RISK FACTORS FOR PRESSURE ULCER DEVELOPMENT IN CRITICALLY ILL PATIENTS

By

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DEDICATION

This dissertation is dedicated primarily to patients who need care in an intensive care unit. I hope that this study will provide some guidance to their caregivers.

Additionally, this dissertation is dedicated to my friends and family with special attention to the following individuals:

To my mother, father, brother, and other family who never seemed to tire of listening to my vicissitudes and who encouraged me every step of the way.

To David Metz, my best friend, who never complained about the countless hours of study that removed me from home activities. He never complained about the mountains of laundry he washed, the countless meals he cooked, or doing the daily chores that I did not. His presence made this dream possible.

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CHAPTER I

INTRODUCTION

Statement of the Problem

Pressure ulcers and the risk factors associated with their development have been studied for almost 50 years yet the temporal, qualitative, and quantitative relationship between pressure ulcer risk factors and pressure ulcer incidence is still poorly understood. The literature suggests that specific risk factors for pressure ulcer incidence are associated with specific patient populations (de Laat, Schoonhoven, Pickkers, Verbeek, & van Achterberg, 2006); however, methodological strategies to explain associations between risk factors and pressure ulcer incidence generally do not reflect a specific patient population orientation. The literature identifies over 200 risk factors that may contribute to pressure ulcer development (Anthony, Parboteeah, Saleh, & Papanikolaou, 2008), but methodological and definitional inconsistencies complicate and slow the process of translating research into clinical practice (Keller, Wille, van Ramshorst, & van der Werken, 2002). Consequently, clinicians lack a specific set of risk factors on which to focus their prevention efforts, resulting in the diffuse application of preventive measures with limited effectiveness. Hospital acquired pressure ulcer (HAPU) rates increased by 63% between 1993 and 2006 (Russo & Elixhauser, 2006). These statistics have not been risk-adjusted for severity of illness; however, hospital admission rates increased only 11% during the same period, and hospital stays for patients over 65 years old increased by 14%, suggesting that the observed increase in HAPU rates are not

entirely a function of the patient demographic. This increase in HAPUs contributes to higher health care costs, increased morbidity and mortality rates (Russo & Elixhauser, 2006), and raises concerns about the quality of care delivered in US nursing homes and hospitals (Needleman, Kurtzman, & Kizer, 2007).

Of the populations studied, patients who are critically ill (i.e., receiving care in an intensive care unit [ICU]) are the most prone to the development of pressure ulcers (Bours, de Laat, Halfens, & Lubbers, 2001; de Laat, et al., 2006), yet few investigators have systematically evaluated the predictive relationships between risk factor presence and pressure ulcer development in this population. The most recent International Pressure Ulcer Prevalence Survey (IPUPS; VanGilder, Amlung, Harrison, & Meyer, n.d.), conducted in 2008 through 2009, substantiates the disproportionate prevalence of pressure ulcers in ICUs. Pressure ulcers acquired in the ICU had a prevalence rate of 8.8% to 12.1% in 2008 and 2009, respectively representing approximately 8,000 to 11,000 patients annually who developed a pressure ulcer while in the ICU in the US. In 2009, 3.3% of US ICU patients developed a severe facility-acquired pressure ulcer defined as Stage III, Stage IV, unstageable, or deep tissue injury (VanGilder et al., n.d.). These findings suggest that clinicians working in ICUs need prevention strategies focused on risk factors specific to their patient population.

Purpose of the Study

Pressure ulcer prevention interventions are predicated on identifying salient risk factors for pressure ulcer development in specific patient populations (de Laat, et al.,

2006). The descriptive research identifies multiple patient specific risk factors that contribute to pressure ulcer incidence in a variety of patient populations; however, with the exception of increased age, no single or combination of risk factors predicts pressure ulcer incidence equally well among various patient populations. Braden and Bergstrom's (1987) and Defloor's (1999) conceptual models identify pressure ulcer risk factors, but have not been extensively studied in various patient populations, specifically the ICU population. Critically ill patients, the most prone to pressure ulcer development, are the least studied patient population reported in the literature. A search of the PubMed database conducted using the search terms 'risk factors' and 'pressure ulcers,' with the limits of all adult, humans, core clinical and nursing journals, and English with no date constraints yielded 574 articles published between 1975 and 2011. To refine the search to risk factors for pressure ulcer development in critically ill patients, the search term 'intensive care' was added using the same limits. The search returned 57 articles published from 1975 to 2011. Of those, eleven were prospective studies designed to identify causality between pressure ulcer risk factors and pressure ulcer incidence. Further studies to evaluate causal relationships between risk factors in critically ill patients and pressure ulcer development are needed to further understand, prevent, and mitigate the effects of pressure ulcers in this vulnerable population. The purpose of this study was to identify risk factors that contributed to pressure ulcer development in critically ill patients.

Significance

The significance of pressure ulcers is viewed within the broader contexts of their significance to society, healthcare, and specifically to the nursing profession.

Significance to Society

Prevalence and incidence of pressure ulcers in the US. National estimates of pressure ulcer prevalence rates vary widely in the literature. In a summary of findings by the 2004 National Nursing Home Survey, Park-Lee and Caffrey (2009) reported that about 159,000 (11%) of nursing home residents had a pressure ulcer. This statistic is somewhat higher than those released by the Agency for Healthcare Research and Quality (AHRQ) in 2004. According to AHRQ, pressure ulcer rates in nursing homes ranged from 8.5% to 8.7% (Agency for Healthcare Research and Quality [AHRQ], n.d.). National pressure ulcer prevalence rates in acute care facilities are less precise than those reported in nursing homes, possibly because of the dynamic nature and increased acuity of the acute care patient populations. Using data from secondary sources, the Institute for Healthcare Improvement (IHI) estimated pressure ulcer prevalence rates in acute care facilities ranged from 0.4% to 38% (Lyder, 2003). The National Pressure Ulcer Advisory Panel (NPUAP) estimates pressure ulcer prevalence rates in acute care facilities at 15% and incidence rates in acute care facilities at 7% (Cuddington, Ayello & Sussman, 2001).

National statistics on pressure ulcer prevalence and incidence in critically ill patients in the US are difficult to locate. Estimates of pressure ulcer prevalence and incidence rates in the ICU patient population are higher than those of the general acute care facility population because of their increased association with risk factors that are

generally thought to contribute to pressure ulcer development (Carlson, Kemp, & Shott, 1999). In a national benchmarking study conducted in US acute care facilities in 1999, Amlung, Miller, and Bosley (2001) found pressure ulcer incidence rates among critically ill patients to be 13%. This statistic falls within the 7% to 15% identified by Cuddington, et al. (2001), although some estimates of pressure ulcer incidence rates in ICUs approach 50% in US ICUs (Cuddington et al., 2001; Fife et al., 2001; Jiricka, Pyan, Carvalho, & Bukvich, 1995).

Healthcare costs of pressure ulcers in the US. In 2006, the national estimates on the costs of treating pressure ulcers in the US ranged between $1.3 and $3.5 billion per year (Courtney, Ruppman, & Cooper, 2006). These costs are similar to earlier estimates by Whittington and Briones (2004) of between $2.2 and $3.6 billion per year for the treatment of pressure ulcers. By 2008, the Institute for Healthcare Improvement (IHI) estimated a total national cost of $11 billion per year to treat pressure ulcers (Institute for Health Care Improvement [IHI], 2008). The IHI also estimated that the cost of treating a single full-thickness pressure ulcer to be as high as $70,000 per ulcer (IHI, 2008). Although there is no specific rationale that explains the 214% to 746% increase in estimated pressure ulcer treatment costs between 2006 and 2008, Leape and Berwick (2005) suggested that the increasing complexity of both healthcare systems and patients contribute to the rising costs demonstrated by these cost statistics.

Morbidity and mortality associated with pressure ulcers. In addition to the high cost of treatment, pressure ulcer presence is a poor prognostic factor (Reddy, Gill, & Rochon, 2006). Prior to 2005, pressure ulcer associated morbidity and mortality in the US was significantly underestimated. In a cross-sectional descriptive study of mortality

causes, Redelings, Lee, and Sorvillo (2005) reviewed death records of the 27,572,153 persons who had died in the US between 1990 and 2001. The study found that 114,380 (0.41%) death records listed pressure ulcers as a contributing cause of death. Of those, 80% of pressure ulcer associated deaths occurred in persons 75 years of age or older. In a prospective cohort study designed to compare hospital length of stays and complications in pressure ulcer positive patients compared with pressure ulcer negative patients, Allman, Goode, Burst, Bartolucci, and Thomas (1999) found that patients who developed pressure ulcers were more likely to develop nosocomial infections (45.9% vs. 20.1%, p = 0.001). Severity of illness adjusted costs of hospital stays were also statistically significantly higher in those patients who developed pressure ulcers ($14,260 vs. $12,382, p = 0.03) (Allman et al., 1999).

Significance to Healthcare

Pressure ulcers are among the serious events listed by the National Quality Forum (NQF) in their 2006 update (National Quality Forum [NQF], 2006). Specifically, the NQF states that pressure ulcers are a product of lapses of care management, and that nosocomially acquired stage III or IV pressure ulcers are a serious event. The NQF acknowledges that pressure ulcers may not be preventable in all cases, but suggests that their incidence in healthcare settings warrants scrutiny of the systems and processes designed to prevent and treat pressure ulcers (NQF, 2006).

The National Quality Measures Clearinghouse (NQMC) provides 18 metrics for pressure ulcers that are included in either the outcome or the process domains (National Quality Measures Clearinghouse [NQMC], n.d.). While most of the measures focus on aspects of appropriate treatment and prevalence rates of pressure ulcers within acute or

long-term care facilities, five evaluate the identification of pressure ulcer risk and presence or absence of preventive measures. The measures do not identify a preferred risk-stratification tool, nor do they speak to the quality of the preventive interventions. The lack of specificity regarding pressure ulcer risk stratification and prevention measures suggests a lack of consensus on stratification of pressure ulcer risk and best pressure ulcer prevention practices. Adequate risk stratification is essential for accurate comparisons of adverse event rates across hospitals (Needleman, et al., 2007). The lack of empirical data supporting the putative link between nursing processes and pressure ulcer incidence (Needleman et al., 2007) suggests a need for a more rigorous risk adjustment method to control for the multiplicity of pressure ulcer risk factors that may be functioning as confounding variables in pressure ulcer research.

Significance to Nursing

According to the American Nurses Association (ANA), pressure ulcer prevention is primarily a nursing responsibility. In 1995, the ANA introduced 10 quality measures described as most sensitive to nursing care (Montalvo, 2007) and integrated those measures into the NQF's voluntary consensus standards for evaluating nurse sensitive care (Kurtzman & Corrigan, 2007). Nosocomially acquired pressure ulcers are among the nurse sensitive outcomes adopted by the NQF and considered to be within the domain of patient-centered outcomes (Kurtzman & Corrigan, 2007). To date, the nurse-specific quality metrics suggested by the ANA and the NQF are associated with patient outcomes, but do not imply causality. The empirical evidence to support a causal link between nursing quality of care and pressure ulcer development is lacking.

Research Aims

Further study is needed to understand the relationship between pressure ulcer risk factors and pressure ulcer development in critically ill patients. The resulting knowledge can help more accurately stratify pressure ulcer risk in this vulnerable population and help nurses target prevention measures to decrease the incidence of pressure ulcer development in the critically ill patient population. The aims for the proposed study were:

1. To compare the frequency and magnitude of pressure ulcer risk factors between critically ill patients that do and do not develop a pressure ulcer during their ICU stay and evaluate their influence on the associations between the Braden subscales and pressure ulcer outcome; and
2. To compare the frequency and magnitude of pressure ulcer risk factors between critically ill patients that have progression of their Stage I pressure ulcer during the ICU stay to those who do not have a progression of their Stage I pressure ulcer during the ICU stay.

The study was accomplished using a prospective matched case-control study design using convenience sampling in five ICUs at Vanderbilt University Hospital (VUH). Risk factors were identified using a previously published conceptual model (Benoit & Mion, 2012). Datasets were constructed that described the study sample and to conduct analyses that addressed the study aims.

Summary

Nursing care processes correlate with various quality outcomes, including pressure ulcer development. Despite the abundance of pressure ulcer risk factors identified in the literature, the HAPU incidence rate continues to rise, suggesting that current prevention interventions are inadequate, possibly because they lack specificity to various patient populations. Critically ill patients are the most vulnerable to pressure ulcer formation, but commonly used risk assessment tools lack the specificity needed to guide focused prevention efforts in the ICU patient population. By identifying risk factors that disproportionately contribute to pressure ulcer formation in the ICU patient population, nursing can improve patient outcomes by refining and selectively targeting pressure ulcer prevention efforts.

CHAPTER II

LITERATURE REVIEW AND THEORETICAL FRAMEWORK

The historical perspective of pressure ulcers indicates they have been a concern to the sick and injured for nearly 4000 years, but their relative importance to healthcare providers has fluctuated as the prevailing science and theoretical approaches to human disease have evolved (Parish, Witkowski, & Crissey, 1997; van Rijswijk, 2001). Prior to World War I (1914-1918), the medical community largely viewed pressure ulcers as an unavoidable consequence of illness, and prevention efforts were virtually nonexistent (Parish et al., 1997). As the prevailing view of pressure ulcers shifted toward a more preventive stance, the medical community began to identify risk factors for pressure ulcer development. The growing body of medical evidence on pressure ulcer risk factors indicates that some risk factors, such as advanced age and poor nutritional status, are common among various patient groups, while other risk factors may be unique or exhibit disproportionate importance within specific patient groups, such as the critically ill (de Laat, et al., 2006). The purpose of this chapter is to:

1. Identify and describe constructs related to pressure ulcer development;
2. Discuss the relationships among those constructs as described in two previously published conceptual frameworks;
3. Present a critical analysis of the extant literature on pressure ulcer risk factors;

4. Describe the validity, reliability, specificity and sensitivity of the most commonly used pressure ulcer risk assessment scale in the US and discuss its predictive ability in critically ill patient populations;
5. Present the conceptual framework used in this study that incorporates those risk factors identified in the literature review.

Theoretical Framework

Pressure Ulcer Constructs

Factors contributing to pressure ulcer development comprise three separate but interrelated constructs. External factors include compression, friction, and shearing forces on the skin and underlying connective tissue. Patient-specific factors include the characteristics of the skin and underlying connective tissue that affect their ability to withstand the external forces without consequent damage (Defloor, 1999; Thompson, 2005). Environmental factors refer to the characteristics of the environment in which medical and nursing care is received that may contribute to pressure ulcer development.

External Factors

Pressure ulcers develop as compressive, friction and shearing forces overwhelm the tissues' ability to withstand those forces. The resulting pressure damage can range from superficial disruption of the epidermis to deep ulceration involving muscle and associated connective tissues. The relative importance of the type and magnitude of the

destructive forces and the characteristics affecting the tissues' tolerance for those forces are not well understood (Thompson, 2005).

Pressure as a construct. Early conceptual models for pressure ulcer formation focused on describing the compressive force, or pressure, necessary to occlude capillary blood flow, creating ischemia to the involved tissues. In 1930, Landis (cited in Defloor, 1999) first described capillary closing pressures of 12 and 32 mm Hg at the venous and arterial end of a human finger capillary, respectively. Defloor (1999) suggested that the commonly accepted arterial capillary closing pressure of 32 mmHg be re-evaluated with regard to its clinical appropriateness because Landis' study was conducted on healthy persons. Defloor reasoned that persons who were ill enough to develop pressure ulcers would have pathophysiologic processes that influence capillary closing pressures. Early animal experiments conducted by Kosiack in 1959 (cited in Nixon, 2001) and a later study outlining tissue tolerance for pressure over time by Reswick and Rogers (1976) support an inverse parabolic relationship between the pressure intensity and time. These findings suggest that minimal amounts of compressive force over long periods had the same effect on blood flow as did high amounts of compressive force over shorter periods. The findings by Reswick and Rogers (1976) and Kosiack (cited in Nixon, 2001), obviate the utility of capillary closing pressures in describing the pathogenesis of pressure ulcers in favor of multifactorial explanations.

Compressive forces, which are those forces applied perpendicularly to the skin, seem to have the least destructive effects, especially when applied for short periods at a low magnitude (Nixon, 2001). Uniformly distributed compressive forces briefly applied to the body's surface do not have any long-term effects on the tissues. For example, a

scuba diver in 33 feet of water experiences an external compressive force of about 760 mm Hg (Springle, 2000) but does not develop pressure ulcers because the external force is uniformly applied and of short duration. This observation of uniform pressure distribution suggests that other forces, combined with pressure, may be more destructive than pressure alone.

Friction and shear as constructs. In 1958, the concept of shearing forces was added to compressive forces as a second causal factor in the development of pressure ulcers (Defloor, 1999). Shearing forces are those forces applied along a plane parallel to the skin and supporting structures. The effects of shear and friction in combination with compressive forces more completely explain the synergistic effects that these forces have on pressure ulcer development. Shearing forces, in combination with compressive forces, contribute to deformation of the deep tissues, thereby occluding blood flow and causing ischemic damage (Nixon, 2001). Friction contributes to pressure ulcer development by mechanical debridement of the epidermal and dermis layers rather than through ischemic mechanisms. Nixon (2001) described research done by Dinsdale in 1973, when he reported that friction initially removed the stratum corneum and separated the epidermis from the dermis. It was established that friction forces alone did not result in ischemia, but rather produced its effects through mechanical disruption of the epidermis. When combined with compressive forces, shearing and friction decrease the pressure required to occlude blood flow by approximately one half (Springle, 2000). The additive effects of pressure, friction, and shear can overcome the skin and connective tissues' tolerance for these forces, producing a disruption in the skin's integrity. The intensity and duration

of the external forces necessary to cause tissue damage is determined by the tissues' ability to tolerate them.

External factors are categorized according to their mechanism of action on the skin and underlying connective tissue and are composed of compressive, friction, and shearing forces. These external forces, however, are not enough to produce pressure ulcers by themselves (Defloor, 1999). Pressure ulcer development also depends on the general health of the individual, skin, and associated tissues. These patient-specific characteristics determine the duration and magnitude of external forces necessary to produce pressure ulcers.

Patient-Specific Factors

Patient-specific risk factors constitute the individual's overall tolerance of the tissue to withstand external forces without damage (Braden & Bergstrom, 1987). The interplay between the external forces of compression, friction, and shearing forces with aspects of tissue tolerance are dynamic and multifactorial (Nixon, 2001), explaining pressure ulcer incident differences among individuals with varying exposure to external forces. The concept of tissue tolerance includes factors that are known to influence the risk of pressure ulcer development, but do not directly affect the pressure, shear, and friction forces. Risk factors are, however, just as important in the etiology of pressure ulcer development as the accompanying pressure, shearing, and friction forces (Meijer, Germs, Schneider, & Ribbe, 1994).

Tissue tolerance as a construct. Tissue's tolerance for pressure, friction, and shear is a function of the homeostatic factors that maintain skin structure, blood and lymph flow to the skin and supporting structures. The dermal layer of the skin is a

critical determinate in its ability to tolerate pressure, friction and shearing forces. The dermis is composed of the papillary layer and the reticular layer and is responsible for most of the structural strength of the skin (Seeley, Stephens, & Tate, 2006). The papillary layer is composed of papillae that extend upwards into the epidermis. The dermal papillae contain an arteriolar and venous capillary necessary for nutrient and waste exchange with cells in the epidermis. The reticular layer is composed of a mat of collagen, elastin, and reticular fibers that contribute to the tensile strength of the skin (Seeley et al., 2006). The subcutaneous layer, or hypodermis, has an abundance of fat. In addition to its insulating and energy storage capabilities, fat is critical in dispersing the effects of extraneous pressure (Nixon, 2001).

Cutaneous blood flow is proportional to the metabolic needs of the tissues. Local blood flow is controlled by a combination of nervous and local factors associated with cell metabolism, such as the accumulation of metabolic byproducts. Cutaneous blood flow is also affected by the nervous system, which responds to various intravascular systemic conditions, such as blood pressure fluctuation and fluid and electrolyte balance. Vasoconstrictive nerve fibers from the sympathetic nervous system extend to most parts of the circulatory system and are prominent in the skin.

In addition to the extensive blood supply, human skin is permeated with a mesh of lymphatic vessels. Because lymph vessels have minimal or no musculature in their walls, the circulation of lymph is sluggish and largely controlled by forces such as pressure, skeletal muscle action, massaging, and heat. Any external pressure exerted, such as from a fixed dressing, interferes with its flow. Since skin plays a major role in immunologic

responses of the body, its lymphatic drainage is as significant as its blood vascular system (Skin Anatomy, n.d.).

In addition to the structural components of the skin, numerous types of sensory nerve fibers transmit signals to the brain, relaying a vast amount of information about the skin's immediate environment. Of primary importance to the concept of pressure ulcers are the mechanoreceptors and pain receptors located throughout the epidermis, dermis, and subcutaneous layers. The ability to respond to these sensory stimuli requires an intact central nervous system and functional effector organs, such as muscle, to alter a noxious stimulus. Alterations in any component of the central nervous system or the effector organs will affect the skin and supportive structure's tolerance for pressure.

Lymphocytes, macrophages, and mast cells are intimately associated with the skin and surrounding structures. When there is damage to the skin, these cells release inflammatory cytokines and chemical mediators. These chemical mediators increase vascular blood flow and vascular permeability at the injury site. Increased vascular permeability alters the capillary exchange mechanism on both the arterial and venous ends, resulting in an increase in net hydrostatic pressure combined with a decrease in net osmotic pressure. The result is interstitial edema because of the increase in net filtration pressure. As edema increases, the metabolic demands of the tissue increase and local factors favor vasodilation. Vasodilation increases edema and the cycle worsens. Eventually, increased edema overcomes the pressures in the capillaries and they close, creating an ischemic environment that leads to cell death.

Environmental Factors

Additionally, environmental elements may contribute to pressure ulcer development. For institutionalized (i.e. hospitalized and long-term care) patients, environmental variables that influence the delivery of care are important because they constitute elements of the clinical setting that affect patient outcomes (Kane, 2006). Kane described outcomes as a function of the patient's baseline clinical, psychosocial, and demographic characteristics influenced by the treatments received and the setting in which those treatments occur. When written as a formula, the relation between outcomes and contributing factors becomes "Outcomes = *f* (baseline, patient clinical characteristics, patient demographic/psychosocial characteristics, treatment, setting)" (Kane, 2006, p. 9).

Kane classified outcome measures as generic or condition-specific and suggested that outcomes under investigation should be selected based on a clear idea of what needs to be measured and why. Pressure ulcers qualify as a generic outcome because their occurrence relates to numerous intrinsic and extrinsic factors (Nixon, 2001) and is associated with multiple health conditions. Treatment and setting influences on patient outcomes can be categorized as nurse characteristics, such as educational level, attitude, and age (Aiken, Clarke, Cheung, Sloane, & Silber, 2003), and administratively mediated variables, such as nurse staffing levels, nurse skill mix, hospital structural characteristics, patient care environments, and equipment (Aiken, Clarke, Sloane, Lake, & Cheney, 2008).

Although environmental variables are increasingly recognized as important contributors to patient outcomes such as pressure ulcer development (Horn, Buerhaus,

Bergstrom & Smout, 2005; Seago, Williamson, & Atwood, 2006), this research focused on the effects of the external forces of compression, friction, and shear and those patient-specific risk factors that comprise the tissue's tolerance to the external forces.

Theoretical constructs contributing to pressure ulcer development are compressive forces, shearing, and friction forces, and the tissues' tolerance for those forces (Bergstrom, Braden, Laquzza, & Holman, 1987; Thompson, 2005). For purposes of this research, pressure ulcer risk factors were categorized as either external (pressure, friction and shear) or patient-specific risk factors that affect the tissues' ability to withstand the external forces.

In summary, pressure ulcers are a localized area of damage to the skin and underlying structures caused by compressive forces, shearing and friction, or a combination thereof. The skin and underlying tissues' ability to tolerate varying degrees of these forces is a function of the structural integrity of the skin, the blood and lymph flow to the cutaneous tissues, and an intact central nervous system required to reduce the destructive effects of those forces. Damage to the skin or underlying tissues results in an inflammatory immune response that ultimately contributes to localized ischemia and cell death, if the damaging element such as prolonged pressure, persists.

Conceptual Models for Pressure Ulcer Development

Prior to 2012, there were two conceptual models demonstrating the relationships between patient specific risk factors and the development of pressure ulcers. They are the Braden and Bergstrom conceptual model (Figure 2.1), and the Defloor conceptual model (Figure 2.2).

Braden and Bergstrom conceptual model. Braden and Bergstrom (1987) published the first conceptual model to explain the patient specific etiology of pressure ulcers (Figure 2.1). Their model was the first to identify components that contributed to the tissues' tolerance for pressure.

Figure 2. 1. Braden and Bergstrom's Conceptual Schema Depicting Factors in the Etiology of Pressure Sores.

(Braden and Bergstrom, 1987)

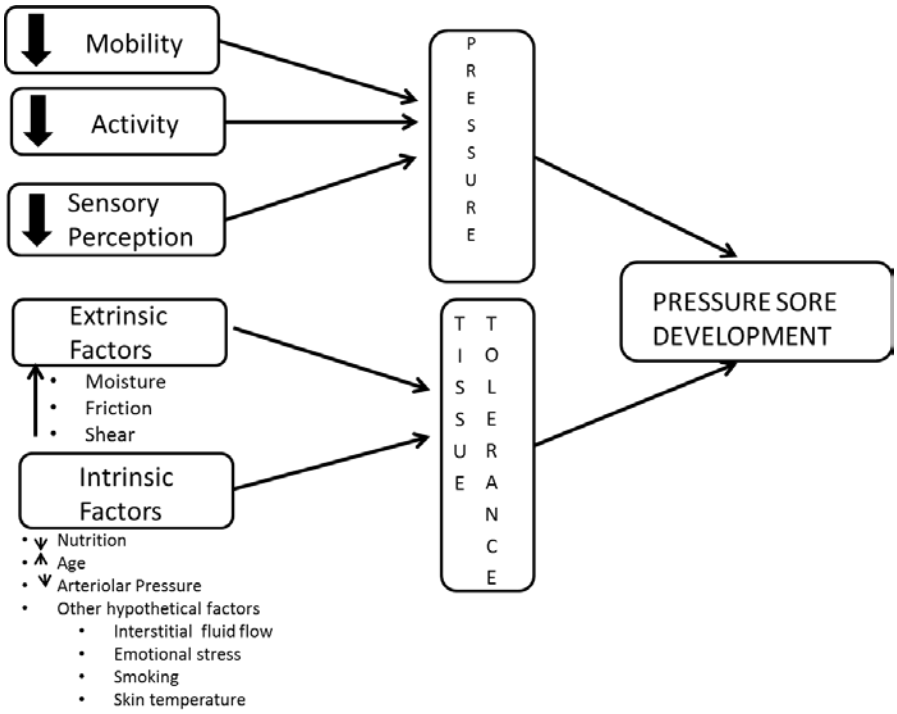


Figure 2.1. Braden and Bergstrom's Conceptual Schema Depicting Factors in the Etiology of Pressure Sores. From "A Conceptual Schema for the Study of the Etiology of Pressure Sores" by B.J. Braden and N. Bergstrom, 1987, *Journal of Rehabilitation Nursing, 12*, p. 9. Reprinted with permission.

The conceptual model proposed by Braden and Bergstrom (1987) identifies two critical determinants in the development of pressure ulcers: (1) intensity and duration of pressure, and (2) the tissues' ability to tolerate pressure. In the model, Braden and Bergstrom identified decreased activity, mobility, and sensory perception as those characteristics that influence the intensity and duration of compressive forces.

To explain the variability in the tissues' tolerance for any given intensity and duration of compressive forces, Braden and Bergstrom (1987) drew heavily from the literature published on pressure ulcer incidence in patients with spinal cord injuries. Cross sectional, descriptive studies published in journals such as *Archives of Physical Medicine and Rehabilitation* and the *Journal of Plastic and Reconstructive Surgery* provided Braden and Bergstrom with the empirical evidence to include general and patient specific factors in their model. Using the descriptive evidence in the literature, Braden and Bergstrom identified intrinsic and extrinsic factors known to affect skin integrity and included them in their construct for tissue tolerance. Among them are friction and shearing forces, moisture, age, arteriolar pressure, and nutritional status. This model, now commonly known as the Braden model, served as the basis for the Braden Scale for Predicting Pressure Sore Risk© (Copyright by Barbara Braden & Nancy Bergstrom, 1988; Bergstrom, Braden, Laquzza, & Holman, 1987) discussed later in this chapter.

Defloor Conceptual Model. Defloor (1999) modified Braden and Bergstrom's conceptual framework to include two specific components that affect tissue tolerance (Figure 2.2). Rather than the intrinsic and extrinsic components of tissue tolerance identified by Braden and Bergstrom (1987), Defloor suggested that the overall concept of tissue tolerance is composed of unique factors that influence the tissue's tolerance for pressure and its tolerance for alterations in oxygen supply and demand. According to Defloor, the tissue's tolerance for pressure is dependent on factors that help to distribute pressure. Defloor defined pressure as the amount of force distributed over a surface area and reasoned that factors that increase surface area will decrease the force on any given

plane of the skin/pressure interface. Tissue mass and factors that affect the skin's ability to distribute pressure, such as amount and quality of collagen, are examples of factors that Defloor suggested influence the tissue's tolerance for pressure and are conceptually similar to those identified by Braden and Bergstrom. Defloor further modified Braden and Bergstrom's conceptual model by adding the construct of tissue oxygenation as a determinate of tissue tolerance. Tissue oxygenation status is a function of the supply and demand of the oxygen traveling to the skin and supporting connective tissues. Defloor theorizes that mean arterial pressure, medications, and characteristics of the circulating hemoglobin will affect oxygen supply and waste removal of the involved tissues, thereby influencing the tissue's tolerance for pressure.

Braden, Bergstrom, and Defloor Conceptual Model Comparison

Despite the multiple similarities in intrinsic, extrinsic, and determinants of intensity and duration of pressure, Defloor enriched Braden's concept of tissue tolerance by describing factors that may contribute to either the structural or the physiologic components of tissue that affect its tolerance for pressure. Although not mutually exclusive, the elements in Defloor's tissue tolerance concept elaborate on characteristics commonly encountered in the clinical setting that are not explained in Braden's conceptual model.

Figure 2. 2. Defloor's Conceptual Scheme Depicting Risk Factors in the Etiology of Pressure Sores.

