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Subsyndromal Delirium And Postoperative Pain In Older Adults

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SUBSYNDROMAL DELIRIUM AND POSTOPERATIVE PAIN IN OLDER ADULTS

by

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Dawn LuJean Denny
September 10, 2014

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

I would like to dedicate this undertaking to those people who have been instrumental in helping me reach this point in my life. To my mother, Donna Jean Fuller, who instilled a love of learning in me and provided encouragement, thank you. I also want to recognize my son, Matthew J. Denny, who has been such a help to me in practical ways, such as serving as one of my critical resources for technological support. My biggest supporter has been my husband, John R. Denny, without whose support, love, and encouragement, I could not have accomplished this milestone. Thank you all. Last, but not least, I want to acknowledge my Savior, Jesus Christ, who gave me strength and intellect for this dissertation work. This work was completed in memory of my father, Donald C. Fuller, whose unwavering belief in my potential continues to inspire me; and my son, John M. Denny, one of the most courageous individuals I have ever known.

ABSTRACT

Study Purpose and Design: The purpose of this study was to determine the relationship between subsyndromal delirium and pain in older adults following major elective orthopedic surgery. The design of this correlational study was based on Inouye and Charpentier's (1996) multifactorial model of delirium.

Methods: Delirium assessments of 62 older adults were completed at 24, 48, and 72 hours following major elective orthopedic surgery. Study measures included: a) the Iowa Pain Thermometer (0-10) pain intensity scale; and b) the Confusion Assessment Method (short form). Data were analyzed for relationships among delirium symptoms and pain, and secondarily, 24-hour opioid intake controlling for preoperative risk factors.

Findings: Subsyndromal delirium occurred in 67.9 percent of participants in this study. Increased pain from 0 to 24 hours after surgery had a significant ($p<.05$) relationship with subsyndromal delirium on the second postoperative day. Similarly, increased pain from 24 to 48 hours had a significant ($p<.05$) relationship with delirium symptoms on the second postoperative day. Opioid intake was not significantly related to subsyndromal delirium.

Conclusions and Implications for Clinical Practice: Findings from this study suggest older adults with higher levels of pain are at higher risk for developing delirium symptoms and subsyndromal delirium on the second day following major elective orthopedic surgery. Improved pain management may help reduce subsyndromal delirium when attention is given to pain on the second postoperative day.

CHAPTER I

INTRODUCTION

Subsyndromal delirium is a common complication in hospitalized older adults with incidence rates of up to 68% in those who undergo major elective orthopedic surgery (Liptzin, Laki, Garb, Fingeroth, & Krushell, 2005). Subsyndromal delirium may precede delirium and is thought to occur midway on a continuum from no symptoms of delirium to delirium (Trzepacz et al., 2012). Delirium symptoms are extremely distressing for patients as well as their families (Partridge, Martin, Harari, & Dhesi, 2012). Subsyndromal delirium refers to subclinical symptoms that are often unrecognized by nurses as well as physicians and may never progress to delirium (Vollmer et al., 2010). Although symptoms are less severe, patients with subsyndromal delirium have similar risks for adverse outcomes to those who suffer from delirium, including increased lengths of hospital stays and admissions to long-term care, increased falls, and higher mortality rates (Cole, McCusker, Dendukuri, & Han, 2003; Cole et al., 2011; DeCrane, Culp, & Wakefield, 2012). The pathophysiology of postoperative delirium is unknown (Maldonado, 2008a), but it is thought to result from a complex interaction of multiple risk factors (Inouye & Charpentier, 1996). Postoperative pain is an important factor related to delirium (Bjoro, 2008; Lynch et al., 1998; Morrison et al., 2003; Vaurio, Sands, Wang, Mullen, & Leung, 2006) occurring up to nine times as frequently in patients with high pain ratings (Morrison et al., 2003). The full syndrome of delirium is costly and

represents a national burden of an estimated $152 billion each year (Leslie, Marcantonio, Zhang, Leo-Summers, & Inouye, 2008), with negative outcomes of increased lengths of stay, increased morbidities, and three times the mortality rate of those without delirium (Ely et al., 2007).

