employers than from non-spousal caregivers, whose roles were less recognized, causing them more stress, especially in the terminal phase of their loved one's illness (Coristine, Crooks, Grunfeld, Stonebridge, & Christie, 2003). Raveis, Karus, and Siegal (1998) found that assuming multiple roles, such as wife and mother, may serve as protective mechanisms for daughters of cancer patients or as a buffer against the negative impact of caring for a parent with cancer.

Responsibilities for detecting and reporting untoward effects of treatment, identifying the care needs, dealing with unpleasant symptoms, and coping with the devastating possibilities of the disease can be overwhelming to both the patient and support persons (Carey, Oberst, McCubbin, & Hughes, 1991). Healthcare professionals have begun to appreciate fully the magnitude of demands that cancer treatment (Carey et al.,1991; Cassileth et al., 1985) and palliative care (Kinsella, Cooper, Picton, & Murtagh, 1998, 2000; Proot et al., 2003) place on family caregivers. Some investigators have distinguished between differences in *burden of care* on family caregivers, comparing curative and palliative care treatment settings (Weitzner, McMillan, & Jacobsen, 1999). Others have examined the disruptions in lifestyles of family caregivers of persons with advanced cancer, stressing how important it is to maintain the valued aspects of daily living during this experience (Cameron, Franche, Cheung, & Stewart, 2002). However, more information and understanding are needed concerning the burden of care experience for family caregivers in HSCT therapy.

Difficulty during the bone transplant process can have profound effects on later coping because of the intensity of short-term treatment and the high likelihood of serious life-threatening effects (Stetz, McDonald, & Compton, 1996). More information is needed, however, to help healthcare professionals better understand the stressors experienced by family caregivers of these patients in order to recognize opportunities to intervene and reduce the stress and the associated burden for these family caregivers.

Perhaps the most compelling need to advance knowledge and understanding of the caregiver experiences, especially in relationship to cancer, is the realization that

caregiver stress can lead to psychological morbidity. Yet, in a recent systematic review of interventions and their effectiveness, Harding and Higginson (2003) found that few effective approaches had been identified to help caregivers cope with the change in responsibilities for providing care. In part, such a paucity of research in this area exists because investigators have not fully identified all the factors that affect perceptions of burden of care and the realization of what is most burdensome and how these differ by the relationships of the caregivers and their personal characteristics. Therefore, the problem of addressing caregiver burden is dependent on knowing how different concepts and experiences contribute to this high risk phenomenon.

The cognitive feature of *uncertainty*, that is, the inability to make sense of a situation or an event (Mishel, 1981), bears some relationship to how people appraise aspects of managing illness and how they deal with the stress of the danger and threat of what might be, and what is to come (Mishel & Sorenson, 1991). While uncertainty has been studied in patients with acute and chronic illnesses, including cancer, it has not been studied as a predictor of perceived burdens of care by caregivers of persons with HSCT. It would be expected that uncertainty would run high with caregivers in situations such as HSCT where treatment and eventual outcome are unpredictable. A study focusing on families of heart transplant patients examined uncertainty and found that in the pre-transplant phase, the families were predominantly focused on finding a suitable heart for transplant, but that the post-transplant focus shifted to the reality of the enormous care demands and uncertainty over the outcome (Mishel & Murdaugh, 1987). These investigators characterized a shift in thinking to focus on the paradigms of pre- and post-

transplant uncertainty experiences. It seems likely that perceptions of uncertainty may also affect the degree of caregiver burden that is experienced before and after a stem cell transplant.

There are experiential and anecdotal reports describing caregivers' experiences with cancer patients and caregiver requirements for information and assistance in providing ongoing care to their loved ones (Pasacreta & McCorkle, 2000). Support and care during the cancer experience involve many areas such as physical care, emotional support, and symptom control (Allen, Haley, Small, & McMillan, 2002; B. A. Given, C. W. Given, & Kozachik, 2001; Northouse, Mood, Templin, Mellon, & George, 2000; Thomas, Morris, & Harman, 2002). Role responsibilities also change, causing added caregiver stress (Oberst et al., 1989).

Family caregivers are responsible for observing and reporting patient symptoms. McMillan and Moody (2003) discussed the need for a standardized strategy to evaluate patients and the caregivers' reports of symptoms. Another study suggests that caregivers who possess a high self-efficacy in pain control report less caregiver burden and their loved ones report higher well-being, indicating that caregiver knowledge is a key component to successful and effective care (Keefe et al., 2003). Differences in caregiver responses were found to be further complicated by the presence or absence of pain (Miaskowski et al., 1997), with caregivers in general overestimating the pain in home hospice patients (Redinbaugh, Baum, DeMoss, Fello, & Arnold, 2002). It is not known how stress for family caregivers could affect their ability to report patient symptoms effectively.

The vulnerability of family caregivers and their need to balance their responsibilities can affect their own health and well-being (Proot et al., 2003). Carter and Chang (2000) describe a risk for clinical depression and sleep disorders in the caregivers of cancer patients. Caregiver vulnerability suggests a need for professionals to be very aware of the risks to the caregivers and to find ways to assist them in assuming the tasks and responsibilities required for providing care.

Uncertainty may be a mitigating factor in how well caregivers can cope with providing care. Although a well-developed framework for understanding the levels of uncertainty in patients has been established by Mishel (1990), there are no systematic approaches to dealing with the uncertainty experienced by caregivers of HSCT patients. In a doctoral dissertation, Eilers (1996) examined the relationship of uncertainty to optimism and danger among caregivers of HSCT patients. She concluded that when uncertainty is viewed as introducing danger, caregivers will make attempts to alter or decrease the uncertainty, whereas if the perceptions of uncertainty are viewed as presenting an opportunity, there is less motivation to change the uncertainty.

The Problem

During the acute phase of an HSCT, patients may not be able to express their distress or warn their healthcare providers of impending complications. The caregiver therefore acts as the surrogate for the patient. If the messages to the provider from the patient and the caregiver are not congruent, however, mixed messages may cause treatment to be less effective or delayed. The seeming stress of increased burden and uncertainty of caregiver and patient may further cloud their perceptions of observed

symptoms. Thus, an improved understanding of caregiver burden, uncertainty, and the perceptions of patient symptoms in HSCT treatment may help healthcare providers find ways to improve support for family caregivers and to improve patient care. An enhanced understanding of both the patient's and caregiver's perceptions during the acute HSCT phase could also help healthcare providers identify problems with the alignment of the patient's and caregiver's perceptions of the symptoms, and suggest areas for improvement where caregiver support is most needed. HSCT family caregivers have increased responsibility to monitor patient response to treatment and report early warning signs of problems to the transplant team, yet very little is known about the experience of caregivers with the shift to outpatient care.

Significance of the Study

The high cost of HSCT treatment makes it critical to develop cost-effective strategies that assure that quality of care is maintained. The greatest cost in stem cell transplant treatment is for the time the patient spends in the hospital. Decreased hospital stays for HSCT patients and increased involvement of family caregivers during the acute phase of treatment after transplant make it important to improve understanding of the HSCT caregiver experience to support their needs. Therefore, examination of HSCT caregiver burden and uncertainty during the acute phase of treatment can help identify areas of risk for the patient. How caregiver perceptions may change over the course of even a short-term aggressive treatment and the great risks involved in the decision to choose this treatment alternative also make it important to understand the relationship between uncertainty and caregiver burden. The results of this study will add information

that can be useful for planning interventions with the HSCT caregiver and thus support improved HSCT patient care.

The influence of patient symptomatology on family caregivers' experiences has been examined in those caring for patients with lung cancer and palliative care (Keefe et al., 2003; Porter et al., 2002). However, it is not known how patient experiences of symptoms during and after HSCT affect the caregivers. The severity and seriousness of side effects and the pre-existing effects of cancer can have a profound impact on caregivers. Several investigations have shown that patient symptoms such as pain can induce a high level of tension, depression, and overall mood disorders among caregivers (Hinds, 1985; Juarez & Ferrell, 1996; Keefe et al., 2003). It seems logical, therefore, to expect the same to hold true for HSCT outcomes.

This current research study explored a model for evaluating the impact of HSCT on the following areas:

1. Individual/patient - potential for uncomplicated recovery and improved quality of life;
2. Family/caregiver - ability to actively engage in care of a loved one;
3. Nursing - evidence-based information to direct nursing interventions;
4. Society - potential to support the HSCT patient in the home environment while avoiding costly hospitalization.

The relationship between caregiver burden and uncertainty as it relates to the increasing demand on family members in today's healthcare environment provides an ongoing challenge to healthcare providers. Better evidence and tools to define patient

care priorities and establish appropriate interventions are needed for caregivers and HSCT patients. A number of authors have recommended further studies and the development of standardized interventions (Eilers, 1996; Stetz et al., 1996). The need for longitudinal studies after the acute transplant experience has also been identified (Boyle et al., 2000). An ever-escalating amount of care and decision making is delegated to the caregiver by virtue of the treatment location.

The majority of cancer treatments are increasingly performed on an outpatient basis, with the caregiver being more responsible for complex aspects of care, including direct physical care, medication administration, transportation, and decisions about when to seek immediate attention for the patient. The complexity of the caregiver situation is further complicated by economic and healthcare reimbursement issues as well as the ensuing strain on the patient-caregiver relationships and roles. Caregiver burden is particularly relevant to today's healthcare environment with the increased emphasis on limited resources and cost cutting, especially through shorter hospitalizations (Thomas, 1999; Weeks et al., 1997). In the current healthcare environment, the family, particularly the significant caregiver, often becomes responsible for all aspects of their loved one's outpatient care with little preparation or training. The ability to determine those at significant risk is needed to facilitate the design of interventions specific to each phase of treatment. The literature on the geriatric caregiver suggests that caregivers who view the experience negatively have significantly higher levels of depression. Individuals who do not have active support systems also do less well than those who have and utilize their support system (Northouse et al., 1995).

One potential area for intervention is in teaching the caregiver the best use of available social support, which includes family and friends as well as community resources such as church and civic groups. Social support can directly help the caregiver and provide direction to others who strongly want to provide help. Examples include suggesting the best timing for providing assistance with child care, meals, emotional support, transportation, and respite, as well as raising funds to assist caregivers financially. Some caregivers are naturally inclined to reach out to others, yet many who need help the most, often fail to use available resources (Kilpatrick, Kristjanson, & Tataryn, 1998; Boyle et al., 2000).

Significance of the Study to Nursing

The results from this study can provide a base for the professional nurse to improve the care of the HSCT patients and their caregivers. More significantly, the study identifies types of information that best support the creation of effective interventions for these caregivers. Currently, inpatient settings must focus on acute care needs. Studies of caregiver issues can help identify the needs of the caregiver and provide data to design effective interventions for the HSCT patient's short-term hospital stay and later community-based care (Speice et al., 2000).

In the acute setting, families and designated caregivers may not be viewed as significant members of the team (Williams, 2007). Scientific inquiry that validates the importance of skilled family caregiver support in assuring positive patient outcomes can enhance understanding of the value of having family caregivers present. Nurses are in a unique position to provide the education, training, and direction to caregivers because of

their ongoing professional role in patient care at all stages of HSCT care. Teaching technical skills to the caregiver provides opportunities for interaction with family members that encourage an ongoing assessment of knowledge and internalization of the tools necessary to care for their family member.

Statement of the Purpose

Reduced hospitalization for HSCT therapy has placed an increased burden on family members who are already emotionally challenged and uncertain as to the predictability of the outcomes of the cancer diagnosis and the HSCT treatment. Accurate identification and interpretation of patient symptoms by the caregivers is crucial to ensure timely and appropriate interventions for that individual during the various treatment phases following the transplant. The responsibility to assess the patient symptoms and initiate interventions also places increased burden and uncertainty on the caregiver. Literature on care in Alzheimer's disease suggests that social support, past experiences, and respite can affect the ability of caregivers to integrate caregiving into their daily routines (Aneshensel, Pearlin, & Schuler, 1993; Montgomery et al., 1985; Pearlin et al., 1990; Zarit et al., 1986). However, little is known about outpatient caregiver experiences or, specifically, the HSCT caregiver experience in the context of early hospital discharge to home care in the acute phase of treatment.

The purpose of this study therefore was to examine the patterns of burden and uncertainty in caregivers of patients involved in the acute phase of HSCT. Associations between patient and caregiver perceptions of the patient's symptoms and caregiver burden and uncertainty were also explored.

It is proposed that establishing a connection between caregiver uncertainty and caregiver burden can help identify persons at risk for negative outcomes and suggest strategies to improve the HSCT caregiver experience. This study examined the relationship between burden and uncertainty during the acute phase of the HSCT treatment process. In addition, associations between the patient's stated symptoms and the caregiver's perceptions of those symptoms during the same time period were examined, along with possible links between caregiver burden and uncertainty and their influence on the caregiver's perceptions of patient symptomatology during each phase of the HSCT. This study also investigated differences in the experience of caregiving with regard to type of transplant (autologous or allogeneic).

Conceptual Framework

Models that define the caregiver experience have been proposed (Pearlin et al., 1990; Zarit, 1989). However, researchers have noted the lack of a universally accepted theoretical framework with conceptual and operational definitions that fully explicate the significant factors in this experience. The interaction between caregiver burden, uncertainty, and caregiver interpretation of symptomatology among HSCT recipients has not been studied. Thus, Mishel's model of uncertainty in illness (1988) was used as a basis for this study, with the addition of caregiver burden as an aspect of uncertainty that is defined as the caregivers' subjective appraisal of danger or optimism. Since Lazarus' theory of stress (1984) is used as a basis for caregiver burden and uncertainty theories, stress is assumed to be integral to the caregiver experience (Lazarus & Folkman, 1984). They proposed that stress perception is a linear event; later, researchers including Zarit,

Reever, & Bach-Peterson (1980) and Mishel (1988) proposed that multiple factors interact to cause the appraisal of stress. The focus of the framework developed for the current study is on the identification of the significance of interactions among burden, uncertainty, and caregiver-perceived patient symptomatology during the HSCT caregiver experience and the HSCT caregiver appraisal process.

Within the conceptual framework for this study (Figure 1.1), a number of concepts are identified that potentially influence the individual, in this case the caregiver's appraisal of a situation. These concepts—burden, uncertainty, and symptom pattern—are on the input side of the model, encompassing factors that may interact with each other in the individual's perceived threat or opportunity of an event. The event in this specific situation is the acute HSCT experience. The trilogy of caregiver burden, uncertainty, and perceived symptomatology of the patient are proposed to interact with each other in the patient-caregiver dyad to affect their interpretation of the event. This perception or appraisal, in turn, is expected to potentially affect the individual's perception of the event and thus the potential outcomes.

Caregiver burden is represented in Figure 1.1 as "Subjective Caregiver Burden" in the model for the current study. Since the primary focus of this study is the individual who provides the care, perceived burden was measured from the perspective of the caregiver. Uncertainty is represented in the model as applied in Mishel's and Lazarus' models. The concept of symptom experience is represented by the term "Symptom Pattern" in the stimuli frame. In this proposed conceptual framework, the symptom experience of the patient is measured as perceived by both the patient and the caregiver.

The conceptual schema illustrates that the symptom pattern is viewed as having an impact on both the subjective caregiver burden and uncertainty.

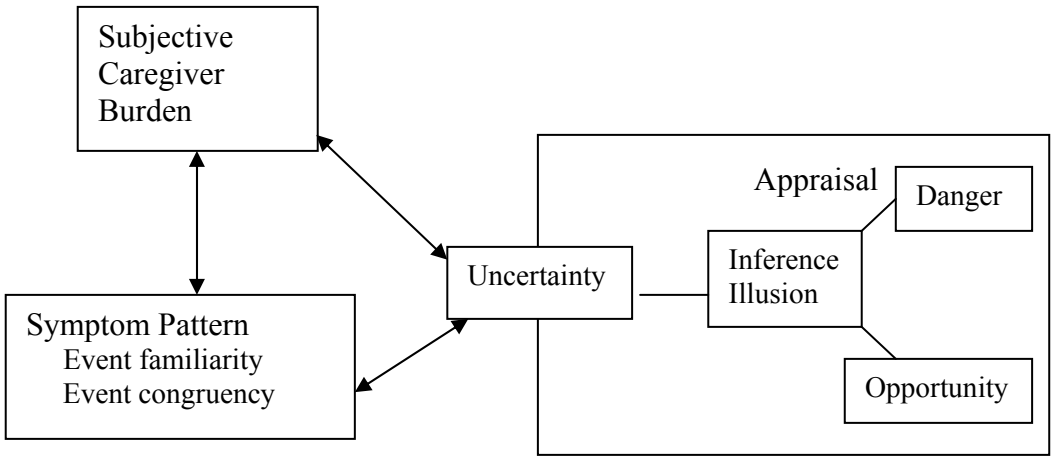

***Figure 1.1*. Conceptual framework.**

The adaptation of Mishel's 1988 model of uncertainty in illness for this study is focused on the subjective caregiver burden and uncertainty as elements that could contribute to altering caregiver perceptions of patient symptomatology that could in turn modify their appraisal of the patient's symptoms. An effective assessment is critical to assure an appropriate response to the needs of the HSCT recipient and eventual adaptation to the event. The possible interactive effects of subjective caregiver burden, uncertainty, and symptom pattern assessment are viewed as multiplying the effects of appraisal in the care situation.

The Aims of the Study

The following were the specific aims of this study:

1. To characterize the status of caregiver burden, uncertainty, and perceptions of symptom pattern (patient symptomatology) at each of the four phases of the acute HSCT treatment regimen.
2. To determine possible associations between caregiver burden, uncertainty, and perceived symptom patterns throughout the four phases of the acute HSCT treatment regimen.
3. To identify associations between demographic characteristics (age, gender, education, number of caregivers), and caregiver burden, uncertainty and caregivers' perceptions of patients' symptomatology at each of the four phases of the acute HSCT treatment regimen.
4. To determine the possible relationship between the patient's and caregiver's perceptions of the patient's symptoms during the HSCT experience.

Research Questions

The research questions explored in this investigation are as follows:

1. What is the relationship of caregiver burden to the phase of treatment during the acute transplant experience for the combined caregiver group?
2. What is the relationship of caregiver burden to the acute phase of treatment during the acute transplant experience for the caregivers of the autologous HSCT patients?

3. What is the relationship of caregiver burden to the phase of treatment during the acute transplant experience for caregivers of the allogeneic HSCT patients?
4. What is the relationship of uncertainty to the phase of treatment during the acute transplant experience for the combined caregiver group?
5. What is the relationship of uncertainty to the phase of treatment during the acute transplant experience for caregivers of the autologous HSCT patients?
6. What is the relationship of uncertainty to the phase of treatment during the acute transplant experience for the caregivers of the allogeneic HSCT patients?
7. What is the relationship of caregiver burden to caregiver assessment of the patient's symptoms during the acute transplant experience for the combined caregiver group?
8. What is the relationship of caregiver burden to caregiver assessment of the patient's symptoms during the acute transplant experience for caregivers of the autologous HSCT patients?
9. What is the relationship of caregiver burden to caregiver perceptions of the patient's symptoms during the acute transplant experience for the caregivers of the allogeneic HSCT patients?
10. What is the relationship of caregiver uncertainty to caregiver assessment of the patient's symptoms for the combined caregiver group?

11. What is the relationship of caregiver uncertainty to caregiver assessment of the patient's symptoms in the caregivers of the autologous HSCT patients?
12. What is the relationship of caregiver uncertainty to caregiver perceptions of the patient's symptoms in the caregivers of the allogeneic HSCT patients?
13. What are the patterns of caregiver and patient perceptions of symptoms and caregiver level of uncertainty throughout the acute transplant process for the combined caregiver group?
14. What are the patterns of caregiver and patient perceptions of symptoms and caregiver level of uncertainty throughout the acute transplant process for the caregivers of the autologous HSCT patients?
15. What are the patterns of caregiver and patient perceptions of symptoms and caregiver level of uncertainty throughout the acute transplant process for the caregivers of the allogeneic HSCT patients?
16. What is the relationship between the caregiver descriptive characteristics and uncertainty across the four phases of the acute transplant process the combined caregiver group?
17. What is the relationship between the caregivers' descriptive characteristics and burden across the four phases of the acute transplant process for the combined caregiver group?
18. What are the differences in caregiver burden and uncertainty based on the type of transplant?

19. How does the level of HSCT caregiver burden compare to that of caregivers of patients with other chronic diseases?
20. How does the level of HSCT caregiver uncertainty compare to that of caregivers of patients with other chronic diseases?
21. When is caregiver support most needed during the phases of the HSCT?

Conceptual Definitions

For the purpose of this investigation, the variables are described in terms of conceptual derivation to more precisely characterize the measurement domains for the relevant concepts of interest and outcomes of the study. When appropriate, the concepts are defined according to their origin and how they have been utilized in the literature. The relationships of the primary concepts of interest—caregiver burden, uncertainty, and symptomatology—are represented in the conceptual framework for this study (Figure 1.1). The conceptual links of this model to the HSCT caregiver experience provide a basis for this study, and are defined in the following.

1. ***Uncertainty*** is conceptually defined as "the inability to determine the meaning of illness related-events" Mishel (1988, p. 225). Mishel further defines uncertainty as the lack of cues to determine or predict the outcomes related to an illness. Managing this uncertainty is viewed as a necessary step towards adaptation.
2. ***Caregiver*** is conceptually defined as a family member or significant other identified by the patient and acknowledged by the caregiver to be the person who will assume the primary caregiving role.

3. ***Caregiver burden*** refers conceptually to "the emotional cost of caregiving and the feeling of oppression associated with embarrassment and overload, disruptions or change in various aspect of the caregiver's life, financial difficulties, role strain, and physical health deterioration" (Lim et al., 1996, p. 253). Caregiver burden in this study refers to the overall perspective of the HSCT caregiver.

4. ***Symptom pattern*** refers to the degree to which the patient symptoms during and after HSCT present with sufficient consistency to be perceived as having a pattern or configuration (Mishel, 1988, p. 225). Patient symptomatology denotes those physical and emotional experiences that arise as a result of the cancer or its treatment, which were measured from both the patient's and the caregiver's perspectives or the patient-caregiver dyad symptom experience.

5. ***HSCT***, or Hemopoietic Stem Cell Transplantation, formerly known as Bone Marrow Transplant (BMT) and Peripheral Stem Cell Transplant (PSCT), is defined as "procedures that restore stem cells that have been destroyed by high doses of chemotherapy and/or radiation therapy" (National Cancer Institute, 2004). HSCT is an intense protocol which may include administration of high doses of chemotherapy, immunotherapy, radiation therapy, or any combination of these treatments. Transplants can be divided into two general categories depending on the source of the transplanted graft: (a) autologous, which refers to a transplant in which the individual is his/her own donor, and (b) allogeneic,

which refers to a transplant in which someone other than the patient is the donor (NCI).

6. ***Phases of an HSCT.*** For the purpose of this study, four phases of the acute transplant process are identified: (a) Phase 1 - immediate pre-transplant or immediate preparatory regimen; (b) Phase 2 - the period of the bone marrow infusion and three days post infusion; (c) Phase 3 - the period seven days post discharge from the hospital or for patients who are not hospitalized, the period immediately after three days post infusion; and (d) Phase 4 - the period marked by one month post discharge from the hospital or for those patients not hospitalized, the care rendered as an outpatient, that is, three weeks post phase 3 testing.

Assumptions

The following assumptions were made for this study:

1. The patient and caregiver have been through previous treatment for the cancer and have been attempting to mobilize resources to maximize their ability to cope with the intense and potentially fatal HSCT treatment.
2. The patient and caregiver understand the gravity of the situation regarding survival, both immediate and long term.
3. The caregiver is an active participant in the patient's care and has the patient's approval to access information from healthcare providers.
4. The identified caregiver will be significantly involved in the care both before and after the transplant procedure.

5. Other members of the family or significant support persons acknowledge the role of the identified caregiver.
6. The caregiver as well as the patient will be affected by the disease process.

Delimitations

The findings from this study may be useful in adding to the understanding of the HSCT caregiver experience but cannot be assumed to be representative of all HSCT caregiver populations.

Limitations

There were several limitations in this study. One was the use of two medical facilities at opposite ends of the country for the recruitment of subjects, which could account for basic differences in the subjects recruited. A second limitation was the use of the descriptive repeated measures study method, which yielded a description of the experience for the subjects over a short period of time, but did not provide cause-and-effect explanations for the study findings. Nonetheless, the results of this study do add to the body of knowledge previously reported on caregivers of BMT/HSCT patients, although analysis of site differences at study completion found no significant variance between the sites. A third limitation was the requirement that caregivers and patients complete instruments at four sequential times, which may have limited the findings to dyads with fewer complications and thus produced limited data from dyads with more stressful experiences. A fourth limitation was the requirement that the participants be screened by clinical staff prior to being approached to participate in the study. This screening process created some unexpected selection bias in order to avoid dyads where the patient was judged by staff as ‘too ill’ to participate. A fifth limitation was the potential that the pre-identified phases were not the key times for detection of changes in caregiver burden, uncertainty, and perceived patient symptomatology, although these

times were based on previous studies. A sixth limitation was the potential for the tools not to be sufficiently sensitive to detect changes over the short data collection period (4 to 6 weeks). In choosing the various tools to represent the given concepts, particular attention was paid to the length of time that would be required to complete the task. Knowing that this might be a demanding time physically and emotionally for the patients and the caregivers, the researcher did not want the survey length to prevent completion of the study or agreement to participate. It was also possible that the patient and caregiver collaborated on the answers to the questions since they completed the questionnaires at their convenience.

A final limitation was that Mishel's Uncertainty in Illness Scale (MUIS) tool had been used with patients and parents of young children but not with caregivers of adults. The results of the current study, which used caregivers of adults, will be reported to Mishel as required for receiving permission to use her tool.

Chapter Summary

The HSCT procedure is a high-cost and high-risk treatment option for cancer patients that is associated with numerous side effects and can be life threatening. Earlier discharge from the hospital to outpatient care in recent years has created an environment for added stress for the patient and caregiver that is poorly understood. It is not clear what kind of support this dyad may need that is not being addressed. Previous research on caregivers in other populations suggests that caregiver burden, uncertainty, and symptom distress may have significant roles in how well the HSCT patients and their families tolerate the acute phase of the treatment experience. Previous research on caregiver

burden in cancer and non-cancer conditions has provided a basis to study elements of the caregiving experience for cancer patients. The development of a body of literature related to uncertainty supports the existence of certain pre-conditions and antecedents that may be expected to contribute to the lack of ability for patients and caregivers to make sense of the HSCT experience.

The proven validity of the tools utilized in this study allowed measurement of symptoms to determine the actual distress the patient experiences throughout the HSCT acute phase, as well as the extent of caregiver burden and uncertainty. This research builds on the existing work on caregiver burden and uncertainty by examining a population at risk for physical and emotional sequelae, namely, caregivers of HSCT patients. This study also extends Mishel's work on uncertainty in illness by application of this concept to an adult caregiver population. In the present study, the researcher attempted to determine the degree of caregiver burden, uncertainty, and the perceptions of patients and caregivers related to selected common symptoms associated with the HSCT experience. The findings from this study suggest areas of need for phase-specific interventions that could improve/support measures for caregivers and their HSCT patients.

Chapter 2

LITERATURE REVIEW

The purpose of this chapter is to present a review of the research and to highlight strengths and gaps in knowledge concerning the HSCT caregiver experience. This study was designed to examine the experience of HSCT family caregivers, specifically the relationships and differences between these caregivers and the experiences of caregivers in other situations. Personal discussions among healthcare providers suggest that the HSCT caregiver experience is very stressful, particularly in the acute phase of treatment, and that this stress has increased because of the decreased length of HSCT patient hospitalization. However, very little is known about the experiences of the HSCT caregiver or the types of support they may need in the changing healthcare environment.

As healthcare costs escalate and healthcare providers strive to be more economically efficient, inpatient length of stay has been reduced considerably, placing a greater burden on the patient's caregiver to learn how to care for and assume responsibility for them at home (B. A. Given et al., 2001; Grimm, Zawacki, Mock, Krumm, & Frink, 2000). Many, if not all, healthcare organizations have made sustained efforts to decrease costs and enhance utilization of healthcare services and resources. The high cost of the HSCT procedure and market competition for health care insurer contracts for services have made earlier discharge from the acute hospital setting a reality. As a result, patients spend less time in the hospital under the watchful eye of nurses and other healthcare professionals, and are discharged with expected continuation of care at home,

but with greater potential for developing complications outside the hospital. This early discharge imposes significant strains on caregivers who must not only monitor the patient's progress and condition but also transport the patient back and forth from the hospital for follow-up appointments and additional treatments in outpatient settings. Ultimately, the day-to-day responsibilities of caregivers include attention to physical care needs, symptom management, monitoring adverse effects as well as acting as an interpreter and advocate for their loved ones (Personal communication, Sivley, 2004).