(Defloor, 1999)

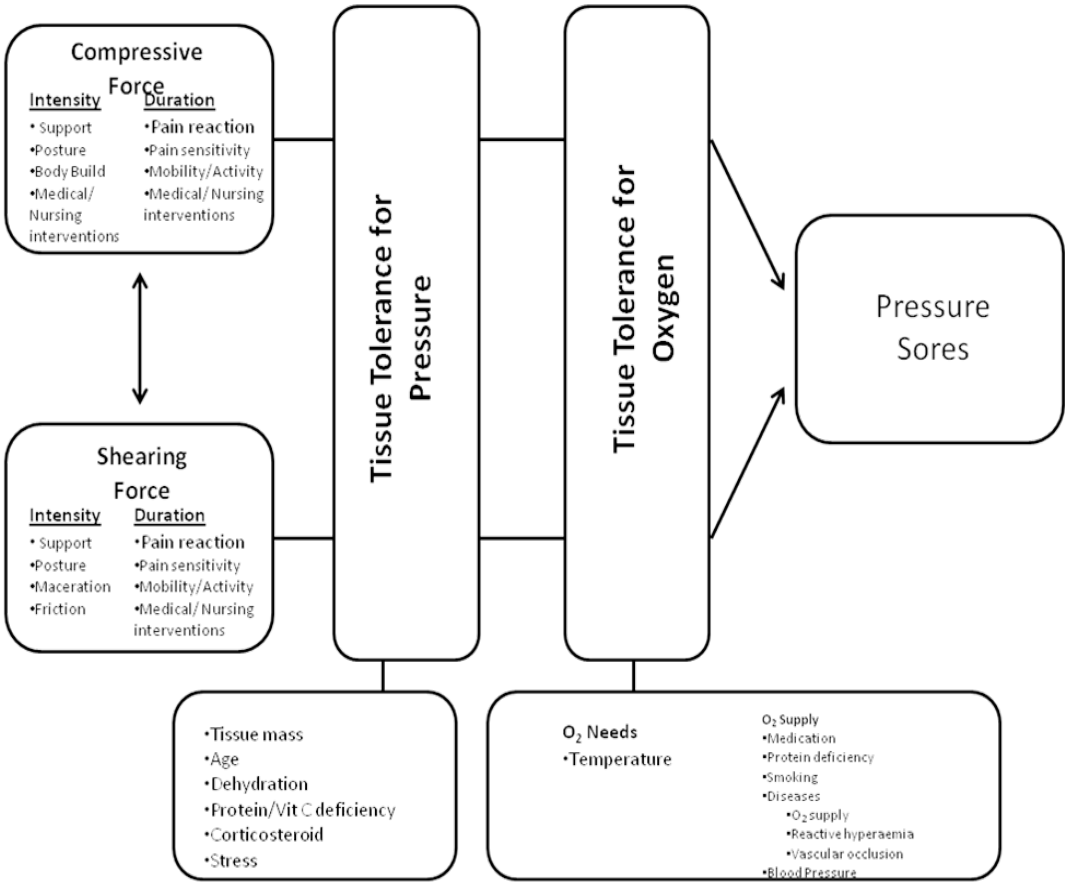


Figure 2.2. Defloor's Conceptual Scheme. From "The Risk of Pressure Sores: A Conceptual Schema" by T. Defloor, 1999, *Journal of Clinical Nursing, 8,* p. 208. Reprinted with permission.

For example, body build and tissue mass are characteristics that influence the development of pressure ulcers. Several research studies support an inverse relationship between body mass index (BMI) and a patient's tendency to develop a pressure ulcer. Fife et al. (2001), Kernozek, Wilder, Amundson, and Hummer (2002), Stinson, Porter-

Armstrong, and Eakin, (2003), and Lindgren, Unosson, Krantz, and Ek (2005) all documented that patients with lower than normal body weights tend to develop pressure ulcers more frequently than those of normal weight or obese patients. By including characteristics such as body weight, medications, and diseases known to affect oxygen demand and delivery, Defloor provided a more comprehensive approach to the study of the etiology of pressure ulcer development. Table 2.1 compares the concepts in the Braden Bergstrom conceptual model with the Defloor conceptual model.

Table 2. 1. Comparison of the Braden and Bergstrom and Defloor Conceptual Models

Conceptual Component	Braden[a]	Defloor[b]
Mobility	Affects intensity and duration of pressure	Affects intensity and duration of pressure and shear
Activity	Affects intensity and duration of pressure	Affects intensity and duration of pressure and shear
Sensory Perception	Affects intensity and duration of pressure	Affects intensity and duration of pressure and shear
Extrinsic Factors	Affects tissue tolerance for pressure Includes moisture, friction and shear	Affects tissue tolerance for pressure Includes moisture (maceration) and friction Adds support surface, medical/nursing interventions.
Intrinsic Factors	Affects tissue tolerance for pressure Includes nutrition, age, arteriolar pressure, and hypothetical factors (i.e., edema, stress, smoking and skin temperature)	Affects tissue tolerance for pressure and oxygen Includes specific components of nutrition (tissue mass, protein, and vitamin C), stress, smoking, temperature, hydration status Adds medications that affect tissue integrity (i.e. corticosteroids) or blood pressure

[a] Adapted from "A conceptual schema for the study of the etiology of pressure sores," by B. Braden and N. Bergstrom, 1987, *Rehabilitation Nursing, 12*(1), 8-12, 16.
[b] Adapted from " The risk of pressure sores: A conceptual scheme," by T. Defloor, 1999. *Journal of Clinical Nursing, 8*(2), 206-216.

Critical Analysis of the Relevant Literature

State of Pressure Ulcer Risk Factor Science

Knowledge progression and associated research questions described by Wood and Ross-Kerr (2006) suggests that subject knowledge progresses from descriptive, observational studies aimed at identifying important components of a phenomenon to understanding the relationships between those variables. Once the relationships are well understood, the knowledge progresses to explaining cause and effect relationships between the variables, requiring an experimental research design (Wood & Ross-Kerr, 2006). The current literature about pressure ulcer risk factors suggests that the constructs of pressure and friction/shear are commonly accepted risk factors for pressure ulcer development. A search of the PubMed database using the search terms "pressure ulcers" and "risk factors", with the limits of all adult, humans, and English, but with no date restraints yielded 1054 articles published between 1975 and August 2012. Of those, 206 were cross sectional or cohort studies that described pressure ulcer risk factors in 585,729 subjects in various settings. Sixty-two were experimental treatment studies evaluating the efficacy of pressure reduction and redistribution devices in 10,168 subjects in various settings. None of the experimental studies evaluated treatments aimed at improving tissue tolerance for pressure. This finding suggests that the relationship between the magnitude and duration of pressure and pressure ulcers is understood well enough to warrant experimental research; however, the knowledge surrounding components of tissue tolerance is not advanced enough to warrant experimental intervention. de Laat et al. (2006) assert that interventions for pressure ulcer preventions are predicated on

identifying salient risk factors for pressure ulcer development in specific patient populations. As medical science evolves and patients with multiple comorbidities survive longer, the search for pressure ulcer risk factors segregates among various target populations, requiring additional study to identify salient pressure ulcer risk factors. The literature is replete with studies designed to identify unique pressure ulcer risk factors in various patient populations. The same literature search identified 39 studies evaluating pressure ulcer risk in spinal cord injury patients, 14 evaluating risk factors in patients with hip fractures, 13 for patients in the operating room, and 21 for critically ill patients.

Despite the abundance of findings reported in the literature for specific patient populations, there is a demonstrated lack of any theoretical framework guiding the research efforts (de Laat et al., 2006). Indeed, the only studies citing a theoretical framework were those evaluating the predictive ability of various risk assessment scales. The resulting findings describe a wide range of risk factors derived from author-hypothesized risk factors and others identified by researchers through literature searches. According to Anthony et al. (2008), over 200 risk factors for pressure ulcer development are identified in the literature. However, the ability to generalize these findings becomes increasingly limited as various target populations assume unique characteristics (Hulley, Newman, & Cummings, 2007). Additionally there are measurement and definitional differences among the study variables reported in the literature (de Laat et al., 2006), contributing to the lack of generalizability of the risk factors identified. Use of an accepted conceptual framework to guide risk factor study in the critically ill patient population will standardize the identification and measurement of variables, thereby

enhancing the generalizability of the findings to guide nursing interventions aimed at pressure ulcer prevention.

Theoretical frameworks to guide risk factor study. To evaluate the conceptual frameworks used to identify pressure ulcer risk factors for study, the search term "prospective" was added to the search limits described earlier. "Prospective" was chosen because of the temporal association between prospective study designs and risk factor identification supporting causality. That search returned 252 articles published between 1982 and June 2012. Of those, 175 were excluded because they were not relevant to pressure ulcer risk factors, were literature summaries, or evaluated pressure ulcer prevention or treatment interventions. Of the 77 remaining, 32 evaluated risk factors that the authors identified from literature reviews or were included via expert opinion. None of those 32 articles cited a theoretical framework guiding the research. Fifteen of the articles evaluated the predictability of various pressure ulcer risk assessment scales by examining specificity and sensitivity results in prospective incident studies. Braden and Bergstrom's (1987) conceptual model provided the theoretical framework guiding risk factor identification in 30 of the studies.

Study populations. Study populations in the 77 articles evaluating pressure ulcer risk were widely distributed. Table 2.2 provides a summary of the study populations evaluated relative to pressure ulcer risk factors.

Table 2. 2. Study Populations Included in Risk Factor Studies N = 77

Study Population	Number of Studies (%)
Acute care setting	20 (26)
Intensive care setting	17 (22)
Hospitalized elderly or geriatric not confined to long term care	15 (19)
Spinal cord injury/neurologic impairment	8 (10)
Long term care	7 (9)
Operating rooms	7 (9)
Traumatized patients	3 (4)

Braden Risk Assessment Scale

The predictive ability of the Braden Scale has been evaluated extensively in the literature (Pancorbo-Hidalgo, Garcia-Fernandez, Lopez-Medina, & Alvarez-Nieto, 2006), however its predictive ability in critically ill patient populations has not been widely evaluated. The Braden Scale is derived from Braden and Bergstrom's (1987) conceptual model.

Validity of the Braden risk assessment scale. Content and construct validity are important components that potentially affect the Braden risk assessment scale (RAS') accuracy in predicting pressure ulcer development. Content validity of an instrument depends on the extent to which a measurement tool adequately captures all aspects of a phenomenon that are relevant to the content under study (Mishel, 1989; Hulley, Martin,

& Cummings, 2007). Construct validity refers to how well the tool in question adheres to a set of theoretical constructs believed to influence the outcome (Hulley, Martin, & Cummings, 2007). Although there is expert consensus on the validity of the Braden RAS (Braden & Frantz, 2004), its predictive ability when used in various patient populations varies because the theoretical constructs of the tool are based on patients in long-term care facilities (Kottner, Dassen, & Tannen, 2009). Because the etiology of pressure ulcer development is multifactorial (Nixon, 2001) and pressure ulcer etiology varies among different patient populations (DeLaat et al., 2006), the content validity of the Braden Scale may affect the accuracy of the tool in predicting pressure ulcer incidence in disparate populations.

Reliability of the Braden risk assessment scale. The reliability of an instrument refers to its consistency in assessing a phenomenon over time and is primarily dependent on the degree of random error that is experienced during measurement (Mishel, 1989). Reliability of a measure is a prerequisite for validity (Kottner & Dassen, 2010). To determine the amount of reliability testing on the Braden RAS, a literature search was conducted in PubMed using the search terms Braden scale/score and reliability with the limits of humans, English, core clinical journals, nursing journals, and all adult. The search returned 21 results. An additional search using identical limits and the search terms pressure ulcer risk scales and reliability returned 19 results, 11 of which were duplicates. Of the remaining 29, one was an incidence study, three were unrelated articles, and six evaluated the interrater reliability of a modified version of the Braden Scale. Three were designed as pre-test post-test evaluations of interrater agreement after

a web based educational initiative. Additionally, 12 were meta-analysis or review articles.

The remaining four articles reviewed interrater reliability findings of the Braden RAS in a multi-center, long-term care, home care, and intensive care unit (ICU) environment. In their prospective study to evaluate the interrater reliability of the Braden RAS in various acute care wards in multiple settings, Halfens, Van Achterberg, and Bal (2000) evaluated the Braden scores of 320 patients collected by staff nurses on 11 acute care wards. Various nurses rated each patient five times during the course of the study. The interrater reliability for the Braden subscales varied from 0.71 to 0.86 (Cohen's kappa) with the moisture subscale demonstrating the lowest interrater reliability at 0.54 (Halfens et al., 2000).

In a cross-sectional study to evaluate the interrater reliability among nurses in two German long-term care facilities, Kottner and Dassen (2008) evaluated data on 152 long-term care residents. The first Braden score was obtained during a routine pressure ulcer prevalence study then repeated scores were obtained by staff nurses up to three days later. Kottner and Dassen (2008) reported intraclass correlation coefficients (*ICC*) on individual subscore items from 0.06, 95% CI [-0.31, 0.48] to 0.97, 95% CI [0.93, 0.99] with the *ICC* being lowest for the sensory perception subscale (*ICC* range 0.16 to 0.62) and nutrition subscale (*ICC* range 0.17 to 0.89). Overall Braden scores demonstrated a higher interrater agreement ranging from an *ICC* of 0.73, 95% CI [0.26, 0.910] to 0.95, 95% CI [0.87, 0.98]. Kottner, Halfens, and Dassen (2009) reported similar findings in a cross sectional study designed to evaluate the interrater reliability of nurses using the Braden RAS in a home care environment. Data were collected during pressure ulcer

prevalence surveys of 691 home care patients during 2007 and 2008. Patients were scored twice; once by the home health nurse and a second time by a certified wound nurse during each data collection period. Range values for the *ICC* of the Braden subscales is not presented for either year; however, the overall summative Braden summative scores from 2007 demonstrated an *ICC* of 0.90, 95% CI [0.88, 0.92] and an *ICC* of 0.88, 95% CI [0.85, 0.91] in 2008.

One study evaluated the interrater reliability of the Braden RAS in two ICU settings (Kottner & Dassen, 2010). Sequential cross-sectional studies were conducted in two ICUs of a large university hospital in Germany between January and April of 2009. Three nurses were randomly selected from each ICU to do Braden assessments on a total of 45 patients. Range values for the *ICC* of the Braden subscales was not presented for the study; however, the overall summative Braden summative scores demonstrated an *ICC* of 0.72, 95% CI [0.52, 0.87] for one ICU and 0.84, 95% CI [0.72, 0.92] for the second ICU (Kottner & Dassen, 2010). Based on the 0.71 to 0.86 range of Cohen's Kappa coefficients from the Halfens et al. (2000) study, the reliability of the Braden RAS is considered good to very good (Newman, Browner, Cummings, & Hulley, 2007). Because *ICC* agreement levels are considered much like the Kappa agreement levels, (Reliability Analysis, n.d.), the 0.72 to 0.95 *ICC* range of Braden summative scores reported by Kottner and Dassen (2008), Kottner, Halfens, and Dassen (2009), and Kottner and Dassen (2010), indicate a similar ranking of good to very good.

Specificity and sensitivity of the Braden risk assessment scale. The predictive ability of the Braden Scale has been evaluated extensively in the literature (Pancorbo-Hildalgo, et al., 2006). As outlined in Table 2.3, most of the specificity and sensitivity

studies of the Braden RAS were conducted in long term and acute care settings. In three studies evaluating optimum scores for ICU patients, cutoff scores of 16 or less yielded a sensitivity range from 97% to 66.6% with associated specificities ranging from 63.9% to 22%. In two of the three studies with larger sample sizes specificities were lower (<30%). The same cutoff score had associated positive predictive values (PPVs) ranging from 15.3% to 60.6%. The results of these studies indicate that a Braden Scale score of 16 or less adequately identifies patients at risk that do develop a pressure ulcer, but the score is not specific enough to adequately screen out patients that do not develop a pressure ulcer.

These values indicate that ICU clinicians may lack an accurate tool that accounts for unique pressure ulcer risk factors associated with critically ill patients, resulting in a diffuse application of prevention efforts to patients incorrectly identified to be at risk. Multiple studies of the sensitivity and specificity of various RAS, including the Braden Scale, indicate that none of them adequately identifies pressure ulcer risk across various patient populations (Anthony, et al., 2008), raising doubt about the efficacy of any one tool to guide treatment decisions in nursing homes, in acute care facilities, and ICUs.

Table 2. 3. Summary of Studies Evaluating the Specificity, Sensitivity, Positive, and Negative Predictive Values of the Braden Pressure Ulcer Risk Scale in Various Settings

Author	Cutoff score	Setting	Sample size	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Barnes and Payton (1993)	≤16	Acute Care	361	72.7	90.6	33.3	98.1
Bergstrom, Braden et al. (1987)	≤ 16	Acute Care	100	100	90.2	43.8	100
Bergstrom, Demuth et al. (1987)	≤ 16	ICU	60	83.3	63.9	60.6	85.2
Bergstrom et al. (1998)	≤19	Combined	843	51.9	77.8	25.6	91.7
Braden and Bergstrom (1994)	≤ 18	Long term care	123	78.6	74.3	53.7	90.2
Capobianco and McDonald (1996)	≤16	Acute Care	50	71.4	83.3	62.5	88.2
Goodridge et al. (1998)	≤19	Long term care	330	50.0	52.3	10.1	90.7
Hagisawa and Barbenel (1999)	≤ 16	Acute Care	275	38.9	100	100	91.6
Halfens et al. (2000)	≤20	Acute Care	320	61.7	79.9	34.5	92.4
Langemo et al. (1991)	≤ 16	Acute Care	1244	54.5	93.7	60.0	92.2
Langemo et al. (1991)	≤ 18	Long term care	74	57.1	61.1	36.4	78.6

Author	Cutoff score	Setting	Sample size	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Lewicki et al. (2000)	≤14	ICU (cardiac surgery)	337	66.6	29.6	4.5	94.7
Lyder et al. (1999)	≤16	Acute Care	84	77.0	50.0	77.0	50.0
Pang and Wong (1998)	≤ 18	Long term care	138	90.5	62.4	37.3	96.4
Salvadalena et al. (1992)	≤ 18	Acute Care	100	60.0	54.4	25.0	84.3
Schoonhoven et al. (2002)	≤18	Acute and Geriatric	1229	43.5	67.8	8.1	94.9
Seongsook et al. (2004)	≤ 16	ICU	125	97.0	26.0	37.3	95.0
VandenBosch et al. (1996)	≤17	Acute Care	103	58.6	40.5	27.9	71.4

Augmented Braden and Bergstrom Model

To provide a conceptual framework that incorporates pressure ulcer risk factors specific to critically ill patients, the focus of this research, Benoit and Mion (2012) augmented Braden and Bergstrom's (1987) conceptual model with risk factors identified in well-designed prospective studies. Multivariate findings from studies having high or medium design quality as defined by the National Institute of Health and Clinical Excellence (NICE, 2005) standards were conceptually grouped and subsequently integrated into Braden and Bergstrom's (1987) conceptual model, retaining their original constructs and augmenting their concept of intrinsic factors for tissue tolerance. Thirty-seven non-unique risk factor variables for pressure ulcer development were identified as statistically significant ($p \leq .05$) at the multivariate level in eight studies identified as higher quality using the NICE criteria (Benoit & Mion, 2012). These were condensed into 18 unique risk factors that augment Braden and Bergstrom's (1987) construct of intrinsic Tissue Tolerance.

The additional risk factors were categorized as affecting metabolic supply and demand, pressure distribution capacity, and threats to skin integrity. Metabolic supply and demand included perfusion and oxygenation parameters, Braden's nutrition subscale, surgical treatment, severity of illness, and other physiologic alterations. Pressure distribution capacity included gender, body habitus, and age. Threats to skin integrity included preexisting pressure ulcers, dry or thin skin, edema, skin problems in pressure prone areas, and chemical exposure, such as with fecal incontinence. The resulting conceptual model (Figure 2.3) indicates that Tissue Tolerance is composed of Braden et al.'s (1987) extrinsic concepts of Moisture and Friction/Shear and that the augmented

intrinsic factor concept includes Metabolic Supply and Demand, Pressure Distribution Capacity, and Threats to Skin Integrity. Additionally, Tissue Tolerance assumes a moderating effect between Pressure and Pressure Ulcer. The specific risk factors identified by Benoit and Mion (2012) are identified in Table 2.4.

Figure 2. 3. Conceptual Model for Pressure Ulcer Etiology in Critically Ill Patients (Benoit & Mion, 2012)

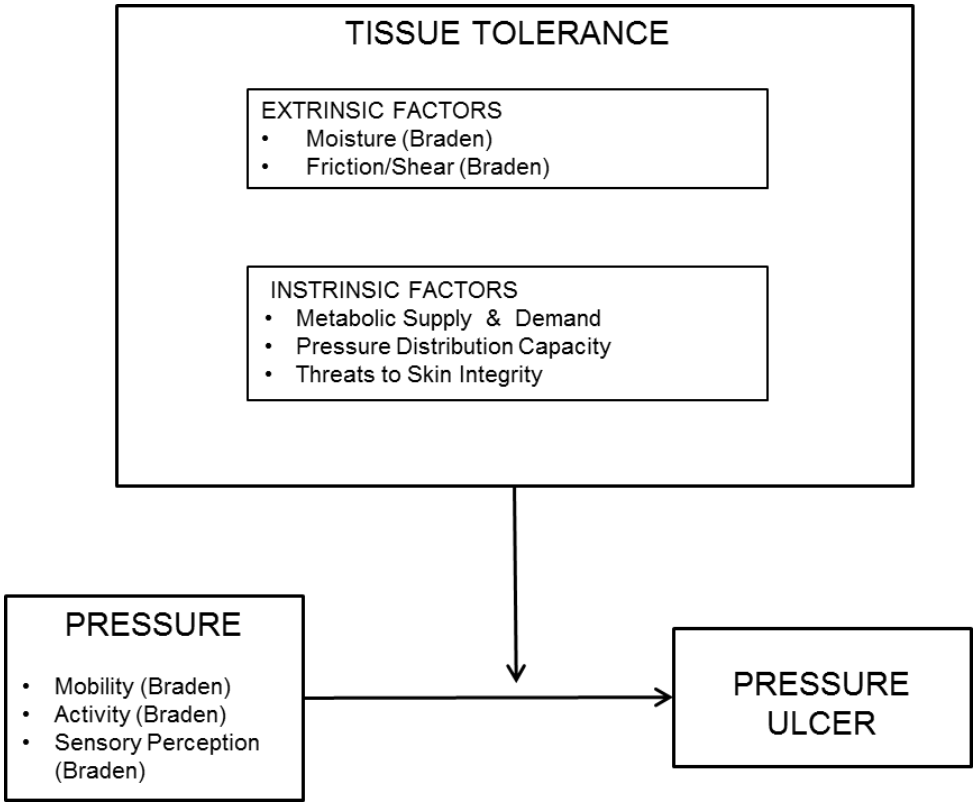


Figure 2.3. Conceptual model for pressure ulcer etiology in critically ill patients. Metabolic supply includes the concepts of perfusion/oxygenation, and the Braden Scale's nutrition subscale. Metabolic demand includes surgical treatment, severity of illness, and physiologic alterations. Pressure distribution capacity includes gender, body habitus, and age. Threats to skin integrity include preexisting pressure ulcer, dry/thin skin, edema, skin problems in pressure prone areas, and chemical exposure such as with fecal incontinence. Items identified as ''Braden'' are risk factors from The Braden Scale for Predicting Pressure Sore Risk_ (Copyright by Braden & Bergstrom, 1988).
From "Risk Factors for Pressure Ulcer Development in Critically Ill Patients: A Conceptual Model to Guide Research," by R. Benoit and L. Mion, 2012. *Research in Nursing & Health*, *35*(4), 340-362. Used with permission.

Table 2. 4. Specific Risk Factors Used to Augment Braden and Bergstrom's Concept of Intrinsic Tissue Tolerance

Concept	Concept Components	Risk Factor Measure
Metabolic Supply	Perfusion/Oxygenation	• Type/amount of IV vasopressor use • Vascular disease of any type except coronary artery and cerebral vascular disease • Hemoglobin/hematocrit • Nicotine use 1.
	Nutrition	• Braden Nutrition subscale score 2.
Metabolic Demand	Surgical Treatment	• Required surgery during hospital stay 3.
	Severity of Illness	• APACHE II Score on admission • NYHA** score • Hospital LOS • Ventilator use • ASA* score
	Physiologic Alterations	• Requires dialysis of any type during hospital stay • Body temperature • Steroid/Anti-Inflammatory use
Pressure Distribution Capacity	Gender	• Gender
	Body Habitus	• BMI (weight indexed with height)
	Age	• Age
Threats to Skin Integrity	Existing and potential threats to skin integrity not captured in Braden Moisture subscale score	• Skin problems in areas at risk for pressure ulcer development (sacrum, elbows, heels) • Current Stage II or worse pressure ulcer • General skin problems (thin, edema) • Chemical exposure (e.g. fecal incontinence)

*American Society of Anesthesiologists; **New York Heart Association functional classification
Adapted from "Risk Factors for Pressure Ulcer Development in Critically Ill Patients: A Conceptual Model to Guide Research," by R. Benoit and L. Mion, 2012. *Research in Nursing & Health, 35*(4), 340-362.

Braden and Bergstrom's modified conceptual framework served as the theoretical framework for this study. Risk factor measures were selected from each of the conceptual components based on their feasibility of study in the sample population. Their measures and operational definitions are included below.

Definition of Terms

Primary Outcome Measure

The definition for pressure ulcer most commonly cited in the US is from the National Pressure Ulcer Advisory Panel (NPUAP). According to the NPUAP, a pressure ulcer is a "localized injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure, or pressure in combination with shear and/or friction. A number of contributing or confounding factors are also associated with pressure ulcers; the significance of these factors is yet to be elucidated" (NPUAP, 2007, Updated staging systems, ¶ 2). The NPUAP also provides the most commonly used pressure ulcer severity or staging system used in the US (NPUAP, 2007). In 2006, the NPUAP updated its staging system to include six categories of pressure ulcer stages that includes stage I, stage II, stage III, stage IV, unstageable, and suspected deep tissue injury (SDTI). Because of its widely accepted use in the US, the NPUAP definitions from 2006 were used to describe pressure ulcer severity in this study (NPUAP, 2007). The definitions for pressure ulcer stages are:

- Stage I: Intact skin with non-blanchable redness of a localized area usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its color may differ from the surrounding area.
- Stage II: Partial thickness loss of dermis presenting as a shallow open ulcer with a red pink wound bed, without slough. This stage may also present as an intact or open/ruptured serum-filled blister.
- Stage III: Full thickness tissue loss. Subcutaneous fat may be visible but bone, tendon or muscle is not exposed. Slough may be present but does not obscure the depth of tissue loss. This stage may include undermining and tunneling.
- Stage IV: Full thickness tissue loss with exposed bone, tendon or muscle. Slough or eschar may be present on some parts of the wound bed. This stage often includes undermining and tunneling.
- Unstageable: Full thickness tissue loss in which the base of the ulcer is covered by slough (yellow, tan, gray, green or brown) and/or eschar (tan, brown or black) in the wound bed.
- Suspected Deep Tissue Injury (SDTI): Purple or maroon localized area of discolored intact skin or blood-filled blister due to damage of underlying soft tissue from pressure and/or shear. The area may be preceded by tissue that is painful, firm, mushy, boggy, warmer, or cooler as compared to adjacent tissue. (NPUAP, 2007, updated staging systems).

In case subjects with multiple pressure ulcers, the most severe pressure ulcer stage was used.

Demographic and Pre-hospital Admission Variables

Demographic and pre-hospital admission variables were obtained from the nursing admission history and/or the admission history and physical examination. They included:

- Age defined in years. Age was recorded as a continuous variable.
- Pre-existing skin disease was defined as the presence of any diagnosed skin disease or alteration in skin integrity including current or past history of pressure ulcers, edema, jaundice, or skin described as fragile and or thin. Pre-existing skin disease was recorded as a dichotomous variable.
- Diabetes was defined by diagnosis of the disease as a past medical diagnosis on admission to the hospital and included Type I and Type II. Diabetes diagnosis was recorded as a dichotomous variable.
- Body mass index (BMI) was defined as the subject's admission body weight divided by the subject's height squared. BMI was recorded as a continuous variable.
- Corticosteroid use was defined as any use of oral, topical, or IV corticosteroid use within two weeks of the hospital admission. Preadmission corticosteroid use was recorded as a dichotomous variable.
- Nicotine use was defined as the use of any products containing nicotine within one year prior to the current hospital admission. Nicotine use was recorded as a dichotomous variable.

Post-Admission Clinical Study Variables

Post-admission study variables were obtained from the subject's electronic medical records (EMR). They included:

- Ventilator use: The continuous or discontinuous presence of a ventilator delivering respiratory support on any mode via tracheal or endotracheal tube within 48 hours of study enrollment. Ventilator use was recorded as a dichotomous variable.
- The lowest subscale score of the Braden RAS (Braden & Bergstrom, 1987) within a 24 and 48-hour period prior to study enrollment. A complete list of the Braden subscales and their weighted definitions are presented in Table 2.5.
    - Moisture: degree of skin exposure to moisture. Ranked as an ordinal variable from least to greatest level of skin exposure on a 4-point scale.
    - Friction/Shear: no overall summary definition given. Ranked as an ordinal variable from least to greatest level of severity on a 3-point scale.
    - Nutrition: usual food intake pattern. Ranked as an ordinal variable from least to greatest level of intake on a 4-point scale.
    - Sensory/Perception: ability to respond meaningfully to pressure related discomfort. Ranked as an ordinal variable from least to greatest level of ability on a 4-point scale.
    - Mobility: ability to change and control body position. Ranked as an ordinal variable from least to greatest level of mobility on a 4-point scale.
    - Activity: degree of physical activity. Ranked as an ordinal variable from least to greatest level of activity on a 4-point scale.

- Serum albumin: Primary protein found in blood plasma (Seeley et al., 2006). Serum albumin was used as proxy measure for protein stores. The most recent value obtained while the subject was in an ICU prior to study enrollment was used. Normal ranges are 3.5 – 5.0 grams per deciliter (g/dl) per VUH laboratory standards. Serum albumin was recorded as continuous level data.
- Pre-albumin: Metabolic precursor to serum albumin. Pre-albumin was used as proxy for protein stores. The most recent value obtained while the subject was in an ICU prior to study enrollment was used. Normal ranges are 18.0 – 45.0 mg/dl per VUH laboratory standards. Pre-albumin was recorded as continuous level data.
- Total lymphocyte count: The total number of lymphocyte types detected in a microliter of blood. Total lymphocyte count was used as proxy for protein stores. The most recent value obtained while the subject was in an ICU prior to study enrollment was used. Normal ranges are 1.1 – 3.5 thousand per microliter of blood. Total lymphocyte counts were recorded as continuous level data.
- Total Protein: A calculated study variable consisting of categorical serum albumin, pre-albumin and total lymphocyte count. Each of these variables was separately categorized as high, medium or low, depending on the specified normal ranges included in their definitions. In subjects that had a serum albumin reported, that categorical rating was used as the overall Total Protein category rating. Serum albumin was used as the default rating because of its prevalence in the nutritional literature as the gold standard proxy measurement for protein reserve (Cereda, Zagami, Vanotti, Piffer, & Pedrolli, 2008; Jeejeebhoy, 2004). In

subjects that did not have a reported serum albumin, the lowest categorical value of pre-albumin or total lymphocyte count was used.

- Hematocrit: Percentage of red blood cells found in whole blood. Hematocrits reported 24 and 48 hours prior to study enrollment were used. Normal ranges are 36 -43% for females and 41-49% for males per VUH laboratory standards. Hematocrit was recorded as continuous level data.