Although risk factors for subsyndromal delirium are presumed to be the same as for full delirium (Cole et al., 2003; Cole et al., 2011; DeCrane et al., 2012; Marcantonio et al., 2003), a recent literature review found an unexplained heterogeneity in the results of existing evidence (Cole, Ciampi, Belzile, & Dubuc-Sarrasin, 2012). The presence of pain is expected following major elective orthopedic surgery, and treatment with opioid medication is standard clinical practice. However, a gap in knowledge exists concerning the relationship between pain intensity level and subsyndromal delirium, as well as in the relationship between opioid intake and subsyndromal delirium. Thus, research is needed to better understand these relationships to reduce adverse outcomes associated with subsyndromal delirium.

The purpose of this study was to determine the relationship between subsyndromal delirium and pain in older adults following major elective orthopedic surgery. The specific aims examined in this study were: a) to determine the frequency of delirium symptoms and the frequency distribution of preoperative risk factors, pain intensity ratings and 24 hour opioid intakes of patients age 65 years and older following major elective orthopedic surgery; b) to determine the relationship between delirium symptoms and the preoperative risk factors in older adults following major elective orthopedic surgery; c) to determine the relationship between delirium symptoms and pain intensity ratings controlling for preoperative risk factors in older adults following major

elective orthopedic surgery; and, d) to determine the relationship between delirium symptoms and 24 hour opioid intakes controlling for selected preoperative risk factors and pain intensity ratings in older adults following major elective orthopedic surgery. In this first chapter, the significance of the problems of delirium and subsyndromal delirium in older adults are discussed.

Significance and Background

Subsyndromal delirium occurs when one or two of the core symptoms of delirium are present without meeting the criteria for full delirium (DeCrane et al., 2012). Recognized clinical features of delirium include an acute onset and fluctuating course, inattention, and disorganized thinking with or without altered level of consciousness (Inouye et al., 1990). Similar to delirium, subsyndromal delirium is a marker of poor prognosis and adverse outcomes (Marquis, Ouimet, Riker, Cossette, & Skrobik, 2007) and may announce an imminent occurrence of full delirium (Cole et al., 2003; Hakim, Othman, & Naoum, 2012).

Incidence of Delirium Symptoms

Full delirium develops in up to 46 percent of older adults following major elective orthopedic surgery (Vaurio et al., 2006). In comparison, subsyndromal delirium occurs in up to 69 percent of older orthopedic patients (Liptzin et al., 2005). Ten percent of all acute care patients admitted from home who develop subsyndromal delirium while hospitalized are discharged to an institution (Cole et al., 2003). Furthermore, subsyndromal delirium is often preventable (Cole, McCusker, Ciampi, & Belzile, 2008). Clearly, early detection and treatment of subsyndromal delirium is imperative to help

reduce adverse outcomes related to delirium symptoms in hospitalized older adults (Hakim et al., 2012).

Interaction of Risk Factors for Delirium Symptoms

Although the pathophysiology of postoperative delirium is unclear, multiple risk factors have been proposed to help explain the development of delirium. Surgery exposes patients to multiple factors simultaneously that may precipitate delirium symptoms in older patients (e.g., stress related to the surgical procedure, exposure to multiple medications, and pain). Following surgery, hospitalized older adults are at risk for developing delirium symptoms as a result of the accumulative impact of predisposing factors from baseline vulnerability and surgery-related precipitating factors. Previous studies have identified several preoperative risk factors for postoperative delirium. Abnormal laboratory tests -- specifically albumin, sodium, potassium, glucose, hemoglobin increased delirium risk (Popeo, 2011). Although relevant, abnormal preoperative laboratory values were anticipated to be infrequent in patients scheduled for major elective surgery due to the requirement for medical clearance prior to the procedure. The medical clearance typically involves the use of the American Society of Anesthesiologists (ASA) score, as well as a medical clearance from the patient's primary physician, to estimate risk for mortality (Schwarzkopf, Katz, Walsh, Lafferty & Slover, 2011).