Interventions need to be developed, tested, and revised to offer the most effective, timely, and efficacious assistance during HSCT post discharge care. An exemplar of the complex responses and feelings related to such care is contained in the following scenario. *A young man was told by his physician that he could go home to complete his recovery from his HSCT if there was someone who could care for him there. The gentleman, eager to leave the confines of the hospital and be in his own comfortable surroundings, quickly assured the healthcare team that his wife would be thrilled to have him home that day. The wife, when told of this decision, expressed concern and alarm that she would have problems managing their three children, a dog, and work, as well as caring for her husband's medical needs, medication administration, the required frequent monitoring of symptoms, physical assistance for his mobility, and daily transportation to the hospital for illness-related appointments. Moreover, she expressed a need to work in order to maintain their healthcare benefits, since the couple was financially compromised with the husband receiving no salary or benefits. Although she had been told that his inpatient stay would be brief, she was not prepared for the degree of assistance her*

husband needed once he returned home. When she approached the medical staff with her concerns, she was told that there was nothing that was being done for her husband that could not be managed in the outpatient setting, where he would be seen at least three times per week, and that her husband was looking forward to going home. How could she say no? But what would make it possible for her to agree?

This scenario is not unusual. Naturally, the HSCT patient is eager to return to comfortable surroundings that can be individualized to his/her desires. But the pressure, responsibilities, and expectations that are placed on the caregiver can have lasting effects which have been shown to affect negatively the caregiver's physical and mental health, at the time of care and in future years (Langer, Abrams, & Syrjala, 2003; Williams, 2003). The caregiver may be overwhelmed by the potential of caring for her very ill and needy spouse as she continues to work and care for the rest of the family. In addition to the actual tasks that need to be done, the potential "what ifs" are significant. Examples include: "What if a symptom is missed?", "What if the dog gives him an infection?", or "What if I give him the wrong medication?" The list of "what ifs" can be endless and add to the burden of the caregiver at home.

Conceptual Background for the Study

This literature review centers on the conceptual focus for this study: *caregiver burden* which refers to "the emotional cost of caregiving and the feeling of oppression associated with embarrassment and overload, disruptions or change in various aspects of the caregiver's life, financial difficulties, role strain and physical health deterioration" (Lim et al., 1996, p. 253); *uncertainty* which relates to the lack of predictability and sense

of reference as it relates to a given situation (Mishel, 1981), and *patient symptomatology* which denotes the physical and emotional experiences that arise as a result of the cancer or its treatment, which were measured from both the patient's and caregiver's perspectives, or what is called the *patient-caregiver dyad* in this study. Definitions for these concepts are provided in Chapter 1. An overview of the phenomenon of stress precedes the literature review on caregiver burden, uncertainty, and patient symptomatology.

Stress

Richard Lazarus (1999, 1984) is frequently cited by many writers in the caregiver burden and uncertainty fields for his work on stress. His 1966 and 1984 works are cited frequently as singular sources that have collated previous information on stress and provided a workable twentieth-century concept from which to develop other more specific models for a variety of psychological problems (Lazarus & Folkman, 1984). Lazarus refers to stress as an organizing framework in the development of a psychopathology, which is more frequently referred to as anxiety. Freud also identified anxiety as a central element in the development of psychopathology. Other researchers in the 1940's and 1950's frequently referred to anxiety as a learned behavior and classic conditioned response. However, Lazarus implies that the stimulus response theories are too simple to explain the variation in response to situations by individuals. He suggests that there is an intermediary step, appraisal, whereby the individual, using past and present experience as well as personal background, can interpret the stressors for a response and outcome. This basic understanding of the response to stress has also been

cited by other researchers on caregiver burden (Zarit et al., 1980; Zarit et al., 1986) and uncertainty (Mishel, 1981). Lazarus and Folkman (1984) further expanded the appraisal steps to include primary and secondary, which have been re-defined numerous times by various theorists, reflecting both cognitive processes that recognize an event as stressful, and provide the background information to determine if the stressor is a danger or an opportunity.

Specific roles in life have significant potential for development of stress due to the expectations and responsibilities associated with significant life changes, e.g., aging and development (Pearlin, Lieberman, Menaghan, & Mullan, 1981). Skaff and Pearlin (1992) point out that caregiver issues provide rich sources of potential for both the stress researchers and the gerontologists examining the natural aging process, due to the high potential for stress issues to emerge. Pearlin et al. (1990) provide a clear, concise framework that links caregiving and stress. While identifying caring and caregiving as crucial and common to any established relationship, there is the potential for it to be a stressful experience, particularly when the reciprocal relationships and roles are changed by illness or incapacity. Noting the proliferation of research on caregiving, and a lack of any clear conceptual framework or definition, Pearlin et al. indicate that volumes of work are available that do not agree on definitions of caregiver stress or converge on proven recommendations for caregiver stress. Pearlin's team, supported by their research, developed, a model of caregiver stress to for others to use in developing their research designs. They acknowledged that others may use different definitions of caregiver stress, but provided a goal to stimulate discussion and debate to determine the agreed-upon

definitions. Nonetheless, stress is decidedly an element associated with caregiver burden (Zarit et al., 1980).

Caregiver Burden

Caregiver burden is an ongoing, developing, and expanding area of concern and investigation in the current healthcare environment, having its origins in the mental health and geriatric research literature. Inquiry about caregiver burden has been reported for conditions of several populations, including mental health, geriatric, dementia, and Alzheimer's disease (AD), as well as for other types of chronic illnesses. Common chronic health issues of concern related to caregiver burden include cancer, palliative care, renal disease, and progressive neurological diseases. A review of the pertinent research on caregiver burden will be presented here, first from the viewpoint of chronic progressive mental deterioration, then from the perspective of diseases which remit, yet compromise, the independent nature of the patient, requiring intermittent caregiving by another. The key approach is the comparison of chronic progressive diseases, the remitting conditions, and the acute phases of chronic illnesses. It is significant to note that cancer can manifest features of chronic as well as acute caregiver burden.

Pearlin et al. (1990) define caregiver stress as a "consequence of a process comprising a number of interrelated conditions, including the socioeconomic characteristics and resources of caregivers that the primary and the secondary stressors to which they are exposed" (p. 583). Caregiver burden is also referred to by Pearlin as an outcome variable, including increased health outcomes and decreased well-being. Ory et al. (1985) define caregiver burden as "the impact of the changes in cognition and

behavior of the Alzheimer patient on the family and the patient's subsequent need for care and supervision" (p. 623).

Caregiver burden is associated with a number of concepts that refer to the caregiver's perception of the responsibility of providing care to another individual. Gilbar and Ben-Zur (2002) refer to caregiving as offering help to the care receiver, noting that caregiving differs from social support in that it is not a reciprocal relationship. Another definition encompasses physical care and household maintenance as well as essentially any service required by the care receiver (Biegel, Magaziner, & Baum, 1991). Thompson and Doll (1982) define caregivers as providing care to "an individual whose presence and performance aroused either fear or shame and must be burdensome" to the caregiver (p. 380). Grad and Sainsbury (1963) define caregiver burden as any cost to the family. None of the existing definitions encompasses all of the elements that define, include, or exclude caregivers. A comprehensive definition would include the effect on the family as well as possible positive and negative impacts on individuals and the family (Coeling, Biordi, & Theis, 2003).

Another approach to defining caregiver burden counts the number of tasks involved in providing care (Montgomery et al., 1985). However, this method measures only what some would call the objective caregiver burden while ignoring the subjective aspects of the tasks as well as their consequences, namely the caregiver's emotional response. The objective burden is comprised of the observable elements involved in providing care to an individual, whereas the subjective burden refers to the perceptual issues related to caregiving. The effects of caregiving have been studied in various

populations, including dementia (Alspaugh, Stephens, Townsend, Zarit, & Greene, 1999), specifically AD (Aneshensel, Pearlin, & Schuler, 1993; Gallagher, Rose, Rivera, Lovett, & Thompson, 1989; Lawton, Moss, Kleban, Glicksman, & Rovine, 1991; Montgomery et al., 1985; Parks & Pilisuk, 1991; Skaff & Pearlin, 1992; Zarit et al., 1980; Zarit et al., 1986); mental illness, including schizophrenia (Chang & Horrocks, 2006; Oyebode, 2003; Rudge & Morse, 2004); AIDS (Pearlin, Aneshensel, & LeBlanc, 1997), renal dialysis (Beanlands et al., 2005; Ekelund, Westman, & Andersson, 2004), palliative care (Cameron, Franche, Cheung, & Stewart, 2002; Kinsella, Cooper, Picton, & Murtagh, 1998, 2000; Proot et al., 2003; Weitzner, Jacobsen, Wagner, Friedland, & Cox, 1999), and cancer (Gaston-Johansson, Lachica, Fall-Dickson, & Kennedy, 2004; Gilbar & Ben-Zur, 2002; Raveis, Karus, & Siegel, 1998; Thomas, Morris, & Harman, 2002). For the most part, these studies have been descriptive in nature, elucidating the important issues related to providing care to persons with chronic illnesses rather than testing interventions that might alleviate the physical and emotional toll that accompanies the responsibilities of caring for the sick.

The study of family members caring for their loved ones has been scrutinized over the past decades by many leading authorities for lack of a universally agreed-upon theoretical framework, lack of conceptual clarity as to what comprises caregiver burden, diversity of reliable and valid instruments to measure caregiver burden, as well as shortcomings related to the systematic evaluation of interventions through randomized clinical trials (Zarit, 1989). Additionally, data collected prior to 1990 were often generated from a single observational time during the continuum of individuals' illness

experience. Specifically, these were investigations of the AD population, who had already been identified as needing services and had previously been receiving services to support the patient and the caregiver.

Zarit et al. (1980) published their first article on the evaluation of caregiver burden in Alzheimer's type dementia with the development of a self-report tool, the Zarit Burden Interview (ZBI). While the focus of their study was on identifying how burden was perceived by the Alzheimer patient caregivers, the major, enduring contribution of this research has been an assessment tool that has been widely employed in subsequent research on caregiver burden, and continually tested and revised to more accurately capture the experience. Zarit et al. (1986) conducted a longitudinal study, retesting the factors of strain that caused family members to resort to institutionalization of the patient. While the objective caregiver burden is a contributing factor, the subjective evaluation by the caregiver was found to be a more significant factor affecting decisions regarding placement.

Some researchers have developed working definitions related to objective and subjective aspects of caregiver burden (Montgomery et al., 1985). They found that different aspects of burden predicted subjective and objective features, with characteristics specific to the caregiver predicting the subjective, while objective factors were predicted by the types of tasks performed.

Caregivers may experience negative consequences of their own by assuming sustained responsibilities for the welfare of sick family members. Depression has been identified in family caregivers of AD patients, and investigators have examined patterns

among those who sought help and those who did not. In a longitudinal study, help seekers were found to be more prone to have depression, with women experiencing it more frequently than men (Gallagher et al., 1989). The level of assistance that was required by patients had little bearing on the severity of depression experienced by the caregivers. These results were corroborated in caregivers of cancer patients, which showed that the number of care demands also did not correlate with the degree of caregiver depression (Carey et al., 1991). Their findings warrant further investigation of critical factors that contribute to caregiver psychological distress. Caregivers of patients undergoing HSCT are often part of the acute phase of treatment, and even though these patients may be hospitalized, and the primary responsibility for their care and safety lies with health care providers, the caregivers' perceived burden and responsibility for the patient's outcome may have profound effects on their own physical and emotional health.

While some research results have only focused on the negative experiences of caregiving, including caregiver burden (Zarit et al., 1980) and caregiver stress (Pearlin et al., 1990), others have identified some of the positive effects of the caregiving experience (Wrubel, Richards, Folkman, & Acree, 2001). Such outcomes include the following: improved caregiver self-esteem (B. A. Given & C. W. Given, 1992), caregiver satisfaction (Lawton et al., 1991), caregiver appraisal (Lawton et al., 1991) and gain of caregiver experience (Hunt, 2003; Kramer, 1997). The negative side of the caregiver process is most generally known, but the positive side may provide the most memorable experiences, such as the caregiver's gratitude for being able to care for a parent,

providing a safe environment for a parent in a home setting, or being able to spend precious time with a loved one (Stuckey, Neundorfer, & Smyth, 1996).

Studies have specifically explored components of caregiver experiences and how they manage the burden of caregiving. Parks and Pilisuk (1991) found that the use of fantasy by women caregivers as a coping mechanism was precipitated by increased anxiety. Male caregivers were more often helped by having adequate social support, which men are less likely to develop and use, according to Kilpatrick et al. (1998). By examining role engulfment and loss of self, Skaff and Pearlin (1992) found that certain groups are more likely to get lost in their caregiving responsibilities. Spouses, females, and younger caregivers are more likely to be immersed in the responsibilities of assuming the caregiving role. Aneshensel et al. (1993) studied the changes in caregiver burden as a result of the increasing care needs of a family member. Caregivers were interviewed at three annual periods, with results indicating that while the patient may require increased care, issues such as role captivity and economic strain have more influence on determining the institutionalization of the patient (Aneshensel, et al.). Specifically, these researchers indicate that primary stressors, including direct care provision, may not be determining factors in placement decisions. They report that secondary stressors, or elements that cause additional stress, may be the proverbial "straw that breaks the camel's back," for example, the car breaking down, a long wait at a physician's office, or a rude sales clerk. Primary and secondary stressors are viewed as mechanisms to cause proliferation of strain and overload, leading either directly to depression or contributing to it (Pearlin et al., 1997). This paradigm could be applied to the HSCT caregiver

population as the acute trajectory of treatment-recovery and possible relapse-complications impose enormous burdens that may cause role overload, role captivity, and work strain.

Alspaugh et al. (1999), using a theoretical model of mover-stayer, developed a framework to predict which caregivers would be depressed or remain stable over a year's time. Their study reflects growth in the use of theoretical models in the field of caregiver research. In the mover-stayer model, individuals are examined for their emotional stability. A basic tenet of this model is that individuals either exhibit depressive behaviors or do not. These individual stayers tend to be stable in their demonstrations over time. The mover is the subgroup of individuals who vacillate between depressive symptoms or not. One belief about this model is that the movers have potential for their symptoms to be moderated by interventions.

Oyebode (2003) reports the development of government standards in England to ensure that caregivers are provided the support necessary to care for both the patient and themselves. This provision reflects the movement towards social responsibility to ensure that those who provide care to their loved ones are afforded the opportunity to get assistance themselves. When patients are hospitalized, there is a tendency for healthcare providers to ignore or seldom acknowledge the family caregivers at the beside. During the patient's hospitalization, the caregivers experience the stressful circumstances of medical interventions, sharing a sense of responsibility and subsequently guilt when the outcome not may not be favorable in the patient's recovery. Therefore, it is critical that

healthcare professionals gain understanding of the caregiver burden and identify ways to reduce perceived stresses associated with patient care.

Caregiver burden in chronic conditions.

The use of previous work on caregiver burden with regard to the elderly in progressive decline is a firm basis for describing caregiver issues of other health conditions. There is a subset of chronic diseases where the illness trajectory is not a steady decline. Rather there is, in each disease, a specific manner of progression and improvement with treatment. The observation can be made that modern science has made treatment available for many previously terminal diseases. Conditions that fall into this category include end-stage renal disease (ESRD), multiple sclerosis, and cancer. Each disease is unique in how it is manifests in individuals, yet follows a set pattern of general disease progression. Palliative care is a phase of an illness where comfort not cure is the primary concern. Of the chronic conditions or phases, palliative care is most prominent in the focus on caregiver burden investigations.

Caregiver burden and cancer.

Research into the effects of a patient's cancer on caregivers has been categorized as psycho-oncology, with the majority of research having been done in the area of palliative care (Thomas et al., 2002). Investigations have been done on the specific consequences of caregiving in the oncology population, which has focused on specific cancer stages (i.e., newly diagnosed, treatment, recurrence) with commonly occurring cancers (i.e., breast, lung, colon). Much of this literature has focused on oncology caregiver issues and has examined the caregiver's impact on the patient, not the effect of

the caregiving on the caregiver (Thomas et al.). Little research has been conducted on the caregiver's experience while at the bedside during intensive treatments (such as with HSCT) and life-threatening clinical outcomes (such as infection and graft-versus-host disease (GVHD). Under intensive treatment conditions, the goal is cure, and aggressive therapies can produce fluctuating states in the patient's status. On occasion, treatment fails, the patient's condition can progressively worsen, and there is a shift in treatment goals from curative therapies to supportive terminal care. The rapid changes in goals can be an overwhelming experience for caregivers, since unlike other patients with progressive types of cancer, there is a very rapid decline in health status when HSCT treatment fails.

The burden of caregiving in cancer may not end upon the death of a loved one, however. Some studies have demonstrated that the effects of caregiving linger into the grieving period (Chentsova-Dutton et al., 2002). The relationship of the caregiver to the patient may be one of spouse, child, or child's spouse, but the caregiver may also be a friend and companion (Thomas et al., 2002). The nature of the burden and the severity of the perceived burden can differ according to the type of relationship the caregiver has with the sick person, the characteristics of the caregiver, and the length of time in providing care. The existing literature has determined that caregivers are more commonly female (Gilbar, 1999), but males also frequently provide care. Females are less likely to identify the full depth of their role as explained by societal expectations; however, they are more susceptible to experiencing psychological distress from their roles (Thomas et al.). Spouses are frequently caregivers (Coristine et al., 2003), but when non-spouses

provide care, the roles of decision-making can prove to be increasingly complex. Differences are also attributed to an established history of spouses routinely discussing all decision rules and understanding the other's wishes prior to making decisions.

The experience of caregiving in cancer is also mediated by the age of the caregiver as well as the relationship to the patient (Dellasega, 1990a; Gilbar, 1999). Gilbar found that husbands and age were predictors of a greater burden, but not psychological distress. Kinsella, Cooper, Picton, and Murtagh (2000) suggest that older individuals while potentially more accepting of the caregiver role are at risk for increased stress due to lower average incomes and potentially poorer health. Dellasega (1990a) discovered that employed women perceived less stress than unemployed women. Employment does not appear to affect the stress related to caregiving. In fact, it may appear to buffer the perceptions, particularly when compared to the women who were not employed. Those who were employed were more likely to be caring for a parent, while those who were unemployed were more likely to be caring for a spouse. Finally, a similar amount of time was spent by each group on caregiver activities. Raveis et al. (1998) had similar findings in that multiple roles may be a protective buffer against the negative effects of caregiving. Their study also found that increased education as well as having other roles may help caregivers in dealing with issues that arise in the process. Kleban, Brody, Schoonover, and Hoffman (1989) found that husbands and wives disagreed on how the caregiving situation affected their life, providing a high potential for miscommunication.

The areas of care that are provided to the patient by the caregiver vary, depending on the individual's needs—physical, emotional and disease-related, and may change based on the patient's condition. The condition outcome is also affected by the patient's age, other health conditions, as well as psychological background. The scope of this care may include any of the following: physical care, emotional support, symptom management, transportation, bill negotiation, and other indirect care needs (B. A. Given et al., 2001). Wochna (1997) identified the family needs of patients undergoing HSCT as needing information, understanding treatment, and being able to retain hope.

Caregiver burden and the family.

Patients undergoing HSCT fall into one of four general age groups according to the Hershey Medical Center BMT office (Personal communication, Sivley, 2004). Patients younger than 20 made up 11.4% of the patients receiving transplants at this center; ages 18 to 45 constituted 34.4% while ages 46 to 64 contributed 48.2%, with ages greater than 65 making up approximately 6% of the patient population. Since the population for this investigation included adults over the age of 18, a primary caregiver could be a parent, spouse, sister or brother, daughter or son.

Most patients undergoing HSCT are generally in the age range of 46 to 64 and have a cancer diagnosis. The cancer would typically have been diagnosed and treated with at least several cycles of chemotherapy to determine if a long-lasting remission or absence of the disease could be achieved with chemotherapy alone. Some patients may have also been exposed to intermittent radiation therapy as a part of their treatment protocol. In this age group, patients are frequently at a point in their life where they are

raising children, working on a career, and planning for the future. It is not uncommon for some patients in this age category to be dealing with the "empty nest syndrome," after children have left the household, or changes in their own health as a result of aging (Dellasega, 1990b). Brody (1985) has called the women of this age group, the "women in the middle" as they may have children who demand their time, as well as parents and a spouse. They are not at a point where they will be immediately entering retirement, but are considering such an option. The unexpected diagnosis of cancer and the possibility of having to have an HSCT might be met with a broad spectrum of emotional reactions (fear of imminent death, concerns over income and financial stability, worries over who will assume their family roles). Unlike patients with dementia or AD, persons who are undergoing HSCT and their caregivers are generally employed and have ongoing financial and personal responsibilities.

The needs of the patient and the changes incurred as the disease progresses will dictate the type of care that the caregiver provides. Hilton, Crawford, and Tarko (2000) note that for families coping with breast cancer, "learning to live with someone else's cancer may be more difficult than dealing with the cancer" (p. 88). From their study, three themes became most important to the caregivers: taking care of the cancer, family patterns, and managing other issues. Taking care of the cancer included such concerns as uncertainty, waiting, hearing, facing the disease, and living with the news.

Kilpatrick et al. (1998) measured the information needs of husbands of women with breast cancer, investigating the social support of patients and husbands and how it affected their adjustment to the breast cancer. The couples who indicated that they had

more social support reported fewer adjustment problems. Men felt less a "part" of the support network of medical personnel. These findings sparked interest in determining factors that affected adjustment psychologically. Kilpatrick et al.'s findings indicate that support from others, the type of disease, and disease-related treatments as well as amount of information affect adjustment to the condition.

Carey et al. (1991) studied family caregivers of patients undergoing chemotherapy, and learned that the majority of their time was spent on providing transportation, running errands, and giving emotional support, with the latter being the most time consuming. A study by Oberst et al. (1989) also confirmed that a large percentage of time was spent providing transportation and emotional support. These physical and emotional demands take an enormous toll on the caregiver's physical stamina and emotional reserves. Therefore, if health professionals could identify the most critical period for the greatest degree of caregiver burden, intervention might be possible, thus lessening these negative experiences. Munkres, Oberst, and Hughes (1992), who examined the patient's own perceptions of their care burden, showed that the recurrence of cancer was associated more with perceptions of being a burden than with those who were newly diagnosed with cancer. All of these studies provide research-based evidence that, in most circumstances, caring for someone with cancer during routine treatment causes a significant degree of burden of care that in some situations may go undetected or unaddressed. Moreover, these findings must be interpreted cautiously as the perceptions of caregivers were measured or assessed at a single point or by a "snapshot" of what is commonly a longer-lasting circumstance for many. These studies did not elucidate the

descriptions of the responsibilities of the caregivers and fluctuations in levels of care burden during the acute episodes associated with cancer treatment.

Morse and Fife (1998) concluded that many of the studies investigating caregiver burden in cancer populations only focused on one part of the diagnosis and treatment. Few studies have noted the changes that occur in a patient's condition, symptoms, and outlook during the process of the cancer experience. Cancer has been identified as a process disease with changes in symptoms, responses to treatment, and, at times, fluctuating periods of progression and remission (Morse & Fife). Patients' symptoms and functional status can have a great impact on caregiver risk for developing depression (Kurtz et al., 1995). Post-traumatic stress disorder (PTSD) has been identified in parents of children undergoing solid organ transplants (Young et al., 2003). Some investigators have documented that a recurrent disease has a particularly strong impact on family dynamics and the degree of perceived burden (Munkres et al., 1992; Northouse, Laten, & Reddy, 1995). This impact of longer term care substantiates the need for longitudinal studies, which Zarit (1989) has advocated for the geriatric caregiver population, in order to identify factors that increase or decrease caregiver burden, and to better characterize fluctuations or patterns in this experience over time. It can be difficult to maintain adequate participation in studies involving geriatric patients due to changes in a patient's condition, the chronicity of health problems, the unpredictable nature of the disease, and the eventual deaths of the patients. Longitudinal studies can also be problematic with cancer populations, especially those undergoing treatment, and can be even more unpredictable than in the geriatric dementia patient population.

If investigators can adapt models from the geriatric literature and apply them to various populations of patients with types of cancer involving more uncertainty and unpredictability, it may be possible to make important contributions to a better understanding of the caregiver burden experience and the vulnerability that is associated with intensive cancer treatment and symptom management. Morse and Fife (1998) studied 175 partners of patients with cancer at various stages of cancer treatment as falling into one of four specific intervention intervals. A questionnaire was completed by each partner at a single point over time. The results indicated that the stress for the partners increased over the time of the disease, with the time of recurrence being the period in which stress levels were the greatest. Additionally, women reported more distress than men during the phases of cancer treatment. These findings support the possibility of detecting fluctuations in caregivers' perceived stress, which if known might prompt more effective strategies to alleviate stress burden.

In another study, Weitzner et al. (1999) identified 267 family caregivers of patients who were undergoing curative/active treatment and 134 caregivers of patients in hospice treatment receiving palliative care. They administered several instruments, including self-report measures, and collected demographic information. Their results showed that caregivers of family members receiving palliative care who had lower levels of formal education and lower quality of life scores were associated with the poorer performance status of their loved one and poorer physical health. These authors concluded that a difference in education may also correlate with differences in socioeconomic status. This descriptive study provides information consistent with other

findings related to caregivers, but in the context of cancer diagnoses and care. Further research is necessary to determine the consistency of the income and education of caregivers as a risk factor that needs to be considered when planning interventions to maximize the caregivers' ability to cope with the change in a caregiver role.

While there are no published data, it is expected that having a family member undergoing HSCT, even if there is hope for recovery, will cause some economic impact due to decreased wages or the increased requirement for outside assistance to maintain the responsibilities of a household. As noted by Thomas and Morris (2002), the care that is provided to the patient, is not only direct care but includes factors that can be collectively called indirect care, and may include tasks previously performed by the patient. Examples include yard work, car repair, meal preparation, laundry, and other daily chores necessary in today's complex world.

Caregiver burden has been studied extensively in caregivers of patients with dementia and mental health issues, but studies that investigate the burden on caregivers of patients undergoing HSCT are rare. Another gap is that multiple tools have been used to measure surrogates of stress in this caregiver population. HSCT is unique in that it is a potential cure, but a transplant also has its own chronic implications. Changes in burden levels over time are also poorly understood. More information is needed to understand changes in burden over time to help determine the type and timing of interventions that could be implemented to decrease the HSCT caregivers' perceived burden.

Uncertainty

Uncertainty in the healthcare context is defined as "the inability to determine the meaning of illness-related events" (Mishel, 1990, p. 225). Mishel (1981) built this mid-range theory based on a cognitive appraisal model, including additional constructs from several theorists including Moos and Tsu (1977), Norton (1975), and chaos theory. Moos and Tsu identified four general classes of illness experience including: (a) discomfort, incapacitation, and other symptoms of the illness itself; (b) the management of special treatment procedures and their side effects; (c) special technical environments with their unfamiliar routines; and (d) assessing the future and reassessing independence. Additional factors included elements internal to the person and characteristics of the stimuli that will influence the perception of illness-related events. Aspects within the person can affect the selection of objects and how they will be perceived. Norton's work clarified other areas of uncertainty. Norton maintains that one of the following must be present to qualify as uncertainty: vagueness, lack of clarity, ambiguity, unpredictability, inconsistency, probability, multiple meanings, and/or lack of information. Cancer diagnosis and the HSCT experience, or the caregiver and patient's perception of the experience, could easily fit these descriptors of uncertainty.

Certainly cancer has multiple meanings for many individuals, ranging from an expectation of immediate death to prolonged unpleasant treatments and painful death. While cancer is generally not viewed as a positive event in one's life, current treatments have reduced some of the side effects and made the experience more tolerable. The HSCT procedure has been viewed as potentially the ultimate cure, eagerly sought, and

greeted with cheers when a donor is identified. An opposite assessment of the HSCT process is that it is an acute life-threatening experience with long-term complications that may alter the remainder of life. Certainly the lack of predictability in the current scientific understanding of cancer survival and side effects would qualify as uncertainty. Current cancer survivorship statistics are frequently discussed in terms of five-year survivals. While this means a probability of surviving five years after diagnosis, it does not guarantee the actual time for the individual, further contributing to uncertainty. Even with survival, there are changes in health, roles, and income that need to be resolved. Many aspects of HSCT therapy include elements of uncertainty.