Table 2. 5. Braden Sub-Scale Definitions

Risk Factor Variable	Scoring Criteria			
SENSORY PERCEPTION ability to respond meaningfully to pressure-related discomfort	1. Completely Limited Unresponsive (does not moan, flinch, or grasp) to painful stimuli, due to diminished level of consciousness or sedation. OR limited ability to feel pain over most of body	2. Very Limited Responds only to painful stimuli. Cannot communicate discomfort except by moaning or restlessness OR has a sensory impairment which limits the ability to feel pain or discomfort over ½ of body.	3. Slightly Limited Responds to verbal commands, but cannot always communicate discomfort or the need to be turned. OR has some sensory impairment which limits ability to feel pain or discomfort in 1 or 2 extremities.	4. No Impairment Responds to verbal commands. Has no sensory deficit which would limit ability to feel or voice pain or discomfort.
MOISTURE degree to which skin is exposed to moisture	1. Constantly Moist Skin is kept moist almost constantly by perspiration, urine, etc. Dampness is detected every time patient is moved or turned.	2. Very Moist Skin is often, but not always moist. Linen must be changed at least once a shift.	3. Occasionally Moist Skin is occasionally moist, requiring an extra linen change approximately once a day.	4. Rarely Moist Skin is usually dry, linen only requires changing at routine intervals.
ACTIVITY degree of physical activity	1. Bedfast Confined to bed.	2. Chairfast Ability to walk severely limited or non-existent. Cannot bear own weight and/or must be assisted into chair or wheelchair.	3. Walks Occasionally Walks occasionally during day, but for very short distances, with or without assistance. Spends majority of each shift in bed or chair	4. Walks Frequently Walks outside room at least twice a day and inside room at least once every two hours during waking hours
MOBILITY ability to change and control body position	1. Completely Immobile Does not make even slight changes in body or extremity position without assistance	2. Very Limited Makes occasional slight changes in body or extremity position but unable to make frequent or significant changes independently	3. Slightly Limited Makes frequent though slight changes in body or extremity position independently.	4. No Limitation Makes major and frequent changes in position without assistance.

Risk Factor Variable	Scoring Criteria			
NUTRITION usual food intake pattern	1. Very Poor Never eats a complete meal. Rarely eats more than a of any food offered. Eats 2 servings or less of protein (meat or dairy products) per day. Takes fluids poorly. Does not take a liquid dietary supplement OR is NPO and/or maintained on clear liquids or IV=s for more than 5 days.	2. Probably Inadequate Rarely eats a complete meal and generally eats only about 2 of any food offered. Protein intake includes only 3 servings of meat or dairy products per day. Occasionally will take a dietary supplement. OR receives less than optimum amount of liquid diet or tube feeding	3. Adequate Eats over half of most meals. Eats a total of 4 servings of protein (meat, dairy products per day. Occasionally will refuse a meal, but will usually take a supplement when offered OR is on a tube feeding or TPN regimen which probably meets most of nutritional needs	4. Excellent Eats most of every meal. Never refuses a meal. Usually eats a total of 4 or more servings of meat and dairy products. Occasionally eats between meals. Does not require supplementation.
FRICTION & SHEAR (no definition given)	1. Problem Requires moderate to maximum assistance in moving. Complete lifting without sliding against sheets is impossible. Frequently slides down in bed or chair, requiring frequent repositioning with maximum assistance. Spasticity, contractures or agitation leads to almost constant friction	2. Potential Problem Moves feebly or requires minimum assistance. During a move skin probably slides to some extent against sheets, chair, restraints or other devices. Maintains relatively good position in chair or bed most of the time but occasionally slides down.	*3.* No Apparent Problem Moves in bed and in chair independently and has sufficient muscle strength to lift up completely during move. Maintains good position in bed or chair.	N A

Braden Scale for Predicting Pressure Sore Risk© (Copyright by Braden & Bergstrom, 1988).

- Corticosteroid use: The total dose of each corticosteroid administered during the current hospital stay for up to two weeks prior to enrollment. Corticosteroids that were included for analysis in this study are the short to medium acting corticosteroids. They were
    - Hydrocortisone;
    - Prednisolone;
    - Methylprednisolone; and
    - Prednisone.

Corticosteroid dosage was recorded as continuous level data for dosages administered during the hospital stay.

- Mean arterial pressure (MAP): An expression of the geometric mean for arterial pressures created during the systolic and diastolic phases of the cardiac cycle. Under normal conditions when the heart rate is not accelerated and the central venous pressure is at or near zero, the mathematic equation where P is pressure is expressed as

$$MAP = P_{dias} + 1/3\ (P_{sys} - P_{dias})$$

Because the amount of time the heart spends in diastole is shorter when the heart rate accelerates, the relationships between systole and diastole change and are calculated more accurately by the cardiac monitor. The most accurate calculations rely on an electronic analysis of the arterial waveform obtained from an invasive arterial line (Cardiovascular Physiologic Concepts, n.d.). Normal MAP is 70-105 mmHg. MAP was recorded as continuous level data. In situations where MAP was recorded from an invasive arterial pressure monitoring line and a blood pressure cuff, the value from the

arterial pressure was used. The lowest documented MAP during the 24 and 48-hour period prior to pressure ulcer development was used.

- Oxygen saturation of hemoglobin: Percentage of the number of circulating hemoglobin oxygen binding sites saturated with oxygen (Cardiovascular Physiologic Concepts, n.d.). Values were obtained using an externally placed pulse oximeter, usually located on the fingertip or forehead that provided a continuous read out of oxygen saturation values. Normal ranges are 95% – 100%. Oxygen saturation of hemoglobin was recorded as continuous level data. The lowest documented oxygen saturation during the 24 and 48-hour period prior to pressure ulcer development was used.
- Vasopressors: Pharmacologic agents that produce an increase in the smooth muscle tone of the vascular system walls by increasing the level of intracellular calcium in vascular smooth muscle (Forrest, n.d.). Table 2.6 provides an overview of the physiologic effects of each of the vasopressors included. They were:
    - Norepinephrine;
    - Epinephrine;
    - Dobutamine;
    - Milrinone;
    - Midodrine; and
    - Vasopressin.

With the exception of Vasopressin, each vasopressor was calculated in total micrograms/kg (μg/kg) each day for 24 and 48 hours prior to study enrollment. Vasopressin was calculated as total units each day for 24 and 48 hours prior to study enrollment. Vasopressor doses were recorded as continuous level data.

- Prior vasopressor use: The use of any additional vasopressor prior to study enrollment. Vasopressors in use at the time of study enrollment were excluded. Prior vasopressor use was recorded as dichotomous data.
- Restraint Use: The continuous or discontinuous use of wrist restraints at any time during the 24 and 48 hours prior to study enrollment. Restraint use was recorded as dichotomous level data.

Table 2. 6. Overview of the Physiologic Effects of Selected Vasopressors

Vasopressor	Half-life and excretion	Effect on skin blood flow	Comments
Dobutamine	2 min – renal	Primarily a beta 1 agonist with minimal effect on peripheral vascular constriction	
Epinephrine	2 min – renal	Non-selective adrenergic agonist Alpha receptor stimulation produces pronounced vasoconstriction	Cutaneous vasoconstriction leads to rise in temperature and metabolic activity
Midodrine	25 min – unclear	Alpha adrenergic agonist Alpha receptor stimulation produces pronounced vasoconstriction	
Milrinone	2.4 hours – renal	Phosphodiesterase inhibitor Produces vasodilation and has positive inotropic effects	
Norepinephrine	Termination of effects related to degradation to metabolites and presynaptic uptake	Less potent than epinephrine at alpha receptor sites	
Vasopressin	10-20 min-liver, renal	Directly stimulates smooth muscle V1 receptors but effects on skin blood flow uncertain	

Adapted from “Vasopressors” by P. Forrest (n.d.).

Summary

As medical science progresses and patients are living longer with multiple comorbidities, pressure ulcer risk becomes stratified among various patient populations, requiring additional research to completely understand pressure ulcer etiology in any given patient population. Pressure ulcer risk factor studies are well documented in the literature; however, the results have limited generalizability because of methodological and definitional inconsistencies. Additionally, a conceptual framework does not guide the majority of studies, producing a myriad of findings that do not substantially contribute to evidence-based prevention interventions by clinicians. Prior to 2012, Braden and Bergstrom (1987) and Defloor (1999) provided the only conceptual models to guide risk factor research. Because neither was specifically designed for evaluating risk factors in the critically ill patient, the focus population of interest, Braden and Bergstrom's conceptual model was augmented to identify pressure ulcer risk factors that disproportionately contributed to pressure ulcer incidence in this patient population. The augmented model (Benoit & Mion, 2012) served as the conceptual model for this study. The following chapter describes the methodology employed to meet the aims of this study.

CHAPTER III

STUDY METHODOLOGY

Overview

This chapter presents the methodology used to investigate the significance of patient-specific risk factors identified in the conceptual model for pressure ulcer development in critically ill subjects (Figure 2.3). The methodology is presented in the order of:

1. Design of the research study;
2. Assumptions surrounding the research design;
3. Description of the research setting;
4. Sample and sampling plan;
5. Data collection methods; and
6. Data analysis.

Research Design

This study utilized a prospective, case-control design. This design is best suited for evaluating the effect of risk factors on the development of a relatively rare outcome, pressure ulcer development (Cummings, Newman, & Hulley, 2007).

Assumptions Surrounding the Research Design

Theoretical Assumption

Braden and Bergstrom's (1987) augmented conceptual model (Figure 2.3) served as the theoretical basis for this study. By enhancing the explanatory model, the assumed criterion-related validity of the model improved, thereby theoretically enhancing its predictive ability (Cummings, et al., 2007). The predictive ability of the associated Braden Scale score, discussed in Chapter 2, could be improved by enhancing the criterion-related validity for critically ill patients. This study did not intend to test a modified Braden Scale; its goal was to validate the enhanced model. Subsequent research using the risk factors validated in this study to evaluate the Braden Scale score's predictive ability in critically ill patients will support or refute the assumptions made about the criterion-related validity of the enhanced model.

Methodological Assumptions

Literature describing the timeframes for pressure ulcer onset is scant leading to assumptions about when to measure both dependent and the independent variables in this study. Because time-to-event of pressure ulcer genesis is not fully understood, and because the temporal relationships between tissue insult and pressure ulcer development probably vary with each individual (Nixon, 2001; Pronovost, Goeschel, & Wachter, 2008), the timing of data collection in this study is based on clinical judgment and consensus of the dissertation committee. Gefen (2008) integrated evidence from various studies and concluded that pressure ulcers may form within one to six hours of insult.

However, in a multisite study of pressure ulcer incidence, Bergstrom et al. (1998) observed some new pressure ulcer onset at 21 days; although it is unclear if the authors were able to relate tissue insult to the new pressure ulcer occurrences.

Annual admissions to the study ICUs, based on fiscal year (FY) 2009 data, were 7,654 adult patients. Of those, 5,514 (72%) had a length of stay (LOS) greater than 48 hours in the ICU. To minimize sample bias incurred by including case patients with a non-ICU acquired pressure ulcer, and to maximize case enrollment, any pressure ulcer occurring after 48 hours of admission to an ICU was considered ICU acquired for purposes of this study. This timeframe provided some assurance that tissue insults resulting in pressure ulcers occurring before the ICU admission would be evident within 48 hours and not erroneously considered ICU acquired.

Similarly, there is no evidence in the literature suggesting optimal timeframes to capture cause and effect of vasopressor use, physiologic parameters, and resulting pressure ulcer incidence. Clinical judgment and consensus of the dissertation committee suggested that these data be collected retrospectively at 48 and 24-hour increments prior to pressure ulcer development.

If vasopressor use and alterations in the physiologic parameters identified for study occurred prior to the 48-hour cutoff disproportionately contributed to pressure ulcer incidence, their effects were not recognized with the timeframe constraints in this study, contributing to a Type I error in the interpretation of the findings. To account for this possibility, vasopressor use at any time during the ICU stay prior to pressure ulcer development was captured as a dichotomous variable. Further research using varying

timeframes for physiologic data capture will yield better estimates about the temporal relationships of these variables to pressure ulcer incidence.

Description of the Research Setting

The study took place in five adult intensive care units (ICUs) at VUH in Nashville, TN. VUH is an 847-bed teaching hospital that operates the only Level 1 Trauma Center, and the only Level 3 Burn Unit in Middle Tennessee. The five ICUs are Cardiovascular ICU (CVICU, 27 beds), Medical ICU (MICU, 34 beds), a combined neuro-medicine and neuro-surgical ICU (NICU, 34 beds), Surgical ICU (SICU, 34 beds), and Trauma ICU (TICU, 14 beds).

Study Concepts and Variables

The conceptual model used as the theoretical basis for this study (Figure 2.3) identifies two constructs containing eight concepts that can be measured by 23 variables (Table 3.1). The three Braden Scale's sub scores of Mobility, Activity, and Sensory Perception exclusively measure the construct of Pressure. Likewise, the Braden Scale's sub scores of Moisture and Friction/Shear exclusively measure extrinsic factors related to Tissue Tolerance. Intrinsic factors related to Metabolic Supply and Demand contain 10 risk factors. Of those, the presence of surgical procedures was not captured because of the mixed ICU population used in this study. Ventilator use, a proxy measure for severity of illness, was used to match cases and controls, so was not evaluated as an independent risk factor. Body temperature and the use of hemodialysis were not captured.

Table 3. 1. Constructs, Concepts, and Associated Risk Factors for the Development of Pressure Ulcers in Critically Ill Patients

Pressure Construct	Tissue Tolerance Construct
Risk Factors Mobility (Braden) Activity (Braden) Sensory Perception (Braden)	Concept of Extrinsic Factors Risk Factors Moisture (Braden) Friction/Shear (Braden) Concept of Intrinsic Factors Risk Factors • Metabolic Supply o Vasopressor use o Vascular disease of any type except cerebral and cardiovascular o Nicotine use o Lower hemoglobin/hematocrit o Nutrition (Braden)/Protein reserve • Metabolic Demand o Surgical procedure o Increased severity of illness • Physiologic demands o Dialysis of any type o Body temperature o Corticosteroid use • Pressure Distribution o Gender (male) o Body habitus o Increased age • Threats to Skin Integrity o Pre-existing pressure ulcer o Dry, thin skin o Edema o General skin problems in pressure prone areas o Chemical exposure, such as with incontinent diarrhea

Pressure distribution capacity contains three risk factors, all of which were included in the study. They are BMI, age, and gender. Threats to skin integrity include

five unique risk factors. Four of those (pre-existing pressure ulcer, dry, thin skin, edema, and skin problems) were captured as nominal variables. Chemical exposure, such as with diarrhea, was not captured because of the variability of its use as a descriptive term in the nursing documentation, and its presence and magnitude could not be visually verified by the investigator. Of the 23 variables identified by the conceptual model, 18 were included for data collection. Table 3.2 summarizes concepts, variables, and variable levels collected for data analysis. Refer to Chapter II for a complete list of term definitions and measurement frequency.

Table 3. 2. Variables Included for Study

Variable	Type	Aim	Purpose[†]
Pre-Admission variables			
Diabetes history	Dichotomous/Nominal	1,2	D, C
Nicotine history	Dichotomous	1,2	D, C
Steroid history	Dichotomous	1,2	D, C
Pre-existing skin disease	Dichotomous/Nominal	1,2	D, C
Demographic variables			
ICU	Nominal	1,2	D, C
Gender	Dichotomous	1,2	D, C
Age	Continuous	1,2	D, C
Pressure ulcer risk			
Braden Subscale Score	Nominal	1,2	D, C
Threats to skin integrity			
BMI*	Continuous	1,2	D, C
Corticosteroid dose	Continuous	1,2	D, C
Restraint use	Dichotomous	1,2	D, C
Albumin	Continuous	1,2	D, C
Pre-Albumin	Continuous	1,2	D, C
Total lymphocytes	Continuous	1,2	D, C
Total Protein	Nominal	1.2	D, C

Variable	Type	Aim	Purpose†
Perfusion			
High and low hematocrit	Continuous	1,2	D, C
Lowest MAP**	Continuous	1,2	D, C
Lowest oxygen saturation	Continuous	1,2	D, C
Vasopressor use	Continuous	1,2	D, C
Outcome variable			
Pressure ulcer and stage	Nominal	1,2	O

*Body mass index; **Mean arterial pressure; † D – descriptor; C – covariate; O – outcome

Sample and Sampling Plan

Nature and Size of the Sample

Standard referenced best practices and statistical powering approaches were used to determine the sample size for this research. The conceptual model guiding this research identifies 23 independent variables; however, 18 were measured. Stability of standard errors in logistic regression requires at least 10 cases for each independent variable in the smallest of the dependent variable categories (M. Dietrich, personal communication, 2009). Therefore, at least 180 cases were required. Each case has one matched control subject making the total sample size 360 subjects. Statistical powering for minimally detectable effects of a given independent variable (IV) is based on not only the desired statistical power and alpha level, but also on the amount of variance in the outcome variable that is already explained by the other IVs in the analysis. For a continuous IV, a total sample size of 360 with an observed proportion of the event of interest set at 0.50 (50% of the participants had a pressure ulcer), provided 80% statistical

power to detect an odds ratio of 1.34 if there was no variance explained by the other IVs. If as much as 30% of the variance in the likelihood of a pressure ulcer was explained by the other IVs, the sample provided 80% statistical power to detect an odds ratio of 1.42 (alpha = .05). For a dichotomous IV, those respective odds ratios were between 1.82 (0% variance explained by other IVs) and 2.06 (30% variance explained by other IVs).

Inclusion, Exclusion, and Matching Criteria

Inclusion criteria for both cases and controls were:

1. 18 to 79 years of age; and
2. Admission or transfer within to any of the five ICUs identified above.

Exclusion criteria for cases were:

1. Presence of any pressure ulcer on admission to the ICU;
2. Any pressure ulcer that developed within 48 hours of admission to the ICU;
3. Cardiopulmonary resuscitation requiring chest compressions and/or resuscitation drugs within 48 hours of pressure ulcer development;
4. Discharge from ICU prior to visual verification of pressure ulcer; and
5. ICU length of stay less than 48 hours.

Exclusion criteria for controls were:

1. Any stage pressure ulcer on admission to the ICU;
2. Any pressure ulcer that developed during the ICU stay;
3. Cardiopulmonary resuscitation during the ICU stay;
4. ICU length of stay less than 48 hours.

Matching criteria were:

1. Must be from the same ICU;
2. Must have been in the same ICU within 90 days of each other (i.e., up to 90 days prior to the case index date or up to 90 days after the case index date);
3. ICU length of stay for controls was at least as long as the length of stay as the case subjects' length of stay upon developing a pressure ulcer; and
4. Must be matched on ventilator use during the 48 hour period prior to case index date.

See Table 3.3 for a summary of the inclusion, exclusion, and matching criteria.

Table 3. 3. Inclusion, Exclusion, and Matching Criteria

Criteria	Case Subjects	Control Subjects
Inclusion Criteria	• Admission to ICU • 18 to 79 years of age	• Admission to ICU • 18 to 79 years of age
Exclusion Criteria	• Stage I or worse pressure ulcer on admission to ICU • Stage I or worse pressure ulcer that develops within 48 hours of admission to ICU • Cardio-pulmonary resuscitation requiring chest compressions and/or resuscitation drugs within 48 hours of stage I or worse pressure ulcer development • Discharge from ICU prior to visual assessment of pressure ulcer • ICU length of stay <48 hours	• Stage I or worse pressure ulcer on admission to ICU • Stage I or worse pressure ulcer that develops during ICU stay • Cardio-pulmonary resuscitation during ICU stay • ICU length of stay <48 hours
Matching Criteria	• Same ICU • Same period in ICU within 90 days of each other • Presence or absence of ventilator use within 48 hours of enrollment • ICU length of stay – control must be in ICU for at least the same number of days as case at time of control enrollment	

Rationale for the proposed exclusion criteria in this study was to enhance the identification of incident pressure ulcer development that allows for examination of patient-specific risk factors. Persons with pre-existing pressure ulcers were excluded because their presence would confound findings intended to identify unique risk factors associated with critical illness and consequent ICU placement for medical care. Persons requiring cardiopulmonary resuscitation were excluded because they are subjected to periods of unmeasured hypo-perfusion states that affect the skin's mechanical and physiologic tolerance to pressure. Additionally, resuscitation drug administration practices often include intra-venous boluses from existing vasopressor infusions that are

recorded on the resuscitation forms used by VUMC, but not necessarily captured on the nursing flow sheet, which was the documentation record used in collecting vasopressor dosage data. Case subjects who were discharged from the ICU prior to visual verification of the pressure ulcer were excluded because of the difficulty in locating and visually confirming pressure ulcer presence in a timely manner following ICU discharge. Subjects whose ICU length of stay is less than 48 hours were excluded because other risk factor influences prior to ICU placement may disproportionately contribute to pressure ulcer incidence in case subjects with less than a 48-hour ICU stay.

The matching criteria increase the comparability of cases and controls (Newman et al., 2007). By matching on the same ICU within 90 days prior or post pressure ulcer development, unique nursing practice and staffing patterns associated with the particular ICU during a similar period were matched, thereby minimizing potential confounders. Additionally, matching on ventilator use enhanced the validity because ventilator use is considered a proxy for severity of illness in critical care settings (Horner, Sloane, & Kahn, 1998). Other, established severity of illness scores, such as the APACHE II, are not consistently gathered in all VUH ICUs and therefore not available for analysis. Because of geographic limitations and fluctuating non-ICU bed availability at VUH, not all patients housed in a VUH ICU have the same severity of illness.

Subject Recruitment Methodology

Institutional Review Board (IRB) approval at Vanderbilt University Medical Center (VUMC) was sought and the study was approved. A convenience sample of potential subjects was identified using ICU census data and Star Panel. The PI then

verified inclusion and exclusion criteria. To help with subject enrollment, Carolyn Watts, MSN, RN, CWON and Christy Thomas, RN were recruited by the PI and trained in recruitment methodology. Patients meeting the inclusion criteria were then approached by the PI, Carolyn Watts or Christy Thomas for study enrollment using the procedures outlined below. Methods to ensure inter-rater reliability among the PI, Carolyn Watts and Christy Thomas are discussed later in this section.

Human Subjects Protection

Informed consent. The patient's cognitive and sedation status dictates their ability to understand and give informed consent. One study found that more than 75% of ventilated patients in an ICU were unable to give informed consent for participation in research because of confusion and delirium that persisted after ventilator use was discontinued (Fan et al., 2008). At VUH, sedation status is indicated by the Richmond Agitation Sedation Scale (RASS). The tool is well validated by several studies and is a commonly accepted way of objectively measuring the sedation status of a patient (Sessler et al., 2002; Ely et al., 2003). The tool ranges from -5 (unarousable) to +4 (combative). A RASS of zero is calm, awake, and alert. A RASS of +1 is described as restless (anxious or apprehensive but movements not aggressive or vigorous). A RASS of -1 is described as drowsy (not fully alert, but has sustained periods of awakening with eye contact to verbal stimuli). Fan et al. (2008) used the RASS range of -1 to +1 in their study about obtaining informed consent and it is the evidence on which this study criteria for obtaining informed consent is based. The RASS score is routinely assessed and documented by VUH ICU nurses every four hours.

Delirium in the ICU patient is measured with the Confusion Assessment Methodology for ICU patients (CAM-ICU). Delirium is indicated as a positive or negative finding and depends on the RASS score as part of its algorithm. As with RASS, the CAM-ICU is well validated in clinical practice (Ely, Inouye, et al., 2001; Ely, Margolin et al., 2001). Fan et al. (2008) used a CAM-ICU negative for their criteria in obtaining informed consent and it is the evidence on which this study criteria is based. Similar to the RASS score, all ICU nurses at VUH assess the patients for delirium and document the CAM-ICU each shift.

Per the approved IRB protocol, two face-to-face attempts and one phone attempt with a surrogate who could give consent were conducted for potential case patients that could not give consent themselves. Consent was waived after the three attempts to obtain it were unsuccessful. Potential case subjects who could not give consent and who did not have a contact person or next of kin indicated in the medical record were not enrolled.

Dignity and Personal Privacy. The following procedures were used to ensure patient dignity and privacy:

1. The PI, Carolyn Watts or Christy Thomas contacted the nurse caring for the patient and arranged a mutually agreeable time to visualize the patient's skin, such as during a bath or during the pressure ulcer dressing change, if applicable. Not all pressure ulcers require a dressing.
2. To maintain respect, the nurse then introduced the PI, C. Watts, or Christy Thomas to the patient and/or family, analogous to introducing a medical or nursing student.

3. The patient's privacy was ensured by closing room curtains or shades and room door.
4. The nurse then repositioned the patient, if necessary, so that the pressure ulcer could be visualized.
5. The nurse then removed the dressing, if applicable, and the PI, Carolyn Watts, or Christy Thomas visualized the ulcer.
6. The PI, Carolyn Watts, or Christy Thomas then offered assistance to the nurse to re-dress the ulcer, if applicable.

Protection of personal health information. The data collected involved patient demographic and health information, such as age, gender, body mass index, and presence of various pre-existing diseases, such as diabetes. Physiologic data, such as blood pressure and oxygen saturation were also collected, as were specific medications that were of interest, such as vasopressors. Patient confidentiality was assured by entering medical record numbers and associated demographic information directly from the EMR onto the paper Data Collection Form, which remained under double lock in the PI's office. Data were then entered into Vanderbilt University's Research, Electronic Data Capture (REDCap) database using the completed Data Collection Forms, which remained under double lock in the PI's office. REDCap is a secure, web-based application that is flexible enough to be used for a variety of types of research. REDCap provides an intuitive user interface that streamlines project development and improves data entry through real-time validation rules with automated data type and range checks. REDCap also provides easy data manipulation with audit trails for reporting, monitoring and querying patient records, and an automated export mechanism to common statistical

packages (Harris et al., 2009). REDCap servers are housed in a local data center at Vanderbilt, and all web-based information transmission is encrypted. REDCap was developed specifically around HIPAA-Security guidelines and is recommended to Vanderbilt researchers by both the Privacy Office and Institutional Review Board. Upon completion, all paper forms were destroyed using the shredder in the SICU (where the PI's office is located).

All data were kept in the REDCap database for the duration of the study. The REDCap data base was de-identified at the conclusion and will be indefinitely maintained for reference, should a secondary data analysis be required. Paper data collection forms were maintained under double lock until the PI was satisfied that all data were entered correctly, then were shredded. The Screening Tracking Tool, Data Management Tool, and Consent Tracking Tool were maintained on Vanderbilt's SICU secure 'M' drive and were only accessible by the PI or Carolyn Watts (Appendix A). The completed tools were deleted from the Vanderbilt's secured 'M' drive at the completion of the study.

Data Collection Methods

Procedures

Case enrollment. At least twice a week, the following steps were taken to identify case subjects.

1. The PI reviewed the Star Panel census for each ICU. The census indicates which patients are designated as having a pressure ulcer by the nursing staff. Information about the location and stage of the pressure ulcer was also available

in Star Panel. Recording pressure ulcer characteristics is a standard of care and is routine care for every patient at VUH.

2. The Inclusion/Exclusion Screening Tool (Appendix A) was used by the PI to determine case eligibility for study enrollment.
3. Once inclusion criteria were met, the PI, Carolyn Watts, or Christy Thomas approached the nurse assigned to the patient. That nurse determined the patient's ability to consent based on the CAM and RASS assessments that are standard nursing assessment practices in all ICU's at VUH. At a time designated by the nurse caring for the patient, the PI, Carolyn Watts, or Christy Thomas entered the room with the nurse. To maintain respect, the nurse introduced the PI, Carolyn Watts, or Christy Thomas, analogous to introducing a medical or nursing student.
4. Patients who were awake and able to understand (i.e., CAM negative with current RASS score of 0, +1 or -1 as documented by the nurse) were asked to give written consent for pressure ulcer visualization and access to PHI from the medical record using the Informed Consent Form (Appendix A). Carolyn Watts, the PI, or Christy Thomas then visualized the pressure ulcer to ensure that the staff nurse documents the location and stage correctly.
5. The PI or co-investigator did not touch the patient unless the primary nurse giving care to the patient requested assistance.
6. In cases where the patient was unable to give consent (i.e. CAM positive with current RASS score of anything other than 0, +1 or -1), family was sought to obtain surrogate consent on two face to face attempts and one phone contact attempt using the Surrogate Informed Consent Rider (Appendix A). After three

failed attempts to obtain informed consent, consent was waived and the patient enrolled into the study. A Patient Information Sheet (Appendix A) was left in the patient's room for those patients identified to be possible case or control subjects. This information sheet informed family who may not be present that the patient was considered for entry into a research study. Carolyn Watts, the PI, or Christy Thomas then visualized the pressure ulcer to ensure that the staff nurse documented the location and stage correctly. The PI or co-investigators did not touch the patient unless the primary nurse giving care to the patient requested assistance.

7. Case patients unable to give consent were periodically reevaluated by the PI or co-investigators in conjunction with the nurse to determine their ability to give written consent. If a patient became capable of giving consent, the consent process was completed.
8. A copy of the informed consent document was given to the patient or surrogate, one copy was placed in the patient's paper medical record, and the original was retained by the PI in accordance with the approved IRB protocol for protecting personal health information.
9. All attempts to obtain informed consent were tracked in the Consent Tracking Tool. (Appendix A)

Control enrollment. After a case subject was identified, the PI used the following method to identify control subjects. Efforts were made to match the ICU admission dates as closely as possible.

1. Each time a case subject was identified, the EMR was used to identify potential control subjects using the matching criteria outlined above.
2. If no control match was located for the case subject on the day of case subject enrollment, a period of 10 days elapsed before a second attempt. On day 11, a second search was completed for a control subject within +/- 10 days of the case index date. The process proceeded incrementally until the search for control subjects reached 90 days +/- the case index date.
3. If no control was found, data on the case subject was kept and labeled as an unmatched case subject.
4. All control subjects who were currently in the ICU underwent the same consent process as that for cases.

Data collection. All data were collected by the PI using either the Case Data Collection Form or the Control Data Collection Form (Appendix B) approved by the IRB. Data were collected using the EMR. Immediately after the data were collected on the paper form, the completed forms were stored in a locked file cabinet in the PI's locked office. For case subjects, the PI entered the medical record number, ICU, length of ICU stay, and ventilator use (if patient was ventilated) into the Data Management Form spreadsheet (Appendix A). The spreadsheet automatically calculated the required matching criteria for ICU admission dates to assist in identifying a matched control subject. Once a control subject was identified, the medical record number and ICU were entered into the Data Management Form, indicating that a match has occurred. The spreadsheet was kept on Vanderbilt's secure data drive, the SICU's 'M' drive, accessible from workstations in Carolyn Watt's and the PI's office, or remotely from the PI's home

computer on Vanderbilt's secured drive. The data drive is password protected and only the PI and Carolyn Watts had access.

Data for case and control subjects were transcribed from the paper data collection sheets into REDCap by the PI. The paper data collection sheets remained under double lock in the PI's office at VUH until the completion of the study, at which time they were shredded. Christy Thomas did not do data entry and therefore did not have access to the REDCap database or data collection spreadsheets.

Data source. All data were collected from the EMR using Star Panel or the nursing documentation system, Horizon Expert Documentation (HED). Star Panel serves as the primary clinical database for VUH. Star Panel acquires information from numerous other databases used in VUH to consolidate patient-specific information into one place. All variables identified in this study were acquired from Star Panel through interfaces with provider documentation, laboratory results, medication administration, and the Nursing Flow Sheet.

Reliability and Validity of Instruments

The instruments used in this study (Appendix B) were designed to capture patient demographic data and risk factors identified in the conceptual model. Therefore, the validity, reliability, and credibility of these instruments are assumed because they are specific to this study and were not used as measurement instruments. For this study, reliability and validity issues were identified in the methodology, discussed below.

Reliability and Validity of the Study Methods

To assess the reliability and validity of staff nurse documentation of pressure ulcers, a feasibility study was conducted prior to the start of this study. The study, designed to determine the completeness and accuracy of documentation regarding pressure ulcer presence and stage, demonstrated 100% agreement between the expert rater and staff nurses on the presence/absence of a pressure ulcer. The study also demonstrated 100% agreement between staff and expert rater on pressure ulcers with regard to location, and 83.3% agreement between staff and expert rater with regard to stage of pressure ulcer. Appendix C presents a detailed description of the feasibility study and its findings.