Other risk factors for incident subsyndromal delirium in surgical patients include advanced age, dementia, and more co-morbidity (Cole, Ciampi, Belzile, & Dubuc-Sarrasin, 2012). Opioids are often implicated as a cause of postoperative delirium. However, growing evidence refutes that opioids increase the incidence of postoperative

delirium (Morrison et al., 2003; Sieber, Mears, Lee, & Gottschalk, 2011). Although delirium symptoms have been shown to result from overmedication (Inouye, 2002), the risk for delirium may actually increase when patients are given ineffective doses of opioids following major elective orthopedic surgery as compared to larger, more effective doses (Morrison et al., 2003). In addition, pain was found to be an independent risk factor for delirium in hospitalized older patients (Ely et al., 2007, Morrison et al., 2003; Vaurio et al., 2006).

Postoperative Delirium and Pain

Well-managed pain appears to be an important aspect of preventing postoperative delirium. Patients with higher pain scores during the first 3 days following surgery may have a higher incidence of delirium (Lynch et al., 1998) and a slower recovery from delirium once it develops (DeCrane et al., 2011). Vaurio et al., (2006) concluded that pain management has a greater impact on postoperative delirium incidence than all other risk factors except age.

Although no studies were identified examining the relationship of subsyndromal delirium and postoperative pain, some suggest risk factors are the same for subsyndromal delirium as for full delirium (Cole et al., 2003; Cole et al., 2011). However, some have noted that subsyndromal delirium may possess its own risk factors, outcomes, and management (Trzepacz et al., 2012). Therefore, the evidence is inconsistent and sometimes contradictory in regards to subsyndromal delirium. In a systematic review of published literature regarding subsyndromal delirium, heterogeneity was noted regarding the prevalence, incidence, and some of the risk factors (Cole et al., 2012). The risk factors for subsyndromal delirium identified in the review included dementia, admission from an

institution, increasing severity of medical illness, and vision impairment. Pain was not one of the risk factors considered by the researchers conducting the review.

Importance of Identifying Subsyndromal Delirium

Subsyndromal delirium has consistently been associated with poor outcomes (Cole et al., 2011). Identification of delirium symptoms may signal the need for early intervention paramount to prevention of the devastating effects of the full syndrome. Several evidence-based algorithms are recommended for use by bedside clinicians to assist in identification of delirium versus no delirium (for example, Inouye et al., 1990). However, no clear what actions are indicated if delirium symptoms are identified prior to the development of full delirium, thereby not meeting the algorithm criteria for further action.

Early intervention involves identifying potential causes of delirium symptoms and initiating attempts to eliminate precipitating factors, such as poorly controlled pain. Multidisciplinary efforts to prevent delirium through identification of risk factors in older patients on admission may or may not include attention to pain management. Furthermore, the relationship between subsyndromal delirium and postoperative pain in older adults following major elective orthopedic surgery remains unclear in the literature. Therefore, if subsyndromal delirium could be reversed in some cases and thereby prevent progression to full delirium, a shift in the emphasis of current delirium detection efforts from merely identifying the full syndrome of delirium to also identifying early delirium symptoms may be indicated.

Theoretical Framework

This dissertation study was built upon Inouye and Charpentier's (1996) predictive model for delirium. Delirium is a syndrome characterized by an acute onset and fluctuating course, inattention, disorganized thinking with or without altered level of consciousness, and evidence of an external cause (Inouye et al., 1990). The pathophysiology of delirium is not fully understood, but is thought to be multifactorial. Delirium occurs on a continuum from no delirium to delirium, with subsyndromal delirium between the two as subclinical symptoms of delirium that may either precede or never progress to delirium (Vollmer et al., 2010). Delirium has a multifactorial etiology with multiple plausible theories regarding possible etiologies of the syndrome; however, the pathophysiology of delirium is unknown (Maldonado, 2008b) and no known biological markers for delirium have been identified (Robertsson, 2002; Van Munster, de Rooij, & Korevaar; 2009).