Treatment protocols outline the dosage and frequency of treatment. However, many cancer treatment episodes are not that straightforward. Complications such as neutropenia, sepsis, and disease progression frequently change the course of treatment What starts out as a clear roadmap to cure, frequently becomes a vague and ambiguous road with a lack of real concrete information or direction. For individuals who like to plan, the lack of clarity of the treatment plan and the expected response are exercises in patience and toleration of uncertainty.

Using Wyler's pattern recognition work, Mishel (1990) proposed three categories of uncertain responses, namely: (a) not recognized, (b) recognized but not categorized, and (c) recognized but categorized incorrectly. When an event, episode, or interaction is not interpreted correctly, according to the individual's previous experiences, it becomes increasingly difficult to accurately plan future actions. The lack of certainty in developing

appropriate actions can result in increased stress, decreased coping, and unproductive decisions**.**

Mishel (1981) perceives uncertainty as a judgment about an identified event or situation as contributing to a stress response in a hospitalized adult patient. The degree of successful coping is influenced by their ability to resolve uncertainty in the situation. Mishel and Murdaugh (1987) write of the adjustments required in heart transplant patients' families as they continue to deal with uncertainty after the transplant. Using a grounded theory methodology, Mishel and Murdaugh conducted family support groups over a 12-week period. The resulting theory regarding adjustment after a heart transplant includes immersion, passage, and negotiation, which parallel the stages of waiting for a donor, hospitalization, and recovery. In the development of her grounded theory, Mishel (1988) noted that little attention had been paid to the family's issues as the patient went through the process. In this theory, unpredictability refers to the unknowns involved in heart transplantation, including the underlying disease, the transplantation, and the future. The study identifies waiting for an organ as very difficult, and the adjustment after the transplant requiring a redefinition of what a "happy" life would be from then on. This readjustment includes changing roles and focus, from waiting for the future to enjoying the present.

Three major themes relating to uncertainty include: (a) antecedents of uncertainty, (b) the process of uncertainty appraisal, and (c) coping with uncertainty (Mishel, 1988). This theory explains how patients cognitively process illness-related stimuli and construct meaning through these events. Uncertainty or the inability to structure meaning can

develop if the patient does not form a cognitive schema for illness events, as interpreted subjectively by the patient. Mishel also identifies some of the antecedents of uncertainty as belonging to one of two phases, i.e., a stimuli frame or structure providers. The stimuli frame includes symptom patterns and event familiarity. This is consistent with the need to make sense of the input stimuli, where physical symptoms or experiences will be an interpreter of uncertainty. Increased patterns would suggest increasing familiarity and more sense, thus less uncertainty in the individual. The other antecedents are credible authority, social support, and education. Within this frame, Mishel identified the resources the individual uses to make sense of such experiences. Certainly, having credible authorities such as doctors, nurses, teachers, parents (at a particular age) can provide a sense of security and an understanding of events. These credible authority figures also represent power, which has the ability to make uncertainty better or worse. An example of credible authority would be the physician providing an interpretation of a diagnosis which provides information as well as a sense of hope. The patient and caregiver, holding the physician as an authority figure, have a perspective from which to view the illness. Also, as in caregiver support, social support provides a framework to decipher the meanings of events. And education provides the tools either to be able to understand experiences via reading or other stimuli, or to know where to find the information; however, lack of education leaves the interpretation of events to lived event experiences only.

In 1990 Mishel revised her uncertainty-in-illness theory, which addressed ongoing uncertainty, particularly as seen in chronic conditions including cancer. With this revision

she evaluated uncertainty through critical social theory to "examine the established view of the world" (Mishel, p. 257). She also compared her theory to the scientific theory which has little or no room for uncertainty. In the scientific view, accuracy, exactness, and predictability are highly valued, and the inability to make sense and predict the future does not fit. This lack of "fit" makes uncertainty all the more intolerable in today's society. Mishel suggests that with acute illness, adaptation and a return to the pre-illness state is expected. With chronic disease, where the unpredictability is ongoing, these may not be realistic goals. It is also suggested that returning to a pre-illness state does not allow, or support, growth and change.

In her re-conceptualization of uncertainty in illness, Mishel chose chaos theory as the parent theory for two main reasons (McDaniel, 1997). First, it reflects the notion of an open systems theory, taking into account the interactions between systems and the environment. Second, it also potentially addresses the exposure and changes with new and developing information. Mishel particularly addresses the concept of a far-from-equilibrium system that allows for minor changes to have far-reaching effects up to and including completely changing pre-existing organizations and conditions. Additionally, the change provides an opportunity to develop interventions to assist individuals in moving to a new plane in their dealings with uncertainty and their view of the world. An example of this would be that the caregiver would have unlimited possibilities to be creative in identifying new ways to cope with situations, as opposed to a mechanistic view, which as a closed system, would only predict the use of existing coping skills.

Mishel (1990) observes that "uncertainty surrounding a chronic . . . condition qualifies as a sufficient fluctuation to threaten the pre-existing organization of the person, a far-from-equilibrium system" (p. 259). The lack of information and ability to make sense of a chronic condition, in an environment that values predictability, creates tension and uncertainty for caregiver and patient. For the uncertainty to become a potentially positive force, the tension created must increase in a non-linear fashion, causing increased and undesirable tension within the system. Only this increased conflict will cause the system to change or re-organize, resulting in a new perspective that will make sense of the chronic uncertainty (Mishel).

Penrod (2001) found the uncertainty concept to be at different states of maturity depending on the discipline being reviewed. In psychology, she found the concept to be most mature but also more narrow in scope. In medicine, the literature indicates that uncertainty is focused on clinical uncertainty with partial maturity, whereas in nursing the focus is on the illness experience, whereas uncertainty has a broader scope and is moving towards maturity. To refine the concept to promulgate its maturity, Penrod recommends three areas for development: (a) the development of conceptual components or attributes, (b) the level of strategies or interventions to decrease discomfort, and (c) continuing efforts to measure the concept. Increased understanding of caregiver uncertainty in the context of HSCT treatment is needed to develop effective support strategies.

Uncertainty has the potential to be a key indicator of increased levels of concern in caregivers experiencing HSCT with their loved ones. Mishel's theoretical development provides a strong base and conceptual framework to develop schemas to evaluate the

level of uncertainty. However, little has been published on the impact of the illness experience for caregivers. Previous work has focused on patients and parents of children. But better understanding of the experience from the caregivers' perspective would assist healthcare providers in developing interventions for them. Mishel's current work is focused on newly diagnosed cancer patients and interventions to assist them in decreasing their uncertainty. For HSCT patients and caregivers who have known the diagnosis for over six weeks, different interventions may be indicated. Since actual changes in levels of uncertainty over time are poorly understood, longitudinal prospective studies of uncertainty in the context of specific care experiences would be useful.

Patient Symptomatology

In this study, patient symptomatology is of concern to the caregiver as well as the patient. Patient symptomatology denotes the physical and emotional experiences that arise as a result of the cancer or its treatment, which are measured from both the patient's and the caregiver's perspectives in what is called the patient-caregiver dyad. The symptomatology itself can alter the caregiving experience, acting as both a stressor and a factor altering the level of burden and uncertainty experienced (Mishel, 1999). Research that increases knowledge related to the possible relationships between the perception of symptomatology, levels of burden, and uncertainty for caregivers over time could help define points when caregiver support is most critical in order to reduce the risk of a perception that the symptoms observed are more serious than the patient would confirm. Patient symptomatology is more specifically discussed in relation to caregivers of HSCT patients in the next section, which provides the context of their caregiving.

Hematopoietic Stem Cell Transplantation

Hematopoietic Stem Cell Transplantation (HSCT) is a complex medical procedure that demands a great deal from the patient and their caregiver. This segment of the literature review provides the background for the study of caregivers of HSCTs. The following defines Hematopoietic Stem Cell Transplantation:

> A bone marrow transplant is a procedure that transplants healthy bone marrow into a patient whose bone marrow is not working properly. A bone marrow transplant may be done for several conditions including hereditary blood diseases, hereditary metabolic diseases, hereditary immune deficiencies, and various forms of cancer (http://www.nlm.nih.gov/medlineplus/ency/article/003009.htm).

There are two general categories of HSCT according to donor type. With autologous HSCT, the individual is their own bone marrow donor for the procedure. The patient receives chemotherapy, then recovers with the assistance of high-dose leukocyte growth factors, which both combine to increase the harvest of stem cells. In an allogeneic HSCT a person other than the patient is the donor. The donor could be a sibling, a matched unrelated donor (MUD), or a cord donor (stem cells from placenta and umbilical cord).

Until recently, the sequencing of aggressive therapies designed to eliminate cancer cell growth totally has resulted in lengthy hospitalizations for HSCT patients. As many as 100 inpatient days were once required for observation or treatment related to neutropenia (e.g., a decreased number of neutrophils or granulocytes), fever, infections, graft-versus-host disease (a complication of allergeneic transplants), and other life-

threatening events. The advent of newer treatment protocols, and the drive to reduce healthcare expenditures associated with the costly HSCT procedure, has prompted a shift to decreased hospital stay and more intensive outpatient care (Grimm, Zawacki, Mock, Krumm, & Frink, 2000).

An analysis by the Center for International Bone Marrow Transplant Registry (CIBMTR, 2004) indicates that the single largest cost driver in HSCT is in-hospital length of stay. Redaelli, Stephans, Brandt, Botteman, and Pashos (2004) also identified length of hospital stay along with HSCT (BMT and PSCT) as significant drivers of the cost of treatment for leukemia. National-length-of-stay data are difficult to obtain since submission of these data is required only for patients covered by Medicare, which represents only a small subset of transplants performed. Anecdotal comments from HSCT centers' staff indicate that efforts are made to discharge patients from in-hospital settings as soon as they have either received stem cell infusions or have recovered from acute infections, or HSCT patients may not be admitted to the hospital at all (Personal communication, Sivley, 2005). The decreased length of stay and shift from intensive inpatient care to frequent outpatient visits and closely supervised home health care has placed an increasingly significant burden of care on patients and their caregivers. Provisions for care that were previously provided by licensed, experienced health professionals are now the shared responsibilities of patients and their families. Greater emphasis on preparing HSCT recipients and caregivers to meet the challenges and demands of community-based care has become a clinical care priority for nurses.

HSCT Patient Populations

The CIBMTR reported that approximately 50,000 to 60,000 HSCT procedures were completed in 2006, of which 20,000 were allogeneic transplants and 35,000 transplants were autologous. The most common diseases involving transplants were acute myologenous leukemia (AML), acute lymphatic leukemia (ALL), non-Hodgkin's lymphoma (NHL), Hodgkin's disease, and multiple myeloma for autologous transplants. In allogeneic transplants, the most common diagnosis included AML, ALL, NHL, Hodgkins' disease, multiple myeloma, aplastic anemia, and myelosysplastic disease. The most common cause of death in autologous transplants was recurrence of the disease (CIBMTR), accounting for over 70% of mortality. In matched sibling transplants, the number one cause of death was disease recurrence at 41%, followed by infection at 17%, and graft versus host disease (GVHD) at 13%. For matched unrelated donors (MUD) relapse caused death in 34% of the patients. Infection caused 20%, and GVHD caused 14% of the mortality (CIBMTR).

Today HSCT involves a reduced hospital stay, increased care at home, and the expectation that caregivers will accurately monitor and report significant symptom changes in the patient. Therefore, it is critical to understand this experience sufficiently to provide the type of caregiver support needed in this unique setting.

Phases of Acute Transplant Experience

The treatment of HSCT patients can be viewed as a continuum of care from pre-HSCT evaluation through the post-recovery phase. Previous studies have identified various phases of the HSCT experience. Brown and Kelly (1976)

identified eight stages from a psychiatric perspective, ranging from the acceptance of the treatment prior to the HSCT to adaptation after discharge from the hospital. In a study, Zabora, Smith, Baker, Wingard, and Curbow (1992) followed the family caregivers of HSCT patients for 12 months and found specific challenges during the post-transplant period or recovery period. Stetz et al. (1996) collected information on the HSCT experience from family caregivers within 90 days of the completion of the relative's HSCT, including both inpatient and outpatients. Eilers utilized similar phases in her research (1996) and recommended future research to investigate care issues in the engraftment and post-discharge phases.

Common practice and previous research would support a study of four separate HSCT phases (Eilers, 1996; Stetz et al., 1996) to clarify the HSCT caregiver's experience: (a) pre-transplant chemotherapy and/or radiation treatment and marrow infusion, (b) acute recovery, (c) immediate home care, and (d) home care one month post discharge from the hospital. Taken together, these four phases constitute the acute transplant experience. The chemotherapy treatments in the pre-treatment phase are intensive; however, life-threatening and other serious effects can be experienced during any of the subsequent phases. Many adverse HSCT sequellae are neither foreseeable nor preventable. Therefore, there is a tremendous sense of uncertainty surrounding the entire HSCT experience for patients, families, and healthcare professionals.

HSCT Research

Studies of caregiver burden and uncertainty among individuals involved with cancer patients continue to increase. Yet, despite the growing attention to the burden of caregiving in cancer care, studies are very limited on the caregiver experience during Bone Marrow Transplantation (BMT) or Peripheral Stem Cell Transplant (PSCT), now called Hematopoietic Stem Cell Transplant (HSCT).

Only two prospective studies related to caregiver needs during the HSCT experience, by Foxall and Gaston-Johansson (1996), have explored issues in regard to the stressful experience of caring for the BMT patient, which potentially causes negative effects on the caregiver's physical and mental health. Eilers (1996) examined a population of 90 family caregivers of adult transplant recipients, using three data collection points: pre-HSCT, 24 to 72 hours post-HSCT, and 7 to 10 days later, focusing on the acute phase of the HSCT experience. She found that uncertainty was elevated in some caregivers but not universally, and social support was important in many caregivers but did not impact the outcome of uncertainty. Eilers' study is very similar to the one reported here, but different in certain significant details. In 1996, when Eilers published the study, most transplants were being performed in the inpatient environment. Many changes have occurred in the HSCT process since then. Length of hospital stay is shorter, so many of these caregivers now have to care for the patient at home for a longer period and for a patient who requires more care. Also, as Eilers notes, these HSCTs were done at one large university hospital where patients were required to stay in close proximity for a period of time. This particular institution has a hotel-like environment on campus with

healthcare providers immediately available on site, unlike the majority of centers where patients need to commute as outpatients from a local hotel or home.

Stetz et al. (1996) studied the needs of family caregivers of BMT (now HSCT) patients in a descriptive study of 19 family members. Data were collected during three focus groups using a semi-structured interview format, with a fourth focus group being used to validate the observations. The participants, family caregivers whose loved one had already received their transplant, responded to fliers posted in the hospital or clinic to volunteer for the project. In their findings, Stetz et al. identified five themes from the focus groups: (a) preparing for caregiving, (b) managing the care, (c) facing challenges, (d) developing supportive strategies, and (e) discovering unanticipated rewards and benefits. This is one of a group of studies published independently of each other in 1996 that dealt with the issue of family caregivers of HSCT patients. The results of Stetz et al.'s study provided an early glimpse of the concerns and worries from the family perspective. However, these data were collected after the transplant, so it is difficult to understand completely the prospective experience of the family as the patient underwent evaluation for the transplant. Additionally, the small sample size, a convenience sample from two hospitals, in Stetz et al.'s study may not have adequately represented issues and concerns for the HSCT population in general.

Patient Symptomatology in HSCT Treatment

Since more of the patient's acute transplant time occurs at home with family caregivers providing care and determining symptoms, information on the ability of the caregivers to communicate patient changes and accurately report patient experiences

becomes more urgent. Little information is available on the degree of consistency with which family members report symptomatology in the acute setting. Therefore, data representing common symptoms were examined in the present study, using established patient self-report tools.

Porter et al. (2002) describe self-efficacy as representing communication between patient and family caregivers regarding management of pain. Several studies have reported that patients and their caregivers' perceptions of their symptoms are commonly not in alignment, with caregivers frequently overestimating the patient's pain (Clipp & George, 1992; Ferrell, Eberts, McCaffery, & Grant, 1991; Miaskowski et al., 1997). These differences are an indication of inadequate communication and a potential source of distress for the caregiver. In a study of patients with lupus, Daltroy, Lewis, McGee, and Kissin (1999) found that significant differences in the perception of disease management often led to higher caregiver distress, which were an indicator of poor communication. Mazanec and Bartel (2002) proposed different pathways on how patients and caregivers perceive pain based on Ferrell et al.'s report. The patient's experience pathway is directly related to the pain perception, and the pain experience is related to factors such as neurophysiological response, associated emotions, suffering, and associated physical symptoms (Ferrell et al.). Caregivers may have a different pathway, which starts with the perception of the patient's pain. It is further moderated by suffering and caregiver burden, and results in the expression of pain. The tools that were used in this study to measure patient

symptomatology included: (a) the Brief Pain Inventory, (b) the Brief Fatigue Inventory, and (c) the Memorial Symptom Assessment Survey.

Pain

Pain is a difficult symptom for the person experiencing it to adequately explain and describe, much less for caregivers to accurately report, describe, and administer interventions based on the patient's report. Pain can be a symptom of expected discomfort or a signal of new complications in the HSCT patient. Being able to advocate for their loved one in communications to healthcare providers from home is a necessary component of the caregiver experience.

Pain is a difficult symptom to define. One commonly used definition is that it is whatever the patient says it is (McCaffery, 1968). A more formal definition is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. While pain is unquestionably a sensation in a part or parts of the body, it is always unpleasant and therefore an emotional experience" (Merskey & Watson, 1979). This definition was used by the American Pain Society in their 2005 publication on pain. It is noted that chronic pain may not be accompanied by the outward signs of grimacing or tachycardia that are expected in acute pain. In addition to the pain that the patient experiences, the presence of that pain may have deep emotional meaning for the individual and may signal a new complication, old complications, or cancer recurrence.

The tool that was used in the present study to evaluate the patient's pain, the Brief Pain Inventory, or BPI, is a self-report measure that includes valid scales of pain intensity. The instrument has been well validated in cancer pain populations (Cleeland & Ryan, 1994) and has been studied in a variety of languages, including Chinese, French, German, Hindi, Italian, Japanese, and Vietnamese (Caraceni et al., 1996; Larue, Colleau, Brasseur, & Cleeland, 1995; Radbruch et al., 1999; Uki, Mendoza, Cleeland, Nakamura, & Takeda, 1998; Wang, Mendoza, Gao, & Cleeland, 1996). In the BPI, patients are asked to self-report their pain intensity since their last visit for pain intensity, according to "on average", "at its worst", "at its least" and "right now" on a 10-point scale. Seven questions ask the participant to score how pain has interfered with various aspects of their life. There are also questions related to the degree of pain relief they experience from pain interventions, using a percent scale and pain sites (Breitbart et al., 1996, p. 316; Daut, Cleeland, & Flanery, 1983).

Fatigue

Fatigue is also a difficult symptom to quantify. It can have many etiologies, including anemia, heart failure, infection (bacterial, viral, or fungal) as well as non-specific causes, including depression, malnutrition, and insomnia. Like pain, fatigue can also be identified as whatever the patient says it is. However, a more formal definition of fatigue is "a subjective state of an imbalance in the availability of inner resources needed to perform physical or mental activities" (Yang & Wu, 2005). Yet others have referred to the fact that sleep does not restore energy in cancer patients. Reports have listed fatigue as the most prominent symptom among cancer patients as well as one of the most

distressing (Mendoza et al., 1999). Many fatigue-measuring instruments are available, including the Pearson-Byars Fatigue Feeling Checklist (Pearson, 1957). the Functional Assessment of Cancer Therapy – Fatigue (FACT-F) (Yellen, Cella, Webster, Blendowski, & Kaplan, 1997), the Profile of Mood States (POMS); fatigue and vigor subscales (McNair, Lorr, & Droppelman, 1971), and the Fatigue Symptom Inventory (Hann et al., 1997). However, many tools are excessively time consuming and exhausting for patients and caregivers to complete, encompassing many pages of questions aimed at capturing the elusive nature of fatigue. A short but comprehensive instrument was sought to limit the burden of completing the tools to a reasonable level. The Brief Fatigue Inventory was chosen for the present study for its brevity and comprehensive design, and the fact that it has been utilized in multiple settings with good established reliability and validity testing (Mendoza et al.).

Measuring Patient Symptomatology

Since the HSCT experience includes the potential for more symptoms than pain and fatigue, an instrument was sought in this study that allowed for a relatively comprehensive overview of potential symptom reports and could be completed in a reasonable time by patients and caregivers. The Memorial Symptom Assessment Survey (MSAS) was chosen because it met these requirements and had pre-established reliability and validity testing. The MSAS is a symptom checklist that elicits information about the intensity, frequency, and distress associated with 32 physical and psychological symptoms. Patients are asked to rate their symptoms within the previous week and provide information on frequency, severity, and distress. The instrument has been

demonstrated to have internal consistency and adequate reliability (Portenoy et al., 1994). Factor analysis identified three specific groups within the symptom constellation: psychological, high frequency, and low frequency symptoms.

Strengths and Gaps in the Caregiver Research

With increased outpatient care, it has become imperative to learn to identify areas where education and training can make a difference, both for the outcome of the patient and the long-term mental and physical health of the caregiver. The results of this research study, therefore, have the potential to identify both the timing and elements that are most problematic for the caregiver during the acute phase of HSCT. With a better understanding of these factors, healthcare professionals can develop better interventions, both in timing and content, and implement them when most needed.

As indicated in this literature review, there is limited availability of caregiver burden research on the cancer population, and virtually none on the HSCT patient caregiver in outpatient populations. There is also a need to identify how the geriatric literature on caregiving applies to the cancer experience, particularly in the acute episode of HSCT. While there are similarities in the level of responsibility, there are significant differences including age, family responsibilities, and the remitting nature of some types of cancer, to name a few. Given the specifically unpredictable nature of cancer and HSCT, as a treatment option, the addition of uncertainty as a major concept and theoretical base in this area of study seems reasonable. Since caregiver burden has had a limited theoretical framework development, and the root theory for both uncertainty and

caregiver burden is based in Lazarus's work (1984), it would seem logical to combine these two concepts to investigate the effects of the HSCT experience on caregivers.

Mishel's work (1981, 1990) is an example of model building that encompasses the introduction of a new theory with her analysis of constructs, interrelationships, and interrelatedness. By using a mid-range theory that has a strongly developed theoretical base, and one that has been adapted to specifically address the chronicity of diseases such as cancer, research can focus on developing interventions. As mentioned previously, Mishel's reconstructed view of uncertainty allows for movement in an open system that can move the caregiver to a completely different view of the illness. This change from a mechanistic closed system allows for increased options for a new vision of the world. A key component of her proposal is to adapt a framework used for chronic conditions and massage it for use in the evaluation of an acute phase of a chronic disease. This sets the stage for a model to evaluate and implement interventions for acute changes in chronic conditions where caregivers are actively involved.

The findings of the present study contribute to the theory of uncertainty in illness as well as improve the potential for caregivers to develop grounded interventions that are theoretically consistent with their actual experience. Since there is a paucity of information on uncertainty in HSCT, this study has provided a basis for documenting the need and timing for interventions that will address broader issues. The results of this study could also help serve as a basis for other researchers to build on the relationship of caregiver burden and HSCT, as well as serve as a beginning model for linking uncertainty to the HSCT experience. By showing the relationships of symptom

experiences with caregiver uncertainty and caregiver burden in HSCT, this research potentially broadens the implications for caregiver research in other populations.

The HSCT experience is currently viewed as a continuum with little demarcation of different stresses during particular periods of the transplant procedure. It would seem reasonable to identify methods to identify times of high and low pressure as healthcare professionals develop strategies for interventions for both HSCT patient and caregiver.

The results of this research can provide a basis for how best to provide information, support, and interventions to caregivers and patients in the context of an increased amount of care in the outpatient setting. The results also may show that the shortened hospitalization of the HSCT patient affects the caregiver in a way that increases their burden. It has been suggested by Oyebode (2003) that failure to provide care to the caregiver may result in their future health problems, both physically and mentally. One of the antecedents to uncertainty is the presence or absence of authority figures who can assist in developing a perspective or pattern to a situation (Mishel, 1988). With the patient having little or no time in the hospital setting, the caregiver may have difficulty identifying who the authority resources are, how to use these supports, and how to access the resources in an appropriate and timely manner when dangers and risks develop outside the hospital setting.

The repeated measures and longitudinal design of this study, enabled exploration of the continuum of caregiver burden, uncertainty, and perceived symptomatology across the four phases of HSCT acute care treatment. With this information, it will be possible

to identify treatment phases that are more inclined to be high uncertainty periods and to develop interventions focused on these points.

Based on the findings of this study, it may be possible to design future interventions, including educational programs, to address high stress, uncertainty, and caregiver burden prior to their occurrence, and thus facilitate the experience of caregivers and patients on this path. Prospective studies are ideal to allow maximum use of subjects and data from a limited pool of HSCT patients and caregivers. Prospective studies also support conceptual framework development and improved understanding of the actual issues and concerns of HSCT caregivers.

Chapter Summary

This chapter has presented a review of the literature encompassing the pertinent concepts of this study, including stress, caregiver burden, uncertainty, and patient symptomatology. Additionally, details on the Hematopoietic Stem Cell Transplantation procedure and related information have set the context for the purpose of this study: to examine the patterns of burden and uncertainty in caregivers involved in the acute phase of HSCT in order to ascertain their needs.

Chapter 3

METHODOLOGY

Hematopoietic Stem Cell Transplantation (HSCT), formerly called Bone Marrow Transplantation (BMT), is an aggressive, life-threatening but potentially curative procedure used in the treatment of cancers, including leukemia, lymphomas, and other malignancies. In recent years, due to new treatment protocols and pressures to decrease length of hospitalization, HSCT patients are spending less or no time at all in the hospital, and depending on family members or other caregivers to provide care that was previously provided by licensed, experienced healthcare professionals. Increasing amounts of the acute care for these patients are being provided in the home or outpatient clinic (Frey, 2002).

It is logical to assume that this change in the care environment has placed an enormous burden on family members who are already emotionally challenged and uncertain as to the predictability of the outcomes of the cancer diagnosis and HSCT treatment. It is not known if the caregiver has the tools to communicate with the healthcare providers. Accurate identification and interpretation of patient symptoms by caregivers is crucial in order to get timely and appropriate interventions for the individual during the various treatment phases for a transplant patient. The responsibility for assessing the patient's symptoms and initiating interventions places additional stress, burden, and uncertainty on the HSCT caregiver. Previous literature on Alzheimer's disease suggests that social support, previous experiences, and respite affect how well

caregivers are successful in integrating caregiving into their life, but little is known about the experience of HSCT caregivers in the outpatient setting and the effects on them.

The purpose of this chapter is to describe the study design, the operationalization of the variables and concepts, the research instruments used to explore aspects of the patient-caregiver experience, and the processes and procedures implemented to complete the study.

Research Design

This study is a descriptive, repeated measures longitudinal study of the experiences of the caregiver and patient in the acute phase of HSCT treatment. The study was reviewed and approved by The Pennsylvania State University Office for Research Protection and the Penn State Milton S. Hershey Medical Center Institutional Review Board (IRB) in 2004 and Stanford University Hospital IRB in 2007. Yearly updates were completed and approved by these entities (Appendix A).

Operationalization of Variables/Concepts

Stress in the caregiver is defined by the level of caregiver burden and uncertainty perceived at the four points of measurement before, during, and after the caregiver experience as described in the Conceptual Definitions in Chapter 1. For the purpose of this investigation, the variables are described in terms of conceptual derivation to more precisely characterize the measurement domains for the relevant concepts of interests and the outcomes of the study. When appropriate, the concepts are portrayed as they relate to their conceptual origin and the manner in which they have been previously utilized in the literature. The relationships of the primary concepts of interest—caregiver burden,

uncertainty, and symptomatology—are presented in the conceptual framework (Figure 1.1). The conceptual links of this model to the HSCT caregiver experience provide a basis for this study.