To ensure that proper pressure ulcer identification and staging was documented for each case patient, the PI, Carolyn Watts or Christy Thomas visually inspected the pressure ulcer during the process of enrollment. In cases of disagreement with the staff nurse staging, the PI, Carolyn Watts, or Christy Thomas assigned the pressure ulcer stage used.

To ensure inter-rater reliability among Carolyn Watts, Christy Thomas, and the PI during the enrollment process, the PI visually validated the presence and stage of every tenth case patient that Carolyn Watts and Christy Thomas each enrolled. An educational session and more frequent validations were planned in the case of any discrepancies that were noted; however, the inter-rater reliability demonstrated 100% agreement obviating the need for education or more frequent inter-rater reliability validations.

Data Analysis Strategy

Data Cleaning Procedures

After all data were collected and prior to analysis, variable data for 18 random case subjects and 18 random control subjects were examined for errors and omissions. No errors or omissions were found. Frequencies were checked for all identifier variables to ensure that there were no repeated subjects and that no control patient was coded as having a pressure ulcer. Matching criteria for each case-control pair were also analyzed to ensure that ICU, ventilator use, and ICU length of stay were identical. No errors in matching were identified. Unmatched cases (n = 12) were described and removed from the database for further analysis (see Chapter 4).

Statistical Methods

All data analyses were conducted using SPSS software (SPSS for Windows, Graduate Student Version, Rel. 16.0.1. 2007. Chicago: SPSS Inc.). Initially an investigation of the nature of the missing data values was undertaken to determine if there were any systematic patterns. None were detected in the primary study variables and thus missing was assumed to be random. Subsequently, multiple imputations were used to estimate the missing values. Results from both completed and imputed data sets are reported.

Aim 1. To compare the frequency and magnitude of pressure ulcer risk factors between critically ill patients that do and do not develop a pressure ulcer during their ICU stay and evaluate their influence on the associations between the Braden subscales and pressure ulcer outcome.

Descriptive statistics were generated to summarize the variables in each of the patient groups (with and without pressure ulcers). Frequency distributions summarized nominal variables. Due to the skewed nature of the continuous variables, median and 25th to 75th interquartile range (IQR) were used to summarize those distributions.

Logistic regression analysis was used to generate both unadjusted and adjusted associations of each risk factor (IV) with the presence of a pressure ulcer (DV). The conceptual model guiding this research identified 18 independent variables. Simple univariate logistic regressions were used to generate estimates of the unadjusted associations. Odds ratios with 95% confidence intervals (CI) were obtained for each variable (IV).

Multiple hierarchical logistic regression was used to generate adjusted odds ratios. Age was entered in the first step of this analysis. Braden subscale values were entered in the second step followed lastly by the other proposed risk variables. Odds ratios with 95% CI were generated. Both the univariate and adjusted analyses were conducted separately for variables collected at 24 hours and at 48 hours of the case index date. An alpha of 0.50 was used for determining statistical significance.

Sample size and power. Stability of standard errors in logistic regression requires at least 10 cases for each IV in the smallest of the dependent variable categories (Dietrich, 2009). Because a case-control design was proposed, the dependent variable categories would be of equal size. Therefore, for 18 IVs, at least 180 cases (and correspondingly 180 controls) were required to meet the minimal sample size requirement. The minimally detectable effects of a given risk factor (IV) in multiple regression analyses is based on not only the desired statistical power and alpha level, but

also on the amount of variance in the outcome variable that was already explained by the other IVs in the analysis. A total sample size of 360 with an observed proportion of the event of interest set at 0.50 (50% of the participants had a pressure ulcer), provided 80% statistical power to detect an odds ratio of 1.34 for a continuous IV if there was no variance explained by the other IVs. If as much as 30% of the variance in the likelihood of a pressure ulcer was explained by the other IVs, the sample provided 80% statistical power to detect an odds ratio of 1.42 (alpha = .05). For a dichotomous IV, those respective odds ratios were between 1.82 (0% variance explained by other IVs) and 2.06 (30% variance explained by other IVs).

Aim 2. To compare the frequency and magnitude of pressure ulcer risk factors between critically ill patients that have progression of their Stage I pressure ulcer during the ICU stay to those who do not have a progression of their Stage I pressure ulcer during the ICU stay.

No statistical analysis of subjects with a Stage I pressure ulcers was performed because four (1.1%) subjects had their pressure ulcers deteriorate into a Stage II or worse during their ICU stay. Because of the low percentage of those subjects that experienced a worsening pressure ulcer during their ICU stay, no statistical inferences can be made. Data were examined qualitatively.

CHAPTER IV

RESULTS

This chapter provides the results of a prospective case-control study examining risk factors for pressure ulcers in critically ill patients. A review of the primary aim, a description of unmatched cases, missing data, and variables with no data are presented. Characteristics of case and control subjects, pressure ulcer findings, and unadjusted and adjusted OR findings are also presented. Finally, the secondary aim is reviewed with its findings.

Unmatched Cases

There were 12 unmatched case subjects. Statistically significant differences between unmatched and matched (n = 180) case subjects were noted in five variables. Unmatched case subjects had statistically significantly less frequency of norepinephrine use prior to study enrollment (X^2 = 6.49, p = 0.011) than did matched case subjects. Unmatched case subjects had statistically significantly lower scores on the Braden Mobility subscale scores 24 hours (z = -2.20, p = 0.028) prior to study enrollment and the Braden Moisture subscale scores 48 hours (z = -2.04, p = 0.041) prior to study enrollment than did matched case subjects. Lowest oxygen saturation 24 hours prior to enrollment was statistically significantly lower in matched case subjects (z =-2.41, p = 0.016) than in unmatched case subjects. ICU length of stay was statistically significantly higher in

unmatched cases than matched cases (z =-5.58, p <0.001). ICU length of stay prior to pressure ulcer development in the unmatched case subjects was the primary reason these subjects were not matched. No further considerations of the unmatched cases were required, so they were removed from the data set for further analysis. See Appendix D, Tables 1, 2 and 3 for complete description of the comparisons between unmatched and matched case subjects.

Missing Data

Missing data were identified in the pre-admission variables describing presence or absence of diabetes, nicotine use within one year of hospital admission, corticosteroid use prior to hospital admission, and pre-existing skin disease. Hematocrit values measured at 24 and 48 hours prior to study enrollment and measures of protein reserve also contained missing data. Table 4.1 details the variables with missing data and their frequencies. Appendix D, Table 4 provides an expanded detail of the variables with missing data.

Pre-Admission Variables

Frequencies for missing data among the pre-admission variables ranged from 6.1% for nicotine use to 18.1% for history of diabetes (see Table 4.1). Variables with more than 10% missing values were excluded from analysis because of the possibility of biasing the conclusions (Duffy & Jacobsen, 2005; Cummings, Browning, & Hulley, 2007). Consequently diabetes, pre-existing skin disease, and pre-admission corticosteroid use were eliminated as variables and not included in further analyses. Aspects of pressure ulcer risk contributed by the eliminated variables shared some

conceptual overlap with other variables, thereby potentially minimizing the risk of losing any explanatory power these variables may have contributed to the study. Presence and type of diabetes had originally been included because of its association with vascular disease and detrimental effect on metabolic supply to the tissues. Other study variables, vasopressor use, hematocrit values, nicotine use, and the Braden nutrition subscale scores are related to this conceptual component of pressure ulcer risk. Pre-existing skin disease is conceptually identified as a threat to skin integrity. The Braden moisture subscale, also related to the skin integrity concept, provided the one measure to assess the concept of skin integrity threats. Because steroid use was also measured during the hospital admission, the effects of steroid use, a conceptual component of metabolic demand, was retained for further analyses. See Table 2.4 for a summary of pressure ulcer risk factor concepts and measures.

Nicotine Use Variable

Nicotine use was missing in 11 (6.1%) each of case and control subjects. Consequently, nicotine use was retained for further analyses and missing nicotine values were imputed using a regression equation to predict missing values (Duffy & Jacobsen, 2005).

Hematocrit Variables

High and low hematocrit levels at both 48 and 24 hours were reported in 351(97.5%) subjects. Values for the nine remaining subjects were imputed for further data analysis using a regression equation. After the missing variables were imputed, collinearity statistics revealed a collinearity tolerance of 0.165 for high hematocrit and 0.162 for low hematocrit 24 hours prior to study enrollment and similar collinearity

statistics were identified for high (0.177) and low (0.181) hematocrits 48 hours prior to study enrollment. Further analyses were conducted using only the low hematocrit values because of the collinearity tolerance values.

Protein Reserve Variables

Laboratory values for serum albumin, pre-albumin, and total lymphocyte count were not reported in a number of case or control subjects. None of these protein variables were reported in 22 (12.2%) of case subjects and 15 (8.3%) of control subjects. Serum albumin levels were not reported in 112 (62.2%) of case subjects or 113 (62.7%) of control subjects. Pre-albumin levels were not reported in 100 (55.5%) of case or control subjects, and total lymphocyte counts were not reported in 51 (28.3%) of case subjects and 41 (22.8%) of control subjects. To retain any explanatory contribution that protein reserve may have on pressure ulcer incidence, a new variable, 'Protein Store', was calculated to capture the presence of any protein store variable in study subjects (see Chapter II for complete definition). To accommodate for the frequency of un-reported protein store measures, values were categorized as high, normal or low, using references from the VUH clinical laboratory. In subjects with values reported for more than one of the protein reserve variables, the value for serum albumin (high, normal or low) was the default ranking. If serum albumin was not reported the value for either pre-albumin or total lymphocyte count was used. When values for two variables differed, the lower of the two was used. Serum albumin was used as the default ranking because of its use as the standard of measure in multiple studies examining nutrition status (Jeejeebhoy, 2004). After the variable was categorized into high, normal, and low, seven subjects (1.9%) were ranked as 'high' and data were missing for 27 subjects. Because the missing data

occurred at random, imputed values were added and analyses from both sets of data (with and without imputed values) were analyzed and compared. Missing variables for protein reserve ranged from 25.5% to 62.5% of subjects. Distributions between all variables for protein reserve (serum albumin, pre-albumin, total lymphocyte count) were equally distributed between case and control subjects. The Protein Store variable reduced the frequency of missing data from 62.5% to 10.3% in total subjects. However, there were only seven subjects (1.9%) with a protein reserve variable rated as high, so the categorical variable was further consolidated to a dichotomous variable representing normal and low protein levels. Data for the 10.3% of missing variables was imputed using the regression equation method used for nicotine use and hematocrit.

Table 4. 1. Frequency of Missing Data for Case and Control Subjects*

Missing Variable	Matched Cases *N* = 180 *n* (%)	Matched Controls *N* = 180 *n* (%)	*p* value†	Frequency of missing variable in both case and control pair
Pre-Admission Demographic Variables				
Diabetes	35 (19.4)	32 (17.8)	0.755	13 (7.2)
Nicotine use	11 (6.1)	11 (6.1)	1.000	2 (1.1)
Corticosteroid use	31 (17.2)	32 (17.8)	1.000	11 (6.1)
Skin Disease	27 (15.0)	29 (16.1)	0.874	8 (4.4)
Perfusion Parameter Variables				
Highest hematocrit 48 hours prior to enrollment	5 (2.8)	4 (2.2)	1.000	0 (0.0)
Lowest hematocrit 48 hours prior to enrollment	5 (2.8)	4 (2.2)	1.000	0 (0.0)
Highest hematocrit 24 hours prior to enrollment	4 (2.2)	5 (2.8)	1.000	0 (0.0)
Lowest hematocrit 48 hours prior to enrollment	4 (2.2)	5 (2.8)	1.000	0 (0.0)
Protein Reserve Variables				
Serum Albumin	112 (62.2)	113 (62.7)	1.000	75 (41.7)
Serum Pre-albumin	100 (55.5)	100 (55.5)	0.560	71 (39.4)
Total Lymphocyte Count	51 (28.3)	41 (22.8)	0.522	14 (7.8)
Any Protein Store	22 (12.2)	15 (8.3)	0.281	0 (0.0)

†McNemar *No missing data for all other demographic variables; no missing data for ICU administered medications; no missing data for all Braden subscale scores.

Recoded Variables

After investigating the initial variable distributions, variables with low response rates were either dichotomized or included with similar variables to create a global categorical variable. Table 4.2 provides summaries of the lack of any vasopressor use in case and control subjects. Vasopressor use frequency ranged from 55 (30.6%) occurrences to one occurrence (0.6%) in case subjects and 50 (27.8%) occurrences to zero occurrences in control patients. Because of the high frequency of zero doses across types of vasopressor, a global vasopressor variable was included that combined the specific types into a single global ordered categorical variable (zero, one, two, and more than two vasopressors received).

Table 4.2. Frequency of Zero Dose Vasopressor Occurrences in Case and Control Subjects

Vasopressor	Matched Cases $N = 180$		Matched Controls $N = 180$		p value†
	n	(%)	n	(%)	
Dobutamine	177	(98.3)	174	(96.7)	0.508
Epinephrine	174	(96.7)	174	(96.7)	1.000
Milrinone	166	(92.2)	170	(94.4)	0.481
Midodrine	179	(99.4)	180	(100.0)	1.000
Norepinephrine	125	(69.4)	139	(77.2)	0.115
Vasopressin	149	(82.8)	163	(90.6)	0.050

† McNemar

Similarly, Table 4.3 presents the summaries of the number of subjects in the two groups that did not receive corticosteroids during the current hospitalization. Subjects

receiving corticosteroids during the current hospitalization ranged between 25% to zero for case subjects and 16.7% to zero for control subjects. Because of the low frequency of corticosteroid administration, the multiple corticosteroids were combined into a single global dichotomous variable for analyses (0 = none received, 1=at least one received).

Table 4.3. Frequency of Zero Dose Corticosteroid Occurrences in Case and Control Subjects

Corticosteroid	Matched Cases $N = 180$		Matched Controls $N = 180$		p-value†
	n	(%)	n	(%)	
Hydrocortisone	135	(75.0)	150	(83.3)	0.268
Prednisone	163	(90.6)	155	(86.1)	0.560
Methylprednisone	160	(88.9)	158	(87.8)	0.864
Prednisolone	180	(100.0)	180	(100.0)	

† McNemar

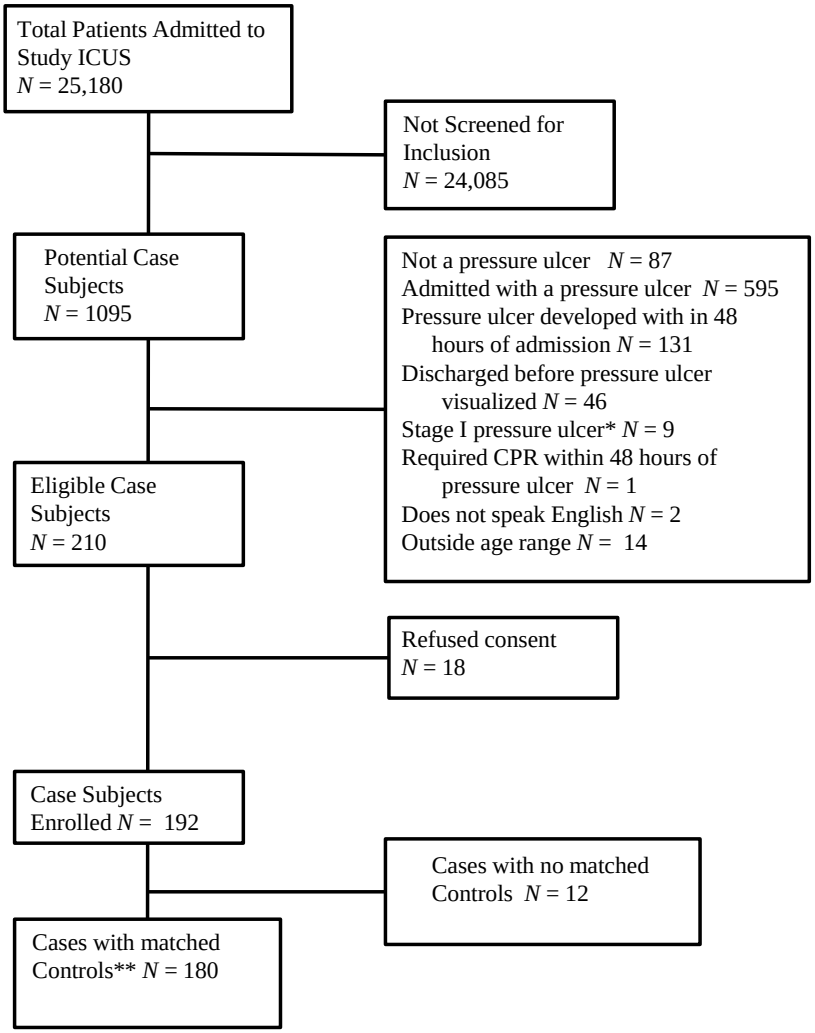
Primary Aim

To compare the frequency and magnitude of pressure ulcer risk factors between critically ill patients that do and do not develop a pressure ulcer during their ICU stay and evaluate their influence on the associations between the Braden subscales and pressure ulcer outcome. To examine any temporal differences in importance of pressure ulcer risk factors, they were measured at 48 hours and 24 hours prior to study enrollment.

Subject Profile

Case subject enrollment followed a defined process (Figure 4.1). During the data collection period from October 2010 through October 2012, 25,180 patients were admitted to the study ICUs. A convenience sample of 1,095 (4.35%) patients was screened as potential case subjects. Eight hundred and eighty-five (80.8%) of the potential case subjects did not meet enrollment criteria, leaving 210 potential case subjects. Eighteen of those were not enrolled due to lack of consent. Of the 192 case subjects that were enrolled, 12 (6.3%) did not have matched controls, so were excluded from further study leaving 180 case subjects. Comparative demographic data between subjects and patients admitted to study ICUs during the data collection period are not available given patient confidentiality issues. Matching control subjects were identified through the EMR after each case subject was identified.

Figure 4. 2. Process for Enrolling Case Subjects for Dissertation Study



*Later removed as exclusion criterion
**Identified through medical record documentation

Characteristics of Case and Control Subjects

Matching Criteria and Consent Type

Matched pairs were most frequently drawn from the SICU (31.1%) and least frequently from the Neuro ICU (5.6%). The Trauma ICU contributed 23.9% of the matched pairs, 20.0% were drawn from the MICU, and 19.4% from the CVICU. Ventilator use was present in 79.4% of the matched pairs.

Sixteen percent of case subjects gave consent for study participation. Surrogates gave consent for 49.4% of case subjects. Following the consent process established for the study protocol, 34.4% of consents were waived in case subjects and 99.4% of control subjects.

Description of Variables Assessing Pressure Distribution Capacity

Table 4.4 provides descriptive statistics and unadjusted odds ratios for likelihood of pressure ulcer for variables assessing pressure distribution capacity. Males comprised 63.9% of the subjects enrolled. A statistically significantly higher percentage were in the cases (71%) than in the controls (57%) ($p = 0.005$). Subjects' age ranged from 18 to 89 years (median = 58, IQR = 47.2 – 67.0). Average age for patients admitted to the study ICUs during the data collection period was 54.7 years. Subject body mass index ranged from 12.8 to 78.27 (median = 27.3, IQR = 23.6 – 32.9) kg/m^2. No statistically significant associations with the presence of a pressure ulcer were observed for age or BMI.

Description of Variables Assessing Metabolic Supply

Table 4.5 provides descriptive statistics and unadjusted odds ratios for likelihood of pressure ulcer for variables assessing metabolic supply. No statistically significant

associations with development of a pressure ulcer were observed for nicotine use, vasopressor administration, Braden Nutrition scores, or oxygen saturation of hemoglobin values ($p > 0.05$).Nicotine use within one year prior to hospital admission was present in 39.9% of subjects. Vasopressor administration was measured at 24 hours prior to study enrollment, 48 hours prior to study enrollment, and at any time during the ICU stay prior to the 48-hour measure. A majority of subjects (69.7%) did not receive vasopressors within 24 or 48 hours of study enrollment (69.2%). Vasopressor use prior to the 48-hour measure occurred in 44.4% of subjects. See Appendix D, Table 5 for a complete description of vasopressor use prior to study enrollment. Using VUH laboratory ranges as the reference, the combined measures of protein reserve (serum albumin, serum pre-albumin, and total lymphocyte count) were in the clinically "low" range in 79.3% of subjects. Within the 24 hours prior to study enrollment, minimum Braden Nutrition subscale scores were in the low risk range (scores of 3 or 4) in 54.1% of study subjects and thus in the high risk range (scores of 1 or 2) in 45.8% of subjects when measured at 24 hours prior to study enrollment. Within 48 hours prior to study enrollment, those values shifted slightly (Braden Nutrition low risk: 51.9%; high risk: 48.0%). Lowest observed oxygen saturation of hemoglobin measured at 24 hours before study enrollment ranged from 71% to 100% (median = 93.0, IQR = 90.0 – 96.0) and measures at 48 hours before study enrollment ranged from 67% to 100% (median = 92.0, IQR = 89.0 – 95.0).

Statistically significant associations with the development of a pressure ulcer were observed for hematocrit levels and for MAP (see Table 4.5). Within 24 hours prior to study enrollment, the minimum observed hematocrit levels in case subjects had a median hematocrit level of 26.0 (IQR = 24.0 – 29.0) while the controls had a median of 29.0

(IQR = 26.0 – 32.0) ($p < 0.001$). Highest observed hematocrit levels during the same time demonstrated a similar pattern (cases: median = 28.0, controls: median = 29.0, $p < 0.001$). Within 48 hours prior to study enrollment, the minimum observed hematocrit levels in case subjects had a median hematocrit level of 27.0 (IQR = 24.0 – 30.0) while controls had a median of 29.0 (IQR = 26.0 – 33.0) ($p = 0.011$). Highest observed hematocrit levels during the same 48 hour period before study enrollment demonstrated a similar pattern (cases: median = 28.0, controls: median = 30.0, $p = 0.008$).

Within 24 hours prior to study enrollment, the minimum observed MAP in case subjects had a median value of 61.0 (IQR = 56.0 – 67.0) mm Hg while the controls had a median of 64.0 mm Hg (IQR = 58.0 – 70.0) ($p = 0.012$). MAP values obtained 48 hours prior to study enrollment demonstrated a similar pattern (cases: median = 61.0, controls: median = 63.0, $p = 0.023$)

Table 4. 4. Frequencies and Unadjusted Odds Ratios for Variables Assessing Pressure Distribution Capacity with Pressure Ulcer

Variable	Variable Descriptor	Total *N* %	Cases *N* %	Controls *N* %	O.R.	*p*-value	CI 95%
Variables Assessing Pressure Distribution Capacity							
Gender	Female	130 (36.1)	52 (28.9)	78 (43.3)	Referent		
	Male	230 (63.9)	128 (71.1)	102 (56.7)	1.88	0.005	1.22 – 2.91
		Median (IQR)	Median (IQR)	Median (IQR)			
Age	Years	58.0 (47.3 – 67.0)	59 (48.3 – 68.0)	57.5 (46.0 – 67.0)	1.01	0.221	0.99 – 1.02
BMI*	Value	27.3 (23.6 – 32.9)	27.6 (23.0 – 33.6)	27.19 (23.9 – 32.5)	1.00	0.775	0.98 – 1.03
		Total *N* %	Cases *N* %	Controls *N* %			
	Normal	101 (28.1)	53 (29.4)	48 (26.7)	--	0.677	--
	Underweight	20 (5.6)	12 (6.7)	8 (4.4)	1.36	0.538	0.51 – 3.60
	Overweight	107 (29.7)	50 (27.8)	57 (31.7)	0.79	0.408	0.46 – 1.37
	Obese	132 (36.7)	65 (36.1)	67 (37.2)	0.88	0.625	0.52 – 1.48

*Body Mass Index: definitions for categorical ranking from www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html

Table 4. 5. Frequencies and Unadjusted Odds Ratios for Variables Assessing Metabolic Supply with Pressure Ulcer

Variable	Variable Descriptor	Total *N*	Total %	Cases *N*	Cases %	Controls *N*	Controls %	O.R.	*p*-value	CI 95%
Prior nicotine use	No	203 [213	(60.1) (59.2)]*	96 [101	(56.8) (56.1)]	107 [112	(63.3) (62.2)]	Referent		
	Yes	135 [147	(39.9) (40.8)]	73 [79	(43.2) (43.9)]	62 [68	(36.7) (37.8)]	1.31 [1.29]	0.222 [0.239]	0.85 – 2.03 [0.85 – 1.96]
Number of vasopressors used 24 hours prior to study enrollment	0	251	(69.7)	117	(65.0)	134	(74.4)	--	0.313	--
	1	63	(17.5)	36	(20.0)	27	(15.0)	1.53	0.136	0.88 – 2.67
	2	29	(8.1)	17	(9.4)	12	(6.7)	1.62	0.224	0.74 – 3.54
	3	12	(3.3)	8	(4.4)	4	(2.2)	1.64	0.333	0.60 – 4.44
	4	4	(1.1)	1	(0.6)	3	(1.7)			
	5	1	(0.3)	1	(0.6)	0	(0.0)			
Number of vasopressors used 48 hours prior to study enrollment	0	249	(69.2)	117	(65.0)	132	(73.3)	--	0.366	--
	1	68	(18.9)	37	(20.6)	31	(17.2)	1.35	0.279	0.79 – 2.31
	2	27	(7.5)	17	(9.4)	10	(5.6)	1.92	0.119	0.85 – 4.35
	3	9	(2.5)	6	(3.3)	3	(1.7)	1.45	0.474	0.52 – 4.02
	4	6	(1.7)	2	(1.1)	4	(2.2)			
	5	1	(0.3)	1	(0.6)	0	(0.0)			
Previous vasopressor use prior to 48 hours of study enrollment	No	200	(55.6)	93	(51.7)	107	(59.4)	Referent		
	Yes	160	(44.4)	87	(48.3)	73	(40.6)	1.37	0.138	0.90 – 2.08

Variable	Variable Descriptor	Total *N* %	Cases *N* %	Controls *N* %	O.R.	*p*-value	CI 95%
Minimum protein level recorded during ICU stay prior to enrollment	Normal	67 (20.7) [83 (23.1)]*	30 (19.0) [43 (23.9)]	37 (22.4) [40 (22.2)]	Referent		
	Low	256 (79.3) [277 (76.9)]	128 (81.0) [137 (76.1)]	128 (77.6) [140 (77.8)]	1.23 [0.91]	0.447 [0.707]	0.72 – 2.12 [0.56 – 1.49]
Lowest Braden nutrition score 24 hours before study enrollment	4	3 (0.8)	2 (1.1)	1 (0.6)	--	0.224	--
	3	192 (53.3)	88 (48.9)	104 (57.8)			
	2	121 (33.6)	64 (35.6)	57 (31.7)	1.31	0.244	0.83 – 2.06
	1	44 (12.2)	26 (14.4)	18 (10.0)	1.69	0.123	0.87 – 3.28
Lowest Braden nutrition score 48 hours before study enrollment	4	3 (0.8)	1 (0.6)	2 (1.1)	--	0.730	--
	3	184 (51.1)	89 (49.4)	95 (52.8)			
	2	133 (36.9)	70 (38.9)	63 (35.0)	1.19	0.427	0.77 – 1.87
	1	40 (11.1)	20 (11.1)	20 (11.1)	1.08	0.830	0.54 – 2.13
		Total Median (IQR)	Cases Median (IQR)	Controls Median (IQR)	O.R.	*p*-value	CI 95%
Lowest hematocrit recorded 24 hours prior to study enrollment		28.0 (24.0 – 31.0) *n* = 351 [28.0 (24.0 – 31.0)] *n* = 360	26.0 (24.0 – 29.0) *n* = 176 [26.0 (24.0 – 29.0)] *n* = 180	29.0 (26.0 – 32.0) *n* = 175 [29.0 (26.0 – 32.0)] *n* = 180	0.90 [0.91]	<0.001 [<0.001]	0.86 – 0.95 [0.87 – 0.95]

Variable	Variable Descriptor	Total *N* %	Cases *N* %	Controls *N* %	O.R.	*p*-value	CI 95%
Highest hematocrit recorded 24 hours prior to study enrollment		28.0 (26.0 – 31.0) *n* = 351 [28.0 (26.0 – 31.0)] *n* = 360	28.0 (25.0 – 30.0) *n* = 176 [28.0 (25.0 – 30.0)] *n* = 180	29.0 (26.0 – 33.0) *n* = 175 [29.0 (26.0 – 33.0)] *n* = 180	0.91 [0.91]	<0.001 [<0.001]	0.87 – 0.95 [0.87 – 0.96]
Lowest hematocrit recorded 48 hours prior to study enrollment		28.0 (25.0 – 31.0) *n* = 351 [28.0 (25.0 – 31.0)] *n* = 360	27.0 (24.0 – 30.0) *n* = 175 [27.0 (24.0 – 30.0)] *n* = 180	29.0 (25.0 – 32.0) *n* = 176 [29.0 (25.0 – 32.0)] *n* = 180	0.95 [0.95]	0.011 [0.010]	0.91 – 0.99 [0.91 – 0.99]
Highest hematocrit recorded 48 hours prior to study enrollment		29.0 (26.0 – 32.0) *n* =351 [29.0 (26.0 – 32.0)] *n* =360	28.0 (26.0 – 31.0) *n* = 175 [28.0 (26.0 – 31.0)] *n* = 180	30.0 (27.0 – 32.8) *n* = 176 [30.0 (27.0 – 33.0)] *n* = 180	0.94 [0.94]	0.008 [0.005]	0.90 – 0.99 [0.90 – 0.98]
Lowest MAP† recorded 24 hours prior to study enrollment		63.0 (57.0 – 69.0)	61.0 (56.0 – 67.0)	64.0 (58.0 – 70.0)	0.97	0.012	0.96 – 0.99
Lowest MAP† recorded 48 hours prior to study enrollment		62.0 (56.0 – 67.0)	61.0 (55.0 – 66.0)	63.0 (57.0 – 69.8)	0.98	0.023	0.96 – 0.99

Variable	Variable Descriptor	Total *N* %	Cases *N* %	Controls *N* %	O.R.	*p*-value	CI 95%
Lowest oxygen saturation recorded 24 hours prior to study enrollment		92.0 (90.0 – 95.8)	92.5 (90.0 – 95.0)	92.0 (90.0 – 96.0)	1.01	0.631	0.97 – 1.05
Lowest oxygen saturation recorded 48 hours prior to study enrollment		92.0 (90.0 – 95.0)	92.0 (89.3 – 95.0)	92.0 (90.0 – 95.0)	0.99	0.572	0.98 - 1.01

*Brackets indicate analyses with imputed values †Mean arterial pressure

Description of Variables Assessing Metabolic Demand

Metabolic demand summaries are presented in Table 4.6. No statistically significant differences were demonstrated between case and control subjects. Steroid administration during the hospitalization up to 14 days prior to study enrollment occurred in 36.7% of case subjects and in 30.6% of control subjects. See Appendix D, Table 5 for a complete description of the type and amount of steroid administration received during the hospitalization.

Description of Variables Assessing Threats to Skin Integrity

Table 4.6 provides summary and unadjusted associations with pressure ulcers for the Braden Moisture (skin integrity) score. A statistically significantly association with pressure ulcer development was observed for values with 24 hours of study enrollment ($p = 0.002$) but not for 48 hours prior to enrollment ($p = 0.080$). When measured at 24 hours prior to study enrollment, low Braden Moisture subscale scores of 1 or 2, indicating greatest risk of pressure ulcer incidence, were noted in 31.7% of case subjects and 18.3% of control subjects ($p < 0.001$). Braden moisture subscale scores of 3 were observed in 56.1% of case subjects and 57.8% of control subjects ($p = 0.031$).