Inouye and Charpentier's (1996) predictive model for delirium theorizes delirium as resulting from the complex interaction of predisposing risk factors (e.g., age, cognitive impairment) and precipitating risk factors (e.g., major surgery, pain). Each additional risk factor increases risk for delirium. In recent years, research has moved away from trying to determine a specific cause for delirium toward trying to find ways to remove or decrease the impact of precipitating risk factors (Maldonado, 2008a). Delirium prevention strategies aimed at reducing the impact of modifiable risk factors are needed to improve the clinical outcomes of high-risk patients (Irving & Foreman, 2006). However, Inouye and Charpentier's (1996) predictive model for delirium describes delirium as an interaction between vulnerability and noxious insults. Figure 1 depicts two

older patients who present with low risk toward delirium prior to surgery; one patient developed delirium symptoms and the other patient did not. Following surgery, *Patient 1* experienced severe pain, whereas *Patient 2* experienced mild to moderate postoperative pain. According to Inouye and Charpentier's predictive model, if all of the other delirium risk factors for both patients were equal, the patient with increased strength of a noxious insult, such as severe pain, would be at higher risk for developing delirium symptoms than the patient with mild to moderate pain.

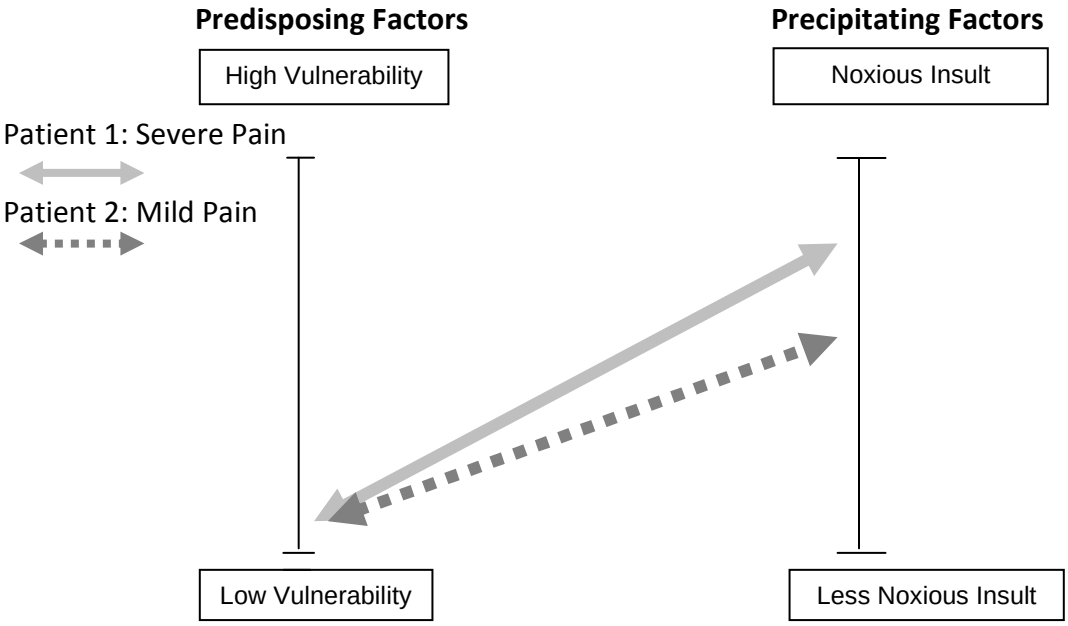


Figure 1. Differences in risk for subsyndromal delirium in older adults with severe versus mild postoperative pain. Higher pain levels increase vulnerability to subsyndromal delirium. Adapted from "Precipitating factors for delirium in hospitalized elderly persons: A predictive model and interrelationship with baseline vulnerability," by S. K. Inouye and P. A. Charpentier, 1996, *Journal of the American Medical Association, 275*, p. 853. Copyright 1996 by the American Medical Association. Used with permission.

Assumptions of the Predictive Model for Delirium

An assumption underlying this conceptualization of delirium as a syndrome is that delirium does not result from one single cause. This assumption for delirium research

suggests that, rather than searching for a single cause, the consideration of multiple contributing factors is needed. To say that delirium results from a variety of factors, however, is inadequate to guide this investigation; it only describes the existence of delirium.