1. ***Uncertainty*** is operationally defined as the overall score on the Mishel Uncertainty in Illness Scale (MUIS).
2. ***Caregiver*** is the identified individual who provides care to the patient.
3. ***Caregiver burden*** is operationally defined as the score obtained on Zarit's measurement tool, the Zarit Burden Interview (ZBI).
4. ***Symptom pattern*** refers to the scores on the patient symptomatology instruments. Fatigue is defined as the total score on the Brief Fatigue Inventory (BFI). Pain is defined as the total score on the Brief Pain Inventory (BPI). The Memorial Symptom Assessment Survey (MSAS) total score reflects other symptoms.
5. ***HSCT***, formerly known as Bone Marrow Transplant (BMT) and Peripheral Stem Cell Transplant (PSCT), is defined as "procedures that restore stem cells that have been destroyed by high doses of chemotherapy and/or radiation therapy" (NCI, 2004). HSCT is an intense protocol, which may include the administration of high doses of chemotherapy, immunotherapy, radiation therapy, or any combination of these treatments. Transplants can be divided into two general categories depending on the source of the transplanted graft: (a) autologous, which refers to a transplant in which the individual is his/her

own donor, and (b) allogeneic, which refers to a transplant in which someone other than the patient is the donor (NCI, 2004).

6. ***Phases of an HSCT.*** For the purpose of this study, four phases of the acute transplant process are identified: (a) Phase 1 - immediately pre-transplant or immediate preparatory regimen; (b) Phase 2 - the period at the time of the marrow infusion and three days post infusion; (c) Phase 3 - the period seven days post discharge from the hospital or for patients who are not hospitalized, the period immediately three days post infusion; and (d) Phase 4 - the period marked by one month post discharge from the hospital, or for those patients not hospitalized, the care rendered as an outpatient—three weeks post Phase 3 testing.

Instrumentation

This study employed an instrument to measure uncertainty about the HSCT procedure among the patients-caregiver dyads, an instrument to measure caregiver burden, and three instruments to measure patient symptomatology. Each is described in the following sections and copies of permission for their use is in Appendix B.

Measurement of Uncertainty

The Mishel Uncertainty in Illness Survey (MUIS) is a 33-item, Likert-type scale in which participants are asked to identify their responses on a scale from 1-strongly agree to 5-strongly disagree. The tool was factor-analyzed into a four-factor scale including: (a) ambiguity, 17 items, (b) complexity, 7 items, (c) deficient information, 4 items, and (d) unpredictability, 6 items. The reliability of the total scale and each factor

have been demonstrated for the internal consistency of the scale. The total scale had a standardized alpha of 0.90, and the reliability coefficients for the subscales ranged from 0.91 for the largest subscale to 0.70 for the smallest. The validity of this measure has been supported by the finding that the MUIS discriminated significantly among a medical, surgical, and diagnostic patient population in the United States. Initial support for the construct validity of the scale was evidenced by item clustering into factors consistent with theoretical predictions. The MUIS has been administered to patients with a variety of illness diagnoses, including breast cancer, prostate cancer, and gynecological cancer. The tool has been used extensively by Mishel in a variety of settings, and normative data for various populations have been established by a number of researchers and reported by Mishel (1997). However, there are no published reports of usage of the MUIS on caregivers of patients undergoing HSCT treatments. (See Appendix B for permission to use the MUIS.)

Caregiver Burden Interview

The Zarit Burden Interview has been used, in various editions, since 1980 by Zarit and other researchers. Originally developed as a uni-dimensional measure of caregiver burden, later versions of the tool have undergone factor analysis and shortened versions and screening versions have been developed (Zarit et al., 1986). Additionally the instrument has been translated into numerous languages and achieved acceptable degrees of reliability and validity (Schreiner, Morimoto, Arai, & Zarit, 2006). The factor analysis of the original 22-item, Likert-type scale of the ZBI provides subscale scores for *personal strain* and *role strain*. Although first developed for the measurement of caregiver burden

in the elderly and AD patients, the ZBI has been used in other populations, including mental illness, intensive care units, and cancer. It has also been interpreted and used in various other countries including Canada (O'Rourke, & Tuokko, 2004), China (Chou, Jiann-Chyun, & Chu, 2002), Taiwan (Chou, LaMontagne, & Hepworth, 1997), Japan (Schreiner et al., 2006), and Korea (Chou et al., 1999).

The ZBI was chosen to measure caregiver burden in this study for several reasons, including the relative ease of self administration, the short time needed for study participants to complete the survey, and its well-established use in measuring caregiver burden. The tool is sufficiently sensitive to demonstrate change over months, but it was to be determined if this tool would demonstrate sensitivity to change over the expected 6-week course of the acute HSCT experience. The ZBI has an internal reliability of .88 (Hassinger, 1985) and .91 (Gallagher et al., 1989) using Cronbach's alpha and a criterion validity of r = .71. These results indicate a high degree of reliability and validity reflecting the ability of the tool to accurately measure caregiver burden in various populations, but not unnecessarily to require redundant answers to identical questions.

This Likert-type scale for the Caregiver Burden Index consists of 22 questions designed to measure the level of stress experienced by caregivers. Subscale scores can be obtained for personal strain using items 1, 4, 5, 8, 9, 14, 16, 17, 18, 19, 20, 21, with an alpha score of .80. The role strain subscale score can be obtained using items 2, 3, 6, 11, 12, 13 with an alpha score of .81. The measures indicate a highly reliable tool for the subsections. The ability to obtain subscale scores measuring aspects of caregiver burden was expected to be helpful in the analysis and review of the data in this study, providing

more possible explanations and theories of individual caregiver burden. The use of the ZBI tool also allowed for some comparison of burden in HSCT caregivers to caregivers in other populations.

The repeated measures design of this study represents the ability to measure caregiver burden at phases that are thought to be significantly different in both objective and subjective caregiver burden. The capability of documenting significant changes over time provides data to support when target-caregiver interventions are most needed to reduce stress and enhance caregiver coping skills. (A copy of permission to use the Zarit Burden Interview tool is found in Appendix B.)

Measures of Patient Symptomatology

Patient symptomatology was measured in this study by scores on three symptom-measuring tools: the Brief Pain Inventory (BPI), the Brief Fatigue Inventory (BFI), and the Memorial Symptom Survey (MSAS). (Copies of permissions for the use of these tools are provided in Appendix B).

Brief Pain Inventory.

The Brief Pain Inventory is a self-report measure that includes valid scales of pain intensity. The instrument has been well validated in cancer pain populations (Cleeland & Ryan, 1994) and has been studied in a variety of languages, including Chinese, French, German, Hindi, Italian, Japanese, and Vietnamese (Caraceni et al., 1996; Larue et al., 1995; Radbruch et al., 1999; Uki et al., 1998; Wang et al., 1996). Patients are asked to self-report their pain intensity since their last visit, indicating “on average”, “at its worst”, “at its least”, and “right now” on a 10-point scale. Seven questions request the participant

to score how pain has interfered with various aspects of his/her life. There are also questions related to degree of pain relief they experience from pain interventions using a percent scale and pain sites (Breitbart et al., 1996, p. 316; Daut et al., 1983). Reliability testing was measured using a Cronbach's alpha, resulting in ranges from .77 to .91 (Cleeland, 1989). These scores represent an acceptable measurement of a construct without having multiple questions measure the same item. Validity has been measured using the correlation between severity of pain and its impact on life, as well as initial studies examining severity of pain and use of medication to control pain. The initial studies reflected good correlation between the use of medication and reported severity of pain (Daut et al.). There was a statistically significant ($p < 0.002$) percentage of patients taking pain medication who were reporting increased pain; this was true for both narcotic and non-narcotic pain medication. The caregiver instructions for completion of the survey were standardized and presented at the time of survey completion to "provide scores that you believe indicate what the patient is experiencing."

Brief Fatigue Inventory.

The Brief Fatigue Inventory was chosen for this study because of its brevity and comprehensive design, and the fact that it has been utilized in multiple settings with good established reliability and validity testing (Mendoza et al., 1999).

The BFI uses a self-report format that is internally reliable for the measurement of severity of fatigue. It consists of four general questions with the fourth subdivided into six questions. Patients are requested to evaluate their fatigue on a 10-point scale, ranging from does not interfere (0) to completely interferes (10) (Mendoza et al., 1999).

Extensive validity testing of the BFI was performed through a variety of methodologies. Factor analysis was used to determine construct validity to assist in determining which factors were significant in measuring fatigue. In the testing, factor analysis scores ranging from .81 to .92 were obtained, indicating high factor loadings, which are associated with items describing a single factor. Testing was done to correlate the BFI with pre-existing subscales of fatigue to ensure that the newly developed instrument was at least as appropriate a tool as already existed. Results from the correlation of pre-existing scales was $r = .84 - .88$ ($p < 0.001$), indicating high correlations with the other scales. Discriminate validity was done by comparing scores from the BFI with the Eastern Cooperative Oncology Group (ECOG) performance status scores, which are brief scores used to quickly determine a patient's functional abilities. Mendoza et al. used extensive testing and cross-testing of correlations among existing scales, hemoglobin levels, and the BFI, with statistically high correlations at $p < 0.001$. Internal consistency was measured using Cronbach's coefficient alpha with a resulting coefficient of 0.96 which indicates a very high reliability, and indicates that the tool measures fatigue as it says it does, but without item redundancy. The caregiver instructions for completion of the survey were standardized and presented at the time of survey completion to "provide scores that you believe indicate what the patient is experiencing."

Memorial Symptom Assessment Survey.

The Memorial Symptom Assessment Survey (MSAS) used in this study is a symptom checklist that elicits information about the intensity, frequency, and distress associated with 32 physical and psychological symptoms. Patients are asked to rate their

symptoms in the timeframe of the previous week and provide information on the frequency of severity and distress. The instrument has been demonstrated to have internal consistency and adequate reliability (Portenoy et al., 1994). Factor analysis identified three specific groups within the symptom constellation: psychological, high frequency, and low frequency symptoms. Cronbach's alpha was 0.88 - 0.83 for the psychological and high frequency symptoms, and 0.58 for the low frequency symptoms, indicating that there was good internal consistency for the first two groups and less high, but still acceptable consistency for the latter. The caregiver instructions for completion of the survey were standardized and presented at the time of survey completion to "provide scores that you believe indicate what the patient is experiencing."

Research Procedures

This descriptive study of HSCT caregivers is a repeated measures longitudinal design. The acute HSCT experience involves an emotional roller coaster ride for the patient-caregiver dyad during a relatively brief time (approximately 6 weeks). Four distinct phases have emerged to describe this intense event. Eilers described similar phases in a study of adult bone marrow recipients that covered a 100-day hospital stay for treatment, but the shorter hospital stay for the HSCT patients in the present study is a significantly different healthcare environment than the one in which she conducted her study in 1996. The phases for the data collection for the current study were based on information from Brown and Kelly (1976) and adjusted to identify points in time common in the current acute phase of HSCT treatment.

The points established for data collection from the participants in this study were: (a) Interview 1, pre-transplant; (b) Interview 2, immediately after transplant to three days post infusion, (c) Interview 3, one week post discharge, and (d) Interview 4, one month post discharge. Each phase has different stressors and expectations, and potentially various effective interventions. The time period of each stage is a limited "snapshot" of the acute phase of the transplant experience. Ongoing challenges await the patient and caregiver during the continuing treatment, post transplant. Challenges such as a compromised immune system, continued graft versus host disease (GVHD), disease recurrence, and increased risk for secondary cancers and stigma related to cancer survivorship, await the patient and the caregiver in the long term. As an initial study, this limited period covered the most acute as well as the most stressful initial time for both the caregiver and the patient. More specifically, the four HSCT phases include the following:

Phase 1, pre-transplant, covers up to approximately one week prior to the beginning of treatment to prepare for the actual transplant. In addition to the heightened anticipation in the waiting period before the transplant is arranged, anxiety and stress are expected to be high when the transplant is actually scheduled. This represents the actualization of months of planning and testing to evaluate eligibility and to search for a suitable and available donor match. Eilers (1996) used a similar phase to establish a baseline for the patient and caregiver.

Phase 2, immediate post-transplant, covers the immediate transplant period from the actual infusion of bone marrow to approximately three days post infusion. This represents the phase identified by many as the "transplant." For many families and

caregivers, this unrealistically represents the height of complexity during the transplant experience. A similar phase was used by Eilers (1996) in her data collection.

Phase 3, one week post discharge, represents the period around the discharge closest to the infusion of the bone marrow/stem cell. During this phase, the patient and caregiver are "on their own" either at home or at a location near the hospital. They are dependent on each other for daily care, observations, and medication administration that had been done by the healthcare team while the patient was in the hospital. It has been suggested that this may be a honeymoon period with the joy of survival overshadowing any negative or long-term implications.

Phase 4, one month post discharge, represents a longer view of the acute post-transplant experience, covering the time from one week post discharge to approximately one month post discharge. Speculation suggests that this phase may represent a more realistic picture of the adaptive and coping mechanisms in adjusting to life post transplant. Eilers' study (1996) did not include these last two phases, as all of her data collection was completed during the patient's hospitalization. Due to the decreased length of stay and early discharge, the current study provides new information about the time of increased responsibility for the HSCT caregiver while the patient is at home, still actively recovering.

Power Analysis

The sample size for this study was calculated with the assistance of the statistical staff at the Penn State University Health Evaluation Sciences Department. The number of participants needed to achieve a 95% confidence interval that had the upper and lower

endpoints +/- .25 was calculated at 50 patient-caregiver dyads (Personal communications, Chinchilli, 2005, 2007). After the loss of subjects following recruitment, the final sample (N = 46) was confirmed as adequate to meet the power criteria (Personal communication, Chinchilli, 2008).

Sample Selection Process

The sample was recruited from two populations of HSCT patients and their identified caregivers at the initiation of a scheduled HSCT transplant in two different hospital settings.

The eligibility criteria were that the participants be 18 years of age or older, be able to read and write English, and not be diagnosed "mentally challenged." A single caregiver must be identified by the patient and the caregiver. Others could participate in the caregiving process, but only the "main" caregiver as identified by the patient would participate in the study. Both members of the patient-caregiver dyad must agree to participate to be included in the study. Eligible participants were identified from the Bone Marrow Transplant Program at the Penn State Milton S. Hershey Medical Center (HMC) and Stanford University Hospital (SUH). The Hershey Medical Center, the only academic medical center in Pennsylvania, located outside the urban hubs of Philadelphia and Pittsburgh, serves more than 2.6 million people in central Pennsylvania. Established in 1970, the Hershey Medical Center has grown to include 504 inpatient beds, 20,669 inpatient admissions, 42,526 emergency room visits, and 624,972 outpatient visits in the most recent year for which statistics are available.

The HMC Hematopoietic Cell Transplant Program was established in 1996 under the direction of Dr. Witold Rybka, with the first transplant occurring in October of that year. Since then, the program has performed 319 adult and pediatric transplants, and provides services for autologous, allogeneic, and non-myeloablative (mini-transplants), matched unrelated donor (MUD), and cord transplants.

The HMC transplant center is accredited by FACT (the Foundation for Accreditation of Cellular Therapies), a national accrediting organization for hematopoietic cell transplantation and is expected to perform approximately 100 transplants per year. As a tertiary referral center, HMC receives patients from Pennsylvania and surrounding states. All patients scheduled for any type of transplantation were considered for inclusion in the study, regardless of disease diagnosis, disease prognosis, or donor status.

Stanford University Hospital and Clinic is a 613-bed hospital associated with the Stanford Cancer Center, a National Cancer Institute Designated Cancer Center, and the Stanford University School of Medicine. Serving northern California, the organization has performed more than 200 autologous and allogeneic transplants yearly. Founded in 1987, the program has performed more than 3,100 adult transplants of all cell types. The program is a fully accredited participating center in the National Bone Marrow Donor Program as well as FACT accredited, and is an active basic research and clinical trial program.

All individuals who met the eligibility criteria were considered eligible for participation in this study. Individuals were first informed of the study by employees of

the organizations, and once permission was obtained from the subjects, their names were forwarded to the primary investigator (PI) by the respective staff. The primary investigator confirmed that all potential participants (HMC and SUH) met criteria before data collection was initiated.

Human Subjects Protection

The study was reviewed and approved by The Pennsylvania State University Office for Research Protection and the Hershey Medical Center IRB in 2004, and the Stanford University Hospital IRB in 2007. Yearly updates on the research procedures were completed for approval by the above entities (Appendix A). All study participants at both sites were given copies of their signed consents (Appendix C). Following the data collection, the study materials were maintained in a secured locked cabinet in a locked room for a minimum of three years. Coded information on the participants' identities was kept in a locked secure cabinet in the PI's residence and was destroyed one year after data were analyzed.

Others were permitted to participate in the caregiving process, but only the main caregiver as identified by the patient could participate in the study. Both members of the patient-caregiver dyad had to agree to participate for the dyad to be included in the study. Persons were deemed ineligible to participate if they were under the age of 18, unable to read or write English, or had a diagnosis of cognitive limitations.

Once the patients and caregivers gave their verbal permission to have their names and phone numbers given to the PI, this information was written on an identified document, which was made available in a secure area of the physicians' work room at

Hershey Medical Center. The names and contact information of these potentially eligible participants were checked three times a week by the PI, who called the patients and caregivers and met with them at the clinic to provide further information about the study and ask if they were willing to participate. The potential subjects had an opportunity to view the survey forms and ask questions. After the PI was assured that the patients and caregivers understood the expectations of their participation and all their questions and concerns were addressed, written informed consent was obtained from each individual. A copy of the signed consent form was given to the patient and caregiver, and the originals were retained by the PI.

For recruitment at Stanford University Hospital, all new HSCT patients were reviewed by the clinical nurse specialist (the co-investigator) for potential participation in the study. Eligible patient-caregiver dyads were given information about the study, and if interested, they were provided necessary information for informed consent. All materials and consents were kept in a locked file in the clinical nurse specialist's office.

Risks to the Participants

There was little or no risk to patients or caregivers in this study other than some possible emotional discomfort. Arrangements were made to refer any study participant to the staff of the appropriate program for counseling at each site if needed during the study.

Data Collection Procedures

Approximately one week prior to the acute transplant phase, all baseline survey data were completed by the patient and caregiver, including a brief demographic information sheet. The patients were asked to complete a series of surveys at four

different phases during the HSCT. The following procedures were used at both medical centers at different times, at HMC from 2004 to 2008 and at SUH from 2007 to 2008:

1a.) Recruitment and informed consent: Consent was obtained from the caregivers and the HSCT recipients by the principal investigator or the co-investigator after recruitment.

1b.) Pre-transplant: The caregiver was asked to complete the demographic information and the following 5 surveys: the Zarit Burden Interview (ZBI), the Brief Pain Inventory (BFI), the Brief Fatigue Inventory (BFI), and the Memorial Symptom Assessment Sheet (MSAS) plus the Mishel Uncertainty in Illness Scale (MUIS). The HSCT patients were asked to complete the 3 surveys, the BPI, BFI, and MSAS.

2.) Immediate post-transplant: The caregivers completed the same 5 surveys. The HSCT recipients were asked to complete the same 3 surveys.

3.) One week post discharge: The caregivers completed the same 5 surveys. The HSCT recipients were asked to complete the same 3 surveys.

4.) One month post discharge: The caregivers completed the 5 surveys. The HSCT patients were asked to complete the 3 surveys.

A summary of the data collection process itself is provided in Table 3.1.

Table 3.1

Data Collection Process

Sessions With the Participants	Caregivers	Patients	Comments
Baseline Data: Approximately one week prior to transplant	ZBI MUIS BPI BFI MSAS Demographic information	BPI BFI MSAS	Administered prior to any preparatory regimens directly related to transplant.
Time 2: Immediately post transplant	ZBI MUIS BPI BFI MSAS	BPI BFI MSAS	Administered within three days of infusion of bone marrow or stem cells.
Time 3: One week post discharge from acute transplant setting	ZBI MUIS BPI BFI MSAS	BPI BFI MSAS	Administered within three to seven days post discharge from acute transplant setting. Acute transplant setting includes inpatient hospitalization or intensive outpatient treatment, greater than three days per seven.
Time 4. One month post discharge from acute transplant setting	ZBI MUIS BPI BFI MSAS	BPI BFI MSAS	To be administered within three days of one month post discharge from acute transplant setting or three weeks from time three.

The data collection for the study took approximately 4 to 6 weeks for each dyad, from the beginning of the acute transplant experience to one month after the patient was discharged from the hospital. The sessions with the participants included one for consent purposes and four for data collection. The caregivers completed the 5 surveys within 30 minutes each time. The HSCT recipients completed the 3 surveys within 15 minutes each time. All data collection was completed at regularly scheduled appointments by the

principal investigator or co-investigator or via mail. The participants were not expected or requested to travel additional distances to the hospital setting for the data collection.

Limitations and Threats to Validity

Threats to validity represented potential limitations to this study. These could be divided into internal, external, and theoretical threats to validity. Shadish, Cook, and Campbell (2002) refer to the repeated measures design as a time series where a number of observations are made of the same variables over time (p. 172). These authors refer to the interrupted time series as a strong quasi-experimental design when randomization is not an alternative. Certainly in the HSCT population, randomization is not a feasible option since this is an intensive treatment for a potentially fatal disease, cancer. Withholding treatment to study caregiver issues is ethically not an option.

A major threat to internal validity was the participants' personal history. Shadish et al. (2002) refer to this as the potential that something other than the intervention caused a particular response. For example, in the case of the HSCT patient, it is possible that marital discord may have been put on hold until the life-threatening transplant was completed. Unfortunately, the public's perception of when the transplant is complete is at the infusion of marrow, whereas the potentially negative impact of the transplant may continue for months or years. In addition to marital issues, there may have been underlying, brewing interpersonal issues that may have affected the scoring of any of the surveys. Another scenario is that there may have been previous interpersonal conflicts that could have affected the scoring on the surveys.

Another threat to internal validity was in the use of the instrumentation (Shadish et al., 2002, p. 179). Changes in how records are kept or procedures are followed in the administration of the surveys can result in significant fluctuations that do not relate to the participants' perceptions. This was a concern in deciding to use two separate sites, HMC and SUH, for the surveys. To minimize this threat, the procedures for the study were established prior to the study and maintained throughout the entire course of data collection through close collaboration with a PI-trained Co-PI at SUH.

Sample selection was also a potential threat to internal validity, referred to as a potential change in the eligible candidates for entry into the study. In the case of this study, the eligibility of all patients who would undergo transplant may appear to have addressed this issue; however, an overrepresentation of one type of transplant might have occurred which could change the caregiver responsibilities. The length of the pre-existing disease or previous number of transplants could also affect the energy reserve of the caregiver. This could change the survey results in an unpredictable direction. The eligibility for the study might need to change if the caregivers changed over the course of treatment and recovery. One of the assumptions of this study was that following the same patient-caregiver dyad throughout the acute transplant experience would help control sampling selection threats. One of the areas of concern in this category, however, was the risk of a selection bias on the part of the hospital staff that first screened the individuals. It was observed that the hospital staff were identifying dyads who were deemed to be successful in compliance and adherence. Unfortunately, not all dyads had this degree of

cooperation; therefore, some were not offered the opportunity to participate in the study, possibly under-representing certain populations and instrument scores.

Statistical conclusion validity represents threats in the following areas: low power, violated test assumptions, and unreliability of measurements (Shadish et al., 2002, p. 180). Low power is reflected in inadequate numbers of subjects recruited to support the conclusions as significant versus chance occurrence. The power criteria were met for this study. However, loss of subjects for repeated measures was an identified limitation. The test assumptions respected the criteria used in the development of the tools. In the case of this study, particular attention was paid to the test assumptions of the uncertainty tool (MUIS), which had been used in adult patients, but not with adult caregivers. It has been used in parents of ill children, but the sensitivity to the adult caregiver has not been demonstrated. It does assist in the use of the tool to perceive the adult caregiver as a patient of a sort also, which is affected by the lack of certainty in the treatment and prognosis of their loved one.

Shadish et al. (2002, p. 180) noted that the use of a clinical time series raises special construct validity threats related to reactivity. This is particularly pertinent when the time to repeat surveys is short as the respondents can remember their previous answers. However, it is vital that the subjects be given clear instructions to answer the questions as they relate to the current period, not the previous periods. It was also important that the patient and caregiver not collaborate on their answers. This was made clear during the instructions to the dyads, which were repeated at each session in order to minimize threats to tool validity.

Another limitation was the attrition of the subjects over the time of the study. This might be due to death, incapacity, or sheer exhaustion of either the caregiver or the patient. This would be an important variable in reviewing the results. Another limitation was the use of two facilities for the study populations. However, the participation samples from each site were very similar in characteristics which are summarized in Chapter 4.

Further limitations related to the measurement tools. One potential limitation was that they might not be sufficiently sensitive to changes in a short period of time. In choosing the various tools to represent the given concepts, particular attention was paid to the length of time that would be required to complete the task. Knowing that this might be a busy time physically and emotionally for the caregivers and patients, the investigator did not want the length of the instruments to discourage their agreement to participate in and complete the study. A second potential limitation relating to the instruments was that the Uncertainty in Illness Scale (MUIS) had been used with patients and parents of young children but not with caregivers of adults. The focus of Mishel's work has been the uncertainty experienced by patients as they go through the illness. The adaptation of the MUIS for caregivers in this current study was approved by Mishel, who has since created a version of the MUIS for assessment of uncertainty in caregivers. Since the focus of this research study on the uncertainty experienced by the HSCT caregiver as their loved one goes through treatment for their illness, this study extends knowledge of uncertainty in illness in the caregiver population.

Data Analysis

Data were entered into individual Excel spread sheets, which were stored in a password-protected file on a computer in the office of the principal investigator. Data were analyzed by the PI with the assistance of the staff of the Department of Public Health Sciences (PHS), College of Medicine, at The Pennsylvania State University. This staff is highly experienced in data analysis. The PHS staff has been responsible for the data analysis of two large, multi-center clinical trials on asthma as well as multiple individual projects for faculty, staff, and students. The analysis for this study included both descriptive and inferential statistics. Specifically, these were measures of central tendency such as mean, mode, and median frequency tables (Pagano, 2001). These data allowed for comparison of subgroups for similarities and differences.

These data were also used to determine the distribution of the data. The data were additionally used to determine variability via standard deviations and ranges. These calculations supported further data analysis using inferential statistics.

The data were summarized on Excel spread sheets and then transformed into data that could be utilized by SAS (Statistical Analysis Software). General descriptive statistics were generated to describe how many subjects' data were included in each data point analysis. Demographic information was generated regarding the population of caregivers and patients. Repeated measurements analysis of covariance (ANCOVA) were conducted on data for each of the following: caregiver burden (ZBI), uncertainty (MUIS), patient symptomatology (BPI, BFI, MSAS). Subscales for ZBI, personal strain and role strain, subscores for uncertainty (MUIS), unpredictability, ambiguity, complexity, and

inconsistency were also analyzed. Scores were compared across visits for changes, using inferential statistics. The covariants included in the repeated measurements ANCOVA were caregiver gender, site, time since cancer diagnosis, and caregiver employment category. Data were compared between patient and caregiver scores for pain, fatigue, and MSAS, and inferential statistics were used to determine statistically significant differences in scores (perceptions of symptoms) occurring at each interview over time.

Chapter Summary

This chapter has described the procedures used to measure and evaluate differences in caregiver and patient scores over the four measurement periods during the acute HSCT experience. The findings of the data analysis are reported in Chapter 4.

Chapter 4

RESULTS

The purpose of this chapter is to report the results of the study. The sample characteristics, demographics of the sample, and results according to caregiver burden, uncertainty, and patient symptomatology are presented. Finally, the findings are delineated in response to the research questions.

The Sample

The data for this study were collected at two university hospital settings with active HSCT programs, one in the mid-Atlantic area and the other on the West Coast. The sample of 46 patient-caregiver dyads included 29 (63%) who were recruited at the Milton S. Hershey Medical Center and 17 (37%) who were recruited from the Stanford University Hospital.

In total, 51 patient-caregiver dyads agreed to participate in the study at one of the two data collection sites. Of these, 46 completed usable data or at least one set of data during the study. Of the 46 caregivers, 17 (37%) were male and 29 (63%) were female. Table 4.1 compares the study participants from each site.

Table 4.1

Descriptive Data for the Sample

Subjects	Hershey Medical Center (HMC)	Stanford University Hospital (SUH)	Total
Male Caregivers	12 (26% of total dyads)	5 (11% of total dyads)	17 (37%)
Female Caregivers	17 (37% of total dyads)	12 (26% of total dyads)	29 (63%)
Allogeneic Transplant	12 (28% of all transplants)	11 (24% of all transplants)	23 (50%)
Autologous Transplants	17 (34.7%)	6 (13%)	23 (50%)
Total Transplants	29 (63%)	17 (37%)	46

Caregivers' Demographics

The data on the caregivers were analyzed by age and gender according to transplant type (autologous caregivers and allogeneic caregivers) as well as by treatment site. The average age of all of the caregivers at both sites was 52, with caregivers for autologous and allogeneic transplant patients ages being an average of 50 and 54, respectively. There were more female caregivers for both types of transplants.