Table 4. 6. Frequencies and Unadjusted Odds Ratios for Variables Assessing Metabolic Demand and Skin Integrity with Pressure Ulcer

Variables Assessing Metabolic Demand							
Variable	Variable Descriptor	Total *N* %	Cases *N* %	Controls *N* %	O.R.	*p*-value	CI 95%
Steroid administration within 14 days prior to study enrollment	No	239 (66.4)	114 (63.3)	125 (69.4)	Referent		
	Yes	121 (33.6)	66 (36.7)	55 (30.6)	1.31	0.220	0.85 – 2.04
Variables Assessing Threats to Skin Integrity							
Lowest Braden Moisture Score 24 hours before study enrollment	4	65 (18.1)	22 (12.2)	43 (23.9)	--	0.002	--
	3	205 (56.9)	101 (56.1)	104 (57.8)	1.89	0.031	1.06 – 3.39
	2	76 (21.1)	45 (25.0)	31 (17.2)	3.38	<0.001	1.73 – 6.59
	1	14 (3.9)	12 (6.7)	2 (1.1)			
Lowest Braden Moisture Score 48 hours before study enrollment	4	66 (18.3)	25 (13.9)	41 (22.8)	--	0.080	--
	3	228 (63.3)	118 (65.6)	110 (61.1)	1.76	0.048	1.00 – 3.08
	2	58 (16.1)	32 (17.8)	26 (14.4)	2.09	0.037	1.04 – 4.19
	1	8 (2.2)	5 (2.8)	3 (1.7)			

Table 4. 7. Frequencies and Unadjusted Odds Ratios for Variables Assessing Intensity and Duration of Pressure and Other Factors with Pressure Ulcer

Variable	Variable Descriptor	Total		Cases		Controls		O.R.	*p*-value	CI 95%
		N	%	*N*	%	*N*	%			
Lowest Braden Sensory score 24 hours before study enrollment	4	70	(19.4)	28	(15.6)	42	(23.3)	--	0.025	--
	3	126	(35.0)	57	(31.7)	69	(38.3)	1.24	0.479	0.69 – 2.24
	2	115	(31.9)	63	(35.0)	52	(28.9)	1.82	0.052	0.99 – 3.32
	1	49	(13.6)	32	(17.8)	17	(9.4)	2.82	0.007	1.32 – 6.03
Lowest Braden Sensory score 48 hours before study enrollment	4	60	(16.7)	21	(11.7)	39	(21.7)	--	0.047	--
	3	129	(35.8)	63	(35.0)	66	(36.7)	1.77	0.076	0.94 – 3.34
	2	121	(33.6)	67	(37.2)	54	(30.0)	2.30	0.011	1.21 - 4.37
	1	50	(13.9)	29	(16.1)	21	(11.7)	2.57	0.017	1.18 – 5.55
Lowest Braden Mobility score 24 hours before study enrollment	4	19	(5.3)	2	(1.1)	17	(9.4)	--	0.002	--
	3	78	(21.7)	34	(18.9)	44	(24.4)			
	2	171	(47.5)	86	(47.8)	85	(47.2)	1.71	0.038	1.03 – 2.85
	1	92	(25.6)	58	(32.2)	34	(18.9)	2.89	<0.001	1.60 – 5.22
Lowest Braden Mobility score 48 hours before study enrollment	4	7	(1.9)	1	(0.6)	6	(3.3)	--	0.012	--
	3	86	(23.9)	35	(19.4)	51	(28.3)			
	2	164	(45.6)	82	(45.6)	82	(45.6)	1.59	0.082	0.94 – 2.66
	1	103	(28.6)	62	(34.4)	41	(22.8)	2.39	0.003	1.35 – 4.25
Lowest Braden Activity score 24 hours before study enrollment	4	4	(1.1)	0	(0.0)	4	(2.2)	--	0.007	--
	3	24	(6.7)	6	(3.3)	18	(10.0)			
	2	83	(23.1)	39	(21.7)	44	(24.4)	3.25	0.021	1.19 – 8.84
	1	249	(69.2)	135	(75.0)	114	(63.3)	4.34	0.002	1.70 – 11.08

Lowest Braden Activity score 48 hours before study enrollment	4	4 (1.1)	2 (1.1)	2 (1.1)	--	0.929	--
	3	16 (4.4)	8 (4.4)	8 (4.4)			
	2	79 (21.9)	38 (21.1)	41 (22.8)	0.93	0.879	0.35 – 2.47
	1	261 (72.5)	132 (73.3)	129 (71.1)	1.02	0.960	0.41 – 2.54
Lowest Braden Friction/Shear score 24 hours before study enrollment	3	35 (9.7)	9 (5.0)	26 (14.4)	--	0.001	--
	2	163 (45.3)	75 (41.7)	88 (48.9)	2.46	0.031	1.07 – 5.58
	1	162 (45.0)	96 (53.3)	66 (36.7)	4.20	0.001	1.85 – 9.54
Lowest Braden Friction/Shear Score 48 hours before study enrollment	3	31 (8.6)	9 (5.0)	22 (12.2)	--	0.018	--
	2	181 (50.3)	87 (48.3)	94 (52.2)	2.26	0.053	0.99 – 5.18
	1	148 (41.1)	84 (46.7)	64 (35.6)	3.21	0.007	1.38 – 7.44
	Other Factors						
Restraint use	No	96 (26.7)	49 (27.2)	47 (26.1)	Referent		
	Yes	264 (73.3)	131 (72.8)	133 (73.9)	0.95	0.812	0.59 – 1.51

Description of Variables Assessing Duration and Magnitude of Pressure and Other Variables

Descriptive statistical summaries and unadjusted associations of the pressure and mobility variables in the model with the development of pressure ulcers are presented in Table 4.7. Statistically significant associations with pressure ulcers were observed for he Braden Sensory Perception, Mobility, and Friction/Shear scores at both 24 hours and 48 hours prior to study enrollment ($p < 0.05$, see Table 4.7). Activity values within 24 hours prior to enrollment were statistically significantly associated ($p = 0.007$) while values within 48 hours were not ($p = 0.929$). When measured at 24 hours prior to study enrollment, low Braden Sensory subscale scores of 1, indicating a high pressure ulcer risk, were observed in 17.8% of case subjects and 9.4% of control subjects ($p = 0.007$). When measured at 48 hours prior to study enrollment, Braden Sensory subscales of 1 and 2 were found to be statistically significantly associated with pressure ulcer (Braden Sensory score of 1, $p = 0.017$; Braden Sensory score of 2, $p = 0.011$). When measured at both 48 and 24 hours prior to study enrollment, all of the Braden Moisture subscale scores were statistically significantly associated with pressure ulcer. Similarly, when measured at 24 hours prior to study enrollment, all of the Braden Friction/Shear subscale scores were statistically significantly associated with pressure ulcer. When measured at 48 hours prior to study enrollment, Friction/Shear subscale scores of 1 and 3 were statistically significantly associated (Braden Friction/Shear score 1, $p = 0.007$; Braden Friction/Shear score 3, $p = 0.018$) while Friction/Shear subscale scores of 2 were not.

There was no statistically significant association of restraint use with the pressure ulcers. Of the subjects enrolled, 73.3% of them were in restraints prior to study enrollment. (See Table 4.7)

Pressure Ulcer Findings

Multiple pressure ulcers occurred in 51 (28.3%) of case subjects. Of those with multiple pressure ulcers, 177 (98.3%) were limited to three or less. One case subject (0.6%) each had four, five, and eight pressure ulcers. The presence of multiple pressure ulcers was confirmed visually per the protocol and had not been documented within 48 hours after the ICU admission. They were therefore considered eligible for study enrollment. Table 4.8 describes the frequency, stage, and location of the most severe pressure ulcer identified in case patients. Deep tissue injury occurred the most frequently in 72 (40.0%) of case subjects followed by Stage II pressure ulcers. The sacrum was the most commonly occurring location for pressure ulcers (*n*= 77; 42.8%) followed by the right (*n*=29; 16.1%) and left (*n*=18; 10.0%) heels.

Table 4. 8. Distribution and Severity of Pressure Ulcers (*N*=180)

	Pressure Ulcer Stage*				
Pressure Ulcer Location	Stage I (*n* = 24)	Stage II (*n* = 68)	Stage III (*n* = 5)	Unstageable (*n*=11)	Deep Tissue Injury (*n* =72)
Occiput (*n*=4)	0	2	0	1	1
Right ear (*n*=3)	0	0	0	1	2
Left ear (*n*=1)	1	0	0	0	0
Face (*n*=2)	0	2	0	0	0
Left elbow (*n*=1)	0	1	0	0	0
Middle back (*n*=1)	1	0	0	0	0
Sacrum (*n*=77)	11	31	4	3	28
Right ischium (*n*=1)	0	1	0	0	0
Left ischium (*n*=3)	0	1	0	0	2
Right buttock (*n*=16)	0	11	0	0	5
Left buttock (*n*=11)	0	6	1	2	2
Right malleolus (*n*=3)	0	0	0	2	1
Right leg (*n*=4)	0	2	0	0	2
Left leg (*n*=1)	0	0	0	0	1
Right heel (*n*=29)	9	6	0	1	13
Left heel (*n*=18)	2	4	0	1	11
Right foot (*n*=1)	0	0	0	0	1
Left foot (*n*=4)	0	1	0	0	3

*No Stage IV pressure ulcers identified

Summary of Unadjusted (Univariate) Findings

Prior to controlling for the inter-correlations among the factors included in this study, gender, a determinate of the capacity to distribute pressure, demonstrated that males were more likely to develop pressure ulcers than females ($p = 0.005$, O.R. = 1.88, 95% C.I. = 1.22 - 2.91). Factors contributing conceptually to metabolic supply that did show statistical significance were lower hematocrit levels at 24 and 48 hours prior to study enrollment, and lower mean arterial pressure recorded within the same timeframe. Braden sub-scale scores comprised 15 (68.2%) of the statistically significant findings. Subjects with low (1 or 2) Braden Moisture subscales, indicating a higher pressure ulcer risk, were statistically significantly more likely to develop a pressure ulcer than subjects with Moisture subscale scores of 3 or 4 which represent less pressure ulcer risk. Similar findings were observed in the Braden subscale components of Sensory Perception, Mobility, Activity, and Friction/Shear (see Table 4.7). Of the Braden sub-scales, only Nutrition subscale scores, a conceptual component contributing to metabolic supply, were not statistically significantly different between case and control subjects.

Multivariate Analysis

Hierarchical multiple logistic regression analysis was conducted controlling for the effects of age, then the Braden subscale scores, with the remaining variables added to test for the combined effects. Data analysis was separated into those variables measured

at 24 hours prior to study enrollment with and without imputed values, and those measured at 48 hours prior to study enrollment with and without imputed values.

Analysis of Variables Measured 24 Hours Prior to Study Enrollment

The adjusted associations of age and Braden scores with the likelihood of a pressure ulcer are summarized in Table 4.9.

Table 4. 9. Summary of Multivariate Associations with Pressure Ulcer Measured at 24 Hours Prior to Study Enrollment for Block One and Two

Variable	Without Imputed Values			With Imputed Values		
	O.R.	p-value	CI 95%	O.R.	p-value	CI 95%
Block 1						
Age	1.01	0.345	0.99 – 1.02	1.01	0.221	0.99 – 1.02
Block 2						
Age	1.01	0.327	0.99 – 1.02	1.01	0.193	0.99 – 1.02
Braden Nutrition subscore 3 and 4	--	0.068	--	--	0.682	--
Braden Nutrition subscore 2	1.64	0.068	0.96 – 2.79	1.21	0.436	0.75 – 1.97
Braden Nutrition subscore 1	2.41	0.062	0.96 – 6.07	1.26	0.550	0.59 – 2.69
Braden Mobility subscore 3 and 4	--	0.753	--	--	0.551	
Braden Mobility subscore 2	1.18	0.667	0.55 – 2.53	1.22	0.583	0.61 – 2.44
Braden Mobility subscore 1	1.48	0.456	0.53 – 4.18	1.67	0.287	0.65 – 4.31
Braden Activity subscore 3 and 4	--	0.153	--	--	0.249	--
Braden Activity subscore 2	4.26	0.054	0.97 – 18.64	2.42	0.112	0.81 – 7.18
Braden Activity subscore 1	3.58	0.107	0.76 – 16.91	1.91	0.285	0.58 – 6.24
Braden Moisture subscore 4	--	0.005	--	--	0.027	--
Braden Moisture subscore 3	2.44	0.024	1.13 – 5.29	1.57	0.185	0.81 – 3.08
Braden Moisture subscore < 3	4.32	0.001	1.79 – 10.43	2.74	0.011	1.27 – 5.92
Braden Sensory Perception subscore 4	--	0.285	--	--	0.574	--
Braden Sensory Perception subscore 3	0.48	0.071	0.21 – 1.07	0.61	0.184	0.29 – 1.26

Variable	Without Imputed Values			With Imputed Values		
	O.R.	p-value	CI 95%	O.R.	p-value	CI 95%
Braden Sensory Perception subscore 2	0.64	0.347	0.26 – 1.62	0.72	0.440	0.31 – 1.65
Braden Sensory Perception subscore 1	0.49	0.273	0.14 – 1.74	0.82	0.729	0.27 – 2.51
Braden Friction/Shear subscore 3	--	0.584	--	--	0.234	--
Braden Friction/Shear subscore 2	1.07	0.911	0.35 – 3.23	1.65	0.297	0.64 – 4.26
Braden Friction/Shear subscore 1	1.42	0.563	0.43 – 4.69	2.28	0.117	0.81 – 6.37

Hierarchical tests without imputed values (N=299): Block 1: Age alone: $X^2_{(df = 1)} = 0.89$, $p = 0.344$; Block 2: Addition of Braden Subscale scores: $X^2_{(df = 13)} = 34.72$, $p = 0.001$; Model: $X^2_{(df = 14)} = 35.62$, $p = 0.001$
Hierarchical tests with imputed values (N=360): Block 1: Age alone: $X^2_{(df = 1)} = 1.51$, $p = 0.219$; Block 2: Addition of Braden Subscale scores: $X^2_{(df = 13)} = 30.96$, $p = 0.003$; Model: $X^2_{(df = 14)} = 32.46$, $p = 0.003$

Consistent with the unadjusted findings, age alone (Block 1) was not statistically significantly associated with pressure ulcer outcome. After controlling for age, there was a statistically significant association of the Braden subscales (Block 2) with pressure ulcer development for both the complete ($X^2_{(df = 13)} = 34.72$, $p = 0.001$) and imputed data sets ($X^2_{(df = 13)} = 30.96$, $p = 0.003$). This finding indicates that the Braden subscales are statistically significantly related to pressure ulcer outcome, after controlling for the effects of age. Within the set of scores, however, only the moisture subscale score contributed uniquely to this effect (see Table 4.9).

To evaluate the effects of the other variables after controlling for the effects of age and the Braden subscales, the remaining variables were entered into the logistic regression analysis. Table 4.10 describes the multivariate associations of all variables measured at 24 hours prior to study enrollment.

Table 4. 10. Summary of Multivariate Associations with Pressure Ulcer Measured at 24 Hours Prior to Study Enrollment for the Entire Model

Variable	Without Imputed Values			With Imputed Values		
	O.R.	p-value	CI 95%	O.R.	p-value	CI 95%
Variables Assessing Pressure Distribution Capacity						
Gender - female	Referent			Referent		
Gender – male	2.99	< 0.001	1.64 – 5.47	3.09	< 0.001	1.69 – 5.64
Age	1.03	0.015	1.01 – 1.05	1.03	0.014	1.01 – 1.05
BMI – normal	--	0.535	--	--	0.112	--
BMI – underweight	1.22	0.766	0.33 – 4.49	1.19	0.789	0.32 – 4.41
BMI – Overweight	0.65	0.249	0.31 – 1.36	0.66	0.265	0.31 – 1.38
BMI – Obese	1.00	0.996	0.49 – 2.02	1.00	0.992	0.49 – 2.03
Variables Assessing Metabolic Supply						
Nicotine use – no	Referent			Referent		
Nicotine use – yes	1.84	0.051	0.99 – 3.41	1.78	0.064	0.97 – 3.27
Vasopressor use – none	--	0.769	--	--	0.841	--
Vasopressor use – 1	1.05	0.891	0.52 – 2.14	1.18	0.653	0.58 – 2.41
Vasopressor use – 2	1.40	0.575	0.43 – 4.54	0.97	0.963	0.31 – 3.05
Vasopressor use > 2	0.53	0.438	0.11 – 2.63	0.51	0.385	0.11 – 2.33
Previous vasopressor use – no	Referent			Referent		
Previous vasopressor use – yes	1.45	0.193	0.83 – 2.52	1.39	0.245	0.79 – 2.43
Minimum Protein Level – normal	Referent			Referent		
Minimum Protein Level – low	0.91	0.798	0.44 – 1.89	0.93	0.835	0.45 – 1.91
Braden Nutrition subscore 3 and 4	--	0.005	--	--	0.160	--
Braden Nutrition subscore 2	1.98	0.029	1.07 – 3.55	1.99	0.027	1.09 – 3.69
Braden Nutrition subscore 1	5.39	0.003	1.79 – 16.22	5.24	0.003	1.76 – 15.61
Low hematocrit	0.89	< 0.001	0.83 – 0.95	0.89	< 0.001	0.83 – 0.95
Low MAP	0.99	0.344	0.96 – 1.01	0.99	0.332	0.96 – 1.01
Oxygen saturation of hemoglobin	1.04	0.176	0.98 – 1.09	1.03	0.256	0.98 – 1.09
Variables Assessing Metabolic Demand						
Steroid use during hospitalization – no	Referent			Referent		
Steroid use during hospitalization – yes	1.15	0.665	0.61 – 2.15	1.19	0.588	0.64 – 2.22

Variables Assessing Threats to Skin Integrity						
Braden Moisture subscore 4	--	0.004	--	--	0.013	--
Braden Moisture subscore 3	2.77	0.024	1.15 – 6.72	2.78	0.023	1.15 – 6.72
Braden Moisture subscore < 3	5.34	0.001	1.96 – 14.56	5.49	0.001	2.02 – 14.95
Variables Assessing Intensity and Duration of Pressure						
Braden Mobility subscore 3 and 4	--	0.770	--	--	0.425	--
Braden Mobility subscore 2	1.09	0.846	0.47 – 2.61	1.13	0.779	0.47 – 2.72
Braden Mobility subscore 1	1.46	0. 526	0.46 – 4.68	1.5	0.498	0.47 - 4.84
Braden Activity subscore 3 and 4	--	0.024	--	--	0.053	--
Braden Activity subscore 2	9.91	0.006	1.90 – 51.64	9.92	0.006	1.91 – 51.59
Braden Activity subscore 1	9.98	0.011	1.71– 58.34	9.53	0.012	1.64 – 55.31
Braden Sensory Perception subscore 4	--	0.140	--	--	0.452	--
Braden Sensory Perception subscore 3	0.44	0.087	0.17 – 1.13	0.45	0.089	0.18- 1.13
Braden Sensory Perception subscore 2	0.74	0.576	0.25 – 2.17	0.75	0.594	0.25 – 2.19
Braden Sensory Perception subscore 1	0.35	0.158	0.08 – 1.51	0.36	0.170	0.08 – 1.55
Braden Friction/Shear subscore 3	--	0.403	--	--	0.237	--
Braden Friction/Shear subscore 2	0.69	0.551	0.19 – 2.37	0.66	0.513	0.19 – 2.29
Braden Friction/Shear subscore 1	1.02	0.975	0.27 – 3.87	1.02	0.973	0.27 – 3.86
Other Factors						
Restraint use – no	Referent			Referent		
Restraint use – yes	0.42	0.022	0.19 – 0.88	0.43	0.025	0.20 – 0.89

Test of the final overall model without imputed data (N = 299): $X^2_{(df = 29)} = 81.17$, $p < 0.001$
Test of the final overall model with imputed data (N = 360): $X^2_{(df = 29)} = 86.53$, $p < 0.001$

The remaining set of variables (nicotine use, BMI, gender, vasopressor use, protein level, steroid use during hospitalization, restraint use, and lowest observed hematocrit, MAP, and oxygen saturation of hemoglobin 24 hours before study enrollment) were added in the final step of the hierarchical analysis. After controlling for age and the Braden scores, the set added statistically significantly to the model (Complete data: $X^2_{(df = 15)} = 45.61$, $p < 0.001$; Imputed data set: $X^2_{(df = 15)} = 54.07$, $p < 0.001$). As would be expected, the overall model containing all of the variables was statistically significant ($p < 0.001$). Within the set of added variables the following variables contributed to that effect: gender, restraint use, and lowest hematocrit levels. The adjusted effects of restraint use on pressure ulcer outcome indicated that restrained subjects were approximately 60% less likely to develop a pressure ulcer than unrestrained subjects using variables with ($p = 0.025$, O.R. = 0.43, 95% C.I. = 0.20 – 0.89) and without ($p = 0.022$, O.R. = 0.42, 95% C.I. = 0.19 – 0.88) imputed data.

Finally, once all variables were adjusted for in the analysis some findings emerged that were not apparent in the unadjusted or in the previous steps. Age became a statistically significant variable. Subjects were 3% more likely to develop a pressure ulcer with each increase in age by one year using variables with ($p = 0.014$, O.R. = 1.03, 95% C.I. = 1.01 – 1.05) and without ($p = 0.015$, O.R. = 1.03, 95% C.I. = 1.01 – 1.05) imputed data. Braden subscales of Nutrition and Activity became statistically significant in the overall test of the model only when data without imputed values were used (Nutrition $p = 0.005$; Activity $p = 0.024$).

Variables remaining statistically significant in the adjusted analysis included Braden Moisture subscale and low hematocrit using the variables with and without

imputed values. Braden Activity subscale maintained the statistical significance demonstrated in univariate associations with pressure ulcer in multivariate analysis using only the variables without imputed values.

Finally, variables that appeared to be statistically significant in the unadjusted or in the model without the last set of variables but were no longer in the full model included Braden Sensory Perception and Friction/Shear subscales. Similarly, MAP was no longer statistically significant in multivariate tests of its association with pressure ulcer outcome.

Analysis of Variables Measured 48 Hours Prior to Study Enrollment

Another multiple hierarchical logistic regression analysis was conducted using variables assessed 48 hours prior to study enrollment. Table 4.11 summarizes that analysis.

Table 4. 11. Summary of Multivariate Associations with Pressure Ulcer Measured at 48 Hours Prior to Study Enrollment for Block One and Two

Variable	Without Imputed Values			With Imputed Values		
	O.R.	p-value	CI 95%	O.R.	p-value	CI 95%
Block 1						
Age	1.01	0.303	0.99 – 1.03	1.01	0.221	0.99 – 1.02
Block 2						
Age	1.01	0.200	0.94 – 1.03	1.01	0.112	0.99 – 1.03
Braden Nutrition subscores 3 and 4	--	0.638	--	--	0.586	--
Braden Nutrition subscore 2	1.24	0.432	0.73 – 2.09	1.22	0.416	0.75 – 1.98
Braden Nutrition subscore 1	0.89	0.788	0.39 – 2.06	0.87	0.715	0.42 – 1.83
Braden Mobility subscore 3 and 4	--	0.167	--	--	0.162	--
Braden Mobility subscore 2	1.72	0.178	0.78 – 3.77	1.47	0.266	0.75 – 2.91
Braden Mobility subscore 1	2.62	0.059	0.97 – 7.09	2.30	0.061	0.96 – 5.51

Variable	Without Imputed Values			With Imputed Values		
	O.R.	p-value	CI 95%	O.R.	p-value	CI 95%
Braden Activity subscore 3 and 4	--	0.135	--	--	0.039	--
Braden Activity subscore 2	0.42	0.203	0.11 – 1.59	0.44	0.154	0.14 – 1.36
Braden Activity subscore 1	0.27	0.058	0.07 – 1.05	0.25	0.019	0.08 – 0.79
Braden Moisture subscore 4	--	0.603	--	--	0.492	--
Braden Moisture subscore 3	1.71	0.178	0.78 – 3.77	1.49	0.234	0.77 – 2.86
Braden Moisture subscore < 3	2.62	0.059	0.97 – 7.09	1.41	0.393	0.64 – 3.08
Braden Sensory Perception subscore 4	--	0.582	--	--	0.605	--
Braden Sensory Perception subscore 3	1.08	0.85	0.48 – 2.43	1.45	0.322	0.69 – 3.05
Braden Sensory Perception subscore 2	1.57	0.345	0.62 – 3.96	1.79	0.175	0.77 – 4.19
Braden Sensory Perception subscore 1	1.03	0.95	0.33 – 3.23	1.67	0.335	0.59 – 4.75
Braden Friction/Shear subscore 3	--	0.300	--	--	0.249	--
Braden Friction/Shear subscore 2	1.95	0.207	0.69 – 5.52	1.95	0.171	0.75 – 5.09
Braden Friction/Shear subscore 1	2.36	0.123	0.79 – 7.05	2.36	0.098	0.86 – 6.51

Hierarchical tests without imputed values (N=301): Block 1: Age alone: $X^2_{(df = 1)} = 1.07$, $p = 0.302$; Block 2: Addition of Braden Subscale scores: $X^2_{(df = 14)} = 19.87$, $p = 0.134$; Model: $X^2_{(df = 15)} = 20.93$, $p = 0.139$
Hierarchical tests with imputed values (N=360): Block 1: Age alone: $X^2_{(df = 1)} = 1.51$, $p = 0.219$; Block 2: Addition of Braden Subscale scores: $X^2_{(df = 13)} = 22.59$, $p = 0.047$; Model: $X^2_{(df = 14)} = 24.09$, $p = 0.045$

Similar to the 24 hour model, age alone (Block 1) was not a statistically significantly associated with pressure ulcer outcome. After controlling for age, addition of the Braden subscales (Block 2) was not statistically significantly associated with pressure ulcer outcome using variables without imputed values ($X^2_{(df = 14)} = 19.87$, $p = 0.134$); however, with the larger sample size of imputed data was statistically significant

($X^2_{(df = 13)} = 22.59$, $p = 0.047$). None of the individual Braden subscales was statistically significantly associated with pressure ulcer outcome in Block 2 of the model. After controlling for age and the Braden scores, the set added statistically significantly to the model when imputed data were used ($X^2_{(df = 14)} = 22.01$, $p = 0.045$) but did not add statistically significantly to the model when the complete data set was used ($X^2_{(df = 15)} = 22.94$, $p = 0.139$).

The results of the final model at 48 hours are presented in Table 4.12. The remaining set of variables (nicotine use, BMI, gender, vasopressor use, protein level, steroid use during hospitalization, restraint use, and lowest observed hematocrit, MAP, and oxygen saturation of hemoglobin 48 hours before study enrollment) were added in the final step of the hierarchical analysis. After controlling for age and the Braden scores, the set added statistically significantly to the model (Complete data: $X^2_{(df = 15)} = 32.09$, $p = 0.006$; Imputed data set: $X^2_{(df = 15)} = 36.42$, $p = 0.002$). As with the variables measured at 24 hours, the overall model containing all of the variables measured at 48 hours prior to study enrollment was statistically significant ($p < 0.001$). Within the set of added variables, gender and low hematocrit contributed to that effect. The adjusted effects of restraint use on pressure ulcer outcome indicated that restrained subjects were approximately 50% less likely to develop a pressure ulcer than unrestrained subjects using variables with imputed data ($p = 0.041$, O.R. = 0.52, 95% C.I. = 0.28 – 0.97); however, restraint use was not statistically significantly associated with pressure ulcer using the complete data set ($p = 0.117$).

Table 4. 22. Summary of Multivariate Associations with Pressure Ulcer Measured at 48 Hours Prior to Study Enrollment for the Entire Model

Variable	Without Imputed Values			With Imputed Values		
	O.R.	p-value	CI 95%	O.R.	p-value	CI 95%
Variables Assessing Pressure Distribution Capacity						
Gender - female	Referent			Referent		
Gender – male	2.52	0.001	1.43 – 4.44	2.29	0.001	1.38 – 3.83
Age	1.02	0.082	0.99 – 1.04	1.02	0.020	1.00 – 1.04
BMI – normal	--	0.341	--	--	0.161	--
BMI – underweight	1.39	0.588	0.42 – 4.68	2.02	0.209	0.67 – 6.06
BMI – Overweight	0.59	0.131	0.29 – 1.17	0.64	0.155	0.35 – 1.18
BMI – Obese	0.75	0.405	0.38 – 1.48	0.78	0.427	0.43 – 1.43
Variables Assessing Metabolic Supply						
Nicotine use – no	Referent			Referent		
Nicotine use – yes	1.32	0.341	0.74 – 2.35	1.53	0.104	0.92 – 2.56
Vasopressor use – none	--	0.529	--	--	0.767	--
Vasopressor use – 1	1.48	0.241	0.77 – 2.85	1.16	0.641	0.63 – 2.14
Vasopressor use – 2	1.88	0.267	0.62 – 5.73	1.37	0.528	0.52 – 3.59
Vasopressor use > 2	1.12	0.882	0.26 – 4.79	0.69	0.544	0.21 – 2.31
Previous vasopressor use – no	Referent			Referent		
Previous vasopressor use – yes	1.53	0.121	0.89 – 2.63	1.32	0.263	0.81 – 2.16
Minimum Protein Level – normal	Referent			Referent		
Minimum Protein Level – low	1.14	0.696	0.59 – 2.20	0.75	0.316	0.43 – 1.32
Braden Nutrition subscore 3 and 4	--	0.831	--	--	0.705	--
Braden Nutrition subscore 2	1.16	0.597	0.66 – 2.05	1.21	0.482	0.72 – 2.03
Braden Nutrition subscore 1	0.94	0.897	0.36 – 2.42	0.91	0.826	0.39 – 2.11
Low hematocrit	0.94	0.030	0.89 – 0.99	0.95	0.017	0.91 – 0.99
Low MAP	0.99	0.454	0.97 – 1.01	0.99	0.240	0.96 – 1.01
Oxygen saturation of hemoglobin	0.99	0.557	0.98 – 1.01	0.99	0.550	0.98 – 1.01
Variables Assessing Metabolic Demand						
Steroid use during hospitalization – no	Referent			Referent		
Steroid use during hospitalization – yes	1.06	0.837	0.59 – 1.93	1.23	0.443	0.72 – 2.09
Variables Assessing Threats to Skin Integrity						
Braden Moisture subscore 4	--	0.566	--	--	0.317	--
Braden Moisture subscore 3	1.50	0.318	0.68 – 3.35	1.70	0.144	0.83 – 3.47
Braden Moisture subscore < 3	1.60	0.326	0.62 – 4.13	1.78	0.188	0.75 – 4.22
Variables Assessing Intensity and Duration of Pressure						
Braden Mobility	--	0.116	--	--	0.094	--

Variable	Without Imputed Values			With Imputed Values		
	O.R.	p-value	CI 95%	O.R.	p-value	CI 95%
subscore 3 and 4						
Braden Mobility subscore 2	1.91	0.128	0.83 – 4.38	1.72	0.147	0.83 – 3.59
Braden Mobility subscore 1	3.12	0.038	1.06 – 9.13	2.87	0.030	1.12 – 7.46
Braden Activity subscore 3 and 4	--	0.137	--	--	0.093	--
Braden Activity subscore 2	0.34	0.151	0.08 – 1.48	0.42	0.165	0.12 – 1.43
Braden Activity subscore 1	0.22	0.051	0.05 – 1.01	0.26	0.038	0.07 – 0.93
Braden Sensory Perception subscore 4	--	0.598	--	--	0.740	--
Braden Sensory Perception subscore 3	0.91	0.839	0.37 – 2.24	1.35	0.481	0.58 – 3.15
Braden Sensory Perception subscore 2	1.43	0.509	0.49 – 4.09	1.68	0.300	0.63 – 4.47
Braden Sensory Perception subscore 1	0.99	0.989	0.28 – 3.55	1.77	0.335	0.55 – 5.69
Braden Friction/Shear subscore 3	--	0.356	--	--	0.297	--
Braden Friction/Shear subscore 2	1.86	0.282	0.60 – 5.74	1.73	0.302	0.61 – 4.91
Braden Friction/Shear subscore 1	2.30	0.163	0.71 – 7.43	2.27	0.143	0.76 – 6.78
Other Factors						
Restraint use – no	Referent			Referent		
Restraint use – yes	0.58	0.117	0.29 – 1.15	0.52	0.041	0.28 – 0.97

Test of the final overall model without imputed data ($N = 299$): $X^2_{(df = 29)} = 81.17$, $p < 0.001$
Test of the final overall model with imputed data ($N = 360$): $X^2_{(df = 29)} = 86.53$, $p < 0.001$

Multivariate associations of age with pressure ulcer outcome again became statistically significant in the overall model with imputed values ($p = 0.020$, O.R. = 1.02, 95% C.I. = 1.00 – 1.04); however, multivariate associations of age with pressure ulcer outcome were not statistically significant using imputed values ($p = 0.082$, O.R. = 1.02, 95% C.I. = 0.99 – 1.04). Braden Activity subscore, identified as a statistically significant association with pressure ulcer in Block 2 ($p = 0.039$) of the 48-hour multivariate analysis was no longer statistically significant in Block 3 ($p = 0.705$).