Operational Definitions

Operational definitions employed for this study are described in Table 1. They were derived from a review of the literature and the conceptual framework provided by Inouye and Charpentier's (1996) multifactorial predictive model of delirium. For this study, subsyndromal delirium excluded cases of subsyndromal delirium that progressed to full delirium or from full delirium. More specifically, subsyndromal delirium was defined as the presence of one or two of the four core symptoms according to the delirium diagnostic detection tool -- Confusion Assessment Method (CAM) -- without meeting full criteria for a diagnosis of delirium, and without preceding or following an episode of delirium.

Assumptions

Assumptions of this study were as follows:

1. The etiology of delirium symptoms is multifactorial in nature with several contributing factors interacting at a specific time (Inouye & Charpentier, 1996).
2. Older patients undergo surgery with some preexisting risk factors that are not easily modified or removed, such as age.
3. Surgery poses multiple strong noxious insults that place older patients at risk for delirium and subsyndromal delirium.

Table 1

Operational Definitions

Concept or Variable	Definitions
Older Adult	Older adult refers to any individual ≥ 65 years of age.
Major Elective Orthopedic Surgery	Orthopedic surgical procedures requiring an anticipated length of stay of 48 hours or more.
Postoperative Delirium	An acute state of transient confusion as measured using a testing method operationalized by the shortened version of the Confusion Assessment Method (CAM) (Inouye, 2003).
Subsyndromal Delirium	One or two positive findings of the four core symptoms of delirium on the CAM, which does not precede or follow delirium (Coe et al., 2003).
Delirium Symptoms	Delirium symptoms were defined according to the core symptoms on the shortened version of the CAM (Inouye et al., 1990) Delirium symptoms were scored on a scale of (0-3): No delirium=0; subsyndromal delirium will be scored as either SSD-1 = 1; or SSD-2 = 2; and Delirium= 3. 1. **Delirium**: An acute state of transient confusion as identified by meeting by a positive finding of the first 2 core symptoms, plus either the 3rd core symptom with or without the 4th core symptom according to the CAM (Inouye, 2003). 2. **Subsyndromal Delirium (SSD-1; SSD-2):** The presence of delirium symptoms according to the CAM that did not precede or follow an episode of delirium (subsyndromal delirium with one symptom, SSD-1; subsyndromal delirium with 2 or 3 symptoms not diagnostic of delirium, SSD-2) (as in Cole et al., 2003). 3. **No Delirium**: No delirium symptoms. Evaluative testing using the CAM failed to identify any core features of delirium.
24 hour Opioid Intake	Opioid intakes will be calculated for each 24 hour period starting from the time of arrival on the post-surgical unit and for each additional 24-hour period thereafter for 72 hours. Totals were converted to morphine sulfate intravenous doses using an equianalgesic calculator to to an estimated dose of parenteral morphine sulfate that would likely result in the same analgesic effect
Pain Intensity	A self-reported pain intensity rating reflecting the degree of pain as measured on the Iowa Pain Thermometer (0-10) (Taylor, Harris, Epps, & Herr, 2005).
Preoperative Risk Factors	Preoperative risk factors for delirium symptoms included a higher comorbidity burden, cognitive impairment, a recent fall history (within 6 months), and longer preoperative fasting times. Comorbidity burden was measured using the Charlson Comorbidity Index (Charlson, Pompei, Ales & MacKenzie, 1987). Cognitive status was scored using the Mini-Cog. The number of falls within the past six months was identified from the medical record or per patient report. Preoperative fasting time was calculated in hours from last known intake prior to surgery start time, or from the midnight prior to surgery, if not otherwise specified.

4. Eligible participants for this study will likely have few predisposing risk factors for delirium. Given the routine practice of strict medical clearance, some patients at the highest risk for delirium symptoms may be deemed unlikely to survive major surgery and denied the option of elective surgery.