The majority of the caregivers at HMC (89%) and SUH (88%) were Caucasian. The caregivers at HMC also included 2 Hispanics and 1 African American with SUH caregivers including 1 Japanese and 1 Korean. The majority of the caregivers were spouses (82% at HMC and 100% at SUH). The remainder of the caregivers at HMC were parents (2) and others (4). Eighteen or 40% of the caregivers reported income over

$60,000 per year. The number of caregivers earning more than $60,000 per year was greater at SUH than at HMC. However, the analysis of covariance, which was controlled for income, showed no statistically significant difference in the income ranges between the two data collection sites.

The majority (54%) of the caregivers worked outside of the home with 6 retired and 9 unemployed. The majority (58%) of the caregivers worked full time (36 to 40 hours per week). The majority of the caregivers worked outside the home and had work-related responsibilities in addition to providing care for the HSCT patient.

Many patient-caregiver dyads lived alone (41%), but 27% had adult children living with them, or young children (22%). Only one caregiver had parents living in the household. This result suggests additional pre-existing responsibilities for the caregiver in some families.

Patients' Demographics

The majority of the transplant patients were male (54.4%) and Caucasian (99%). Approximately half (52%) of the patients were employed. The average age of all of the patients was 52, with the autologous patients ranging in age from 27 to 72 and the allogeneic patients ranging from 40 to 68. The number of transplant types was equally split with 23 or 50% of the patients receiving autologous transplants and 23 or 50% receiving allogeneic transplants.

The diagnoses of the patients reporting included non-Hodgkin's lymphoma (24%), acute lymphoblastic leukemia (20%), multiple myeloma (17%), Hodgkin's disease (11%), myelodysplatic syndrome (6.5%), acute myeloblastic leukemia (6.5%),

and chronic lymphocytic leukemia (4%). These frequencies are not representative of those reported by the American Cancer Society as their data represent the accrual of active clinical trials and the distribution of health insurance approvals in a geographic area.

The time since these patients' cancer diagnoses varied widely, with 30% diagnosed between 6 weeks and 6 months, 46% diagnosed between 6 months and 2 years, and 24% diagnosed more than 2 years before the transplant. However, according to an analysis of covariance (ANCOVA), the time since diagnosis was not a significant covariant.

Differences Between Sample Characteristics by Site

A comparison of patient and caregivers at the two data collection sites was conducted to determine if there were any significant differences in caregiver gender, age, caregiver income, and time since the patient's cancer diagnosis. Comparisons between the characteristics of the caregivers and patients by site determined that they were quite similar except for a higher percentage of allogeneic patients at HMC than at SUH as shown in Table 4.1.

Analysis of Caregiver Burden, Uncertainty, and Patient Symptomatology

This section reports the results on caregiver burden, caregiver uncertainty, and patient symptomatology, with accompanying tables that present the results of the analysis of the data from of the measures used in the study.

Caregiver Burden

Descriptive statistics for the scores for the Zarit Burden Interview data can be found in Appendix D. An analysis of total caregiver burden over time, using an ANCOVA, was conducted on the ZBI data. The analysis revealed a significant difference in scores between Interviews 1 and 2 (p = .07) and Interviews 1 and 3 (p = .03) for the combined group of caregivers (Table 4.2). There were no significant differences in burden across time for the caregivers of the autologous HSCT patients. For the caregivers of the allogeneic HSCT patients, however, there was only a marginally significant difference from Interview 1 to 2 (p = .08), reinforcing the finding that burden is high for caregivers of allogeneic patients at the time of transplant.

Table 4.2

ANCOVA Repeated Measures Analysis of the Burden Subscale Scores for the Combined Caregiver Group

Relationship	Estimate	Standard Error	DF	Value	p Value
Interview 1 vs Interview 2	-1.1663	0.64	0	1.81	0.07*
Interview 1 vs Interview 3	-2.0114	0.89	0	2.25	0.03**
Interview 1 vs Interview 4	-1.5298	1.08	0	1.42	0.16
Interview 2 vs Interview 3	-0.8451	0.71	0	1.19	0.24
Interview 2 vs Interview 4	-0.3636	0.97	0	0.37	0.71
Interview 3 vs Interview 4	0.4815	0.75	0	0.64	0.52

***p < .010, **p < .05, *p < .10

The two subscales of the ZBI tool, personal strain and role strain, were also examined using ANCOVA. For the combined caregiver group, there was a marginally significant decrease in personal strain from Interview 1 to 2 (p = .069) and a statistically

significant decrease from Interview 1 to 3 (p = .025), as reported in Table 4.3. However, personal strain only revealed a significant decrease from Interview 1 to 3 for the autologous patients (p = .08), and no significant decrease for personal strain in the allogeneic caregiver group.

Table 4.3

ANCOVA Repeated Measures Analysis of the Personal Strain Subscale Scores for the Combined Caregiver Group

Relationship	Estimate	Standard Error	DF	t Value	p Value
Interview 1 vs Interview 2	-1.1663	0.6447	0	-1.81	*0.07
Interview 1 vs Interview 3	-2.0114	0.8932	0	-2.25	**0.02
Interview 1 vs Interview 4	-1.5298	1.0774	0	-1.42	0.15
Interview 2 vs Interview 3	-0.8451	0.7117	0	-1.19	0.24
Interview 2 vs Interview 4	-0.3636	0.971	0	-0.37	0.71
Interview 3 vs Interview 4	0.4815	0.7492	0	0.64	0.52

***p < .010, **p < .05, *p < .10

Analysis of the ZBI subscale of role strain revealed no significant differences between any of the interviews for any of the three groups. The ANCOVA of the ZBI subscore for role strain showed no statistically significant differences over time.

Caregiver Uncertainty

Descriptive statistics for the scores of the Mishel Uncertainty in Illness Scale data can be found in Appendix D. The combined group of caregivers revealed no significant change over time. There were varied changes in uncertainty as measured by the MUIS, depending on the type of transplant performed. An analysis of the caregivers of the

autologous transplant recipients revealed a decrease over time on the total uncertainty measure, with the change from the first interview to the subsequent second, third, and fourth interviews found to be statistically significant (Table 4.4). The caregivers of the allogeneic HSCT patients were found to have a marginally significant increase in total uncertainty from Interview 1 to 2 (p = .059), and a statistically significant increase from Interview 1 to 3 (p = .045) (Table 4.5).

Table 4.4

ANCOVA Repeated Measures Analysis of the Total Uncertainty Subscale Scores for the Caregivers of the Autologous HSCT Patients

Relationship	Estimate	Standard Error	DF	t Value	p Value
Interview 1 vs Interview 2	-8.4434	3.8455	1	-2.20	**0.03
Interview 1 vs Interview 3	-10.3672	4.8524	1	-2.14	**0.03
Interview 1 vs Interview 4	-11.4794	5.3984	1	-2.13	**0.04
Interview 2 vs Interview 3	-1.9238	4.0039	1	-0.48	0.63
Interview 2 vs Interview 4	-3.0360	5.0553	1	-0.60	0.55
Interview 3 vs Interview 4	-1.1122	3.9583	1	-0.28	0.78

***p < .010, **p < .05, *p < .10

Table 4.5

ANCOVA Repeated Measures Analysis of the Total Uncertainty Subscale Scores for the Caregivers of the Allogeneic HSCT Patients

Relationship	Estimate	Standard Error	DF	t Value	p Value
Interview 1 vs Interview 2	3.1381	1.6339	3	1.92	*0.06
Interview 1 vs Interview 3	4.9623	2.3771	3	2.09	**0.04
Interview 1 vs Interview 4	4.0886	3.0092	3	1.36	0.18
Interview 2 vs Interview 3	1.8242	1.9192	3	0.95	0.35
Interview 2 vs Interview 4	0.9506	2.7302	3	0.35	0.73
Interview 3 vs Interview 4	-0.8737	2.1159	3	-0.41	0.68

***p < .010, **p < .05, *p < .10

The four factor subscales validated to be contained within uncertainty (Mishel, 1997) that are measured by Mishel's tool include inconsistency, ambiguity, unpredictability, and complexity. Inconsistency refers to information changing frequently or not being in accord with previous information given. Ambiguity refers to cues about the state of the illness being vague and indistinct (Mishel). Unpredictability refers to a lack of contingency between the illness and treatment cures and illness outcomes (Mishel). Complexity refers to situations where cues about treatment and the system of care are multiple and varied (Mishel). These factors were defined in Chapter 3.

An analysis of the combined caregiver group revealed that the scores in the inconsistency subscale decreased significantly from Interview 1 to 2 ($p = .03$), and comparing the results for the interviews of the caregivers of the autologous patients (Table 4.6), the inconsistency scores decreased from Interview 1 to 2 ($p = 0.05$) and decreased marginally from Interview 1 to 4 ($p = 0.75$). However, there was no change in

the inconsistency scores across the interviews for the caregivers of the allogeneic patients.

Table 4.6

ANCOVA Repeated Measures Analysis of the Inconsistency Subscale Scores for the Caregivers of the Autologous HSCT Patients

Relationship	Estimate	Standard Error	DF	t Value	p Value
Interview 1 vs Interview 2	-2.3013	1.1383	1	-2.02	*0.05
Interview 1 vs Interview 3	-2.0662	1.4059	1	-1.47	0.15
Interview 1 vs Interview 4	-2.7886	1.5390	1	-1.81	*0.08
Interview 2 vs Interview 3	0.2352	1.1891	1	0.20	0.84
Interview 2 vs Interview 4	-0.4872	1.4733	1	-0.33	0.74

***p < .010, **p < .05, *p < .10

For the subscale of ambiguity, there were no significant changes in the scores between the interviews for the combined caregiver group. However, there were statistically significant decreases in the ambiguity subscale scores for the caregivers of the autologous patients (Table 4.7) from Interview 1 to 2 (p = .010), Interview 1 to 3 (p = .012), and Interview 1 to 4 (p = .040). An analysis of the caregivers of the allogeneic patients (Table 4.8) revealed that there was a marginally significant increase in the ambiguity subscale score from Interview 1 to 2 (p = .070).

Table 4.7

ANCOVA Repeated Measures Analysis of the Ambiguity Subscale Scores for the Caregivers of the Autologous HSCT Patients

Relationship	Estimate	Standard Error	DF	t Value	p Value
Interview 1 vs Interview 2	-5.3163	2.0442	1	-2.60	**0.01
Interview 1 vs Interview 3	-6.5313	2.5408	1	-2.57	**0.01
Interview 1 vs Interview 4	-5.7880	2.7942	1	-2.07	**0.04
Interview 2 vs Interview 3	-1.2150	2.1333	1	-0.57	0.57
Interview 2 vs Interview 4	-0.4717	2.6579	1	-0.18	0.86
Interview 3 vs Interview 4	0.7433	2.1111	1	0.35	0.72

***p < .010, **p < .05, *p < .1

Table 4.8

ANCOVA Repeated Measures Analysis of the Ambiguity Subscale Scores for the Caregivers of the Allogeneic HSCT Patients

Relationship	Estimate	Standard Error	DF	t Value	p Value
Interview 1 vs Interview 2	2.1856	1.1887	4	1.84	*0.07
Interview 1 vs Interview 3	2.8322	1.6822	4	1.68	0.10
Interview 1 vs Interview 4	1.6797	2.0709	4	0.81	0.42
Interview 2 vs Interview 3	0.6466	1.3776	4	0.47	0.64
Interview 2 vs Interview 4	-0.5059	1.9106	4	-0.26	0.79
Interview 3 vs Interview 4	-1.1525	1.5515	4	-0.74	0.46

***p < .010, **p < .05, *p < .10

In Mishel's subscale of unpredictability, no significant changes were revealed over time in the combined caregiver group. There was a marginally significant decrease in the unpredictability measure from Interview 1 to 4 (p = .06) for the caregivers of the autologous patients and in the allogeneic caregiver group (p = .09).

There was a minimally significant increase for the caregivers of the allogeneic patients in complexity ($p = .097$). There were no statistically significant changes in the scores for complexity for the combined group of caregivers or the caregivers of the autologous patients over time.

Data were available to compare the results of this study with those of previous work by Mishel. Researchers who use the Mishel Uncertainty in Illness Scale (MUIS) are required to submit data for the development of comparisons. The scores on the MUIS and subscales (Table 4.9) are consistent with previous data (Mishel, 1998). Results from each interview for the three types of caregiver groups: allogeneic, autologous, and combined are provided. For comparison, Mishel's scores for cancer ($N = 761$) and chronic illness ($N = 659$) are also listed. Scores in total uncertainty for the current study are generally higher or similar to Mishel's total uncertainty scores for cancer patients, with some variation related to point in time and the type of transplant. Compared with the chronic illness scores in Mishel's database for cancer, the scores for the autologous and combined caregiver groups in this study are higher. The scores from this study, however, are not markedly different from those in Mishel's database.

The most variance in total uncertainty in the current study was found for the group of caregivers of autologous patients in Interview 2 (SD 20.86) and Interview 4 (SD 20.8). The caregivers of the allogeneic HSCT patients showed less variance with a standard deviation between 9.4 and 14.11. The standard deviation of the caregivers of the allogeneic patients is close to those of Mishel's cancer (16.9) and chronic illness (15.6) database. These finding suggest that uncertainty for autologous caregivers in this study

varied more and may be a more pertinent issue in some types of transplant care than in others, supporting individualize assessment of needs in transplant populations.

Table 4.9

Comparison of the Interview Scores for the Caregivers at Each Interview With Mishel's Data (MUIS Adult Form, 1997)

Measures on the MUIS Tool	Combined Caregiver Group	Caregivers of the Autologous Transplants	Caregivers of the Allogeneic Transplants	Mishel's Database Cancer N = 761 (SD)	Mishel's Database Chronic Illness N = 659 (SD)
Total Uncertainty	Interview 1: 84.20 Interview 2: 81.69 Interview 3: 82.38 Interview 4: 79.37	Interview 1: 87.59 Interview 2: 80.4 Interview 3: 77.46 Interview 4: 76.26	Interview 1: 80.8 Interview 2: 82.9 Interview 3: 87 Interview 4: 83.2	79.5 (16.9)	84.2 (15.6)
Inconsistency	Interview 1: 15.34 Interview 2: 13.86 Interview 3: 14.54 Interview 4: 14.03	Interview 1: 16.9 Interview 2: 15 Interview 3: 14.93 Interview 4: 14.13	Interview 1:19.77 Interview 2: 13.1 Interview 3: 14.1 Interview 4:13.91	14.9 (4.7)	15.5 (5.0)
Ambiguity	Interview 1: 37.38 Interview 2: 36.13 Interview 3: 36.04 Interview 4: 34.81	Interview 1: 38.68 Interview 2: 33.73 Interview 3: 32.2 Interview 4: 32.93	Interview 1:36.09 Interview 2:37.9 Interview 3:39.68 Interview 4:37.16	32.3 (9.3)	36 (9.1)
Unpredictability	Interview 1: 16.38 Interview 2: 16.69 Interview 3: 16.16 Interview 4: 15.81	Interview 1: 17.13 Interview 2: 17.06 Interview 3: 15.86 Interview 4: 15.20	Interview 1: 15.6 Interview 2:16.45 Interview 3:16.43 Interview 4:16.58	15.8 (3.7)	16 (4.1)
Complexity	Interview 1: 15.04 Interview 2: 15.16 Interview 3: 15.61 Interview 4: 14.70	Interview 1: 14.86 Interview 2: 14.6 Interview 3: 14.46 Interview 4: 14.0	Interview 1: 5.21 Interview 2: 15.6 Interview 3: 16.6 Interview 4:15.58	16.5 (5.0)	16.6 (5.0)

Patient Symptomatology

Descriptive statistics for patient symptom pattern scores for the BPI, BFI, and MSAS as perceived by both caregivers and patients can be found in Appendix D. Physical and psychological symptoms are a major part of the transplant experience for the patient and were therefore expected to also have some impact on the caregivers' view

of the transplant experience. The degree of the agreement of the caregivers' assessment of the patient's symptoms with that of the patient is important if the patient is unable to verbalize the problems. Pain is a frequent symptom which can be a side effect of HSCT treatment or a warning of new complications. Pain was measured by the score on the Brief Pain Inventory (BPI) (Cleeland & Ryan, 1989). Fatigue is acknowledged as the most frequent symptom experienced by patients with cancer. Fatigue was measured by the scores on the Brief Fatigue Inventory (BFI) (Mendoza, 1999).

The HSCT patient may experience other physical and psychological symptoms. The Memorial Symptom Assessment Scale (Portenoy et al., 1994), which measures multiple symptoms, was used to determine an over-all degree of symptoms, taking into consideration the frequency, severity, and intensity of the patient's symptoms. Subscale scores were determined by factor analysis to represent specific areas of concern, which included a global distress score, psychological score, and physical symptoms. The global distress score represents the symptoms that occur more frequently. The physical symptom score represents symptoms that are less frequent but still bothersome. The psychological score represents the items that have a strong psychological component.

The BPI scores were compared in order to test for significant differences in caregiver and patient perceptions of pain, using an ANCOVA to identify statistically significant differences between the patients and the caregivers at Interview 1 ($p = 0.03$) in the combined caregiver group (Table 4.10). In the caregivers of the allogeneic patients, there were minimally significant differences between Interview 1 and 3 ($p = .075$) and 1 to 4 ($p = .063$). There were no significant differences between the patients' and

caregivers' perceptions of pain in the autologous population (Table 4.11). In the allogeneic population (Table 4.12) there were minimally significant differences between the patients and caregivers at Interview 1 (p = .054), Interview 2 (p = .078), and Interview 4 (p = .059), with the patients' perceptions of pain being lower than the caregivers'.

The results of the ANCOVA of caregiver and patient scores on the BPI (perception of pain) are listed in Tables 4.10, 4.11, and 4.12.

Table 4.10

ANCOVA Repeated Measures Analysis of the Pain Subscale Scores for Patients and Caregivers in the Combined Caregiver Group

Relationship	Estimate	Standard Error	DF	t Value	p Value
Patient vs Caregiver at Interview 1	7.4146	3.2564	21	2.28	**0.03
Patient vs Caregiver at Interview 2	2.8439	3.5576	21	0.80	0.42
Patient vs Caregiver at Interview 3	0.3233	3.8418	21	0.08	0.93
Patient vs Caregiver at Interview 4	3.5992	4.2635	21	0.84	0.39

***p < .010, **p < .05, *p < .10

Table 4.11

ANCOVA Repeated Measures Analysis of the Pain Subscale Scores for the Patients and Caregivers in the Autologous Group

Relationship	Estimate	Standard Error	DF	t Value	p Value
Patient vs Caregiver at Interview 1	6.9411	5.0623	01	1.37	0.17
Patient vs Caregiver at Interview 2	-3.6447	5.9198	01	-0.62	0.54
Patient vs Caregiver at Interview 3	-7.0812	5.8158	01	-1.22	0.23
Patient vs Caregiver at Interview 4	-3.4863	6.3881	01	-0.55	0.59

***p < .010, **p < .05, *p < .10

Table 4.12

ANCOVA Repeated Measures Analysis of the Pain Subscale Scores for the Patients and Caregivers in the Allogeneic Group

Relationship	Estimate	Standard Error	DF	t Value	p Value
Patient vs Caregiver at Interview 1	7.9130	4.0492	12	1.95	*0.05
Patient vs Caregiver at Interview 2	7.4041	4.2124	12	1.76	*0.08
Patient vs Caregiver at Interview 3	6.8747	4.9102	12	1.40	0.16
Patient vs Caregiver at Interview 4	10.5034	5.5340	12	1.90	*0.06

***p < .010, **p < .05, *p < .10

A comparison of the patients' and caregivers' assessments of fatigue in the combined caregiver group (Table 4.13) revealed that there were statistically significant differences in the perceptions of the patients and caregivers at Interview 1 (p = .027) and at Interview 2 (p = .015). A similar difference was found between the allogeneic group (Table 4.14) at Interview 1 (p = .017) and Interview 2 (p = .096), and a significant difference (p = .04) in the autologous group (Table 4.15), indicating that the variance in the combined caregiver group is primarily explained by the findings on the allogeneic

group in the pre-transplant phase and on the autologous group in the immediate post-transplant phase. An ANCOVA of the caregiver and patient scores on the BFI (perception of fatigue) are shown in Tables 4.13, 4.14 and 4.15.

Table 4.13

ANCOVA Repeated Measures Analysis of the Fatigue Subscale Scores for the Patients and Caregivers in the Combined Caregiver Group

Relationship	Estimate	Standard Error	DF	t Value	p Value|
Patient vs Caregiver at Interview 1	7.4053	3.2731	223	2.26	**0.03
Patient vs Caregiver at Interview 2	9.2323	3.6219	223	2.55	**0.01
Patient vs Caregiver at Interview 3	2.1211	3.8725	223	0.55	0.58
Patient vs Caregiver at Interview 4	0.3361	4.3238	223	0.08	0.94

***p < .010, **p < .05, *p < .10

Table 4.14

ANCOVA Repeated Measures Analysis of the Fatigue Subscale Scores for the Caregivers and Patients in the Allogeneic Group

Relationship	Estimate	Standard Error	DF	t Value	p Value
Patient vs Caregiver at Interview 1	9.8261	4.0927	13	2.40	**0.02
Patient vs Caregiver at Interview 2	7.1379	4.2643	13	1.67	0.10
Patient vs Caregiver at Interview 3	6.6071	4.8604	13	1.36	0.18
Patient vs Caregiver at Interview 4	5.9833	5.6136	13	1.07	0.29

***p < .010, **p < .05, *p < .10

Table 4.15

ANCOVA Repeated Measures Analysis of the Fatigue Subscale Scores for the Patients and Caregivers in the Autologous Group

Relationship	Estimate	Standard Error	DF	t Value	p Value
Patient vs Caregiver at Interview 1	4.6810	5.3285	02	0.88	0.38
Patient vs Caregiver at Interview 2	12.8490	6.3172	02	2.03	**0.04
Patient vs Caregiver at Interview 3	-2.3893	6.2790	02	-0.38	0.70
Patient vs Caregiver at Interview 4	-4.7881	6.7619	02	-0.71	0.48

***p < .010, **p < .05, *p < .10

For the MSAS global distress subscale scores, there was a statistically significant difference between the patients and the caregivers at Interview 1 (p = .032) in the combined caregiver group (Table 4.16), but there were no statistically significant differences in the autologous group. Analysis was stopped in the allogeneic group due to excessive findings.

Table 4.16

ANCOVA Repeated Measures Analysis of the MSAS Global Distress Subscale Scores for the Patients and Caregivers in the Combined Caregiver Group

Relationship	Estimate	Standard Error	DF	t Value	p Value
Patient vs Caregiver at Interview 1	0.2251	0.1049	22	2.15	**0.03
Patient vs Caregiver at Interview 2	-0.05413	0.1152	22	-0.47	0.64
Patient vs Caregiver at Interview 3	0.02257	0.1230	22	0.18	0.85
Patient vs Caregiver at Interview 4	-0.06506	0.1377	22	-0.47	0.63

***p < .010, **p < .05, *p < .10

For the MSAS psychological subscale scores there were statistically significant differences between patient and caregiver perceptions at Interview 1 for both the combined caregiver group (p = .006) (Table 4.17) and the allogeneic group (p = .003) (Table 4.18). There were no statistically significant differences in the perceptions of the autologous group (Table 4.19).

Table 4.17

ANCOVA Repeated Measures Analysis of the MSAS Psychological Subscale Scores for the Patients and Caregivers in the Combined Caregiver Group

Relationship	Estimate	Standard Error	DF	t Value	p Value
Patient vs Caregiver at Interview 1	0.3246	0.1183	222	.74	*0.01
Patient vs Caregiver at Interview 2	0.09278	0.1296	222	.72	0.48
Patient vs Caregiver at Interview 3	0.1411	0.1384	222	.02	0.31
Patient vs Caregiver at Interview 4	0.04136	0.1550	222	0.27	0.79

***p < .010, **p < .05, *p < .10

Table 4.18

ANCOVA Repeated Measures Analysis of the MSAS Psychological Subscale Scores for the Patients and Caregivers in the Allogeneic Group

Relationship	Estimate	Standard Error	DF	t Value	p Value
Patient vs Caregiver at Interview 1	0.4381	0.1481	13	2.96	***0.003
Patient vs Caregiver at Interview 2	0.1166	0.1540	13	0.76	0.45
Patient vs Caregiver at Interview 3	0.2498	0.1752	13	1.43	0.16
Patient vs Caregiver at Interview 4	0.1265	0.2024	13	0.63	0.53

***p < .010, **p < .05, *p < .10

There was a minimally significant difference for the autologous group (Table 4.19) at Interview 2 (p = .01). There were no other significant differences.

Table 4.19

ANCOVA Repeated Measures Analysis of the MSAS Physical Subscale Scores for the Patients and Caregivers in the Autologous Group

Relationship	Estimate	Standard Error	DF	t Value	p Value
Patient vs Caregiver at Interview 1	0.1017	0.1339	01	0.76	0.45
Patient vs Caregiver at Interview 2	-0.2581	0.1544	01	-1.67	*0.097
Patient vs Caregiver at Interview 3	-0.06999	0.1544	01	-0.45	0.65
Patient vs Caregiver at Interview 4	-0.2246	0.1669	01	-1.35	0.18

***p < .010, **p < .05, *p < .10

For the MSAS total, there was one minimally significant difference for the caregiver and patient scores for Interview 2 in the allogeneic patients (p = .066) (Table 4.20).

Table 4.20

ANCOVA Repeated Measures Analysis of the MSAS Total Scores for the Patients and Caregivers in the Allogeneic Group

Relationship	Estimate	Standard Error	DF	t Value	p Value
Patient vs Caregiver at Interview 1	0.05729	0.1280	108	0.45	0.66
Patient vs Caregiver at Interview 2	-0.2454	0.1325	108	-1.85	*0.07
Patient vs Caregiver at Interview 3	-0.1519	0.1481	108	-1.03	0.31
Patient vs Caregiver at Interview 4	-0.07061	0.1755	108	-0.40	0.69

***p < .010, **p < .05, *p < .10

Further analysis of the data was completed using Pearson Partial Correlation statistics to identify the relationships between the variables. Partial correlations were used

due to the statistical model for the ANCOVA, which accounts for some of the variance (Table 4.21). The variables used in the model included caregiver gender, time since patient diagnosis, site of data collection, and caregiver employment. Although some relationships approached significance (p = < .10), none met significance criteria for this study (p = <.05).

Table 4.21

Significant Covariants by Type of Transplant

Scores	Combined Caregiver Group	Caregivers of Autologous Patients	Caregivers of Allogeneic Patients
Burden			CG* p = .05*
Role Strain	CG p = .04**		CG p = .06*
Personal Strain			
Total Uncertainty			
Ambiguity			
Complexity			
Inconsistency		CG p = .08*	
Unpredictability		Site p = .09 *	

***p < .010, **p < .05, *p < .10, p > .10 NS (not reported)
CG = Caregiver Gender; Site = HMC & SUH

For the patients of the combined caregiver group, there was a mix of moderate to poor correlations between caregiver burden and the subscore scales with the measurements of patient symptomatology (Table 4.22).

Table 4.22

Pearson Partial Correlation* Tables for Caregiver Burden and Caregiver Perceptions of Patient Symptomatology for the Combined Caregiver Group

Measurement	Personal Strain	Role Strain	Total Strain / Burden
BPI	0.38*	0.34*	0.39*
BFI	0.31*	0.35*	0.33*
MSAS Global Distress	0.41**	0.48**	0.479**
MSAS Psychological	0.46**	0.51**	0.51**
MSAS Physical	0.33*	0.42**	0.39*
MSAS Total	0.33*	0.44**	0.40*

Partial Correlation Coefficient (r): *Low = < .4; **Moderate = > .4 to .7; ***High = > .7

For the caregivers of the autologous patients, there was an overall moderate correlation between burden and measurements of patient symptomatology (Table 4.23).