Using both the complete ($p = 0.001$, O.R. = 2.52, 95% C.I. = 1.43 – 4.44) variables and variables with imputed data ($p = 0.001$, O.R. = 2.29, 95% C.I. = 1.38 –

3.83), male gender demonstrated a statistically significant association with pressure ulcer at 48 hours prior to study enrollment. Similarly, low hematocrit demonstrated a statistically significant association with pressure ulcer at 48 hours prior to study enrollment with both complete (p = 0.030, O.R. = 0.94, 95% C.I. = 0.89 – 0.99) and imputed data ((p = 0.017, O.R. = 0.95, 95% C.I. = 0.91 – 0.99). None of the Braden subscale scores were statistically significantly associated with pressure ulcer in the final model using variables obtained 48 hours to study enrollment.

Summary

Although the Braden subscale scores are statistically significantly associated with pressure ulcer outcomes, the addition of other variables at both 24 and 48 hours did contribute statistically significantly to the overall model. With the exception of nutrition, all of the Braden subscale scores were statistically significant in unadjusted (univariate) analysis. In multivariate analysis, Braden Nutrition (without imputed values), Activity (without imputed values), and Moisture were statistically significantly associated with pressure ulcer when analyzed with scores obtained 24 hours prior to study enrollment, but did not show a statistically significant association with pressure ulcer when analyzed with scores obtained 48 hours before study enrollment. Consequently, none of the Braden subscores were uniquely identified as statistically significant predictors when analyzed with their scores obtained 48 hours prior to study enrollment. Increased age and restraint use, although not identified as statistically significant in unadjusted, did demonstrate statistically significant associations with pressure ulcer when analyzed with data collected

at 24 and 48 hours prior to study enrollment. Male gender and low hematocrit were statistically significantly associated with pressure ulcer in unadjusted and adjusted analyses at both 24 and 48 hours prior to study enrollment.

Secondary Aim

The secondary aim of this study was to compare the frequency and magnitude of pressure ulcer risk factors between critically ill patients that have progression of their Stage I pressure ulcer during the ICU stay to those who do not have a progression of their Stage I pressure ulcer during the ICU stay.

Stage I pressure ulcers were identified in 24 of the case subjects. Of those, four (1.1%) subjects had their pressure ulcers deteriorate into a Stage II or worse during their ICU stay. Ages of these four subjects ranged from 27 years to 74 years (median = 58 years for entire sample), and length of ICU stay until a pressure ulcer developed ranged from nine to 22 days (median = 7 days for the entire sample). Two were males. Low hematocrit ranged from 24% to 36% ($\tilde{\chi}$ = 28.0% for the entire sample). One of the four subjects was quadriplegic requiring permanent ventilator support. Because of the low percentage of those subjects that experienced a worsening pressure ulcer during their ICU stay, no statistical inferences can be made.

CHAPTER V

DISCUSSION

This chapter provides an overview of the primary and secondary aims of this dissertation research and findings for each of the aims are discussed relative to their contributions to the conceptual model identified in Chapter II. Strengths and limitations are presented and the implications of this research are discussed. Finally, an outline of recommendations for future research is presented.

Primary Aim

To compare the frequency and magnitude of pressure ulcer risk factors between critically ill patients that do and do not develop a pressure ulcer during their ICU stay and evaluate their influence on the associations between the Braden subscales and pressure ulcer outcome. To examine any temporal differences in importance of pressure ulcer risk factors, they were measured at 48 hours and 24 hours prior to study enrollment.

Predictive Ability of the Braden Score in Critically Ill Patients

A hierarchical test of the independent variables initially controlled for the effects of age and then tested for the added effect of the Braden subscale scores. As indicated

from the adjusted effects of the association after controlling for age, the Braden subscale scores at 24 hours prior to study enrollment were statistically significant ($p < 0.001$ with and without imputed data). A similar hierarchical test using Braden subscale scores obtained 48 hours prior to study enrollment demonstrated that the added associations of the Braden subscale scores after controlling for age were not statistically significant when analyzed without imputed data ($p = 0.100$). When analyzed with imputed data, the added effects of the Braden subscale scores did reach statistical significance ($p = 0.047$). The findings of this study indicate that the Braden subscale scores reflect more of an association with pressure ulcers when measured within 24 hours of pressure ulcer occurrence than they do when measured within 48 hours of pressure ulcer occurrence.

The temporal relationship between Braden Scale and pressure ulcer has not been widely evaluated in the literature (Brown, 2004). In their study of 843 subjects in tertiary care, skilled nursing facilities (SNFs), and Veteran's Administration Medical Centers (VAMCs), Bergstrom, Braden, Kemp, Champagne and Ruby (1998) evaluated the specificity and sensitivity of the Braden Scale on admission to the facility, 48 to 72 hours after admission. A third measure (indicated as Time 3) was calculated as the time between the last observation and first recorded pressure ulcer. Bergstrom et al.'s findings indicated that Time 3 was least useful in pressure ulcer prediction in tertiary care settings compared to VAMCs and SNFs, but the authors did not indicate the number of days between risk score and pressure ulcers development.

Although the Braden Scale was not evaluated, Nijs et al. (2008) found that factors affecting metabolic supply and demand such as dialysis, vasopressor use, and elevated body temperature were statistically significantly associated with pressure ulcer outcome

when measured at 24 and 48 hours before the occurrence of a pressure ulcer. In their study of 520 critically ill patients receiving care in a surgical unit, use of sedatives, a component that theoretically diminishes a patient's ability to minimize intensity and duration of pressure, was found to be a protective factor 24 hours ($p = 0.006$, O.R = 0.30, 95% C.I = 0.13 – 0.70) and 48 hours ($p = 0.004$, O.R = 0.27, 95% C.I = 0.11 – 0.65). Nijs et al. suggested that reduced muscle tension associated with sedative use may facilitate preventive measures. Multivariate analyses in this study were conducted only on variables that demonstrated a p-value ≤ 0.2 with univariate logistic regression, thereby enhancing the chances of a Type I or II error in the study findings.

There are two possible explanations for the findings in this study. First, it is possible that patients are assessed as low pressure ulcer risk (higher Braden subscale scores) until there is visual evidence of skin damage, such as blanching erythema or dermatitis, that leads to pressure ulcer development. This explanation assumes that the presence of skin damage biases the rater toward lower (higher risk) Braden subscale scores. A second explanation may lie with the acute nature of critically ill patients whose pressure ulcer risk can change significantly over the course of hours. This explanation favors Benoit and Mion's (2012) idea that tissue tolerance serves as a moderating factor between duration and intensity of pressure and pressure ulcer outcomes. Components of tissue tolerance may be the critical determinates of pressure ulcers in critically ill patients. Patients with depleted tissue tolerance reserve may be susceptible to acute changes that pressure ulcers develop more quickly than they would in patients with better tissue tolerance reserves. The implication of this second explanation is that the Braden

Score, when used alone, may lack the sensitivity to capture acute changes in tissue tolerance that quickly lead to pressure ulcer development.

Statistically Significant Variables Assessing Tissue Tolerance for Pressure at 24 Hours

Indeed, when variables that assessed tissue tolerance were added to the multivariate regression, male gender, increased age, lower hematocrit, and Braden Nutrition and Moisture subscale scores were all statistically significant in their associations with pressure ulcer outcome when measured at 24 hours prior to study enrollment. All are included in Benoit and Mion's (2012) conceptual model as affecting tissue tolerance for pressure. Of the remaining variables analyzed in this study, only the Braden subscale score for Activity and restraint use were identified as statistically significant at 24 hours. Neither of these variables was considered by Benoit and Mion to affect tissue tolerance, but do play a role in affecting magnitude and duration of pressure.

Gender

van Rijswijk (2001) and Sayar et al. (2008) questioned the significance of gender as a pressure ulcer risk factor, citing conflicting findings in the published literature on the influence of gender on pressure ulcer development. Fisher, Wells, and Harrison (2004) postulated that females would be more prone to pressure ulcer development because males tend to have better tissue tolerance for pressure due to higher muscle mass and anabolic hormones. Males, however, tend to have less body fat than females,

theoretically reducing their ability to distribute pressure across the body surface (Nixon, 2001), thereby making males more vulnerable to pressure ulcer development.

Male gender was a statistically significant risk factor for pressure ulcer development in both univariate and multivariate analysis findings in this study. This is consistent with those results reported by Nonnemacher et al. (2008); however, female gender as an important risk factor has also been reported. Lindgren et al., 2004 sampled a mixed group of surgical patients (n = 286) and reported female gender to be statistically significantly associated with pressure ulcers in multivariate analysis (p = 0.003; O.R. = 0.27, 95% C.I. = 0.11 – 0.68) although the odds ratios reported indicate female gender is a protective factor. Furthermore, the women in Lindgren et al.'s study were significantly older than males, and demonstrated higher risk for pressure ulcer development on admission to the study, possibly explaining the findings. In a multisite study of 530 subjects admitted to a tertiary care facility and a county hospital, female gender was identified as a risk factor with univariate analysis, but the variable did not maintain significance in multivariate analysis (Lindgren et al., 2005). It is unclear if the sample populations were shared between this study and the previous one by Lindgren et al. published a year earlier. The population in Lindgren et al.'s 2005 study was reported to include 286 surgical subjects- the same number of subjects included in Lindgren et al.'s 2004 study.

Because gender was not controlled for in this study, there was a disproportionate representation of males (63.9%) in this study. This sampling bias could account for the findings in this study.

Age

The relationship between increasing age and pressure ulcer incidence is well documented in the literature. A PubMed search of the literature using the search terms age and pressure ulcer risk with no limits returned 577 articles, indicating that the relationship is well studied. The effects of age on pressure ulcer risk in the critically ill patient population share the positive association documented for subjects with less acute illness, and there is little evidence that the magnitude of the relationship between increased age and pressure ulcers in critically ill patients is more pronounced. In their study of 3,026 critically ill patients, Eachempati, Hydo, & Barie (2001) found increased age to retain its statistical significance with multivariate analysis ($p = 0.003$; O.R. = 1.08, 95% C.I. = 0.003 – 0.013). Increased age was identified as statistically significant with univariate analysis in two other studies of critically ill patients, but age did not maintain its statistical significance in multivariate analyses. In their study of 332 critically ill patients, Theaker et al., 2000 found that the odds of developing a pressure ulcer increased by approximately 80% for each increase in year of age ($p = 0.025$; O.R. = 1.79, 95% C.I. = 0.003 – 0.013). Papantonio, Wallop, & Kolodner (1994) reported categorical findings for age in their study of 136 thoracic surgery patients. Subjects ≥ 70 years of age were five times more likely to develop a pressure ulcer than subjects less than 70 years of age ($p = 0.001$; O.R. = 5.38, 95% C.I. = 1.96 – 14.76).

Age did demonstrate a slight decrease in p-value from 48 hours ($p = 0.020$) to 24 hours ($p = 0.014$) when imputed values were used, and odds ratios remained approximately the same (1.02 at 48 hours; 1.03 at 24 hours). One possible explanation for the lack of statistical change for age in this study was the similar age ranges among

case and control patients. Age ranged between 51 and 70 years for 50.6% of subjects in this study (controls = 46.1%; cases = 55.0%). Subjects older than 70 years accounted for 16.4% (controls = 16.7%; cases = 16.1%) of the study population. Patients older than 89 years were not enrolled in this study because of protective measures of human subjects and concerns for this vulnerable population. The homogenous mix of age in this study is representative of the population most likely to require intensive care during their hospital stay and may explain the lack of statistical change in odds ratios and significance from 48 to 24 hours.

Hematocrit

Hematocrit levels were randomly missing in nine subjects, and values for this variable were imputed. Lower hematocrit values demonstrated statistical significance with univariate and multivariate analyses 24 and 48 hours prior to pressure ulcer development using the variable with and without imputed data. This finding is consistent with those reported in several studies of pressure ulcer risk factors. In studies of 149 acute care patients, Olson et al. (1996) found decreased hemoglobin on admission to be univariately associated with pressure ulcer incidence. Strordeur, Laurent, and D'Hoore (1998) found decreased hemoglobin on admission to be statistically significant in univariate and multivariate analyses of 163 cardiac surgery patients. In studies of critically ill patients, Lewicki et al. (1997) reported a statistically significant difference ($p = 0.004$) between hematocrit values in 337 pressure ulcer positive and pressure ulcer negative patients. Nijs et al. (2008) reported statistically significant univariate findings for hemoglobin 48 hours prior to pressure ulcer development ($p = 0.015$; O.R. 0.78; 95% C.I. = 0.64 – 0.95) in their study of 520 patients receiving care in a surgical ICU, but the

variable did not maintain its statistical significance with multivariate analysis. Theaker et al. (2000) found anemia to be statistically significant when analyzed at both univariate (p = 0.013; O.R. 3.23; 95% C.I. = 1.89 – 5.51) and multivariate (p = 0.013; O.R. 2.81; 95% C.I. = 1.24 – 6.34) levels for 286 patients in a general ICU.

The findings in this study demonstrate stronger p-values at for both imputed and non-imputed variables at 24 hours ($p < 0.001$) than the studies cited above, and similar p-values for imputed and non-imputed variables at 48 hours (without imputed value, p = 0.030; with imputed values, p = 0.017) (see Table 4.8 and 4.10). The implications of this finding are discussed below.

Braden Nutrition Subscale

Of the Braden subscales, Nutrition is the only one requiring some historical knowledge of the patient (see Table 2.5). Temporary food intake restrictions, such as for surgical procedures, do not adversely affect the Braden Nutrition subscale score. Additionally, physicians and dieticians closely monitor nutritional status in the ICUs, and aggressive measures provide adequate nutritional support during critical illness. No studies were located that described statistical significance of Braden Nutrition subscore in isolation; however, depleted protein stores are a common finding among critically ill patients (Anthony, et al., 2000). In their study of 186 patients in a neurologic ICU, Fife et al. (2001) did report low serum albumin to be statistically significant with pressure ulcers (p = 0.033), but it is unclear how the variables for multivariate analysis were selected, and no odds ratios or confidence intervals are reported. Perhaps the largest study to demonstrate a statistically significant multivariate association between nutritional status and pressure ulcer outcome was in Nonnemacher et al.'s (2008) study of

34,238 patients admitted to a large university hospital. Multivariate analysis in that study demonstrated that patients with insufficient nutrition were 60% more likely to develop a pressure ulcer than those patients who did not have nutritional insufficiency (p = 0.002, O.R. = 1.61; 95% C.I. = 1.20 – 2.17). Eachempati et al. (2001) also reported similar multivariate findings.

Measures of protein reserve did not show statistical significance in this study. This finding is understandable given that the majority of both case and control subjects had low protein levels (79.3% without imputed data and 76.9% with imputed data).

Braden Moisture Subscale

Braden's Moisture subscale assesses threats to skin integrity in the conceptual model described in Table 2.4, and is theorized to affect the tissue's extrinsic tolerance for pressure. Prolonged exposure of skin to moisture contributes to skin integrity problems (Nixon, 2001; Sayar et al., 2008), especially with reference to urinary and fecal incontinence. Several studies identified some element of moisture (perspiration, urinary or fecal incontinence) as a statistically significant risk factor in univariate or multivariate analysis of their findings. In their study of 286 patients admitted to an urban teaching hospital, Allman, et al. (1995) found high incidence of fecal incontinence to be a significant risk factor with univariate analysis (p = 0.04, no O.R. reported). Halfens, et al. (2000) found moisture to co-exist with the summative Braden score (that includes the Moisture subscale) as a multivariate statistically significant risk factor (p < 0.01, O.R. = 2.35, 95% C.I. = 1.40 – 3.94) in 320 subjects enrolled in a multi-center study.

Statistically Significant Variables Assessing Intensity and Duration of Pressure at 24 Hours

Braden Activity Subscale

In the study by Lindgren et al. (2004, n = 530) decreased physical activity was identified as a statistically significant predictor of pressure ulcer incidence in univariate analysis of non-ICU patients (p = 0.029, O.R. = 0.77, 95% C.I. = 0.62 – 0.97). In a study of 3026 critically ill patients, Eachempati et al. (2001) identified number of days in bed to be a statistically significant predictor with both univariate (p = 0.0328) and multivariate analysis (p = 0.0064). The odds ratio reported in Eachempati et al.'s study is 1.05 and the 95% confidence interval is reported as -0.0013 – 0.0156. It is unclear with which p-value the odds ratio and confidence interval are associated.

Restraints

Use of upper limb restraints is common in ICUs as a method to prevent tube dislodgement by patients. There is some evidence in the literature suggesting that restraint use pre-disposes patients to pressure ulcers (Castle & Engberg, 2009), but the association has not been widely explored in the literature. This study demonstrated that restraint use was not statistically significantly associated with pressure ulcer incidence with univariate analysis, but did show statistical significance as a protective factor in multivariate analysis at 24 hours prior to study enrollment with imputed values (p = 0.025; O.R. 0.43; 95% C.I. = 0.20 – 0.89) and without imputed values (p = 0.022; O.R. 0.42; 95% C.I. = 0.19 – 0.88). One possible explanation for this finding is that restraint

use reduces the amount of friction and shear experienced by the patient by reducing movement across the surface of the bed. Another explanation for this finding are the regulatory and institutional mandates for repositioning restrained patients every two hours.

Non-Significant Variables Assessing Pressure Ulcer Risk

Remaining Braden subscales

The Sensory, Activity, Mobility, and Friction/Shear subscales were not statistically significant in multivariate tests of the model in this study. They are all variables used to assess intensity and duration of pressure identified in Benoit and Mion's conceptual model (2012). As discussed earlier, the findings of this study suggest that tissue tolerance for pressure may play a more important role in pressure ulcer development than does pressure relief in critically ill patients, especially when considered within the context of the enhanced statistical significance of the findings at 24 hours prior to study enrollment. All of the remaining Braden subscales are possibly affected by sedative use, a common practice in ICUs. As discussed earlier, Nijs et al. (2008) identified sedative use as a protective factor. One possible explanation for the findings in this study and the study by Nijs et al. is that sedated patients are more receptive to nursing interventions to reduce intensity and duration of pressure, such as repositioning; however, Nijs et al. also report nursing interventions identified as prevention measures and frequency of turning to be positively associated with pressure ulcer outcome. Nijs et

al.'s study design was prospective, so the relationship between nursing intervention and pressure ulcer outcome may be causal. As indicated earlier, Nijs et al.'s multivariate analysis consisted of only those variables that demonstrated *p*-values of <0.20. Nonnemacher et al. (2008) reported contradictory findings in their study of 34,238 patients admitted to a large university hospital. Those findings indicated that sedative use ($p = 0.0006$, O.R. = 1.61, 95% C.I. = 1.23 – 2.12) and limited mobility and activity ($p < 0.0001$, O.R. = 4.42, 95% C.I. = 3.50 – 5.59) were statistically significant in multivariate analysis and increased odds of pressure ulcer development. One possible explanation for this finding is that Nonnemacher et al. collected dichotomous data and combined variables scored as 'unknown' with 'no' responses, possibly increasing the chances for a Type I or II error.

Other variables assessing pressure distribution capacity

Body mass index. There is strong evidence in the literature that lower BMIs are disproportionately related to pressure ulcer development. The relationship between BMI and pressure ulcer development is a function of poor nutritional status and resulting loss of body fat that results in exaggerated bony prominences (Jirika et al., 1995) with a consequent loss of pressure distribution capacity. In a prospective study of 286 patients admitted to an urban teaching hospital, Allman et al. (1995) identified lower BMI as a pressure ulcer risk factor ($p = 0.03$; O.R. 2.18; 95% C.I. = 1.05 – 4.52). Fife et al. (2001) reported a negative correlation between pressure ulcer incidence and body mass ($r = -0.258$, $p = 0.002$) in their study of 186 patients in a neurologic ICU. Similarly, Lindgren et al. (2004) identified increased weight as a protective factor ($p= 0.002$; O.R. 0.96; 95% C.I. = 0.94 – 0.99) as did Tschannen, Baates, Talsma, and Guo (2012) in their

retrospective analysis of 3225 patient records ($p < 0.001$; O.R. 0.97; 95% C.I. = 0.95 – 0.98). In a retrospective examination of 64,372 patient records, VanGilder, MacFarlane, Meyer, and Lachenbruch (2009) found a higher prevalence of pressure ulcers in underweight patients (25.3%) than in normal weight or obese patients, but do not hypothesize about the reason for the finding. Categorical measures of BMI were not identified as statistically significant at either univariate or multivariate analyses in this study. One explanation for this finding is the lack of underweight subjects enrolled in this study ($n = 20$; 5.6%) compared to the distribution of normal weight ($n = 101$; 28.1%), overweight ($n = 107$; 29.7%) and obese ($n = 132$; 36.7%) subjects.

Variables assessing metabolic supply

Nicotine use. The study findings indicate that nicotine use was not a statistically significant predictor of pressure ulcer formation with univariate or multivariate analyses. Nicotine use is a component of the Waterlow Pressure Ulcer Prevention/Treatment Policy (Copyright by J. Waterlow, 1985; Revised, 2005). It was included in the conceptual model because of statistically significant findings ($p < 0.001$; O.R. 1.18; 95% C.I. = 1.13 – 1.23) involving high Waterlow risk scores and pressure ulcer incidence (Anthony, et al., 2000) and the positive relationship between nicotine use and vascular disease. Multivariate analyses reported by Nijs et al. (2008) in a study of 520 subjects in a surgical ICU indicated that a history of vascular disease was statistically significant for pressure ulcer incidence at 24 hours in multivariate analysis ($p < 0.001$; O.R. 4.51; 95% C.I. = 1.99 – 10.24) and 48 hours ($p = 0.001$; O.R. 2.85; 95% C.I. = 1.29 – 6.30). Nonnemacher et al. (2008) reported similar findings with vascular disease after multivariate analysis ($p = 0.032$; O.R. 1.80; 95% C.I. = 1.05 – 3.08) in their study of

34,238 subjects admitted to a large university hosptial. Because medical diagnoses were not collected as part of this study, it is unclear if there is any association between nicotine use and vascular disease. Because populations from mixed ICU types were included, it is possible that any significance that nicotine use had with pressure ulcer incidence was obfuscated by medical diagnoses unrelated to vascular disease – a potential result of nicotine use.

Vasopressor use. The findings in this study indicate that vasopressor use was not a statistically significant predictor of pressure ulcer formation with univariate or multivariate analyses. This finding is not consistent with the results reported in the literature, although the studies evaluating vasopressor use as a pressure ulcer risk factor are limited. Nijs et al. (2008) identified low dose dopamine ($\leq$ 5 µg/kg/min) to be an independent predictor of risk 24 hours prior to prior to pressure ulcer development in 520 subjects with multivariate analysis (p= 0.003; O.R. 6.05; 95% C.I. = 1.88 – 19.54). Similarly, Theaker et al. (2000) found norepinephrine to be an independent predictor of pressure ulcers in a multivariate analysis of 22 risk factors (p< 0.001; O.R. 8.11; 95% C.I. = 3.64 – 18.0) in a study of 286 general ICU patients. In a more recent cohort study of 3,225 critically ill patients, Tschannen et al. (2012) identified use of vasopressors to be statistically significant with multivariate analysis (p = 0.03; O.R. 1.3; 95% C.I. = 1.03 – 1.73). Only variables with a univariate p-value of < 0.30 were selected for inclusion into the multivariate analysis conducted by Tschannen et al. which may contribute to Type I or II error in the findings.

The findings in this study are difficult to explain, given that norepinephrine was the most commonly used vasopressor in case and control subjects (26.7%) compared to

the other vasopressors identified for study. Norepinephrine works to increase systemic vascular resistance by stimulating α-1 and α-2 adrenergic receptor cites in the peripheral vasculature (Klabunde, 2011), and has been associated with extremity ischemia when used at high doses for long periods. Because only total amounts of vasopressor infusions were collected instead of infusion rates, any significance that higher infusion rates may have on pressure ulcer incidence were not captured. Additionally, the lack of vasopressor infusions necessitated the use of vasopressor as a categorical variable, possibly contributing to a Type II error with regard to vasopressor use.

Mean arterial pressure. Univariate analyses of lowest recorded MAP was statistically significantly associated with pressure ulcer development at 24 and 48 hours prior to study enrollment; however, it did not maintain its statistical significance with multivariate analysis. A plausible explanation of this finding is because extremes of arterial pressures are treated with medications, such as vasopressors, to maintain arterial pressures within a prescribed normal physiologic range.

Oxygen saturation of hemoglobin. No measure of oxygen saturation of hemoglobin demonstrated statistical significance at either the univariate or multivariate level of analysis. This finding is consistent with ICU practices to provide supplemental oxygen as needed to keep oxygen saturations values near to 100%.

Variables assessing metabolic demand

Steroid use. Steroid use did not demonstrate statistical significance at either the univariate or multivariate level of analysis in this study. Steroid use is included in Waterlow's pressure ulcer risk assessment and was included in the conceptual model because of Anthony et al.'s (2000) finding that summative Waterlow scores were

statistically significant with multivariate analysis of their findings ($p < 0.001$; O.R. 1.18; 95% C.I. = 1.13 – 1.23). In their study of 163 cardiac surgery patients, Stordeur et al. (1998) identified post-operative corticosteroid use as being statistically significant in a multivariate analysis ($p = 0.020$). No odds ratios or confidence intervals were presented in the article. Additionally, the multivariate analysis included only those variables that were statistically significant with univariate analysis, possibly contributing to a Type I or II error in Stordeur et al.'s interpretation of their study results.

Strengths and Limitations

Strengths and limitations of this study were considered within the contexts of the study design, data analysis strategies, and the clinical utility of the findings. These areas are discussed in this section.

Study Design

The use of a prospective cohort case-control design was a strength of this study because it supported the investigation into potential causes of pressure ulcer incidence (Cummings, Newman, et al., 2007) and allowed for the examination of temporal sequencing. Spurious associations due to bias resulting from the study design were minimized by enrolling sample subjects from the targeted ICU patient population. Some measures of predictor variables such as protein reserve, medication administration, and Braden subscale scoring by staff nurses may have contributed to systematic errors because of reduced accuracy of those measures. Spurious associations due to chance were minimized by use of a case-control study design where subjects were individually

matched on ICU type, ICU length of stay before pressure ulcer development (cases), and severity of illness. These matching criteria were considered potentially confounding variables in this study. A limitation of this study was that case-control subjects were not matched on age or medical diagnoses that are other potential confounding variables in this study.

Analysis Strategies

To evaluate the relationships among the variables in this study adequately, it was necessary to apply statistical methods that allowed for paired analysis of case-control subjects and that would allow for evaluation of one set of variables while controlling for potential confounding variables. Analytic strategies that facilitated these statistical evaluations were a strength of this study. Wilcoxon's Signed Rank test and McNemar's Chi Square were used to evaluate differences in the dependent variables for descriptive analysis. Hierarchical tests controlling for age, then Braden scores, allowed for statistical evaluations of the strength of the associations with each variable set. As noted in the previous section, the final block of the model demonstrated that the added associations of the remaining variables after controlling for age and Braden subscale scores enhanced the statistical significance of the model compared to the effects of the Braden subscales alone.

Clinical Utility

A strength of this study was that it identified risk factors for pressure ulcer development that enhance the predictive ability of the Braden RAS with variables that are easily obtained in the ICU setting. Integrating age, gender, and hematocrit levels into a modified Braden RAS would not require extensive effort from clinical staff, especially in

facilities where computerized medical records are readily available for laboratory results. Another strength of this study is that the findings can easily be implemented in smaller community hospitals that do have the resources of tertiary care medical centers.

Implications

The implications of this study are related to healthcare policy and guiding nursing practice in the prevention of pressure ulcers. They are discussed in this section.

Implications for Healthcare Policy

As discussed in Chapter I, there is a lack of empirical evidence needed to link nursing quality of care and pressure ulcer development (Needleman et al., 2007). Despite the lack of empirical evidence, the NQF placed nosocomially acquired pressure ulcers among outcomes considered sensitive to nursing care (Kurtzman & Corrigan, 2007). Using the NQF's list of "never events" published in 2001, The Centers for Medicare and Medicaid Services (CMS) began to scrutinize the Diagnostic Related Group (DRG) complication codes related to the NQF's never events (Wachter, Foster, & Dudley, 2008). In October 2008, CMS began to stop payments for three hospital-acquired infections and five complications of care. Pressure ulcers were among the complications of care that CMS included in that list (Wachter et al., 2008). Wachter et al. (2008) suggested that these sanctions are reasonable if four criteria concerning the never event are met. The criteria include adequate evidence that the event is preventable, the event is accurately measurable, the event results in clinically significant patient harm, and that it is possible

to differentiate among those events that are nosocomial versus those that are present on admission to the healthcare institution (Wachter et al., 2008).

The findings from this study tend to refute the NQF's assertion that pressure ulcer outcomes are primarily functions of nursing care quality. Hematocrit levels demonstrated a statistically significant univariate ($p < 0.001$) and multivariate ($p < 0.001$ within 24 hours; $p = 0.030$ within 48 hours) association with pressure ulcer incidence. The decision to transfuse blood lies within the domain of medicine. Because of limited resources, blood transfusion policies tend to be conservative and the risks of anemia compared to the risks of transfusions are evaluated carefully (Shader, Javidroozi, Ozawa, & Hare, 2011). Enhanced collaboration on pressure ulcer reduction strategies among providers and nursing staff will promote shared responsibility for pressure ulcer prevention by considering more aggressive strategies, such as blood transfusion, that are outside the purview of nursing.