Limitations

This study had several limitations:

1. **Observational design**. The observational design presents limitations as to the inferences that can be drawn from study findings. However, the ethical concerns surrounding the provision of pain relief for some patients and not for others limits the use of more controlled designs. Patients have a right to pain relief and should receive the best possible pain treatment (Blacksher, 2001). Therefore withholding an effective medication from one group of study participants to facilitate a clinical trial may pose ethical concerns.
2. **Sample and sampling method**. The sample was largely homogenous (98% Caucasian, $n = 52$; and, 2% American Indian, $n = 1$) and may not represent the diverse population of older adults who choose to have major elective orthopedic surgery procedures performed. Requirements for medical clearance prior to elective surgery for orthopedic problems may have served to limit the number of individuals with a pre-existing high risk for delirium (for example, those with a diagnosis that prevents surgical clearance for elective procedures due to an anticipated high risk for mortality). However, the restrictive medical requirements for major elective orthopedic surgeries may have served to reduce the number of predisposing risk factors present when compared to those seen in nonsurgical patients.

3. **Missing data**. The presence of missing data regarding pain intensity poses a limitation. To minimize the impact of missing data, mean substitution methods were planned for use prior to final data analyses.
4. **Use of self-reported pain in patients with delirium**. Delirium may represent a barrier to pain assessment. However, self-reported pain intensity was used successfully in previous research involving patients with delirium. For example, Leung et al. (2009) examined the ability of patients with postoperative delirium to use PCA and found their ratings of pain to be consistent with those without delirium. In addition, DeCrane et al. (2011) successfully used a self-report rating scale for the assessment of pain when investigating factors associated with early recovery from postoperative delirium when all of the patients selected for the study were delirious. Furthermore, Kinjo, Lim, Sands, Bozic, and Leung (2012) successfully used the Numeric Rating Scale with adults age ≥ 65 years following unilateral total knee replacement surgery of whom 48.1 percent developed delirium. Through the course of the current study, patients with either subsyndromal delirium or the full syndromal delirium were able to utilize the Iowa Pain Thermometer for attempted pain assessments by either unit nurses or the researcher.

Human Subjects Protection

Approval was obtained from the Institutional Review Board (IRB) at the University of North Dakota for the study prior to the start of the investigation (See Appendix J for IRB materials). The research site, which did not have its own IRB in place, accepted the university's IRB approval for the study. In addition, support for the

project was obtained from the physician groups who were performing surgeries at the research site.

To protect the privacy and confidentiality of participants, data entered into the computerized database were protected through the use of a password known only to the researcher, the utilization of encryption software, and de-identified data collection forms. A unique number for each participant was selected by using a random number table and placed on the data collection tools. Completed data collection forms were kept in a locked cabinet in a locked home office. The code list with the key to the patient's identity and personal information was kept in a separate locked cabinet.

Summary

Delirium is a significant problem for older adults following surgery with serious adverse consequences, including a higher mortality rate. The subclinical symptoms of the syndrome of delirium, subsyndromal delirium, occurs when only one or two of the four core symptoms of delirium are present and may occur on a continuum between the absence of delirium and the full syndrome of delirium (Cole et al., 2008; Li et al., 2014). Subsyndromal delirium has been found to pose similar risks and adverse outcomes as delirium, but of less severity (Cole et al., 2008). Several risk factors for postoperative subsyndromal delirium have been identified in a growing body of evidence. However, even though pain has been identified as a significant predictor of the full syndrome of delirium, investigations into the relationship between subsyndromal delirium and postoperative pain were absent in the literature. Although the evidence negates the notion that opioid medications precipitate delirium when given in recommended doses -- with the exception of meperidine -- the relationship between subsyndromal delirium and

opioid analgesic medications has not yet been described in the literature. Therefore, the purpose of this study was to determine the relationship between subsyndromal delirium and postoperative pain in older adults following major elective orthopedic surgery.

This study expanded on previous research regarding subsyndromal delirium research. A gap in knowledge exists regarding the relationship between subsyndromal delirium and pain. Findings from this study provide information that can be used to inform delirium prevention efforts towards improving outcomes in older adults following major elective orthopedic surgery.