Table 4.23

Pearson Partial Correlation Tables for Caregiver Burden and Caregiver Perceptions of Patient Symptomatology for the Caregivers of the Autologous Group

Measurement	Personal Strain	Role Strain	Total Strain/ Burden
BPI	0.53**	0.54**	0.56**
BFI	0.48**	0.51**	0.48**
MSAS Global Distress	0.59**	0.67**	0.66**
MSAS Psychological	0.62**	0.66**	0.67**
MSAS Physical	0.55**	0.66**	0.61**
MSAS Total	0.52**	0.61**	0.60**

Partial Correlation Coefficient (r): *Low = < .4; **Moderate = > .4 to .7; ***High = > .7

For the caregivers of the allogeneic patients, there was an overall poor correlation between caregiver burden and the subscore scales for the measurements of patient symptomatology (Table 4.24).

Table 4.24

Pearson Partial Correlation Tables for Caregiver Burden and Caregiver Perceptions of Patient Symptomatology for the Caregivers of the Allogeneic Group

Measurement	Personal Strain	Role Strain	Total Strain / Burden
BPI	*0.13	*0.03	*0.08
BFI	*0.001	*0.13	*0.06
MSAS Global Distress	*0.003	*0.12	*0.06
MSAS Psychological	*0.09	*0.26	*0.15
MSAS Physical	*-0.08	*0.04	*-0.02
MSAS Total	*-0.04	*0.16	*-0.02

Partial Correlation Coefficient (r): *Low = < .4; **Moderate = > .4 to .7; ***High = > .7

For the combined caregiver group there was an overall poor correlation with the patient symptomatology measurements and uncertainty and any of the subscales (Table 4.25).

Table 4.25

Pearson Partial Correlation Tables for Caregiver Uncertainty and Caregiver Perceptions of Patient Symptomatology for the Combined Caregiver Group

Measurement	Total Uncertainty	Ambiguity	Complexity	Inconsistency	Unpredictability
BPI	*0.36	**0.41	*0.08	*0.30	*0.13
BFI	*0.23	*0.31	*0.04	*0.08	*0.14
MSAS Global Distress	*0.33	**0.42	*0.10	*0.22	*0.06
MSAS Psychological	*0.34	**0.43	*0.12	*0.26	*-0.03
MSAS Physical	*0.26	*0.34	*0.05	*0.09	*0.16
MSAS Total	*0.26	*0.36	*-0.01	*0.25	*-0.03

Partial Correlation Coefficient (r): *Low = < .4; **Moderate = > .4 to .7; ***High = > .7

For the caregivers of the autologous patients there was a wide range of correlation scores, ranging from .55 and .57 for the MSAS and total uncertainty, respectively, and .57 for ambiguity and MSAS psychological, respectively, to .1 or lower for all of the symptom measurements with unpredictability (Table 4.26).

Table 4.26

Pearson Partial Correlation Tables for Caregiver Uncertainty and Caregiver Perceptions of Patient Symptomatology for the Caregivers of the Autologous Group

Measurement	Total Uncertainty	Ambiguity	Complexity	Inconsistency	Unpredictability
BPI	**0.47	**0.54	*0.27	*0.40	*0.11
BFI	*0.34	**0.434	*0.18	*0.22	*0.08
MSAS Global Distress	**0.47	**0.574	*0.31	*0.38	*-0.00
MSAS Psychological	**0.50	**0.574	*0.35	**0.43	*-0.02
MSAS Physical	*0.35	**0.464	*0.17	*0.21	*0.05
MSAS Total	*0.43	**0.554	*0.18	*0.34	*0.02

Partial Correlation Coefficient (r): *Low = < .4; **Moderate = > .4 to .7; ***High = > .7

For the caregivers of the allogeneic patients there was poor correlation overall between the symptom subscore scales and total uncertainty or any of the subscore scales (Table 4.27).

Table 4.27

Pearson Partial Correlation Table for Caregiver Uncertainty and Caregiver Perceptions of Patient Symptomatology for Caregivers of the Allogeneic Group

Measurement	Total Uncertainty	Ambiguity	Complexity	Inconsistency	Unpredictability
BPI	*0.14	*0.25	*-0.14	*0.04	*0.11
BFI	*-0.01	*0.06	*-0.16	*-0.15	*0.17
MSAS Global Distress	*0.02	*0.12	*-0.24	*-0.06	*0.13
MSAS Psychological	*-0.0	*0.11	*-0.31	*-0.02	*-0.06
MSAS Physical	*0.08	*0.13	*-0.12	*-0.10	*0.26
MSAS Total	*-0.05	*0.04	*-0.29	0.10 *	*-0.08

Partial Correlation Coefficient (r): *Low = < .4; **Moderate = > .4 to .7; ***High = > .7

Results Related to the Research Questions

1. What is the relationship of caregiver burden to the phase of treatment during the acute transplant experience for the combined caregiver group?

Caregiver burden, as measured by the scores on the Zarit Burden Interview (ZBI), with higher scores representing increased burden, revealed a marginally significant increase over time between Interview 1 and Interview 2 ($p = .07$), and Interview 1 to Interview 3 ($p = .03$) had a statistically significant difference as calculated using ANCOVA for the combined group. These findings indicate that overall burden (strain) is greatest and increased early in the acute phase for the combined caregiver group.

2. What is the relationship of caregiver burden to the acute phase of treatment during the acute transplant experience for the caregivers of the autologous HSCT patients?

No statistically significant changes in level of burden were found over time for the caregivers of the autologous transplants. However, the scores for caregiver burden were twice as high as those of the allogeneic group (39 to 20), indicating that the high score for the combined caregiver group related most to the autologous caregiver group findings. These findings show that in this study the caregivers of the autologous patients reported greater burden (strain) than the caregivers of the allogeneic patients.

3. What is the relationship of caregiver burden to the phase of treatment during the acute transplant experience for the caregivers of the allogeneic HSCT patients?

No statistically significant changes in the level of burden were found across the four interviews for the caregivers of the allogeneic patients, although there was a minimally significant difference between Interview 1 and Interview 2 ($p = .08$) as stated earlier. The scores for the caregivers of the allogeneic patients were almost half those for the caregivers of the autologous patients, 21.9 compared to 39, indicating that in this study the caregivers of the allogeneic patients reported less burden than the caregivers of the autologous patients.

4. What is the relationship of uncertainty to the phase of treatment during the acute transplant experience for the combined caregiver group?

There were some statistically significant relationships for total uncertainty (MUIS) and related subscore scales as the caregivers went through the acute transplant

process. This relationship is indicated by the differences between the interview scores of the caregivers over time. For the combined caregiver group, the inconsistency subscore scale showed a statistically significant difference between Interview 1 and 2 ($p = .05$), suggesting that inconsistency is an issue in care that increased uncertainty for this group of caregivers.

5. What is the relationship of uncertainty to the phase of treatment during the acute transplant experience for the caregivers of the autologous HSCT patients?

The total uncertainty scores decreased from Interview 1 to 2 ($p = .026$), Interview 1 to 3 ($p = .03$), and Interview 1 to 4 ($p = .036$) for the autologous caregivers. Analysis of the uncertainty subscore scales for the autologous patients indicated a statistically significant decrease in ambiguity from Interview 1 to 2 ($p = .01$), from Interview 1 to 3 ($p = .012$), and from Interview 1 to 4 ($p = .04$). There was also a significant decrease in scores in inconsistency from Interview 1 to 2 ($p = .05$). Overall, the findings indicate that the caregivers of the autologous patients experienced less uncertainty over time than the caregivers of the allogeneic patients.

6. What is the relationship of uncertainty to the phase of treatment during the acute transplant experience for the caregivers of the allogeneic HSCT patients?

For the caregivers of the patients undergoing an allogeneic transplant, there was a minimally significant increase in total uncertainty from Interview 1 to 2 ($p = .059$). There were no other significant findings. These findings suggest that this group of allogeneic caregivers had the opposite response to that of the caregivers of the autologous patients and experienced more uncertainty over time in the acute phase of treatment.

7. What is the relationship of caregiver burden to caregiver assessment of the patient's symptoms during the acute transplant experience for the combined caregiver group?

For the caregivers of the combined group of HSCT patients there was an overall poor correlation between the patient symptomatology measurements and total burden and any of the subscales. However, there was a moderate correlation for the MSAS global distress and MSAS psychological subscales, which indicates that global distress and psychological characteristics did increase with an increase in caregiver burden. Additionally, an increase in burden scores did not relate to the perception of the severity of pain, fatigue, or MSAS total for the patient-caregiver dyad.

8. What is the relationship of caregiver burden to caregiver assessment of the patient's symptoms during the acute transplant experience for the caregivers of the autologous HSCT patients?

The caregivers of the autologous transplants revealed a moderately positive correlation between patient symptoms and total burden and the subscore scales of personal strain and role strain. Therefore, increased burden in the autologous group was associated with an increased perception of the severity of the patient symptoms by this group of caregivers.

9. What is the relationship of caregiver burden to caregiver perceptions of the patient's symptoms during the acute transplant experience for the caregivers of the allogeneic HSCT patients?

The scores for the caregivers for the allogeneic transplant patients had a low or negative correlation with the subscales of burden. Burden scores were lower in the allogeneic caregiver group than in the autologous group, and there was a minimal relationship between the burden scores and the patient's symptomatology scores in this group, suggesting some tendency for the caregivers with higher scores to perceive symptoms as more severe than did the patients.

10. What is the relationship of caregiver uncertainty to caregiver assessment of the patient's symptoms for the combined caregiver group?

There were poor correlations across all of the subscores for total uncertainty and all of the measurements of patient symptomatology, indicating a poor relationship between uncertainty and perceptions of patient symptoms for this group.

11. What is the relationship of caregiver uncertainty to caregiver assessment of the patient's symptoms in the caregivers of the autologous HSCT patients?

For the caregivers of the autologous patients, there was a range of correlation scores from $r = .55$ and $r = .57$ for the MSAS and total uncertainty respectively, and $r = .57$ for ambiguity and the MSAS psychological subscale. This indicates that increased uncertainty in the autologous population is associated with increased symptomatology in the patient.

12. What is the relationship of caregiver uncertainty to caregiver perceptions of the patient's symptoms in the caregivers of the allogeneic HSCT patients?

For the caregivers of the allogeneic patients there was poor correlation between the perceptions of patient symptoms and total uncertainty and its subscales. Therefore, in

this group, caregiver uncertainty had very little relationship to their perceptions of the patient's symptoms.

13. What are the patterns of caregiver and patient perceptions of symptoms and caregiver level of uncertainty throughout the acute transplant process for the combined caregiver group?

The combined caregiver group had the greatest discrepancy in perceptions of symptoms with the patients at Interview 1 for pain (BPI), fatigue (BFI), and multiple symptoms (MSAS). At Interviews 2, 3, and 4, the patient scored multiple symptoms higher than the caregivers in the MSAS total (Table 4.28). The caregivers' total uncertainty adjusted mean score was the highest during the times of greatest patient-caregiver discrepancy in perception of symptoms, except for the score of Interview 2 in the BFI. Therefore, at times when burden and uncertainty were scored highest in the caregiver group, they perceived symptoms to be of higher severity than were reported by the patients.

Table 4.28

Differences Between Caregiver and Patient Perceptions of Symptomatology in the Combined Caregiver Group

Patient and Caregiver Difference	Interview 1	Interview 2	Interview 3	Interview 4
BPI	7.29 p = .026	2.46	0.12	3.50
BFI	7.28 p = .027	8.78 p = .015	1.97	0.23
MSAS	.014 p = .862	-0.140	-0.150	-0.121
Caregiver Total Uncertainty (adjusted mean score)	93.7	91.56	91.34	89.72
Caregiver Burden (adjusted mean scores)	30.43	28.25	27.43	27.68

Partial Correlation Coefficient (r): *Low = < .4; **Moderate = > .4 to .7; ***High = > .7

14. What are the patterns of caregiver and patient perceptions of symptoms and caregiver level of uncertainty throughout the acute transplant process for the caregivers of the autologous HSCT patients?

The data on the caregivers of the autologous patients indicated marginally significant differences between the patient and caregiver scores (Table 4.29). The results of Interview 2 for fatigue (BFI) and the remaining comparisons of the patient-caregiver dyad scores were not statistically different from each other. The total uncertainty score for these caregivers peaked at Interview 1, then dropped considerably at Interview 2, and continued to drop throughout the remainder of the interviews, showing a decline in uncertainty over time.

Table 4.29

Differences Between Caregiver and Patient Perceptions of Symptomatology in the Autologous Group

Patient and Caregiver Difference	Interview 1	Interview 2	Interview 3	Interview 4
BPI	6.76	-4.44	-7.45	-3.07
BFI	4.32	11.34 p = .074	-2.99	-5.24
MSAS	-0.041	0.000	-0.11	-0.08
Uncertainty	91.59	82.87	81.11	80.08

Partial Correlation Coefficient (r): *Low = < .4; **Moderate = > .4 to .7; ***High = > .7

15. What are the patterns of caregiver and patient perceptions of symptoms and caregiver level of uncertainty throughout the acute transplant process for the caregivers of the allogeneic HSCT patients?

For the caregivers of the allogeneic patients, the total uncertainty scores increased over the four interviews, with statistically significant differences at Interview 1 and 2, when the uncertainty score was the lowest (Table 4.30). There was a minimally significant increase in uncertainty between Interview 1 and 2 (p = .059) and a statistically significant increase between Interview 1 and 3 (.045). Caregiver scores were higher than patient scores for pain (BPI) and fatigue (BFI), but in the MSAS, the patient scores were higher than the caregivers', although only minimally significant at Interview 2 (p = .066). Therefore, the caregivers scored the patients' pain and fatigue higher than the patients reported them during the time when the uncertainty scores were the lowest, although the caregivers scored multiple symptoms lower than the patients over time. However, the

only significant difference was in fatigue where the caregivers scored higher in multiple symptoms (MSAS) than the patients reported over time.

Table 4.30

Differences Between Caregiver and Patient Perceptions of Symptomatology in the Allogeneic Group

Patient and Caregiver Difference	Interview 1	Interview 2	Interview 3	Interview 4
BPI	7.91 p =.054	7.52 p =.078	6.91	10.58 p = .059
BFI	9.82 p = .017	7.13 p =.096	6.59	6.00
MSAS	.059	-0.24 p = .066	-0.15	-0.07
Uncertainty	97.06	100.22	101.96	101.01

Partial Correlation Coefficient (r): *Low = < .4; **Moderate = > .4 to .7; ***High = > .7

16. What is the relationship between the caregiver descriptive characteristics and uncertainty across the four phases of the acute transplant process for the combined caregiver group?

In the ANCOVA model used for the analysis of this study, age, data collection site, caregiver gender, and time since diagnosis were considered covariants. None of the variables in the model had consistent significance over time.

17. What is the relationship between the caregivers' descriptive characteristics and caregiver burden across the four phases of the acute transplant experience for the combined caregiver group?

In the ANCOVA model, age, data collection site, caregiver gender, and time since diagnosis were considered possible variables. In the combined caregiver group, caregiver gender was intermittently statistically significant but was not a consistent factor.

18. What are the differences in caregiver burden and uncertainty based on the type of transplant?

Burden: Burden decreased over time for both the caregivers of the autologous and allogeneic HSCT patients.

Uncertainty: Uncertainty decreased over time for the caregivers of the autologous HSCT patients. The caregivers of the allogeneic patients increased over the time of the acute transplant experience. This suggests that the peak for uncertainty was in the pre-transplant period for the caregivers of the autologous patients, but one week post discharge for the allogeneic patient.

The different patterns of scores for burden and uncertainty suggest they are measuring different concepts. The difference in trends for uncertainty in autologous (decreasing) and allogeneic (increasing) suggest that further studies with larger populations are necessary to determine if the results can be replicated.

19. How does the level of HSCT caregiver burden compare to that of caregivers of patients with other chronic diseases?

The Zarit Burden Interview scores in this population were slightly lower than those from the stroke population but slightly higher than those from the COPD population (Table 4.31). Therefore, burden (strain) may be as great or greater for the HSCT caregivers as for the caregivers of patients with other chronic diseases.

Table 4.31

A Comparison of the ZBI Scores of the HSCT Caregivers and Caregivers for Other Chronic Conditions

	Combined Caregiver Group	**Caregivers of Autologous Transplant**	**Caregivers of Allogeneic Transplant**	**Stroke Caregivers (Schreiner, et al.)**	**COPD (Schreiner et al.)**
ZBI Scores (SD)	Interview1:26(11) Interview2:22(12) Interview3:23(10) Interview4:23(13)	Interview1:26 (13) Interview2:23(15) Interview3:23(13) Interview4:22(15.6)	Interview1:26 (9.2) Interview2:22 (9.4) Interview3:23 (6.6) Interview4:24(9.9)	28.3 (12.7) N = 80	20.35 (13) N = 56

20. How does the level of HSCT caregiver uncertainty compare to that of the caregivers of patients with other chronic diseases?

The levels of uncertainty as measured with Mishel's Uncertainty in Illness Scale (MUIS) have been reported for numerous other research studies. Mishel has collated other researchers' results to provide comparison normative data. She provided only one score for each study, however, since she did not measure total uncertainty over time as was shown in Table 4.9 for this study. Comparison of the means between findings revealed that the caregivers in this study had similar scores to data on caregivers in cancer and other chronic illnesses, indicating that uncertainty is probably also an issue for HSCT caregivers.

21. When is caregiver support most needed during the phases of the HSCT?

For the caregivers of the autologous HSCT patients, the uncertainty scores were highest in Interview 1, with the largest standard deviations for scores and the most discrepancies between patients and caregivers occurring at this time. Although the total uncertainty scores for the caregivers of the allogeneic patients were as high as those of

the caregivers of the autologous patients initially, the allogeneic caregivers' scores continued to rise over the course of the acute transplant experience. Burden scores were overall higher for the caregivers of the autologous HSCT patients than for the caregivers of the allogeneic HSCT patients; however, scores for both groups of caregivers decreased over time, except for a slight increase at Interview 1 for the caregivers of the allogeneic patients. Therefore, the early or pre-transplant and immediate post-transplant phases appeared to be the times when the most support was needed for all caregivers.

Summary tables presenting the results of the statistical analysis of this study are found in Appendix E.

Chapter Summary

This chapter has reviewed the statistical analysis and primary findings of the study. The interpretation and relevance of the findings and recommendations for future research are discussed in Chapter 5.

Chapter 5

DISCUSSION

The purpose of this chapter is to discuss the interpretation and relevance of the principal findings of this study. Recommendations for future research are also proposed.

Principal Study Findings

The research questions have been synthesized to provide a framework for this discussion and to focus this summary of the findings.

Question: *What is the relationship of caregiver burden to the phase of treatment during the acute transplant experience for the combined group of caregivers, caregivers of autologous and allogeneic HSCT patients?*

Burden (strain) was at a high level for all caregivers at all four measurement times compared to the findings for burden in caregivers of other populations. Overall, caregiver burden (stress) decreased over time, although only the change in the pre-transplant and immediately after transplant times were found to be statistically significant. It has been suggested by Mishel (1999) that as the caregiver moves forward, he/she makes sense out of the cancer reality, with the help of support persons familiar with chemotherapy. Thus, seeing the patient progress each day may, even early in the process, can help the caregiver cope.

Although statistics are not available for recent years, it is thought that increasing experience with managing the side effects of bone marrow transplants, white cell growth factors, and better anti-rejection medications have decreased death rates from early transplantation (Bolwell, 2003; CIBMTR, 2008). The improved response may explain the

decrease in burden scores over time for this study population but may not be a consistent finding in other transplant groups. It is interesting to note that burden scores did not increase post discharge.

Question: *What is the relationship of uncertainty to the phase of treatment during the acute transplant experience for all caregivers, and for the caregivers of patients undergoing autologous and allogeneic HSCTs?*

Uncertainty was also high for all caregivers in the initial (pre-transplant) phase. This finding is consistent with the view that uncertainty is worse prior to an event or new treatment (Mishel et al., 1991). There was a significant decrease in uncertainty for the autologous caregivers over the time of this study. However, there was an increase in uncertainty in the allogeneic group, with the highest scores peaking at Interview 3 (one week post discharge). The finding that pre-transplant was the time of highest stress for the autologous patients in this study, but that the caregivers of the allogeneic patients had higher stress one week post discharge, may relate to the differences in the clinical response to treatment common for each group. One difference between these groups is the development of the graft versus host disease (GVHD) in allogeneic transplants, which commonly occurs 7 to 10 days post transplant (CIBMTR, 2008), the point of time in the study for Interview 3. Data were not available on the incidence of GVHD in this study population to determine if this were an explanation for the peaks in uncertainty.

The general decline in uncertainty at the last (fourth) interview, one month post discharge, suggests that the participants completing the study were coping well at home. However, it is possible that patient-caregiver dyads who were not doing well were the

ones who dropped out of the study and that these findings were skewed by sample attrition similar to a study reported by Kurtz et al. (2005).

Question: *What is the relationship of caregiver burden to caregiver assessment of the patient's symptoms during the acute transplant experience for combined caregiver group and for the caregivers of both autologous and allogeneic HSCTs?*

At pre-transplant, when the burden scores were the greatest, the caregiver assessment of the patient's symptoms had the greatest variation with how symptoms were perceived by the patient. Specifically, it was found at pre-transplant that the caregivers overestimated symptoms of pain, fatigue, and multiple symptoms as reflected by the MSAS tool. Therefore, the pre-transplant period may be the time when caregivers are the least accurate in reporting the observed patient's symptoms, which may be an important time to provide added caregiver support.

Question: *Is there a relationship between caregiver descriptive characteristics and uncertainty across the four phases of the acute transplant process for all of the HSCT caregivers?*

No significant relationships were found between caregiver characteristics and their levels of burden or uncertainty over time. According to Boyle (2000), changes related to burden, role, and personal strain may not be exhibited until after the acute transplant experience since it is in the extended post-transplant period when roles are significantly and irreversibly changed that burden becomes a factor. Therefore, a longitudinal study over a more extended period of time may be needed to reveal significant relationships.

Question: *What are the differences in caregiver burden and uncertainty based on type of transplant?*

Differences by type of transplant primarily involved an increase in uncertainty for the caregivers of the allogeneic patients, as compared to the decrease in uncertainty over time for the autologous patient caregivers.

As mentioned previously, the allogeneic HSCT patient experiences more physical changes and tends to have more marked changes in symptoms than the autologous HSCT patient who follows a more established pattern of recovery. According to Eldredge et al. (2006), the increase in uncertainty for caregivers of allogeneic patients reflects their increasing inability to make sense of the progress the patient is making, the graft versus host disease issues, and how to predict what will be next.

Question: *How does the level of HSCT caregiver burden and uncertainty compare to that of caregivers of patients with other chronic diseases?*

Comparing burden and uncertainty scores in published data for other populations, the levels for both caregiver burden and uncertainty were similar to published scores for caregivers involved in other chronic diseases. The caregiver burden scores were slightly lower than those of a stroke population but higher than the scores of those from a population with COPD (Schriener et al., 2006). This finding may reflect that cancer and HSCT treatment, may be perceived to cause less burden than a stroke, which can be life threatening and occupationally disabling. COPD in the extreme forms can also be life threatening and occupationally disabling, but many patients are able to function with minimal daily assistance. Schreiner et al. compared ZBI scores to three measures of

clinical depression in a study of caregivers, and through multiple types of analyses determined that a ZBI score of 25 or higher was highly correlated to a diagnosis of depression in the caregiver. Mean ZBI scores for all caregivers in this study were above 25, suggesting that the HSCT caregiver population may be at relatively high risk for clinical depression.

The individual nature of the caregiver experience, which revealed relatively wide standard deviations in burden scores, supports the need to be aware of the possibility of individual variations in the HSCT experience for this population. A similar situation is true for the total uncertainty scores (Mishel, 1997), which were slightly higher than the cancer database mean, but slightly lower than scores for other chronic diseases. Overall, the wide range of scores for total uncertainty also suggest that the caregiver and patient experiences may be quite different for many caregivers of patients with HSCT.

Question: *What are the points of time in the HSCT acute phase of treatment when the caregiver needs the most support?*

Due to the different nature and spikes in high scores for allogeneic and autologous HSCT caregivers and patients, there appear to be key periods of time when support and intervention might be most helpful. The initial stage of the process revealed the areas of most concern for all of the caregivers in this study. Mishel's (1997) findings on uncertainty in illness have led to the development of repeated education and support to newly diagnosed cancer patients to decrease their uncertainty. Although HSCT patients are not newly diagnosed, they are entering a new phase of their treatment, so therefore more intensive family education might be useful.

Based on the findings of this study, the caregivers of the autologous and allogeneic patients may benefit most from early support, the time when the patient enters the transplant process. However, the caregivers of the allogeneic patients may also need intensive support throughout the transplant experience, particularly at the time when they are at highest risk, e.g., 7 to 10 days post transplant, since the risk of GVHD occurs at this time. Individual supportive counseling at key times may assist in minimizing daily stress and help the caregivers improve their ability to support the patient.

Study Limitations

A number of limitations may have affected the outcomes of this study, as described in the following.

Sampling Method

Access to the subjects for the study depended on the BMT coordinators to identify potential patient-caregiver dyads who met the selection criteria. Some difficulty occurred in stabilizing the coordinators' use of the pre-screening criteria. Therefore, there may have been a tendency to enroll patients who were doing well and to avoid patients who were ill.

The final approach for participant recruitment was to identify the patients shortly prior to transplant and to introduce the study and discuss it with the caregiver and the patient. This approach used a short time period, enrolling both participants when they were feeling reasonably well and had time to complete the surveys. This was also an opportunity to provide information when there were no other critical decisions to be made about medical treatment.

Study Design

As suggested by Williams (2007), following patients over time is an ideal way to collect data about the transplant experience. The concepts chosen to measure uncertainty, caregiver burden, and patient symptomatology are those that are repeatedly mentioned in the literature (Eilers, 1996; Mishel, 1997; Zarit et al., 1986). A representative or larger sample may have improved the data. Additionally, repeated measures over a short period of time may be burdensome to the caregivers and may not adequately reflect changes in a small sample. The findings of this study, due to the sample selection process, cannot be considered representative of caregivers of HSCT patients beyond the study participants.

Attrition of the Sample

The patients' health conditions changed over the approximate six weeks of the treatment. Several patients were unable to complete some of the data points because of their health condition. Some were unable to appropriately concentrate for the required 10 minutes of the data collection. Unfortunately, three patients expired during the data collection phase. One died before transplant but after completing one series of the questionnaires. A second died after transplant in the ICU. A third patient died three weeks after discharge from the hospital. Over the time of the study, dyad attrition evolved as follows: Interview 1: N = 46 dyads, Interview 2: N = 36, Interview 3: N =31, and Interview 4: N = 27.

Sample Diversity

The recruitment of the study participants from primarily Caucasian populations was not demographically representative of the U.S. population. Thus, the results of this

study are not generalizable beyond the specific populations at the medical centers where the dyads were recruited.

Recommendations for Future Research

Differences found in this study between the experiences of the caregivers of autologous and allogeneic patients in this study population support further studies that compare findings between the groups. The use of quantitative methods increases the risk that individual variations among caregivers and patients are less visible in the data. As noted by Frey et al. (2002), the comparison of means in a sample population may result in the loss of individual differences. Eilers (1996) also notes that using only total scores may cause changes to be missed. Other data collection methods may need to be considered in order to capture the best data for this type of study and this population of caregivers. Keogh et al. (1998), in their study of BMT patients, used a mixed methods research, including verbal interviews even for their self-report forms as well as specific qualitative interviews. Zabit (1997) used structured interviews, self-report tools, and psychological screening data available prior to transplant. Frey et al. (2002) used quantitative methods as well as qualitative data from a caregiver diary and financial analysis of medical bills. Other authors (e.g., Williams, 2007) have used qualitative methods to maximize the "story" identified for each caregiver. Efforts should be made to study this population using methods that facilitate identification of the unique features of the autologous and allogeneic transplant experience to create a base for creating patient-caregiver dyad interventions that can meet the needs of both groups.

The examination of the ability of the caregivers in this study to accurately communicate symptoms the patient was experiencing is reflected in the agreement of patient and caregiver scores on common areas of symptoms; the least agreement was at the time that the burden scores were the highest (pre-transplant). It may be that high levels of stress and depression associated with high burden scores negatively affected the ability of the dyad in this study population to communicate the symptoms. The agreement on symptoms by the dyad after the initial phase does suggest that the caregivers in this study were at times also quite accurate reporters of patient symptoms. Further investigation is needed of a representative sample of HSCT caregivers to determine if pre-transplant is the most stressful time for caregivers of both types of transplant patients. Validation of the relationship of the perception of symptoms with the level of burden would also be a worthwhile goal for future studies. Confirmation of findings in a representative sample is needed to help identify interventions that would improve communication within the dyad in the pre-transplant and other phases of HSCT treatment.