Implications for Nursing

The results of this study have the potential to enhance the specificity of the Braden score in critically ill patients. As discussed in Chapter II (Table 2.3) the specificity of the Braden score ranges from 26% to 77.8% in studies of critically patients with cutoff scores between 14 and 16 and from 40.5% to 100% in acute care patients with cutoff scores between 16 and 20. Additionally, the findings of this study indicate that the Braden Scale, when used alone, does not adequately capture pressure ulcer risk at 48 hours prior to pressure ulcer development, suggesting that the tool lacks the sensitivity required to identify rapidly changing moderators of pressure ulcer incidence in critically ill patients. Augmenting the Braden RAS with the findings in this study may provide

higher sensitivity levels in critically ill and acute care patients. The enhanced sensitivity would allow nursing staff to target prevention measures more efficiently.

Recommendations for Future Research

Critically ill patients are a vulnerable and understudied population with regard to pressure ulcer risk factors. Research is needed that is directed at better understanding risk factor measurement strategies and pressure ulcer etiology. This dissertation research contributes to the body of knowledge about risk factors, but more work is needed to enhance the understanding of pressure ulcer risk factors.

A first step for future research is to determine appropriate measurement strategies for risk factors. The decision to evaluate some risk factors, such as medication administration and Braden subscale scores, was primarily based on clinical experiences of the researcher with input from the dissertation committee. Expanded data collection timeframes in future research will provide insight into the optimum time intervals in which to collect data.

A second goal of future research is to evaluate medical diagnoses and any confounding effects that exists between pressure ulcer outcomes and other variables. For example, some studies have identified cancer as having a statistically significant relationship to pressure ulcers (Flattau & Blank, 2012; Fromantin et al., 2011); however, it is unclear if cancer is the direct cause of the pressure ulcer or if cancer is associated with another variable, such as malnutrition and cachexia, which is responsible for pressure ulcer development. Another example is the effect of surgery and surgical

procedures on pressure ulcer development. Several studies have evaluated surgery as a pressure ulcer risk factor; however, standard approaches to studying the surgical variable are lacking. A better understanding of the relationship between disease states and pressure ulcer outcomes may have implications for healthcare policy in the future.

A third direction for future research involves hospital processes that may contribute to pressure ulcer development. Multiple studies identified surgical procedures as a statistically significant effect on pressure ulcer incidence (Nonnemacher et al., 2008; Schoonhoven, et al., 2002). The limited understanding of pressure ulcer etiology combined with the complexity of hospital processes impedes the ability to discern which processes need improvement. Patients with long term ICU stays requiring multiple surgeries may develop a pressure ulcer that is assigned incorrectly to the care received in the ICU. A better understanding of the processes surrounding high risk areas such as ICUs and operating rooms will help to focus prevention and improvement efforts.

Appendix A

Data Management and Study Enrollment Forms

Screening Tracking Tool - Example

Date Screened	ROOM NO.	SCREENED AS	ELIGIBLE?	REASON NOT ELIGIBLE?	CODE	
3/7/2011	8633	CASE	N	PU w/I 48 hours admission	8	Sacrum I
4/25/2011	8615	CASE	N	Admitted to ICU w/ PU	2	Buttock, R/L II
10/17/2011	8642	CASE	N	Admitted w/ PU	2	Sacrum II
8/7/2011	8615	CASE	N	Not a Pressure Ulcer	1	R Ishcium II
12/22/2010	8656	CASE	N	Admitted to ICU w/ PU	2	
1/27/2011	8641	CASE	N	Admitted to ICU w/ PU	2	L Buttock/I
5/4/2011	NA	CONTROL	N	Low Vent	5	
5/9/2011	8619	CASE	N	PU w/I 48 hours admission	8	Sacrum II
2/7/2011	8659	CASE	N	Admitted to ICU w/ PU	2	L Buttock 4
5/15/2011	8639	CASE	N	Admitted to ICU w/ PU	2	L Hip IV
7/6/2011	8603	CASE	N	Admitted to ICU w/ pu	2	L Hip IV
1/23/2012	8655	CASE	N	Admitted w/ PU	2	L Occiput DTI: L ishcium DTI
8/31/2011	8615	CASE	N	Admitted w/ PU	2	Sacrum II
3/27/2011	8657	CASE	Y			
10/21/2010	8613	CASE	N	Stage I	3	
7/6/2011	8649	CASE	N	Admitted to ICU w/ pu	2	Sacrum II
12/22/2010	8625	CASE	N	PU w/I 48 hours admission	8	
6/1/2011	8641	CASE	N	Admitted to ICU w/ PU	2	Sacrum I
10/17/2011	8625	CASE	N	Admitted w/ PU	2	Sacrum I
5/18/2011	8607	CASE	N	PU w/I 48 hours admission	8	Sacrum II
1/27/2011	8621	CASE	N	Admitted to ICU w/ PU	2	Sacrum 2
10/27/2011	8631	CASE	N	Admitted w/ PU	2	R heel, ustg; L/R scrotum II
5/1/2011	8613	CASE	N	PU w/I 48 hours admission	8	Sacrum II

Consent Tracking Tool – Example

ROOM #	CASE/CONTROL	DATE/TIME 1ST ATTEMPT	CONSENT OBTAINED ? (Yes, No, Refused)	DATE/TIME 2ND ATTEMPT	CONSENT OBTAINED ? (Yes, No, Refused)	DATE/TIME PHONE ATTEMPT	CONSENT OBTAINED ? (Yes, No, Refused)	CONSENT WAIVED
	CONTROL							CONSENT WAIVED-D/C at time of enrolloment
	CASE	5/23/2011	Y					
	CASE	6/7/2011	Refused					
	Case	1/12/2011	N	1/13/2011	N	1/13/2011	Y	
	CASE	8/29/2011	Y	8/30/2011	Y			
	CONTROL							CONSENT WAIVED-D/C at time of enrolloment
	CASE	10/27/2011	Y					
	CASE	12/2/2011	N	12/13/2011	Y			
	CASE	5/5/2011	Y					
	CASE	4/26/2011	Y					

Informed Consent Tool-Case Subject

This informed consent applies to Adults.

Name of participant: _____
Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

You do not have to be in this research study. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study.

1. What is the purpose of this study?

You are being asked to take part in this research study because you have developed a pressure ulcer (bed sore) in an intensive care unit. The purpose of this study is to see if you have any additional risk factors that may have caused the pressure ulcer compared to other patients in an ICU that have not developed a pressure ulcer (bed sore). Examples of risk factors that this study evaluates are your average blood pressure, some medications that you may have received, your age and weight, and certain health problems that you may have had before you were admitted to the hospital, such as diabetes. Certain laboratory values from your blood work will also be considered, such as hemoglobin and hematocrit (the amount of red blood cells you have) and albumin (the amount of protein in your blood).

2. What will happen and how long will you be in the study?

Some types of wounds and skin problems are easily confused with a pressure ulcer (bed sore). For that reason, either myself or another investigator will need to look at the wound to make sure it is a pressure ulcer (bed sore). Either myself or another investigator will only look at your skin wound during normal routines that you will experience during your ICU stay. Examples are when your nurse routinely changes the dressing on the wound or positions you to evaluate the wound. Your nurse will be in the room when we look at the wound and will be doing all of the treatments on you. After myself or the other investigator have looked at the wound and have determined that it is a pressure ulcer (bed sore), you will be entered into the study. We will then look at your medical record and use the data about your risk factors to record in a database. The data from your medical record will contain your medical record number so that we can make sure that we have all the data entered correctly. At the end of the study, your medical record number is removed, and the data from your medical record will be analyzed mathematically to see if your risk factors made a difference in why you developed the pressure ulcer (bed sore). We will be evaluating the pressure ulcer (bed sore) only one time.

.

3. Costs to you if you take part in this study:

There is no cost to you for taking part in this study.

However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

4. Side effects and risks that you can expect if you take part in this study:

There are no side effects that are associated with this study because the study does not involve additional or different treatment than you would normally receive because of your illness. The risks involved in this study are minimal and include possible loss of anonymity because your medical record number will be associated with the data we collect about you from the medical record. Multiple safe-guards are in place to prevent this from happening as described in section 13, below. Additional minimal risks involve those associated with routine care in the ICU, such as repositioning in bed and possibly losing a tube that has been inserted as part of your care. Your nurse is experienced at protecting you from accidentally losing a tube and will be the one helping you to turn or reposition in bed.

4. Risks that are not known:

NONE

6. Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

There are no plans for Vanderbilt to pay for the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

7. Good effects that might result from this study:

a) **The benefits to science and humankind that might result from this study**. Patients in ICUs get pressure ulcers (bed sores) more frequently than do other hospitalized patients. This study will help to identify risk factors specific to ICU patients that cause them to get pressure ulcers (bed sores) more frequently than do other patients. If we can identify those risk factors before the pressure ulcer (bed sore) develops, then we can take steps to prevent them.

b) **The benefits you might get from being in this study**. There are no benefits to you from participating in this study.

8. Other treatments you could get if you decide not to be in this study:

Your treatment will be the same if you participate in the study or not.

9. Payments for your time spent taking part in this study or expenses:

You will not be paid for your time spent participating in this study.

10. Reasons why the study doctor may take you out of this study: You may be removed from the study data base if your are discharged from the ICU before either myself or the co-investigator can look at your wound to determine if it is a pressure ulcer (bed sore) or if you require CPR within 48 hours of the time that the nurse first noticed the wound.

11. What will happen if you decide to stop being in this study?

If you decide to stop being part of the study, you should tell either myself of the co-investigator.

12. Who to call for any questions or in case you are injured:

If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Richard Benoit at 322-6565 or the Faculty Advisor, Dr. Lorraine Mion at 343-7098. If you cannot reach the research staff, please page Richard Benoit at 835-7701

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

13. Confidentiality:

All data will be collected by either Richard Benoit, the Principal Investigator (PI) or Carolyn Watts, co-investigator, using a paper data collection form. Immediately after the data has been collected on the paper form, the completed forms will be stored in a locked file cabinet in the PI's locked office in the SICU at Vanderbilt University Hospital. Data will then be transcribed from the paper data collection sheets into Vanderbilt's secured data base by the PI. The paper data collection sheets will remain under double lock at Vanderbilt until the completion of the study, at which time they will be placed in a shredder box located near the PI's office in the SICU. The medical record number will remain attached to the protected health information until the study's completion and the PI is satisfied that the data is complete and accurate. At that time, the records will be de-identified by removing the medical record number. Only Richard Benoit and Carolyn Watts will have access to the paper data collection forms. After the information has been entered into Vanderbilt's secured data base, Richard Benoit, Carolyn Watts, Drs. Lorraine Mion and Anne Minnick, the faculty advisors, Dr. Mary Dietrich, the statistician, and Dr. Oliver Gunter, the physician advisor, will have access to the database.

14. Authorization to Use/Disclose Protected Health Information

All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is, or has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Richard Benoit and his study team may share the results of your study and/or non-study linked information such as lab values,demographic variables, and severity of the pressure ulcer (bed sore) as well as parts of your medical record, to the groups named below. These groups may include people from the Federal Government Office for Human Research Protections, the Vanderbilt University Institutional Review Board, National Database of Nursing Quality Indicators (NDNQI), and the National Pressure Ulcer Advisory Panel (NPUAP). Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

Vanderbilt may give or sell your health data, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Richard Benoit and his staff will comply

with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact Richard Benoit in writing and let him know that you withdraw your consent. His mailing address is

1211 Medical Center Drive
9612B CCT
Nashville, TN 37232-7417

At that time, we will stop getting any more data about you. However, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date	Signature of patient/volunteer

Consent obtained by:

Date	Signature
	Printed Name and Title

SURROGATE RIDER-CASE PATIENT

I, _____ [name of decision-maker/surrogate],
am the _____ [state relationship to participant]
of _____ [state participant's name]. I have read the informed consent document or it has been explained to me. I have had the opportunity to ask any questions and all of my questions have been answered. I believe participating in this research would be in the interests of _____ [participant's name] and is consistent with what he/she would have decided had he/she been able to do so.

Your decision to allow your family member/friend to participate in this research study is voluntary. You may choose not to allow his/her participation and he/she will receive the same treatments. The decision not to participate in the research will not affect his/her healthcare/services or other rights. You are also free to withdraw him/her from this study at any time. In the event new information becomes available that may affect the risks or benefits associated with this research study or your willingness to allow continued participation in this research study, you will be notified so that you can make an informed decision whether or not to continue your family member/friend's participation in this study.

Your family member/friend will periodically be re-evaluated for the capacity to give consent. If he/she is found to be capable, continued participation in this study would only occur with his/her consent.

_____ ___/___/___
Signature of Health Care Decision-Maker/Surrogate Date

_____ ___/___/___
Signature of Witness Date

_____ ___/___/___
Name and Signature of person obtaining consent Date

Informed Consent Tool – Case Subject

This informed consent applies to Adults.

Name of participant: _____
Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

You do not have to be in this research study. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study.

5. What is the purpose of this study?

You are being asked to take part in this research study because you are a patient in an intensive care unit who has not developed a pressure ulcer (bed sore). The purpose of this study is to see if any risk factors you may have for pressure ulcer development are different from other patients that have developed a pressure ulcer. Examples of risk factors that this study evaluates are your average blood pressure, some medications that you may have received, your age and weight, and certain health problems that you may have had before you were admitted to the hospital, such as diabetes. Certain laboratory values from your blood work will also be considered, such as hemoglobin and hematocrit (the amount of red blood cells you have) and albumin (the amount of protein in your blood).

6. What will happen and how long will you be in the study?

Once you give permission, one of the study team will go to your medical record and use risk factor information that has already been collected as part of your routine care at Vanderbilt. There will be no additional tests or procedures performed as a result of your entry into the study. The data from your medical record will contain your medical record number so that we can make sure that we have all the data entered correctly. At the end of the study, your medical record number is removed, and the data from your medical record will be analyzed mathematically to see if your risk factors made a difference in why you did not develop a pressure ulcer (bed sore).

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7. Costs to you if you take part in this study:

There is no cost to you for taking part in this study.

However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

4. Side effects and risks that you can expect if you take part in this study:

There are no side effects that are associated with this study because the study does not involve additional or different treatment than you would normally receive because of your illness. The risks involved in this study are minimal and include possible loss of anonymity because your medical record number will be associated with the data we

collect about you from the medical record. Multiple safe-guards are in place to prevent this from happening as described in section 13, below.

8. Risks that are not known:

NONE

6. Payment in case you are injured because of this research study:

Because we will only be reviewing your medical record, there is no chance of injury to you by participating in this study.

There are no plans for Vanderbilt to pay for the costs of any additional care.

7. Good effects that might result from this study:

a) **The benefits to science and humankind that might result from this study**. Patients in ICUs get pressure ulcers (bed sores) more frequently than do other hospitalized patients. This study will help to identify risk factors specific to ICU patients that cause them to get pressure ulcers (bed sores) more frequently than do other patients. If we can identify those risk factors before the pressure ulcer (bed sore) develops, then we can take steps to prevent them.

b) **The benefits you might get from being in this study**. There are no benefits to you from participating in this study.

8. Other treatments you could get if you decide not to be in this study:

Your treatment will be the same if you participate in the study or not.

9. Payments for your time spent taking part in this study or expenses:

You will not be paid for your time spent participating in this study.

10. Reasons why the study doctor may take you out of this study: You may be removed from the study data base if your are discharged from the ICU and we find that some of the important information in your medical record is missing or incomplete.

11. What will happen if you decide to stop being in this study?

If you decide to stop being part of the study, you should tell either myself of the co-investigator.

12. Who to call for any questions or in case you are injured:

If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Richard Benoit at 322-6565 or the Faculty Advisor, Dr. Lorraine Mion at 343-7098. If you cannot reach the research staff, please page Richard Benoit at 835-7701

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

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All data will be collected by either Richard Benoit, the Principal Investigator (PI) or Carolyn Watts, co-investigator, using a paper data collection form. Immediately after the data has been collected on the paper form, the completed forms will be stored in a locked file cabinet in the PI's locked office in the SICU at Vanderbilt University Hospital. Data will then be transcribed from the paper data collection sheets into Vanderbilt's secured data base by the PI. The paper data collection sheets will remain under double lock at Vanderbilt until the completion of the study, at which time they will be placed in a shredder box located near the PI's office in the SICU. The medical record number will remain attached to the protected health information until the study's completion and the PI is satisfied that the data is complete and accurate. At that time, the records will be de-identified by removing the medical record number. Only Richard Benoit and Carolyn Watts will have access to the paper data collection forms. After the information has been entered into Vanderbilt's secured data base, Richard Benoit, Carolyn Watts, Drs. Lorraine Mion and Anne Minnick, the faculty advisors, Dr. Mary Dietrich, the statistician, and Dr. Oliver Gunter, the physician advisor, will have access to the database.

16. Authorization to Use/Disclose Protected Health Information

All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is, or has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Richard Benoit and his study team may share the results of your study and/or non-study linked information such as lab values,demographic variables, as well as parts of your medical record to the groups named below. These groups may include people from the Federal Government Office for Human Research Protections, the Vanderbilt University Institutional Review Board, National Database of Nursing Quality Indicators (NDNQI), and the National Pressure Ulcer Advisory Panel (NPUAP). Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

Vanderbilt may give or sell your health data, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Richard Benoit and his staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact Richard Benoit in writing and let him know that you withdraw your consent. His mailing address is

1211 Medical Center Drive
9612B CCT
Nashville, TN 37232-7417

At that time, we will stop getting any more data about you. However, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date	Signature of patient/volunteer

Consent obtained by:

Date	Signature
	Printed Name and Title

SURROGATE RIDER – CONTROL PATIENT

I, _____ [name of decision-maker/surrogate],
am the _____ [state relationship to participant]
of _____ [state participant's name]. I have read the informed consent document or it has been explained to me. I have had the opportunity to ask any questions and all of my questions have been answered. I believe participating in this research would be in the interests of _____ [participant's name] and is consistent with what he/she would have decided had he/she been able to do so.

Your decision to allow your family member/friend to participate in this research study is voluntary. You may choose not to allow his/her participation and he/she will receive the same treatments. The decision not to participate in the research will not affect his/her healthcare/services or other rights. You are also free to withdraw him/her from this study at any time. In the event new information becomes available that may affect the risks or benefits associated with this research study or your willingness to allow continued participation in this research study, you will be notified so that you can make an informed decision whether or not to continue your family member/friend's participation in this study.

Your family member/friend will periodically be re-evaluated for the capacity to give consent. If he/she is found to be capable, continued participation in this study would only occur with his/her consent.

_____ ___/___/___
Signature of Health Care Decision-Maker/Surrogate Date

_____ ___/___/___
Signature of Witness Date

_____ ___/___/___
Name and Signature of person obtaining consent Date

Patient Information Sheet

Hello: Your family member/friend is being considered for enrollment in a study at Vanderbilt.

This sheet is provided as information only and does not mean that your family member/friend

has been enrolled. A member of the study team will be attempting to contact you in person or by
phone to get consent from you to enroll your family member/friend in the study.

Information about the Pressure Ulcer Risk Factor Study

What is the Study About?
This is a nursing study we are doing in the intensive care units at Vanderbilt. The study is to
help us see what risk factors cause pressure ulcers in critically ill patients. There are many risk
factors, such as older age or poor nutrition, that can lead to the development of pressure ulcers.
We do not know which combination of risk factors are the ones most likely to predict a pressure
ulcer. The study will help us find out which risk factors are most important. We can then plan
better ways to prevent them from happening.

Why is my family member/friend being asked to participate?
Your family member/friend is a patient in an ICU. Studies show that patients in ICUs have a
higher risk for developing pressure ulcers, commonly known as bedsores. We want to see what
risk factors (such as nutrition status and some types of medications) contribute to pressure ulcer
development. Your family member/friend may or may not have a pressure ulcer. In either case,
we want to compare risk factors between patients that do and do not have a pressure ulcer.

What will happen and how long will my family member/friend be in the study?
If your family member/friend has a pressure ulcer, one of the research nurses will observe the
pressure ulcer when the nurse does usual care and turns him/her. In addition, the research nurse
will get information from the chart on your family member/friend's illness, medications, and
some blood work. Your family member/friend will be in the study until discharged from the
ICU.
If your family member/friend does not have a pressure ulcer, the research nurse will get
information from the chart on your family member/friend's illness, medications, and some blood
work. Your family member/friend will be in the study until discharged from the ICU.

Are there costs to my family member/friend for being in the study?
There are no costs or charges for being in this study.

Are there any side effects or risks?
There are no side effects since we are only looking at the pressure ulcer (if there is one) and gathering information from the chart. The only risk is the loss of anonymity. We will make sure that any study forms with your family member/friend's name or medical record are kept locked in a private office. Only the nurse researchers will be able to see that information. We will destroy all forms with the name and medical record number at the end of this study.

Can my family member/friend expect to get paid?
No. We do not plan on paying people who are in this study.

Are there any good effects for being in this study?
There are no direct benefits to your family member/friend. The findings from this study will help future ICU patients.

If I decide to not enroll my family member/friend in the study, are there other treatments?
The treatment will be the same if your family member/friend participates in this study or not.

Can I stop my family member/friend from being in the study after I give consent?
You may withdraw from participating in the study. Please contact the investigator, Richard Benoit, at 322-6565, to discuss this.

Who do to call for any questions?
If you have questions about the study, please contact Richard Benoit at 322-6565 or on his pager at 835-7701. If you have any questions about your rights in participating in research, please call the Vanderbilt IRB at 322-2918.

How will privacy and information be protected?
The study forms will be in a locked office. Only the nurse researchers will be able to get to the study forms. After the study is over, all paper forms will be shredded. We will enter the study information into the Vanderbilt computer system, but that information will not include the name

or medical record number. All publications will be in group results only; no individual will have
results published. Certain groups, such as the Vanderbilt IRB, the National Database of Nursing
Quality Indicators (NDNQI), may look at the information. Richard Benoit and the other nurse
researchers will comply with any and all laws that protect the privacy of your family member/friend's information.

Will I be able to see the results of the study?
Because the specific results do not include any details other than those located in the medical
record, you will need to follow Vanderbilt's procedures for accessing information in personal
records. You must address your request in writing to the Medical Information Services Department. You may download a copy of the request form at
http://www.vanderbilthealth.com/main/11323 or you may ask your nurse to get a copy of it for
you from E-docs, Vanderbilt's electronic document service.

Mail or fax the completed form to:
Medical Information Services
1211 22nd Avenue N.
B-334 VUH
Nashville, TN 37232
Fax # (615)343-0126

If you have any questions about accessing a medical record, please call: (615) 322-2062.
The overall findings of the study will be published in an appropriate journal after the findings
have been analyzed. If you would like information about the journal name and publication date,
please email the Principal Investigator at Richard.Benoit@vanderbilt.edu to request this information once it is available.

Inclusion/Exclusion Tracking Tool

PRESSURE ULCER RISK FACTOR

Inclusion/Exclusion Tool

Date of Screening: ____/____/____

Your Initials _____

INCLUSION CRITERIA:

Subject 18 years of age or older? _____

Current ICU _____

EXCLUSION CRITERIA:

CASE	CONTROL
ICU LOS < 48 hours	ICU LOS < 48 hours
Stage II or worse pressure ulcer on admission to ICU	Stage II or worse pressure ulcer on admission to ICU
Stage II or worse pressure ulcer that develops within 48 hours of ICU admission	Stage II or worse pressure ulcer development during ICU stay
CPR within 48 hours prior to pressure ulcer development	CPR during ICU stay
Discharge from ICU prior to visual assessment of pressure ulcer	Discharge from ICU with any missing pre-admission or demographic information

Is this subject a CASE or CONTROL? (Circle one)

If this is a CASE subject, is the patient able to give consent as assessed by the nurse? YES NO

If YES, date consent form signed _____

If NO, is there a surrogate present during the pressure ulcer screening? If yes, date surrogate consent form signed _____

If no surrogate and patient unable to consent, date "Written Information about the Pressure Ulcer Study" left in room _____

Study ID: _____ (001- 174 Case numbers for CW)
(1001-1174 Control numbers for CW)
(175-350 Case numbers for RB)
(1175-1350 Control numbers for RB)

Appendix B

Data Collection Forms

Data Collection Form – Case Subjects

Subject Information-CASE

Study ID _____
CASES:(001-350)
(CW Use 001-174; RB use 175 to 350)

Total # P U _____

Wrst P U Stg
Stage II
Stage III
Stage IV
Unstageable
SDTI

Wrst P U location
Occiput
R Ear
L Ear
Face
R Scapula
L Scapula
R Elbow
L Elbow
R Hand
L Hand
Upper Back
Middle Back
Sacrum/Coccyx
R Ischium
L Ischium
R Buttocks
L Buttocks
R Scrotum
L Scrotum
R Trochanter
L Trochanter
R Knee/Peri-knee
L Knee/Peri-knee
R Malleous/Ankle
L Malleous/Ankle
R Leg
L Leg

R Heel
L Heel
R Foot
L Foot

ICU Adm Date _____
(Continuous ICU stay-even if transferred from
another ICU.)

Date P U ided by RN _____

Ht (in) _____
Wt (lbs) _____

Vent use? (Has the patient required a ventilator at ANY TIME
during the ICU stay?)

No
Yes

IF YES: Curr Vent use? (Is the patient CURRENTLY requiring vent use?)

No
Yes

IF NO: Contin Vent use hrs _____ (Longest # hrs continuous vent use up to midnight before study enrollment (Includes time on vent prior to transfer from another ICU, if
applicable)

IF YES: Prior cont Vent use _____ (Longest # hrs continuous vent use up to midnight before study enrollment)

Sens 48 1 2 3 4
(may be from either day or night Braden)
Sens 24 1 2 3 4
(may be from either day or night Braden)

Nut 48 1 2 3 4
(may be from either day or night Braden)
Nut 24 1 2 3 4
(may be from either day or night Braden)

Mob 48 1 2 3 4
(may be from either day or night Braden)
Mob 24 1 2 3 4
(may be from either day or night Braden)

Act 48 1 2 3 4
(may be from either day or night Braden)
Act 24 1 2 3 4
(may be from either day or night Braden)

Moi 24 1 2 3 4
(may be from either day or night Braden)
Moi 48 1 2 3 4
(may be from either day or night Braden)

F/S 24 1 2 3
(may be from either day or night Braden)
F/S 48 1 2 3
(may be from either day or night Braden)

HYDRO? (Hydrocortisone use)

No

Yes
HYDRO 14 d _____

PREDSOL (Prednisolone use)

No

Yes
PREDSOL 14d _____

METH (Methylprednisolone use)

No

Yes
METH 14d _____

PRED (Prednisone use)

No

Yes
PRED 14d _____

Serum Albumin 24 _____
(Enter 888 if no value available)

Serum Albumin 48 _____
(Enter 888 if no value available)

Total Lymphocyte count 24 _____
(Enter 888 if no value available)

Total Lymphocyte count 48 _____
(Enter 888 if no value available)

High Crit 24 _____
(Enter 888 if no value available)

Low Crit 24 _____
(Enter 888 if no value available)

High Crit 48 _____
(Enter 888 if no value available)

Low Crit 48 _____
(Enter 888 if no value available)

MAP 48 _____
(Enter 888 if no value available)

MAP 24 _____
(Enter 888 if no value available)
Ox 24 _____
(Enter 888 if no value available)

Ox 48 _____
(Enter 888 if no value available)

Norepi? (Noreipnepherine use within 48 hours of study enrollment?)

No

Yes

Norepi 48 _____
(In total mcg/kg during 24 hour block 2 days before study enrollment (use midnight of study enrollment as reference))

Norepi 24 _____
(In total mcg/kg during 24 hour block 1 day before study enrollment (use midnight of study enrollment as reference))

Epi? (Epinepherine use within 48 hours of study enrollment?)

No

Yes

Epi 48 _____
(In total mcg/kg during 24 hour block 2 days before study enrollment (use midnight of study enrollment as reference))

Epi 24 _____
(In total mcg/kg during 24 hour block 1 day before study enrollment (use midnight of study enrollment as reference))

Dobut? (Dobutamine use within 48 hours of study enrollment?)

No

Yes

Dobut 48 _____
(In total mcg/kg during 24 hour block 2 days before study enrollment (use midnight of study enrollment as reference))

Dobut 24 _____
(In total mcg/kg during 24 hour block 1 day before study enrollment (use midnight of study enrollment as reference))

Mil? (Milrinone use within 48 hours of study enrollment?)

No

Yes

Mil 48 _____
(In total mcg/kg during 24 hour block 2 days before study enrollment (use midnight of study enrollment as reference))

Mil 24 _____
(In total mcg/kg during 24 hour block 1 day before study enrollment (use midnight of study enrollment as reference))

Mid? (Midodrine use within 48 hours of study enrollment?)

No

Yes

Mid 48 _____
(In total mcg/kg during 24 hour block 2 days before study enrollment (use midnight of study enrollment as reference))

Mid 24 _____
(In total mcg/kg during 24 hour block 1 day before study enrollment (use midnight of study enrollment as reference))

Vaso? (Vasopressin use within 48 hours of study enrollment?)

No

Yes

Vaso 48 _____
(In total units during 24 hour block 2 days before study enrollment (use midnight of study enrollment as reference))

Vaso 24 _____
(In total units during 24 hour block 1 day before study enrollment (use midnight of study enrollment as reference))

Prssors? (Did the patient require pressor use at any point during the ICU stay PRIOR to 48 hours of study enrollment? Use only the pressors identified in this study)

No
Yes

Pressor use Norepinepherine
Epinepherine
Dobutamine
Dopamine
Milrinone
Midodrine
Vasopressin

Restr? (Is the patient currently in wrist restraints or were wrist restraints used within 48 hours of study enrollment (use midnight of study enrollment as reference))

No

Yes

Subject Information-CONTROL

Assigned Study ID _____

CONTROL 1001-1350
(CW use 1001-1174; RB use 1175 to 1350)

ICU Adm Date _____
(Continuous ICU stay-even if transferred from
another ICU.)

Date Control met inclusion criterion for study _____

Ht (in) _____
Wt (lbs) _____

Vent use? (Has the patient required a ventilator at ANY TIME
during the ICU stay?)

No
Yes

IF YES: Curr Vent use? (Is the patient CURRENTLY requiring vent use?)

No
Yes

IF NO: Contin Vent use hrs _____ (Longest # hrs
continuous vent use up to midnight before study enrollment (Includes time on vent prior to
transfer from another ICU, if
applicable)

IF YES: Prior cont Vent use _____ (Longest # hrs continuous
vent use up to midnight before study enrollment)

Sens 48 1 2 3 4
(may be from either day or night Braden)
Sens 24 1 2 3 4
(may be from either day or night Braden)

Nut 48 1 2 3 4
(may be from either day or night Braden)
Nut 24 1 2 3 4
(may be from either day or night Braden)

Mob 48 1 2 3 4
(may be from either day or night Braden)
Mob 24 1 2 3 4
(may be from either day or night Braden)

Act 48 1 2 3 4
(may be from either day or night Braden)
Act 24 1 2 3 4
(may be from either day or night Braden)

Moi 24 1 2 3 4
(may be from either day or night Braden)

Moi 48 1 2 3 4
(may be from either day or night Braden)

F/S 24 1 2 3
(may be from either day or night Braden)
F/S 48 1 2 3
(may be from either day or night Braden)

HYDRO? (Hydrocortisone use)

No

Yes
HYDRO 14 d _____

PREDSOL (Prednisolone use)

No

Yes
PREDSOL 14d _____

METH (Methylprednisolone use)

No

Yes
METH 14d _____

PRED (Prednisone use)

No

Yes
PRED 14d _____

Serum Albumin 24 _____
(Enter 888 if no value available)

Serum Albumin 48 _____
(Enter 888 if no value available)

Total Lymphocyte count 24 _____
(Enter 888 if no value available)

Total Lymphocyte count 48 _____
(Enter 888 if no value available)

High Crit 24 _____
(Enter 888 if no value available)

Low Crit 24 _____
(Enter 888 if no value available)

High Crit 48 _____
(Enter 888 if no value available)

Low Crit 48 _____
(Enter 888 if no value available)

MAP 48 _____
(Enter 888 if no value available)

MAP 24 _____
(Enter 888 if no value available)
Ox 24 _____
(Enter 888 if no value available)

Ox 48 _____
(Enter 888 if no value available)

Norepi? (Noreipnepherine use within 48 hours of study enrollment?)