Uncertainty, while high for both caregivers of allogeneic and autologous stem cell transplant patients initially, continued to rise for the allogeneic caregivers after the pre-transplant phase. Agreement on symptoms was the lowest at the time of the greatest uncertainty scores for the caregivers of the autologous patients (pre-transplant). The uncertainty scores increased over time for the caregivers of allogeneic patients, although the increase was not associated with greater disagreement in the assessment of symptoms. Although there was good agreement on symptom scores in the allogeneic population, the

peak of uncertainty scores one week post discharge is at a crucial time for rapid development of new symptoms related to GVHD. Additional research with a larger representative group of HSCT patient-caregiver dyads is needed to determine if the variance between patient-caregiver dyad assessment of patient symptoms would increase over time in relation to uncertainty scores.

This study examined the HSCT caregiver experience only during the acute phase of treatment. Williams (2007) identified the need for longitudinal studies to understand the full impact of the transplant experience on both caregivers and patients. Extension of the time for data collection is recommended to explore the impact of the acute treatment and recovery phases and more long-term factors impacting this patient-caregiver dyad. More knowledge of the incidence of patient survival, GVHD, disease recurrence, employment changes, and possible return to previous roles over time is needed to fully understand the scope of care needs present in this population.

The review of the literature on caregivers of HSCT patients shows that past research has focused on identifying concepts that help define the experience. Concepts such as caregiver commitment, expectation, and negotiation (Williams, 2007), psychological distress, fatigue, burden of care, and quality of life (Gaston-Johanson, 2004), anxiety, needs, and coping (Wochna, 1997), and uncertainty and hardiness (Eilers, 1996) have been investigated. A variety of tools have been used to measure the concepts of interest in this population.

How caregivers change over the course of the transplant experience as well as identify the times of highest risk times have also been studied (Gaston-Johanson, 2004;

Williams, 2007; Wochna, 1997). However, there has been limited consistency in the findings and no replication of similar studies to facilitate comparison. This study adds to the base of knowledge related to caregiver uncertainty and burden in this population and supports further exploration of these elements of the HSCT caregiver experience.

Overall, a common thread of agreement in the research is that transplantation is as stressful an event for the caregivers as it is for the patients (Keogh et al., 1998). A recent study showing a strong relationship between higher burden scores and clinical depression (Schreiner et al., 2006), and the findings in the current study of high burden scores in the caregivers of HSCT patients support future research to determine the consistency of this finding in a representative group of HSCT caregivers. Studies that focus on testing interventions to reduce the incidence of depression in this high-risk group are also indicated. It has been suggested that the presence of depression in a caregiver can have a negative effect on the HSCT patient (Young, 2003). Knowing when the high-stress periods may occur—suggested in this study to be early in the transplant experience—would be an important consideration for future studies

Chapter Summary

The findings from this study suggest that family caregivers of HSCT patients may benefit from focused caregiver interventions at specific points of time during the HSCT process. This study provides insight into certain aspects of the HSCT caregiver experience not previously reported. Further areas for research are identified based on the findings.

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APPENDIX A

Institutional Review Board and Human Protection Documents

Penn State Office for Research Protection Approval

Date: June 16, 2004

From: Jodi Mathieu, IRB Administrator

To: Margaret D. Harris

Subject: Results of Review of Proposal- Expedited **(IRB #18865)**
Approval Expiration Date: June 3, 2005
"The Perception of Burden, Uncertainty and Symptomatology in Family Caregivers of Peripheral Stem Cell Transplant Patients (PSCT)"

The Social Science Institutional Review Board has reviewed and approved your proposal for use of human participants in your research. By accepting this decision, you agree to obtain prior approval from the IRB for any changes to your study. Unanticipated participant events that are encountered during the conduct of this research must be reported in a timely fashion.

COMMENT: When received, please submit a copy of the IRB approval letter from the Hershey Medical Center.

Enclosed is/are the dated IRB-approved informed consent(s) to be used when recruiting participants for this research. Participants must receive a copy of the approved informed consent form to keep for their records.

If signed consent is obtained, the principal investigator is expected to maintain the original signed consent forms along with the IRB research records for this research at least three (3) years after termination of IRB approval. For projects that involve protected health information (PHI) and are regulated by HIPAA, records are to be maintained for six (6) years. The principal investigator must determine and adhere to additional requirements established by the FDA and any outside sponsors.

If your study will extend beyond the above noted approval expiration date, the principal investigator must submit a completed Continuing Progress Report to the Office for Research Protections (ORP) to request renewed approval for this research.

On behalf of the committee and the University, thank you for your efforts to conduct your research in compliance with the federal regulations that have been established for the protection of human participants.

Hershey Medical Center Acknowledgment of IRB Application

DATE: July 6, 2004

TO: Margaret Davitt Harris, MSN; CRNP; Nursing

FROM: Kevin Gleeson, M.D., Executive Chair
Institutional Review Board

RE: IRB Protocol No. 19085EP - The Perception of Burden, Uncertainty and Symptomatology in Family Caregivers of Peripheral Stem Cell Transplant Patients (PSCT)

Thank you for your application to the Institutional Review Board (IRB). The above IRB protocol number was assigned for the research and should be included on all future correspondence and documentation. The proposed research met the regulatory criteria for expedited review and was reviewed accordingly. Official approval was granted for this research effective *July* 6. *2004,* through *June 30, 2005,* at which time IRB reconsideration will be required. This approval includes the following:

- Research Protocol- Abstract, dated 06/14/2004
- Total entry - One hundred (l00) subjects
- Informed Consent - Consent form (dated 06/22/2004)
- Authorization to use protected health information (PI-II) - Included in consent form
- Advertisement - None
- Questionnaire - Demographic Data Survey; Brief Fatigue Inventory; Memorial Symptom Assessment
- Scale; Brief Pain Inventory; Zarit Burden Interview; Mishel Uncertainty in Illness Scale (all received)
- 06/15/2004)
- Other - Informational Letter to PSCT Patients; Informational Letter to Caregivers (both received)
- 06/15/2004)
- IRB member exclusions: No investigators for this research serve on the IRB.

Informed Consent and Authorization: Only approved investigators may solicit consent for research participation. Subjects or their representatives must receive a copy of the consent form, and for patients include a copy in the medical record along with the protocol abstract. It is the principal investigator's responsibility to keep original consent forms/authorizations filed in a secure place and to retain them for six years after termination of research that accesses protected health information (PHD, or for two years after termination if no PI-IT is accessed. Additional requirements apply for FDA and sponsored trials, which the principal investigator should ascertain, if applicable.

Proposing Changes: Federal regulations require prompt reporting to the IRB of any proposed changes in a research activity and prior approval before changes are initiated, except where necessary to eliminate apparent immediate hazards to the subject. (Submit a Modification Request Form to change an existing investigation.)

Adverse Event Reporting: Serious, life-threatening or unexpected adverse events occurring in subjects participating in this research must be reported immediately to the IRB. (Submit the Adverse Event/Safety Report form). Report all other adverse events (i.e., mild or expected reactions) on the Progress Report for renewal.

The Institutional Review Board appreciates your efforts to conduct research in compliance with the institutional policies and federal regulations that have been established to ensure the protection of human subjects. Please feel free to communicate any future questions or concerns regarding this research to the IRB via its administrative arm, the Human Subjects Protection Office.

Letter to PSU and HMC to Request Approval of Study Changes

To: IRB PSU
IRB HMC

From: Margaret Davitt Harris

Re: Requested changes to IRB approvals
PSU: IRB #18865
HMC: #19085EP

Date: July 22, 2004

I would like to request the following changes in documents approved by the IRBs for my study.

1. Change in title to reflect current title of transplant nomenclature from BMT or PSCT to HSCT (Hematopoietic Stem Cell Transplant). This is a broader term reflecting not only peripheral stem cells, or bone marrow, but also dendritic cells, products what have had elements changed (i.e., T cell depleted) as well as new types of cell products.
2. Change in body of IRB application from PSCT to HSCT: same as Number 1
3. Change in letters to patient and caregiver from PSCT to HSCT; same as Number 1
4. Change in consents from PSCT to HSCT; same as number 1
5. Change in body of IRB application, Letters to patients, caregivers and consent to reflect the following:
   a. Change in data points. There will continue to be four data points for data collection but rather than collect data when patients are identified pre-transplant, data will be collected within the window of one week before their transplant is scheduled to occur. This will allow measurement closer to actual transplant. Additionally, data would be collected one month after discharge in addition to the immediate transplant period, and one week post discharge. The one-month period post transplant would allow us to capture potential indications of adaptation to caregiver burden and uncertainty during the transplant experience.

   Please let me know how to proceed with these changes. Thank you.

PSU Office for Research Protections Approval Letter

Date: July 15, 2004

From: Jody Mathieu, IRB Administrator

To: Magaret D. Harris

Subject: Research Proposal - Modification **(IRB #18865)**
Approval Expiration Date: June 3, 2005
(Note: This date reflects the anniversary date of the actual submission approval date.)

The Perception of Burden, Uncertainty and Symptomatology in Family Caregivers of Peripheral Stem Cell Transplant Patients (PSCT)

The revision(s) to the above-referenced study, outlined in the July 13, 2004 e-mail message from Kathleen Fisher, have been reviewed and approved by the Social Science Institutional Review Board **(IRB).** You may proceed with your study. Please continue to notify the IRB of any further changes to your study.

On behalf of the IRB and the University, thank you for your efforts to conduct research in compliance with the federal regulations that have been established for the protection of human participants.

JLM/slk
cc: Kathleen M. Fisher

Letter to Hershey Medical Center Regarding Title Change

DATE: August 23, 2004

TO: Margaret D. Harris

FROM: Elizabeth Galgocy, RN, BSN
Research Compliance Coordinator
Human Subjects Protection Office

RE: IRB Protocol No. 19085EP

OLD TITLE: The Perception of Burden, Uncertainty and Symptomatology in Family Caregivers of Peripheral Stem Cell Transplant Patients (PSCT): A Prospective Study

NEW TITLE: The Perception of Burden, Uncertainty and Symptomatology in Family Caregivers of Hematopoietic Stem Cell Transplant Patients (HSCT): A Prospective Study

The Human Subjects Protection Office (IISPO) received your August 4, 2004 correspondence with the accompanying documentation regarding the above investigation.

The request for the protocol revisions outlined in the revised abstract (dated 08/01/2004*)* received expedited review and approval was granted on August 23, 2004. The revised consent form (dated *08/0112004),* the revised patient letter and the revised caregiver's letter (both received *08/0412004)* were also approved. The deletion of co-investigator Kathleen Fisher and the title change was noted.

If you have any questions, please phone the IISPO (ext. 5687). Thank you very much.

EAG\

PSU Office for Research Protection Approval of the Study

Date: August 25, 2004

From: Jodi Mathieu, IRB Administrator

To: Margaret D. Harris

Subject: Research Proposal - Modification (IRB #18865)
Approval Expiration Date: June 3, 2005
(Note: This date reflects the anniversary date of the actual submission approval date.)

The Perception of Burden, Uncertainty and Symptomatology in Family Caregivers of Hematopoietic Stem Cell Transplant Patients (HSCT)

The revision(s) to the above-referenced study, outlined in your July 23 and August 24, 2004 e-mail messages, has been reviewed and approved by the Social Science Institutional Review Board (IRB). You may proceed with your study. Please continue to notify the IRB of any further changes to your study.

On behalf of the IRB and the University, thank you for your efforts to conduct research in compliance with the federal regulations that have been established for the protection of human participants.

JLM/slk

Letter from Hershey Medical Center on Research Progress

DATE: June 26, 2006

TO: Margaret D. Harris, CRNP, Nursing

FROM: Kevin Gleeson, M.D., Executive Chair
Institutional Review Board

RE: IRB Protocol No. 19085EP - The Perception of Burden, Uncertainty and Symptomatology in Family Caregivers of Hematopoietic Stem Cell Transplant Patients (HSCT): A Prospective Study

The Human Subjects Protection Office (HSPO) received the progress report for the above titled investigation, with your request for Institutional Review Board (IRB) approval to continue this research. The progress report, protocol, and supporting documentation were considered during the continuation review process. In accordance with Federal guidelines and institutional policy, this request was determined to qualify for expedited review* on behalf of the IRB (*eligible for review by designated IRB reviewers in lieu of convened board review).

Expedited approval was granted to renew this investigation for a twelve-month period, from ***July 1, 2006*** **through** ***June 30, 2007.*** **Use of the attached, stamped consent form is required. The new form supersedes all previous versions, which are now invalid for further use. Prior versions should be retrieved and destroyed, with the exception of reference copies retained for your regulatory binder.**

Please continue to forward all correspondence for the IRB directly to the Human Subjects Protection Office, with the IRB protocol number clearly noted. For research requiring written informed consent, the investigator should keep the original signed consent form and provide the subject with a photocopy. For clinical treatment protocols, include a copy of the consent form and the abstract in the patient's HMC medical record to inform other medical caregivers about this research.

Federal regulations require prompt reporting to the IRB of any proposed changes in a research activity and prior approval before changes are initiated, except where necessary to eliminate apparent immediate hazards to the subject. Please request approval for proposed changes using the Modification Request Form. Federal regulations also require the prompt reporting to the IRB of unanticipated problems involving risks to subjects or others. Please report these problems according to the directions in the "Adverse Event Definitions and Reporting Requirements", using the indicated report form and/or tracking log. (See www.hmc.psu.edulformslstudies)

The Institutional Review Board appreciates your efforts to conduct research in compliance with the federal regulations that have been established to ensure the protection of human subjects.

HMC Letter Renewing Research Approval

DATE: June 20, 2007

TO: Margaret D. Harris, CRNP, Nursing

FROM: Kevin Gleeson, M.D., Executive Chair
Institutional Review Board

RE: IRB Protocol No. 19085EP - The Perception of Burden, Uncertainty and Symptomatology in Family Caregivers of Hematopoetic Stem Cell Transplant Patients (HSCT): A Prospective Study

The Human Subjects Protection Office (HSPO) received the progress report for the above titled investigation, with your request for Institutional Review Board (IRB) approval to continue this research. The progress report, protocol, and supporting documentation were considered during the continuation review process. In accordance with Federal guidelines and institutional policy, this request was determined to qualify for expedited review* on behalf of the IRB (*eligible for review by designated IRB reviewers in lieu of convened board review).

Expedited approval was granted to renew this investigation for a twelve-month period, from ***July 1, 2007*** **through** ***June 30, 2008.*** **Use of the attached, stamped consent form is required. The new form supersedes all previous versions, which are now invalid for further use. Prior versions should be retrieved and destroyed, with the exception of reference copies retained for your regulatory binder.**

Please continue to forward all correspondence for the IRB directly to the Human Subjects Protection Office, with the IRB protocol number clearly noted. For research requiring written informed consent, the investigator should keep the original signed consent form and provide the subject with a photocopy. For clinical treatment protocols, include a copy of the consent form and the protocol summary (abstract form) in the patient's HMC medical record to inform other medical caregivers about this research.

Federal regulations require prompt reporting to the IRS of any proposed changes in a research activity and prior approval before changes are initiated, except where necessary to eliminate apparent immediate hazards to the subject. Please request approval for proposed changes using the Modification Request Form. Federal regulations also require the prompt reporting to the IRS of unanticipated problems involving risks to subjects or others. Please report these problems according to the directions in the "Unanticipated Problems/Adverse Events Report Forms and Instructions", using the indicated report form and/or tracking log. (See www.hmc.psu.edu/irb/forms/studies)

The Institutional Review Board appreciates your efforts to conduct research in compliance with the federal regulations that have been established to ensure the protection of human subjects.

KG\js

Addendum: Approval was granted for the revised caregiver letter and the revised patient letter (both rec'd 6/20/07).

STANFORD UNIVERSITY

Stanford, California 94305 - 5401

David D. Oakes, M.D. (650) 725-9834
CHAIR, PANEL ON MEDICAL HUMAN SUBJECTS (650) 725-8013

Certification of Human Subjects Approvals

Date: June 30, 2008

To: Debra Tierney, RN, PhD, BMT O/P TREATMENT CTR - SUH

From: David D. Oakes, M.D., Administrative Panel on Human Subjects in Medical Research

Protocol Title: Uncertainty and Caregiver Burden and Patient Symptomatic in Caregivers of BMT Patients

Protocol ID: 9107 **IRB Number:** 4947 (Panel: 6)

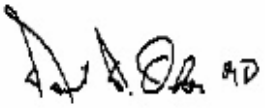
The IRB approved human subjects involvement in your research project on 06/30/2008. Prior to subject recruitment and enrollment, if this is: a Cancer-related study, you must obtain Cancer Center Scientific Review Committee (SRC) approval; a GCRC study, you must obtain GCRC approval; a VA study, you must obtain VA RD Committee approval; and if a contract is involved, it must be signed.

The expiration date of this approval is 05/31/2009 at Midnight. If this project is to continue beyond that date, you must submit an updated protocol in advance for the IRBs re-approval. If this protocol is used in conjunction with any other human use it must be re-approved. Proposed changes to approved research must be reviewed and approved prospectively by the IRB. No changes may be initiated without prior approval by the IRB, except where necessary to eliminate apparent immediate hazards to subjects. (Any such exceptions must be reported to the IRB within 10 working days.) Unanticipated problems involving risks to participants or others and other events or information, as defined and listed in the Report Form, must be submitted promptly to the IRB. (See Events and Information that Require Prompt Reporting to the IRB at http://humansubjects.stanford.edu.)

All continuing projects and activities must be reviewed and re-approved on or before Midnight of the expiration date. The approval period will be less than one year if so determined by the IRB. It is your responsibility to resubmit the project to the IRB for continuing review and to report the completion of the protocol to the IRB within 30 days.

Please remember that all data, including all signed consent form documents, must be retained for a minimum of three years past the completion of this research. Additional requirements may be imposed by your funding agency, your department, or other entities. (See Policy on Retention of and Access to Research Data at http://stanford.edu/dept/DoR/rph/2-10.html.)

This institution is in compliance with requirements for protection of human subjects, including 45 CFR 46, 21 CFR 50 and 56, and 38 CFR 16.



David D. Oakes, M.D., Chair

Approval Period: 06/30/2008 THROUGH 05/31/2009
Review Type: EXPEDITED - CONTINUING REVIEW
Funding:
Expedited Under Category: 7
Assurance Number: FWA00000934 (SHC)

APPENDIX B

Permissions for Use of Instruments

MUIS Approval Letter

March 11, 2004

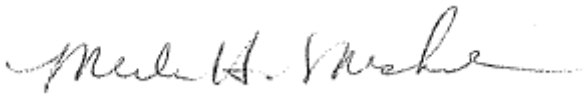
Margaret E. Harris
208 S. 6th St.
PO Box 421
Mount Wolf, PA 17347

Dear Ms. Harris:

I am enclosing a copy of the Adult Uncertainty in Illness Scale you requested. Also enclosed is a copy of the request form countersigned by Dr. Mishel for your records.

This scale may be administered verbally by interview or enclosed in a paperbound scale booklet to be completed by the subject. The Uncertainty Scale cannot be transferred electronically to the Internet, as this is copyrighted material.

Sincerely,



Merle H. Mishel, RN, PhD, FAAN
Keenan Professor
UNC - School of Nursing

Permission for Use of the Zarit Burden Interview

From: z67@psu.edu
To: mdavitt582@aol.com
Sent: 7/18/2008 11:12:36 A.M. Eastern Daylight Time
Subj: Re: Permission to use Burden Interview

Dear Ms. Harris,

You may use the Burden Interview in your research.

Steve Zarit

MSAS Information

Memorial Symptom Assessment Scale

Instrument Name:
Memorial Symptom Assessment Scale (MSAS)
Memorial Symptom Assessment Scale - Short Form (MSAS-SF)

Category:
Clinical Care Tools - Symptom Management

Authors:
Russell Portenoy, MD and colleagues

Author Contact Information:
Russell K. Portenoy, MD
Dept of Pain Medicine & Palliative Care
Beth Israel Medical Center
212-844-1505
RPortenoy@BethIsraelNY.org RPortenoy@BethIsraelNY.org

Keywords:
symptom assessment, symptom level, mutliple symptoms, function, health status

References:
Portenoy RK, Thaler HT, Kornblith AB, Lepore JM, Friedlander-Klar H, Kiyasu E, Sobel K, Coyle N, Kemeny N, Norton L, et al. The Memorial Symptom Assessment Scale: an instrument for the evaluation of symptom prevalence, characteristics and distress. Eur J Cancer. 1994;30A(9):1326-36.
Ingham JM, Portenoy RK. Symptom Assessment. Hematol Oncol Clin North Am. 1996 Feb;10(1):21-39. Review.
Chang VT, Hwang SS, Feuerman M, Kasimis BS, Thaler HT. The memorial symptom assessment scale short form (MSAS-SF). Cancer. 2000 Sep 1;89(5):1162-71.

To use and view this tool:
No permission required. To download tools:
MSAS - PDF 300 KB
MSAS-SF - PDF 203 KB
Scoring information - PDF 61 KB

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER

July 8, 2008

Ms. Margaret Davitt Harris
Pennsylvania State University
3718 Starview Road
Mount Wolf, PA 17347

Dear Ms. Harris:

I am pleased that you have considered using the Brief Fatigue Inventory© (BFI) in your upcoming study. The study description you provided seems to be congruent with the intended use of the BFI. You may reproduce the BFI but your copyright use is limited only to this specific study. In addition, the following should appear in your reproduced copy.

Additional information can be found by visiting our website:
www.mdanderson.org/departments/prg

I look forward to having a summary of your results.

Sincerely,

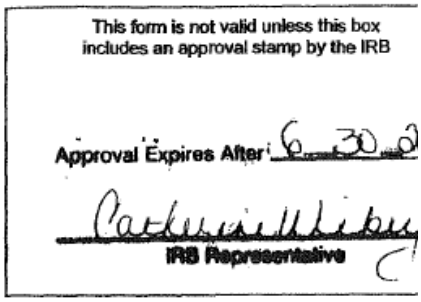
Charles S. Cleeland, Ph.D.
McCullough Professor of Cancer Research
Chairman, Department of Symptom Research
Division of Internal Medicine

CSC:lfs

cc: Tito R. Mendoza, Ph.D.

APPENDIX C

Informed Consent



INFORMED CONSENT FOR RESEARCH

Penn State College of Medicine
The Milton S. Hershey Medical Center

Title of Project: The Perception of Burden, Uncertainty and Symptomatology in Family Caregivers of Hematopoietic Stem Cell Transplant Patients: Prospective Study

Principal Investigator: Margaret Davitt Harris, CRNP
P.O. Box 421, Mount Wolf, PA 17347
(717) 531-4212; Email: mdavitt582@aol.com

Participant's Printed Name:_____

This is a research study, Research studies include only people who voluntarily choose to take part. This consent form gives you information about this research, which will be discussed with you. This consent form may contain words or procedures that you do not understand. You are urged to ask questions about anything that is unclear to you. Discuss it with your family and friends and take your time to make your decision. You will receive a copy of the signed and dated consent form to keep.

1. **Purpose of the Research**: You are being offered the opportunity to take part in this research because you are a patient scheduled to receive a Hematopoietic stem cell transplant for your cancer or you are a caregiver of a Hematopoietic stem cell transplant patient.

The purpose of this research is to identify issues of caregivers of Hematopoietic stem cell transplant patients. A second purpose is to examine patients' and caregivers' awareness of patients' symptoms during the transplant process.

Approximately 50 patients and 50 caregivers will take part in this research at the Hershey Medical Center.

2. **Procedures to be Followed**: Participation in this research for both caregivers and patients will include completion of several brief surveys at four different times during the transplant experience. Surveys will be completed before the stem cell transplant procedure, at some point during the transplant, one week after discharge and one month post discharge. If you are a caregiver, you will complete five brief surveys about your feelings about taking care of another person and about the patient's pain, fatigue and symptoms. If you are a patient, you will be asked to complete three brief surveys about your pain, fatigue and symptoms.

3. **Discomforts and Risks**: Some of the questions are personal and might cause discomfort. You may choose not to answer any questions that you feel uncomfortable answering. There is a risk of loss of confidentiality if your research information or your identity are obtained by someone other than the investigators, but precautions will be taken to prevent this from happening.

4. **Possible Benefits:**
   a. Possible benefits to the participant: You will not benefit from taking part in this research study.
   b. Possible benefits to society: The benefits to society include a better understanding of the issues and concerns of caregivers of patients during Hematopoietic stem cell transplantation. This will help healthcare providers to design better educational and support programs for patients and caregivers.

5. **Other Options that Could be Used Instead of this Research:** You do not have to take part in this research study.

6. **Time Duration of the Procedures and Study**: It will take less than thirty minutes for caregivers to complete the surveys during each of the four points during the transplant experience. It will take the patients approximately 12-15 minutes to complete the surveys during each of the four points during the transplant experience.

7. **Statement of Confidentiality:**

a. **Privacy and Confidentiality Measures** Your research records that are reviewed, stored, and analyzed at The Milton S. Hershey Medical Center (HMC) and Penn State University and College of Medicine (PSU) will be labeled with a code number. The list that matches your name with the code number will be kept in a locked file in Margaret Davitt Harris' office. The research records will be kept in a password-protected computer file and in file cabinets in Margaret Davitt Harris' office.

b. **The Use of Private Health Information:** Health information about you will be collected if you choose to be part of this research study. Health information is protected by law as explained in the HMC Privacy Notice. If you have not received this notice, please request a copy from the researcher. At The Milton S. Hershey Medical Center (HMC) and Penn State College of Medicine (PSU) your information will only be used or shared as explained and authorized in this consent form or when required by law. It is possible that some of the other people/groups who receive your health information may not be required by Federal privacy laws to protect your information and may share it without your permission.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

To participate in this research you must allow the research team to use your health information. If you do not want us to use your protected health information, you may not participate in this research.

Your permission for the use, retention, and sharing of your identifiable health information will expire upon completion of the research study. At that time the research information will be destroyed. Any research information in your medical record will be kept indefinitely.

If you choose to participate, you are free to withdraw your permission for the use and sharing of your health information at any time. You must do this in writing as indicated in the HMC Privacy Notice. Write to Margaret Davitt Harris and let her know that you are withdrawing from the research study. Her mailing address is: P.O. Box 421, Mount Wolf PA 17347

If you withdraw your permission:

- We will no longer use or share medical information about you for the reasons covered by your written authorization, except when the law allows us to do so.
- We are unable to take back anything we have already done or any information we have already shared with your permission.
- We may continue using and sharing the information obtained prior to your withdrawal if it is necessary for the soundness of the overall research.
- We will need to keep our records of the care that we provided to you as long as the law requires.

The research team may use the following sources of health information.

- The information on the completed surveys

Representatives of the following people/groups within HMC and/or PSU are allowed to use your health information and to share it with other specific groups in connection with this research study.

- The principal investigator, Margaret Davitt Harris
- The HMC/PSU Institutional Review Board
- The HMC/PSU Human Subjects Protection Office

The people or groups listed in the above paragraph may share your health information with the following people/groups outside HMC and/or PSU for their use in connection with this research study. These groups, while monitoring the research study, may also review and/or copy your original HMC and/or PSU records.

- The Office of Human Research Protections in the U. S. Department of Health and Human Services
-

8. **Costs for Participation**: There is no cost to you for participating in this study. You are not waiving any legal rights you may have by signing this form.

9. **Compensation for Participation**: You will not receive any compensation for being in this research study.

10. **Research Funding**: The institution and investigators are not receiving any funding to support this research study.

11. **Voluntary Participation**: Taking part in this research study is voluntary. If you choose to take part in this research, your major responsibilities will include: completing the surveys. You do not have to participate in this research. If you choose to take part, you have the right to stop at any time. If you decide not to participate or if you decide to stop taking part in the research at a later date, there will be no penalty or loss of benefits to which you are entitled. In other words, your decision to decline to participate in this research or to stop taking part in the research will not affect your medical care.

12. **Contact Information for Questions or Concerns**: You have the right to ask any questions you may have about this research. If you have questions or concerns or believe you may have developed an injury that is related to this research, contact Margaret Davitt Harris at (717) 531-4212.

If you have questions or concerns regarding your rights as a research participant or about your privacy and the use of your personal health information, you may contact the research protection advocate in the HMC Human Subjects Protection Office at 717-531-5687.

Signature and Consent Permission to Be in the Research

Before making the decision regarding enrollment in this research you should have:

- Discussed this study with an investigator,
- Reviewed the information in this form, and
- Had the opportunity to ask any questions you may have.
-

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Participant: By signing this consent form, you indicate that you are voluntarily choosing to take part in this research.

_____	_____	_____	_____
Signature of Participant	Date	Time	Printed Name

Person Explaining the Research: Your signature below means that you have explained the research to the participant/participant representative and have answered any questions he/she has about the research.

_____	_____	_____	_____
Signature of person who explained this research	Date	Time	Printed Name

(Only approved investigators for this research may explain the research and obtain informed consent.)

INFORMED CONSENT FOR RESEARCH

STANFORD UNIVERSITY MEDICAL CENTER

IRB Meeting Date:

Protocol ID: 9107
Title: Uncertainty and Caregiver Burden and Patient Symptomatic In Caregivers of BMT Patients

Please check one of the following:
_____ You are an adult subject in this study.
_____ You are the parent or guardian granting consent for a minor in this study.
Print Minor's name here: _____

The following information applies to the individual or to his/her minor child. If the subject is a minor, use of "you" refers to "your child".

Are you participating in any other research studies? _____ yes _____no

INTRODUCTION TO RESEARCH STUDIES

A research study is designed to answer specific questions, sometimes about a drug, device or treatment's safety and its effectiveness. Being in a research study is different from being a patient. When you are a patient, you and your personal doctor have a great deal of freedom in making decisions about your health care. When you are a research subject, the Protocol Director and the research staff will follow the rules of the research study (protocol) as closely as possible, without compromising your health.

PURPOSE OF RESEARCH

You are being invited to participate in a research study that will examine the effect the Bone Marrow Transplant has on the Caregiver. You were selected as a possible participant because you have a disease of your blood or lymph system, are a candidate for a BMT, or are a caregiver for a patient undergoing a BMT, are over the age of 18.

Your participation in this study is entirely voluntary.

Your decision whether or not to participate will not prejudice you or your medical care. If you decide to participate, you are free to withdraw your consent and to discontinue participation at any time without prejudice to you or effect on your medical care. If you decide to terminate your participation in this study, you should notify Kate Tierney, PhD, Clinical Specialist in Bone Marrow Transplant.

Approximately, 100 subjects will be enrolled in this study over a three to four year period.

DURATION OF STUDY INVOLVEMENT

This research study is expected to take approximately six to nine weeks. At the end of the study, you will be finished with this study.

PROCEDURES

If you choose to participate, the study plan is as follows:

1. Complete consent procedures for both patient and caregiver.
2. Complete Packet Number One prior to your bone marrow transplant. This will include a short collection of information about your loved one and yourself. And five short questionnaires if you are the caregiver. If you are the patient, you will be asked to complete three short questionnaires on your perception of pain, fatigue, and several other frequently occurring symptoms.
3. Complete Packet Number Two within several days of receiving your stem cells, or marrow. Packet Number Two is identical to Packet Number One with the exception of the information about yourself and the patient.
4. Complete Packet Number Three which will occur approximately seven days after discharge from the hospital or seven days after your receive your stem cells if you are not admitted for your bone marrow transplant.
5. Complete packet number four which will occur approximately one month after discharge from the hospital or one month after you have received your stem cells.

SUBJECT'S RESPONSIBILITIES

You should:

- Complete the questionnaires as honestly as you can.
- Do not compare answers between yourself and your loved one.
- Complete all of the questions.
- Ask questions as you think of them.
- Tell the Protocol Director or research staff if you change your mind about staying in the study.

There is no restriction on your participation in any other clinical trials

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind, you are **free to withdraw** your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled.

If you decide to withdraw from the study at any time you should notify Kate Tierney. There are no consequences for withdrawing from participating in this trial.

The Protocol Director may also withdraw you from the study and the study medication may be stopped without your consent for one or more of the following reasons:

- Failure to follow the instructions of the Protocol Director and/or study staff.
- The Protocol Director decides that continuing your participation could be harmful to you.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the Protocol Director, Kate Tierney, PhD, if you have any questions. Risks with this study should be minimal, limited to emotional distress. If you experience this emotional distress, you may be referred for treatment within the resources available in the Stanford Cancer Center.

POTENTIAL BENEFITS

WE CANNOT AND DO NOT GUARANTEE OR PROMISE THAT YOU WILL RECEIVE ANY BENEFITS FROM THIS STUDY.

Benefits will be to individuals who undergo BMT or have loved ones who under go BMT in the future.

ALTERNATIVES

Every participant has the right to refuse to participate in this research study.

SUBJECT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction.

If you decide not to participate, tell Kate Tierney, PhD. You will still receive care for your disease and will not lose any benefits to which you would otherwise be entitled.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study. You have the right to review your medical records.

CONFIDENTIALITY

Your identity will be kept as confidential as possible as required by law. Except as required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier. Your research records may be disclosed outside of Stanford, but in this case, you will be identified only by a unique code number. Information about the code will be kept in a secure location and access limited to research study personnel.

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. However, your identity will not be disclosed**.**

Patient information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

FINANCIAL CONSIDERATIONS

PAYMENT

You will not be paid to participate in this research study.

COSTS

All costs associated with this treatment will be yours or your insurance companies. There is no additional cost beyond what is customary for any transplant associated with this research study. No labs or blood work will be collected for this study.

USE AND DISCLOSURE OF YOUR MEDICAL INFORMATION

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this

form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my health information be utilized in the study?

The purpose of this research is to continue to explore, understand and improve care and support for caregivers of patients undergoing BMT and their loved ones.

Do I have to sign this authorization form?

You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study. Signing the form is not a condition for receiving any medical care outside the study.

If I sign, can I revoke it or withdraw from the research later?

If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your information (e.g., necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of your health information in this study, you must write to: Kate Tierney, PhD, at Stanford University Medical Center, 300 Pasteur Drive, H3249, Stanford, CA 04305.

What Personal Information Will Be Used or Disclosed?

Your health information related to this study, may be used or disclosed in connection with this research study, including, but not limited to your age, gender, ethnic background, disease and treatment related information.

Who May Use or Disclose the Information?

The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The Protocol Director, Kate Tierney, PhD
- The research team which includes your physician, laboratory research staff, nursing staff and study coordinators who gather and document your data.

- The Stanford University Administrative Panel on Human Subjects in Medical Research and any other unit of Stanford University as necessary.

Who May Receive / Use the Information?

The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- Federal and regulatory agencies as required
- Other investigators for IRB approved research projects

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?

Your authorization for the use and/or disclosure of your health information will expire on February 14, 2050.

_____
Signature of Subject

_____
Date

_____
Signature of Legally Authorized Representative

_____

_____
Description of Representative's Authority to Act for Subject

CONTACT INFORMATION

- If you need to change your appointment, please contact Kate Tierney at (650) 723-0822.
- If you have any questions, concerns or complaints about this **research study**, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Kate Tierney. You may contact him at (650)723-0822.

- In addition, if you are not satisfied with the manner in which this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a research study subject, please contact the Stanford Institutional Review Board to speak to an informed individual who is independent of the research team at (650) 723-5244 or toll free at 1-866-680-2906. Or write the Stanford Institutional Review Board, Administrative Panels Office, Stanford University, Stanford, CA 94305-5401

If you think you have experienced a **research-related injury** call Kate Tierney

COMPENSATION

All forms of medical diagnosis and treatment -- whether routine or experimental -- involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this study. If such complications arise, the Protocol Director and the research study staff will assist you in obtaining appropriate medical treatment but this study does not provide financial assistance for additional medical or other costs. Additionally, Stanford is not responsible for research and medical care by other institutions or personnel participating in this study. You do not waive any liability rights for personal injury by signing this form.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a human subject you have the following rights. These rights include but are not limited to the subject's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might
- be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should rise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without

prejudice;

- be given a copy of the signed and dated consent form;
- and 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 influence on the subject's decision.

YOUR SIGNATURE INDICATES THAT YOU HAVE READ AND UNDERSTAND THE ABOVE INFORMATION, THAT YOU HAVE DISCUSSED THIS STUDY WITH THE PERSON OBTAINING CONSENT, THAT YOU HAVE DECIDED TO PARTICIPATE BASED ON THE INFORMATION PROVIDED, AND THAT A COPY OF THIS FORM HAS BEEN GIVEN TO YOU.

_____ _____
Signature of Adult Participant Date

_____ _____
Signature of Parent, Guardian or Conservator Date

_____
Authority to act for participant

_____ _____
(If available) Signature of Other Parent Date

_____
Authority to act for participant

Signatures of both parents are requested, unless the person obtaining consent has determined that the other parent is not reasonably available.

Person Obtaining Consent

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied – that the subject has been provided with the Experimental Subject's Bill of Rights, if appropriate, that I have discussed the research project with the subject and explained to him or her in non-technical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the subject to ask questions and that all questions asked were answered.

_____ _____
Signature of Person Obtaining Consent Date

APPENDIX D

Descriptive Statistics

Descriptive Statistics of Burden (ZBI) Scores for Combined Caregiver Group

Total Burden Scores (Range)	**Min** (0)	**Max** (88)	**Mean**	**SD**
Interview 1	5.00	52.00	26.04	11.17
Interview 2	3.00	65.00	22.72	12.24
Interview 3	10.26	55.00	22.90	10.25
Interview 4	6.00	55.00	23.07	13.19
Personal Strain Scores(Range)	(0)	(48)		
Interview 1	2	31	12.87	5.97
Interview 2	1	33	11.16	6.40
Interview 3	4	25	10.77	5.11
Interview 4	2	29	11.15	7.18
Role Strain Scores (Range)	(0)	(24)		
Interview 1	0	17	7.29	4.04
Interview 2	0	19	6.59	4.17
Interview 3	0	17	7.10	3.52
Interview 4	0	18	6.63	3.88

Descriptive Statistics of Burden (ZBI) Scores for the Caregivers of the Autologous HSCT Patients

Total Burden Scores (Range)	**Min** (0)	**Max** (88)	**Mean**	**SD**
Interview 1	12.00	52.00	26.36	13.07
Interview 2	7.00	65.00	23.06	15.55
Interview 3	9.00	55.00	22.80	13.37
Interview 4	6.00	55.00	22.46	15.66
Personal Strain Scores (Range) (0) (48)				
Interview 1	4	31	13.27	7.00
Interview 2	3	33	11.31	8.44
Interview 3	4	25	10.53	6.55
Interview 4	2	29	10.53	8.47
Role Strain Scores (Range) (0) (24)				
Interview 1	1	17	7.36	4.46
Interview 2	0	19	7	4.84
Interview 3	0	17	7.33	4.40
Interview 4	0	18	6.47	4.64

Descriptive Statistics of Burden (ZBI) Scores for the Caregivers of the Allogeneic HSCT Patients

Total Burden Scores (Range)	**Min** (0)	**Max** (88)	**Mean**	**SD**
Interview 1	5.00	52.00	26.04	11.17
Interview 2	3.00	65.00	22.72	12.24
Interview 3	10.26	55.00	22.90	10.25
Interview 4	6.00	55.00	23.07	13.19
Personal Strain Scores(Range)	(0)	(48)		
Interview 1	2	31	12.87	5.97
Interview 2	1	33	11.16	6.40
Interview 3	4	25	10.77	5.11
Interview 4	2	29	11.15	7.18
Role Strain Scores (Range)	(0)	(24)		
Interview 1	0	17	7.29	4.04
Interview 2	0	19	6.59	4.17
Interview 3	0	17	7.10	3.52
Interview 4	0	18	6.63	3.88

Descriptive Statistics of Uncertainty (MUIS) Scores for the Combined Caregiver Group

Total Uncertainty Scores (Range)	**Min** (32)	**Max** (165)	**Mean**	**SD**
Interview 1	49	115	84.20	15.44
Interview 2	51	128	81.69	16.60
Interview 3	32	108	82.39	15.53
Interview 4	32	107	79.37	16.83
Ambiguity Scores (Range)	(13)	(65)		
Interview 1	21	56	37.39	7.86
Interview 2	16	56	36.14	9.37
Interview 3	13	50	36.06	8.71
Interview 4	13	50	34.81	8.43
Complexity Scores (Range)	(7)	(35)		
Interview 1	8	24	15.04	4.02
Interview 2	16	56	36.14	9.37
Interview 3	7	23	15.61	3.90
Interview 4	7	20	14.70	3.70
Inconsistency Scores (Range)	(7)	(35)		
Interview 1	8	27	15.34	4.70
Interview 2	7	29	13.86	4.62
Interview 3	7	24	14.55	4.22
Interview 4	7	24	14.04	4.21
Unpredictability Scores (Range)	(5)	(25)		
Interview 1	9	23	16.39	3.25
Interview 2	10	23	16.69	3.09
Interview 3	5	22	16.16	3.37
Interview 4	5	22	15.81	3.85

Descriptive Statistics of Uncertainty (MUIS) Scores for the Caregivers of the Autologous HSCT Patients

Total Uncertainty Scores (Range)	**Min** (32)	**Max** (165)	**Mean**	**SD**
Interview 1	56	115	87.59	16.29
Interview 2	51	128	80.13	20.86
Interview 3	32	108	77.47	18.92
Interview 4	32	107	76.27	20.81
Ambiguity Scores (Range)	(13)	(65)		
Interview 1	22	56	38.68	8.37
Interview 2	16	56	33.75	11.26
Interview 3	13	50	32.20	9.31
Interview 4	13	50	32.93	9.69
Complexity Scores (Range)	(7)	(35)		
Interview 1	9	24	14.86	4.14
Interview 2	9	23	14.63	3.86
Interview 3	7	23	14.47	4.32
Interview 4	7	20	14	4.28
Inconsistency Scores (Range)	(7)	(35)		
Interview 1	8	27	16.91	5.16
Interview 2	7	29	14.75	5.94
Interview 3	7	23	14.93	4.65
Interview 4	7	24	14.13	4.96
Unpredictability Scores (Range)	(5)	(25)		
Interview 1	13	23	17.14	2.88
Interview 2	12	23	17	2.76
Interview 3	5	20	15.87	3.64
Interview 4	5	21	15.2	4.21

Descriptive Statistics of Uncertainty (MUIS) Scores for the Caregivers of the Allogeneic HSCT Patients

Total Uncertainty Scores (Range)	**Min** (32)	**Max** (165)	**Mean**	**SD**
Interview 1	49	107	80.82	14.11
Interview 2	58	105	82.95	12.67
Interview 3	65	102	87	10.08
Interview 4	70	101	83.25	9.43
Ambiguity Scores (Range)	(13)	(65)		
Interview 1	21	46	36.09	7.28
Interview 2	24	50	37.95	7.42
Interview 3	22	50	39.69	6.48
Interview 4	27	45	37.17	6.12
Complexity Scores (Range)	(7)	(35)		
Interview 1	8	24	15.22	3.98
Interview 2	9	21	15.60	2.87
Interview 3	11	23	16.69	3.22
Interview 4	10	19	15.58	2.75
Inconsistency Scores (Range)	(7)	(35)		
Interview 1	9	22	13.77	3.68
Interview 2	8	21	13.15	3.22
Interview 3	9	24	14.19	3.89
Interview 4	9	21	13.92	3.26
Unpredictability Scores (Range)	(5)	(25)		
Interview 1	9	21	15.64	3.49
Interview 2	10	21	16.45	3.38
Interview 3	11	22	16.44	3.18
Interview 4	12	22	16.58	3.37

Descriptive Statistics of the Caregivers' Symptomatology Scores for the Combined Caregiver Group

Pain (BPI) Scores (Range)	**Min** (0)	**Max** (100)	**Mean**	**SD**
Interview 1	0	94	29.98	27.68
Interview 2	0	91	27.58	24.77
Interview 3	0	78	25.57	26.80
Interview 4	0	96	21.81	26.63
Fatigue (BFI) Scores (Range)	(0)	(100)		
Interview 1	0	87	39.36	24.22
Interview 2	0	90	45.17	28.53
Interview 3	0	86	41.81	24.71
Interview 4	0	82	37.85	25.13
MSAS Total Scores (Range)	(0)	(7.36)		
Interview 1	1.17	3.28	2.03	0.55
Interview 2	1.17	2.86	2.02	0.45
Interview 3	1.09	3.44	1.98	0.51
Interview 4	.93	4.07	1.91	.66
MSAS Global Scores (Range)	(0)	(8.3)		
Interview 1	0	3.4	1.18	0.81
Interview 2	0	2.38	1.17	.67
Interview 3	0	4.1	1.19	.88
Interview 4	0	3.6	1.05	.92
MSAS Psychological Scores (Range)	(0)	(8.3)		
Interview 1	0	4	1.40	0.99
Interview 2	0	4.22	1.19	0.91
Interview 3	0	2.89	1.14	0.75
Interview 4	0	3.61	1.05	0.98
MSAS Physical Scores (Range)	(0)	(5.7)		
Interview 1	0	3.05	0.86	0.71
Interview 2	0	2.25	1.13	0.64
Interview 3	0	2.65	1.08	0.75
Interview 4	0	2.59	0.97	0.81

Descriptive Statistics of the Caregivers' Symptomatology Scores for the the Autologous HSCT Patients

Pain (BPI) Scores (Range)	**Min** (0)	**Max** (100)	**Mean**	**SD**
Interview 1	0	94	37.5	30.63
Interview 2	0	91	29.8	30.42
Interview 3	0	78	25.33	29.88
Interview 4	0	96	21.73	27.64
Fatigue (BFI) Scores (Range)	(0)	(100)		
Interview 1	0	87	42.55	27.54
Interview 2	2	90	45	30.91
Interview 3	0	80	36.80	25.84
Interview 4	0	69	31.87	24.82
MSAS Total Scores (Range)	(0)	(7.36)		
Interview 1	1.17	3.28	2.05	0.54
Interview 2	1.17	2.86	2.01	0.51
Interview 3	1.09	3.44	1.99	0.65
Interview 4	0.93	4.07	1.88	0.80
MSAS Global Scores (Range)	(0)	(8.4)		
Interview 1	0	3.44	1.16	.91
Interview 2	0	2.38	1.12	0.71
Interview 3	0	4.10	1.17	1.15
Interview 4	0	3.6	0.87	1.02
MSAS Psychological Scores (Range)	(0)	(5.7)		
Interview 1	0	4	1.37	1.11
Interview 2	0	4.22	1.19	1.18
Interview 3	0	2.9	0.92	0.94
Interview 4	0	3.61	0.91	1.09
MSAS Physical Scores (Range)	(0)	(5.7)		
Interview 1	0	3.05	0.88	0.81
Interview 2	0	2	1.00	0.61
Interview 3	0	2.65	1.11	0.90
Interview 4	0	2.59	0.84	0.83

Descriptive Statistics of the Caregivers' Symptomatology Scores for the the Allogeneic HSCT Patients

Pain (BPI) Scores (Range)	**Min** (0)	**Max** (100)	**Mean**	**SD**
Interview 1	0	73	22.78	22.93
Interview 2	0	70	26	20.48
Interview 3	0	76	25.80	24.39
Interview 4	0	69	21.91	24.08
Fatigue (BFI) Scores (Range)	(0)	(100)		
Interview 1	0	70	36.30	20.73
Interview 2	0	88	45.29	27.49
Interview 3	0	86	46.50	23.43
Interview 4	0	82	45.33	24.47
MSAS Total Scores (Range)	(0)	(7.36)		
Interview 1	1.17	3.17	2.01	0.58
Interview 2	1.24	2.75	2.03	0.41
Interview 3	1.47	2.80	1.97	0.36
Interview 4	1.43	2.93	1.94	0.45
MSAS Global Scores (Range)	(0)	(8.4)		
Interview 1	0	2.32	1.21	0.71
Interview 2	0	2.36	1.21	0.66
Interview 3	0.52	2.50	1.22	0.57
Interview 4	0	2.90	1.27	0.76
MSAS Psychological Scores (Range)	(0)	(8.3)		
Interview 1	0	2.8	1.43	0.88
Interview 2	0	2.54	1.19	0.69
Interview 3	0.61	2.49	1.34	0.48
Interview 4	0	3.14	1.22	0.83
MSAS Physical Scores (Range)	(0)	(5.7)		
Interview 1	0	2.63	0.84	0.61
Interview 2	0	2.25	1.22	0.66
Interview 3	0.24	2.35	1.06	0.62
Interview 4	0	2.51	1.13	0.79

Descriptive Statistics of the Patients' Symptomatology Scores for the Combined Group

Pain (BPI) Scores (Range)	**Min** (0)	**Max** (100)	**Mean**	**SD**
Interview 1	0	82	23.35	24.90
Interview 2	0	92	26.65	25.01
Interview 3	0	83	25.22	28.10
Interview 4	0	71	19.84	20.72
Fatigue (BFI) Scores (Range)	(0)	(100)		
Interview 1	0	83	32.36	23.69
Interview 2	0	79	35.89	23.60
Interview 3	3	75	39.97	19.79
Interview 4	3	90	38.96	24.96
MSAS Total Scores (Range)	(0)	(7.36)		
Interview 1	1	3.28	2.0	.47
Interview 2	.90	3.50	2.18	.54
Interview 3	1.59	3.07	2.13	.40
Interview 4	1.19	3.37	2.09	.53
MSAS Global Scores (Range)	(0)	(8.4)		
Interview 1	0	2.9	.98	.73
Interview 2	0	3.24	1.22	.86
Interview 3	0	3.3	1.18	0.70
Interview 4	0	3.10	1.20	.89
MSAS Psychological Scores (Range)	(0)	(8.3)		
Interview 1	0	3.89	1.11	.97
Interview 2	0	3.12	1.13	.91
Interview 3	0	2.93	.97	.73
Interview 4	0	3	1.16	.90
MSAS Physical Scores (Range)	(0)	(5.7)		
Interview 1	0	2.47	.81	.68
Interview 2	0	2.98	1.28	.79
Interview 3	.12	3.01	1.21	.69
Interview 4	.11	2.62	1.08	.66

Descriptive Statistics of the Patients' Symptomatology Scores for the Autologous Group

Pain (BPI) Scores (Range)	**Min** (0)	**Max** (100)	**Mean**	**SD**
Interview 1	0	82	33.10	29.70
Interview 2	0	92	35.13	28.04
Interview 3	0	83	31.00	32.78
Interview 4	0	71	27.15	24.42
Fatigue (BFI) Scores (Range)	(0)	(100)		
Interview 1	0	77	38.81	26.46
Interview 2	0	72	32.5	25.61
Interview 3	3	75	39.81	20.48
Interview 4	3	90	40.08	29.45
MSAS Total Scores (Range)	(0)	(7.36)		
Interview 1	1	3.28	2.06	.59
Interview 2	.9	2.69	2.05	.54
Interview 3	1.72	3.06	2.15	.44
Interview 4	1.40	3.37	2.16	.60
MSAS Global Scores (Range)	(0)	(8.4)		
Interview 1	0	2.90	1.03	.88
Interview 2	0	3.24	1.99	1.00
Interview 3	0	3.3	1.15	.81
Interview 4	0	3.10	1.30	1.10
MSAS Psychological Scores (Range)	(0)	(8.3)		
Interview 1	0	3.89	1.23	1.17
Interview 2	0	3.12	1.16	1.13
Interview 3	0	2.9	.86	.91
Interview 4	0	3	1.23	1.10
MSAS Physical Scores (Range)	(0)	(5.7)		
Interview 1	0	2.44	.82	.77
Interview 2	0	2.88	1.24	.86
Interview 3	.12	3.01	1.20	.78
Interview 4	.11	2.62	1.16	.80

Descriptive Statistics of the Patients' Symptomatology Scores for the Allogeneic Group

Pain (BPI) Scores (Range)	**Min** (0)	**Max** (100)	**Mean**	**SD**
Interview 1	0	53	14.87	16.13
Interview 2	0	68	20.19	20.86
Interview 3	0	73	19.44	22.06
Interview 4	0	37	11.92	12.42
Fatigue (BFI) Scores (Range)	(0)	(100)		
Interview 1	0	83	26.48	19.61
Interview 2	0	79	38.48	22.24
Interview 3	8	74	40.13	19.75
Interview 4	9	79	37.75	19.98
MSAS Total Scores (Range)	(0)	(7.36)		
Interview 1	1.18	2.58	1.94	.35
Interview 2	1.44	3.5	2.28	.52
Interview 3	1.59	3.07	2.12	.38
Interview 4	1.19	2.90	2.00	.46
MSAS Global Scores (Range)	(0)	(8.4)		
Interview 1	0	1.84	.93	.59
Interview 2	0	2.9	1.23	.75
Interview 3	.28	2.3	1.21	.59
Interview 4	.24	2.64	1.10	.62
MSAS Psychological Scores (Range)	(0)	(8.3)		
Interview 1	0	2.27	1.00	.76
Interview 2	0	2.63	1.10	.73
Interview 3	.20	2.21	1.08	.49
Interview 4	0	2.29	1.10	.66
MSAS Physical Scores (Range)	(0)	(5.7)		
Interview 1	0	2.47	.81	.62
Interview 2	0	2.98	1.32	.75
Interview 3	.34	2.26	1.23	.61
Interview 4	.42	2.12	.99	.49

APPENDIX E

Summary Tables of Statistical Analysis

Summary Table for Caregiver Burden, Uncertainty and Related Subcale Scores by Caregiver Type of Transplant

Measurement	Combined Caregiver Group HSCT Transplants		Caregivers of Allogeneic HSCT Transplants		Caregivers of Autologous HSCT Transplants	
	General Direction of Score	Significance	General Direction of Score	Significance	General Direction of Score	Significance
Total Burden	↓	1-2 * (p =. 04 1-3* (p = .04)	↓	1-2 * (p = .08)	↓	NS
Personal Strain	↓	1- 2* (p = .07) 1- 3* (p = .02)	↓	NS	↓	1-3 * (p = .07)
Role Strain	↓	NS	↓	NS	↓	NS
Total Uncertainty	↓	NS	↑	1-2 (p = .06) 1-3 (p = .05)	↓	
Ambiguity	↓	NS	↑	1-2* (p = .07)l	↓	1-2* (p = .01) 1-3* (p = .01) 1-4* (p = .04)
Complexity	No change	NS	↑	1-3* (p = .09)	↓	NS
Inconsistency	↓	1-2* (p = .03)	↑	NS	↓	1-2* (p = .03)
Unpredictability	↓	NS	↑		↓	

*Legend
1= Interview 1: Pre-transplant; 2 = Interview 2 = Immediately post-transplant; 3 = Interview 3 one week post discharge, 4 = Interview 4 = one month post discharge

Summary Table of Differences Between Patient and Caregiver Subscale Scores for Patient Symptomatology by Type of Transplant

Difference between Patient and Caregiver	Combined Caregiver Group HSCT Transplants		Allogeneic HSCT Transplants		Autologous HSCT Transplants	
	General Direction of Score	Significance	General Direction of Score	Significance	General Direction of Score	Significance
BPI (Brief Pain Inventory)	↓ ↑ at 4	p = .026 at 1	↓ ↑ at 4	p = .054 at 1 p =.078 at 2 p =.059 at 4	↓	ns
BFI (Brief Fatigue Inventory)	↑1-2 ↓	p = .027 1 p = .015 2	↓	p =.017 at 1 p =.096 at 2	↑ 1-2 ↓	p =.074
MSAS (Memorial Symptom Assessment Survey) Total	↓	p = .862 at 1	↓ ↑ at 3 ↓at 4	p=.066 at 2	↓	ns

Vita

Margaret E. Davitt Harris

Education

2008	PhD, The Pennsylvania State University School of Nursing
1995	Nurse Practitioner Certification The Pennsylvania State University School of Nursing Family Nurse Practitioner
1980	MSN, The University of Pennsylvania School of Nursing Adult Health and Illness
1977	BSN, College Misericordia Department of Nursing

Professional Experience

2006 - Present	Administrative Director	Lancaster General Cancer Program, Lancaster General, Lancaster Pa.
2004 - 2005	Educator	Oncology Nursing Society
1990 - 2004	Director Medical Nursing	Penn State Hershey Medical Center Hershey, Pa.
1979 - 1990	Head Nurse	Hospital University of Pennsylvania Philadelphia, Pa.
1977 - 1979	Staff Nurse	Hospital University of Pennsylvania Philadelphia, Pa.

Awards

1980 Sigma Theta Tau

Professional Memberships

Oncology Nursing Society
American Society Blood and Marrow
American Academy of Nurse Practitioners

Certifications

Advanced Oncology Certified Nurse AOCN®
Nurse Practitioner Certified. Family Nurse Practitioner, American Academy Nurse Practitioners