No

Yes

Norepi 48 _____
(In total mcg/kg during 24 hour block 2 days before study enrollment (use midnight of study enrollment as reference))

Norepi 24 _____
(In total mcg/kg during 24 hour block 1 day before study enrollment (use midnight of study enrollment as reference))

Epi? (Epinepherine use within 48 hours of study enrollment?)

No

Yes

Epi 48 _____
(In total mcg/kg during 24 hour block 2 days before study enrollment (use midnight of study enrollment as reference))

Epi 24 _____
(In total mcg/kg during 24 hour block 1 day before study enrollment (use midnight of study enrollment as reference))

Dobut? (Dobutamine use within 48 hours of study

enrollment?)

No

Yes

Dobut 48 _____
(In total mcg/kg during 24 hour block 2 days before study enrollment (use midnight of study enrollment as reference))

Dobut 24 _____
(In total mcg/kg during 24 hour block 1 day before study enrollment (use midnight of study enrollment as reference))

Mil? (Milrinone use within 48 hours of study enrollment?)

No

Yes

Mil 48 _____
(In total mcg/kg during 24 hour block 2 days before study enrollment (use midnight of study enrollment as reference))

Mil 24 _____
(In total mcg/kg during 24 hour block 1 day before study enrollment (use midnight of study enrollment as reference))

Mid? (Midodrine use within 48 hours of study enrollment?)

No

Yes

Mid 48 _____
(In total mcg/kg during 24 hour block 2 days before study enrollment (use midnight of study enrollment as reference))

Mid 24 _____
(In total mcg/kg during 24 hour block 1 day before study enrollment (use midnight of study enrollment as reference))

Vaso? (Vasopressin use within 48 hours of study enrollment?)

No

Yes

Vaso 48 _____
(In total units during 24 hour block 2 days before study enrollment (use midnight of study enrollment as reference))

Vaso 24 _____
(In total units during 24 hour block 1 day before study enrollment (use midnight of study enrollment as reference))

Prssors? (Did the patient require pressor use at any point during the ICU stay PRIOR to 48 hours of study enrollment? Use only the pressors identified in this study)

No
Yes

Pressor use Norepinepherine
Epinepherine
Dobutamine
Dopamine
Milrinone
Midodrine
Vasopressin

Restr? (Is the patient currently in wrist restraints or were wrist restraints used within 48 hours of study enrollment (use midnight of study enrollment as reference))

No

Yes

Appendix C

Feasibility Study

The Efficacy of Using the Electronic Medical Record as a
Data Source for a Prospective Cohort Study to Determine Pressure Ulcer Risk in
Critically Ill Patients

Abstract

Objective: To determine the feasibility of using the electronic medical record (EMR) as a data source for a future study to identify pressure ulcer risk factors in critically ill patients. *Design*: Prospective cohort study. *Setting*: Six intensive care units (ICUs) in a 847 bed tertiary care center. *Subjects*: All patients, aged 18 years, admitted the ICUs during the study without a pre-existing pressure ulcer. *Interventions*: None. *Methods*: Daily concurrent chart reviews for pressure ulcer incidence. Data were abstracted from the EMR and entered into the database for pressure ulcer positive subjects. *Variables*: ICU, age, height, weight, pre-existing skin disease, and history of diabetes or nicotine use. Subsequent measures were collected until subjects were discharged from the ICU, developed a stage I or worse pressure ulcer, or died. *Measures*: Worst mean arterial pressure, oxygen saturation, albumin, vasopressor use, and Braden sub- and summative scores. Expert visual screening assessment and Braden scores were conducted independently to evaluate the validity of the documentation. *Results*: 100 subjects were enrolled; six developed a pressure ulcer. There was 100% agreement between staff nurse and expert on pressure ulcer status among pressure ulcer positive and negative subjects, and 83% agreement on pressure ulcer stage. Braden sub-scores weighted Kappa coefficient agreement ranged from 0.25 to 0.67. Expected electronic medical record (EMR) variable information was available 66% of the time. Transient technical difficulties precluded a higher data retrieval rate. Time required exceeded 100 hours. *Conclusion*: The EMR is a reliable source of data for pressure ulcer research. However, the prospective cohort design used in this study was time intensive. To limit the time required for future studies, a case-control study designed will be used.

Introduction

Pressure ulcers are a complication of acute and chronic illness that affect approximately 8.5% to 15% of institutionalized (i.e. nursing homes, acute care facilities) patients per year, representing between 2.4 and 5.2 million persons annually. Patients who are critically ill and require placement in an ICU during their hospitalization are more likely to develop pressure ulcers than patients who are less critically ill and do not require ICU placement for their care

needs (Bours, De Laat, Halfens, & Lubbers, 2001; De Laat, Schoonhoven, Pickkers, Verbeek, & van Achterberg, 2006; Frankel, Sperry & Kaplan, 2007; Keller, Wille, van Ramshorst, & van der Werken, 2002; Kirby & Gunter, 2008; Shahin, Dassen & Halfens, 2008; Theaker, Mannan, Ives, & Soni, 2000). Pressure ulcer prevention interventions are predicated on identifying salient risk factors for pressure ulcer development in specific patient populations (De Laat et al., 2006).

The predominant approach to studying pressure ulcer risk factors in the related literature is the prospective cohort study. Prospective cohort studies are particularly valuable for establishing causality. By measuring variables in all study subjects before the outcome occurs, the researcher establishes a temporal relationship between pre-existing risk factors and the incidence of the dependent variable (Cummings, Newman, & Hulley, 2007). Prospective cohort studies are not without their limitations, however. Prospective cohort studies can be expensive and time consuming. Many studies designed to identify pressure ulcer risk factors relied on teams of observers to collect data, which adds to study costs and introduces the risk of inter-rater reliability issues. Data availability and inter-rater reliability on pressure ulcer staging and risk scoring are missing in a large number of prospective cohort studies evaluating pressure ulcer risk factors. Prior to initiating a large, prospective cohort study, a feasibility study was necessary to determine the accuracy and timeliness of nurses' documentation of pressure ulcers in the ICU population, and the ease of extraction of physiologic risk factors from the electronic medical record (EMR). This feasibility study was designed to identify potential problems with data collection and evaluate the reliability of staff nurses regarding pressure ulcer presence and staging, and their agreement with expert raters on the Braden score.

Methods

Study Design

This study used a prospective cohort design.

Study Setting

Data were collected in each of the six intensive care units (ICUs) in a 847 bed tertiary care center. The six ICUS included Burn (BICU, 9 beds), Cardiovascular (CVICU, 27 beds), Medical (MICU, 34 beds), combined neuro-medicine and neuro-surgical (NICU, 34 beds), Surgical (SICU, 34 beds), and Trauma (TICU, 14 beds).

Sample

Subjects were recruited to this study if they met the inclusion criteria of:

- 18 years of age or older
- Admitted to one of six ICUs during the course of the study
- Had no pre-existing pressure ulcer on admission to the ICU

Due to the nature of this study, subjects were not excluded based on lack of data in the EMR.

Study Procedures

Beginning on the first Monday of the study, EMR census logs were reviewed by the PI, Richard Benoit, MSN, RN, CCRN, or Carolyn Watts, MSN,RN, CWON, for admissions the previous day. Demographic information on subjects that met the inclusion criteria were entered into the database. The following day, clinical information from the previous 24 hours was abstracted from the EMR and entered into the database. Nursing documentation in the EMR was examined

and the identified physiologic and medication information was entered into the database. The data on subjects was collected each day for 14 days with newly admitted patients captured for study the following day. Any patient that developed a pressure ulcer during the 14-day study (as indicated in the EMR) was visually evaluated by either the PI or Carolyn Watts to ensure accurate staging of the pressure ulcer as entered by the staff nurse. A Braden score was also performed by the PI or Carolyn Watts at the time that the pressure ulcer was evaluated. Each day, study subjects that did not have a documented pressure ulcer in the EMR were randomly selected d by the PI or Carolyn Watts for a skin evaluation and Braden score. Twenty-seven subjects were randomly evaluated.

Data Collection Procedures

The study was approved Vanderbilt University's Institutional Review Board. Written consent was waived in all cases, and verbal consent was required for those patients who were chosen to have a random assessment of their skin by an expert rater. Following a literature review to identify demographic and physiologic variables that potentially contribute to pressure ulcer development in critically ill patients, data extraction from the EMR was conducted over a two-week period on 100 patients meeting the inclusion criteria for the study. Baseline demographic information was entered into the data base on the day the patient qualified for the study, and daily physiologic parameters were entered throughout the duration of the patient's eligibility to be in the study. Subjects in the study were randomly selected for reliability testing on pressure ulcer presence and Braden scores generated by the staff nurses.

Baseline Measures

Baseline measures were collected on any patient meeting the inclusion criterion. Age, weight and height were abstracted from the EMR primarily using the institution's nursing admission and history form. BMI was calculated using the standard formula weight/height^2. History of diabetes and history of nicotine use was located in either the nursing admission form or the physician's history and physical. History of diabetes was recorded as either present or absent. Similarly, nicotine use was recorded as present if the patient admitted to its use within one year of the current hospitalization. Pre-existing skin disease was also coded as present or absent on admission. Where possible, the description of any pre-existing skin disease was noted in the database. The type of ICU the subject was admitted to was recorded in the database. The six possible ICU admissions were to the Trauma, Burn, Medical, Surgical, Neurologic, and Cardiovascular ICUs.

Daily Measures

The day following a subject's enrollment in the study, measures were obtained using data from the previous 24 hours until the subject was either discharged from the ICU, developed a stage I or worse pressure ulcer, died, or the study concluded. All measures but the Braden score and lab values for the previous 24-hour period were extracted from the electronic nursing vital sign flowsheet. For MAP, the worst value during the previous 24 hours from either an invasive arterial line reading or non-invasive cuff reading was utilized. In cases where there

were both types of readings, the arterial line measurement was used. Similarly, the worst oxygen saturation of hemoglobin was used. Vasopressor use was indicated as either present or absent for the previous 24 hours. When vasopressors were used, the type and highest dose during the 24-hour period were recorded. Lowest serum albumin and hematocrit levels from the previous 24-hour period were recorded.

Staff nurses' assessments of the subject's Braden scores are documented with the location and stage of any pressure ulcers present. The Braden score and any associated pressure ulcer documentation are required every 12 hours. The results from the most recent Braden scores and pressure ulcer documentation were used and entered into the study database.

Data Analysis

Data collected in this feasibility study were analyzed based on their availability and reliability. Demographic and laboratory variables were analyzed for their frequency of availability. Daily clinical variables were analyzed for their expected frequency, based on number of subjects enrolled in the study on any given day. Braden scores were analyzed for the level of agreement between staff nurse and expert rater by manually calculating weighted Kappa scores.

Results

Subject Profile

One hundred subjects were enrolled in the study. Subjects ranged in age from 19 years to 94 years, mean 53.5 years. BMI ranged from 16.23 to 54.04 with a mean of 28.6. ICU length of stay ranged from 1 day to 14 days. Thirty eight patients (38%) had a history of nicotine use prior to admission, 9 (9%) had pre-existing skin disease, and 20 (20%) had a history of diabetes. Table 1 represents the frequency of those demographic and clinical variables that were obtained. Given that there were 100 subjects enrolled in the study, the maximum number of results for each demographic variable was 100. As subjects were added and removed from the study, the number of daily maximum clinical variables changed, depending on how many subjects were enrolled on any given day. By calculating the number of subjects enrolled in the study on each of the 14 days, the total number of patient days evaluated were 476. Because of the standard frequency of collecting MAP, oxygen saturation, and Braden scores, at least 476 variables were expected for each of those variables. Laboratory values for hematocrit and serum albumin were collected as they were available.

Table 1 gives a summary of the availability of expected variables. Because vasopressor use in critically ill patients is highly variable, no expected number of variables was possible to calculate. Of the 100 subjects enrolled, 31 received vasopressors during the study, and vasopressors were in use during 85 of the 476 patient days. All data regarding vasopressor type and infusion rates were available in the EMR.

Braden score agreement between staff nurse and expert rater were evaluated using manual calculations of a weighted Kappa score. Twenty-seven subjects were randomly evaluated for their skin integrity and Braden score by an expert rater. Additionally, the expert

raters performed Braden scores on the six pressure ulcer positive subjects. Weighted Kappa scores are presented in Table 2.

Of the six subjects that developed a pressure ulcer during the 14 day study, there was 100% agreement between the staff nurse documentation and expert rater validation regarding presence and location of the pressure ulcer. There was discrepancy on one pressure ulcer stage, giving an 83.3% agreement between staff nurse documentation and expert rater on pressure ulcer staging.

Discussion

The feasibility of data retrieval and the quality of that data are prime concerns to a researcher wishing to use the EMR. Added concerns about the quality of nursing documentation around pressure ulcer presence, staging, and risk stratification are particularly troublesome. The quality and quantity of pressure ulcer documentation is generally poor (Gunningberg & Ehrenberg, 2004). Studies of ward nurses conducted in Europe report that pressure ulcers were often classified incorrectly and report Kappa statistics slightly greater than 0.3 (Beeckman et al., 2007; Defloor, Schoonhoven, Katrien, Weststrate, & Myny, 2006). This study was designed to answer questions about data availability and quality with regard to the study of pressure ulcers and their risk factors.

Demographic and daily clinical information were readily available. The EMR was easily accessible and the information was easily located. The laboratory values of hematocrit and serum albumin were chosen as potential risk variables based on a review of the literature and for their physiologic importance in maintaining skin integrity. Hematocrit values were performed on each subject almost daily. Serum albumin values, used extensively in the literature as a proxy measure for protein stores, were sparse, with only 25 values being recorded during any previous 24 hour observation period for the 100 subjects enrolled. Assuming this level of serum albumin testing will continue, other proxy measures for protein stores or funding for serum albumin testing is necessary.

The 66% availability of the staff nurse Braden scores was primarily a function of the EMR. As each new Braden score was entered into the EMR, the previous one was automatically archived and consequently was not available for analysis. As the data collection was designed to evaluate clinical parameters and Braden scores from the previous 24 hours, Braden score evaluation became problematic if the data collection was occurring in the afternoon. By that time, the nurse had entered a new Braden score for the day, and the scores from the previous day were not accessible. Since the study, the author has learned how to retrieve archived information, so future studies should show higher availability of the Braden scores.

Agreement between Braden scores performed by the staff nurse and those conducted by the expert rater had good to excellent agreement. All weighted Kappa scores were above 0.53 with the exception of the moisture subscale. The low agreement on the moisture subscale is confounding, but probably of little clinical significance. When staff nurse and expert rater Braden scores were dichotomized into high risk (Braden scores ≤ 16) and low risk (Braden scores ≥ 17), the non-weighted Kappa score was 0.698 ($p < 0.001$).

The agreement between staff nurse and expert rater on the presence, location, and stage of pressure ulcer positive subjects is encouraging. It should be noted that the six subjects

that developed pressure ulcers did not have massive tissue damage, and staging was relatively straightforward. One pressure ulcer was stage I, two were stage II, and two were unstageable. The disagreement between nurse and expert rater occurred on a pressure ulcer that developed because of naso-gastric tube erosion into the nares. The staff nurse staged the lesion as a stage II; however, the expert rated it as unstageable a day later because of the scabbing that was obscuring the wound base.

Given the availability and accuracy demonstrated by this study, the EMR can be utilized as a data source for future pressure ulcer studies. The time constraints required to abstract the data, complete random skin assessments, and validate extant pressure ulcers was extensive. The two data collectors spent in excess of 100 hours during the two-week study. To reduce the excessive amount of time required for data collection, future studies will use a case-control study design, thereby eliminating the need for data collection on every patient admitted to the ICU.

Table C.1. Variable availability for Pressure Ulcer Feasibility Study

Variable	Number of times variable present	Maximum no. observations possible	% of times data available
Age	100	100	100
Diabetes	99	100	99
BMI	95	100	95
Nicotine	97	100	97
Skin Disease	99	100	99
Worst MAP	459	476	96
Worst O2 Sat	467	476	94
Hematocrit Level*	433		
Serum Albumin*	25		
Staff RN Braden Scores	317	476	66

*Maximum no. possible observations assuming lab values completed at least once every 24 hours

Table C.2. Weighted Kappa Agreement Between expert and Staff Nurse (N=33)

Braden Sub-Scale	Weighted Kappa Value
Sensory	0.535
Moisture	0.248
Activity	0.666
Mobility	0.577
Nutrition	0.56
Friction/Shear	0.581

Appendix D

Tables

Table D.1. Comparison of Dichotomous Data between Marched and Unmatched Case Subjects

Variable	Unmatched Cases $N = 12$		Matched Cases $N = 180$		p value[†]
	n	(%)	*n*	(%)	
Gender					
Male	10	(83.3)	128	(71.1)	0.362
Female	2	(16.7)	52	(28.9)	
Consent					
Self	2	(16.7)	29	(16.1)	0.421
Surrogate	8	(66.7)	89	(49.4)	
Waived	2	(16.7)	62	(34.4)	
ICU*					
CVICU	3	(25)	35	(19.4)	0.254
MICU	0		36	(20.0)	
Neuro	2	(16.7)	10	(5.6)	
SICU	3	(25)	56	(31.1)	
Trauma	4	(33.3)	43	(23.9)	
Ventilator use*					
No	1	(8.3)	37	(20.6)	0.304
Yes	11	(91.7)	143	(79.4)	
Diabetes					
No	7	(58.3)	96	(53.3)	0.705
Yes	2	(16.7)	49	(27.2)	
Missing	3	(25)	35	(19.4)	
Nicotine					
No	7	(58.3)	96	(53.3)	0.866
Yes	4	(33.3)	73	(40.6)	
Missing	1	(8.3)	11	(6.1)	
Steroid use					
No	9	(75)	124	(68.9)	0.348
Yes	0		25	(13.9)	
Missing	3	(25)	31	(17.2)	
Skin disease					
No	11	(91.7)	114	(63.3)	0.368
Missing	0		27	(15.0)	
Yes	1	(8.3)	39	(21.7)	
Pre-existing pressure ulcer	1	(8.3)	24	(13.3)	0.618
Edema	0		11	(6.1)	0.378
Jaundice	0		5	(2.8)	0.559
Thin, fragile skin	0		1	(0.6)	0.796
IV vasopressor use prior to enrollment					
No	3	(25)	93	(51.7)	0.074

Variable	Unmatched Cases *N* = 12 *n* (%)	Matched Cases *N* = 180 *n* (%)	*p* value†
Yes	9 (75)	87 (48.3)	
Dobutamine	0	14 (7.8)	0.316
Dopamine	0	9 (5.0)	0.428
Epinephrine	1 (8.3)	23 (12.8)	0.652
Midodrine	0	0	--
Milrinone	1 (8.3)	17 (9.4)	0.898
Norepinephrine	9 (75)	68 (37.8)	0.011
Vasopressin	5 (41.7)	39 (21.7)	0.110
Restraint use			
No	6 (50)	49 (27.2)	0.091
Yes	6 (50)	131 (72.8)	

† X^2

*Matching criteria

Table D.2. Comparison of Braden Subscale Scores between Matched and Unmatched Case Subjects

Braden Sub Scale Score	Unmatched Cases *N* = 12 *n* (%)	Matched Cases *N* = 180 *n* (%)	*p* value†
Lowest Sensory 48 hours prior to enrollment			
1	2 (16.7)	29 (16.1)	0.973
2	4 (33.3)	67 (37.2)	
3	5 (41.7)	63 (35.0)	
4	1 (8.3)	21 (11.7)	
Lowest Sensory 24 hours prior to enrollment			
1	2 (16.7)	32 (17.8)	0.953
2	4 (33.3)	63 (35.0)	
3	5 (41.7)	57 (31.7)	
4	1 (8.3)	28 (15.6)	
Lowest Nutrition 48 hours prior to enrollment			
1	1 (8.3)	20 (11.1)	0.587
2	4 (33.3)	70 (38.9)	
3	7 (58.3)	89 (49.4)	
4	--	1 (0.6)	
Lowest Nutrition 24 hours prior to enrollment			
1	1 (8.3)	26 (14.4)	0.133
2	2 (16.7)	64 (35.6)	
3	9 (75.0)	88 (48.9)	
4	--	2 (1.1)	
Lowest Mobility 48			

Braden Sub Scale Score	Unmatched Cases *N* = 12		Matched Cases *N* = 180		*p* value[†]
	n	(%)	*n*	(%)	
hours prior to enrollment					
1	5	(41.7)	62	(34.4)	0.236
2	7	(58.3)	82	(45.6)	
3	--		35	(19.4)	
4	--		1	(0.6)	
Lowest Mobility 24 hours prior to enrollment					
1	6	(50.0)	58	(32.2)	0.080
2	6	(50.0)	86	(47.8)	
3	--		34	(18.9)	
4	--		2	(1.1)	
Lowest Activity 48 hours prior to enrollment					
1	10	(83.3)	132	(73.3)	0.408
2	2	(16.7)	38	(21.1)	
3	--		8	(4.4)	
4	--		2	(1.1)	
Lowest Activity 24 hours prior to enrollment					
1	7	(58.3)	135	(75.0)	0.246
2	5	(41.7)	39	(21.7)	
3	--		6	(3.3)	
4	--		--		
Lowest Moisture 48 hours prior to enrollment					
1	1	(8.3)	5	(2.8)	0.041
2	5	(41.7)	32	(17.8)	
3	5	(41.7)	118	(65.6)	
4	1	(8.3)	25	(13.9)	
Lowest Moisture 24 hours prior to enrollment					
1	1	(8.3)	12	(6.7)	0.050
2	6	(50.0)	45	(25.0)	
3	5	(41.7)	101	(56.1)	
4	--		22	(12.2)	
Lowest Friction/Shear 48 hours prior to enrollment					

Braden Sub Scale Score	Unmatched Cases *N* = 12 *n* (%)	Matched Cases *N* = 180 *n* (%)	*p* value†
1	5 (41.7)	84 (46.7)	0.891
2	7 (58.3)	87 (48.3)	
3	--	9 (5.0)	
Lowest Friction/Shear 24 hours prior to enrollment			
1	6 (50.0)	96 (53.3)	0.756
2	5 (41.7)	75 (41.7)	
3	1 (8.3)	9 (5.0)	

†Mann-Whitney

Table D.3. Comparison of Continuous Data between Matched and Unmatched Case Subjects

Variable	Unmatched Cases *N* = 12 Median (*n*; IQR)	Matched Cases *N* = 180 Median (*n*; IQR)	*p* value††
Age	58.5 (12; 41.3 - 61.8)	59.0 (180; 48.3 – 68.0)	0.530
ICU length of stay before enrollment*	24.5 (12; 21.0 - 27.5)	7.0 (180; 4.0 – 11.0)	< 0.001
BMI**	27.6 (12; 23.9 - 34.3)	27.6 (180; 23.0 - 33.6)	0.826
Total corticosteroid dose 14 days before enrollment			
Hydrocortisone dose	1275.0 (4; 343.8 – 1625.0)	450.0 (45; 200.0 – 1000.0)	0.182
Methylprednisone dose	1250.0 (1; 1250.0 – 1250.0)	342.5 (20; 125.0 - 1117.5)	0.280
Prednisolone dose	0	0	--
Prednisone dose	0	140.0 (17; 62.5 – 230)	--
Protein store			

Variable	Unmatched Cases *N* = 12 Median (*n*; IQR)	Matched Cases *N* = 180 Median (*n*; IQR)	*p* value[††]
Serum albumin	2.8 (7; 2.6 – 3.0)	2.8 (68; 2.4 - 3.2)	0.763
Pre-albumin	12.5 (10; 8.0 – 23.0)	11.0 (80; 8.0 – 14.0)	0.354
Lymphocyte count	1.0 (8; 0.6 - 1.4)	1.0 (129; 0.6 - 1.6)	0.765
Perfusion parameters			
Highest hematocrit 48 hours prior to enrollment	27.0 (11; 23.0 – 32.0)	28.0 (175; 26.0 – 31.0)	0.528
Lowest hematocrit 48 hours prior to enrollment	27.0 (11; 23.0 – 31.0)	27.0 (175; 24.0 – 30.0)	0.871
Highest hematocrit 24 hours prior to enrollment	29.0 (11; 25.0 – 33.0)	28.0 (176; 25.0 – 30.0)	0.624
Lowest hematocrit 24 hours prior to enrollment	29.0 (11; 25.0 – 33.0)	26.0 (176; 24.0 – 29.0)	0.225
Lowest MAP[†] 48 hours prior to enrollment	57.5 (12; 51.5 – 65.0)	61.0 (180; 55.0 – 66.0)	0.197
Lowest MAP 24 hours prior to enrollment	53.0 (12; 42.3 – 66.3)	61.0 (180; 56.0 – 67.0)	0.064
Lowest O_2 saturation 48 hours prior to enrollment	95.0 (12; 87.0 – 98.3)	92.0 (180; 89.3 – 95.0)	0.400
Lowest O_2 saturation 24 hours prior to enrollment	95.5 (12; 93.3 – 98.5)	92.5 (180; 90.0 – 95.0)	0.016
Vasopressor dose in total micrograms/kg			
Norepinephrine dose 48 hours prior to enrollment	73.6 (2; 1.2 – 0.0)	44.5 (49; 15.8 – 86.0)	0.633
Norepinephrine dose 24 hours prior to enrollment	37.1 (1; 37.1 -37.1)	51.3 (43; 9.4 - 117.3)	0.098
Epinephrine dose 48 hours prior to enrollment	0	9.4 (6; 5.9 - 53.2)	--

Variable	Unmatched Cases *N* = 12 Median (*n*; IQR)	Matched Cases *N* = 180 Median (*n*; IQR)	*p* value††
Epinephrine dose 24 hours prior to enrollment	0	17.0 (3; 1.5 - 17.0†††)	--
Dobutamine dose 48 hours prior to enrollment	0	4463.9 (2; 1448.8 - 4463.9†††)	--
Dobutamine dose 24 hours prior to enrollment	0	1373.0 (3; 483.0 – 1373.0†††)	--
Milrinone dose 48 hours prior to enrollment	134.4 (1; 30.3 – 0.0)	150.0 (13; 40.8 - 323.4)	0.751
Milrinone dose 24 hours prior to enrollment	435.7 (1; 199.7 – 0.0)	224.5 (10; 65.8 - 406.1)	1.000
Midodrine dose 48 hours prior to enrollment	0	333.0 (1; 333.0 – 333.0)	--
Midodrine dose 24 hours prior to enrollment	0	333.0 (1; 333.0 – 333.0)	--
Vasopressin dose 48 hours prior to enrollment (total units/kg)	2.4 (1; 2.4 - 2.4)	31.2 (23; 19.2 - 57.6)	0.100
Vasopressin dose 24 hours prior to enrollment	26.4 (1; 26.4 - 26.4)	39.6 (24; 16.9 - 49.8)	0.550

†† Mann-Whitney

*****Matching criteria; **Body mass index; †Mean arterial pressure, † † † 25th and 50th percentile

Table D.4. Summary of Missing Data

Missing Variable	Matched Cases *N* = 180 *n* (%)	Matched Controls *N* = 180 *n* (%)	*p* value[†]
Pre-Admission Demographic Variables			
Diabetes	35 (19.4)	32 (17.8)	0.755
Nicotine use	11 (6.1)	11 (6.1)	1.000
Corticosteroid use	31 (17.2)	32 (17.8)	1.000
Skin Disease	27 (15.0)	29 (16.1)	0.874
Perfusion Parameter Variables			
Highest hematocrit 48 hours prior to enrollment	5 (2.8)	4 (2.2)	1.000
Lowest hematocrit 48 hours prior to enrollment	5 (2.8)	4 (2.2)	1.000
Highest hematocrit 24 hours prior to enrollment	4 (2.2)	5 (2.8)	1.000
Lowest hematocrit 48 hours prior to enrollment	4 (2.2)	5 (2.8)	1.000
Protein Reserve Variables			
Serum Albumin	112 (62.2)	113 (62.7)	1.000
Serum Pre-albumin	100 (55.5)	100 (55.5)	0.560
Total Lymphocyte Count	51 (28.3)	41 (22.8)	0.522
Any Protein Store	22 (12.2)	15 (8.3)	0.281

Table D.5. Summary of Vasopressor Use and Steroid Administration in Case and Control Subjects

Variable	Matched Cases *N* = 180 Median (*n*; IQR)	Matched Controls *N* = 180 Median (*n*; IQR)	*p* value*
Total corticosteroid dose within 14 days of enrollment			
Hydrocortisone dose	450.0 (45; 200.0 – 1000.0)	700.0 (30; 250.0 – 1225.0)	0.223
Methylprednisone dose	342.5 (20; 125.0 - 1117.5)	285.5 (22; 123.8 – 875.0)	0.988
Prednisolone dose	0 (0.0)	0 (0.0)	--
Prednisone dose	140.0 (17; 62.5 – 230.0)	100.0 (25; 37.5 – 215.0)	0.361
Vasopressor dose in total micrograms/kg			
Norepinephrine dose 48 hours prior to enrollment	44.5 (49; 15.8 – 86.0)	41.5 (34; 13.4 – 78.0)	0.095
Norepinephrine dose 24 hours prior to enrollment	51.3 (43; 9.4 - 117.3)	38.3 (31; 14.3 - 128.6)	0.107
Epinephrine dose 48 hours prior to enrollment	9.4 (6; 5.9 - 53.2)	120.1 (6; 28.0 - 518.9)	0.272
Epinephrine dose 24 hours prior to enrollment	17.0 (3; 1.5 – 17.0††)	67.1 (5; 12.4 – 75.4)	0.401
Dobutamine dose 48 hours prior to enrollment	4463.9 (2; 1448.8 – 4463.9††)	3445.5 (4; 858.3 - 5847.0)	0.600
Dobutamine dose 24 hours prior to enrollment	1373.0 (3; 483.0 – 1373.0††)	2610.9 (6; 454.6 - 4474.7)	0.374
Milrinone dose 48 hours prior to enrollment	150.0 (13; 40.8 - 323.4)	294.7 (8; 70.7 -1155.5)	0.936

Variable	Matched Cases *N* = 180 Median (*n*; IQR)	Matched Controls *N* = 180 Median (*n*; IQR)	*p* value*
Milrinone dose 24 hours prior to enrollment	224.5 (10; 65.8 - 406.1)	364.1 (9; 78.7 – 629.0)	0.795
Midodrine dose 48 hours prior to enrollment	333.0 (1; 333.0 – 333.0)	0 (0.0)	--
Midodrine dose 24 hours prior to enrollment	333.0 (1; 333.0 – 333.0)	0 (0.0)	--
Vasopressin dose 48 hours prior to enrollment (total units/kg)	31.2 (23; 19.2 - 57.6)	38.4 (13; 19.8 - 57.6)	0.263
Vasopressin dose 24 hours prior to enrollment (total units/kg)	39.6 (24; 16.9 - 49.8)	52.8 (13; 18.6 - 57.6)	0.138

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