CHAPTER II

LITERATURE REVIEW

The purpose of this study was to determine the relationship between subsyndromal delirium and pain in older adults following major elective orthopedic surgery. The specific aims examined in this study were: a) to determine the frequency of delirium symptoms and the frequency distribution of preoperative risk factors, pain intensity ratings and 24 hour opioid intakes of patients age 65 years and older following major elective orthopedic surgery; b) to determine the relationship between delirium symptoms and the preoperative risk factors in older adults following major elective orthopedic surgery; c) to determine the relationship between delirium symptoms and pain intensity ratings controlling for preoperative risk factors in older adults following major elective orthopedic surgery; and, d) to determine the relationship between delirium symptoms and 24 hour opioid intakes controlling for selected preoperative risk factors and pain intensity ratings in older adults following major elective orthopedic surgery. This chapter will focus on delirium and the influence of pain and exposure to opioid medication in the early postoperative period. Current evidence is discussed relative to the significance of subsyndromal delirium in older adults, and the relationship of those symptoms to risk factors related to surgery, including pain and pain treatment.

Pathophysiology of Delirium

Delirium is an adverse outcome that may be an indicator of the quality of care received by hospitalized older patients (Inouye, Schlesinger, & Lydon, 1999). Length of stay, another quality indicator, is increased for patients who develop delirium (Kerr et al., 2010). Delirium has been found to be a costly complication in terms of elderly patient morbidity and mortality as well as costs to the healthcare system (Ely et al., 2007; Leslie et al., 2008; Leslie et al., 2005). Without prevention strategies, the incidence of delirium is expected to increase as the delivery of healthcare changes with technological advances and as life expectancy increases (Inouye et al., 1999b). Risk factor identification and targeting is a common subject in the literature. Delirium is generally thought to be a syndrome related to global brain dysfunction and the underlying mechanisms are poorly understood (Bagri, Rico, & Ruiz, 2008). Current evidence suggests that delirium may result from multiple pathogenic mechanisms, such as drug toxicity, inflammation and acute stress responses that alter neurotransmitter activity and cognitive function (Fong, Tulebaev, & Inouye, 2009). Despite uncertain pathophysiology, researchers agree the etiology of delirium is multifactorial (Potter & George, 2006).

Subsyndromal delirium occurs when one or two of the core symptoms of delirium are present, but are diagnostic of delirium. Subsyndromal delirium may occur on a continuum between no delirium and the full expression of delirium. Very little literature has been published specific to subsyndromal delirium. Thus, a review of the published literature regarding delirium, as well as the available literature of the impact of subsyndromal delirium, is relevant and pertinent. The following review of the literature

examines available qualitative and quantitative evidence of what is known regarding subsyndromal delirium and postoperative pain in older adults.

Qualitative Studies Describing Delirium

Although investigations into the experience of subsyndromal delirium were not located in the literature, findings from a limited number of studies regarding patient, nurse, and family-member experiences of the full syndrome of delirium help provide some insight into the experience. Studies using qualitative descriptive and phenomenology methodology have shed some light on the experiences of patients with delirium.

Patients have described their delirious experiences as a sudden change in reality in which they experience dramatic scenes that generate strong emotions characterized by opposite pairs. Patients report the delirium experience as one that is incomprehensible - one of being in a world that fluctuated between reality and fantasy, clarity and confusion, fear and pleasure. Some delirious patients reported suddenly finding themselves in a world in which the past and present were interwoven, contributing to feelings of discomfort in the experience. Patients stated that, while in a delirious state, they need understanding, support, explanations, and the presence of family and friends (Bélanger & Ducharme, 2011).

Quantitative Studies Focusing on Delirium

The risk of delirium increases with the number of risk factors experienced by the patient (Inouye et al., 1999b). Therefore, nurses must identify patients with risk factors that may contribute to the development of delirium. Different strategies are needed for addressing preoperative risk factors and postoperative risk factors for delirium (Edlund,

Lundström, Brännström, Bucht, & Gustafson, 2001). Inouye et al. (1999b) divided interacting risk factors for postoperative delirium into predisposing and precipitating factors. Predisposing factors contribute to an individual's vulnerability to developing delirium. The identification of predisposing and precipitating factors of delirium allows for the application of preventive strategies (Inouye & Charpentier, 1996).

Predisposing Risk Factors of Postoperative Delirium

Older age has been consistently identified as a risk factor that predisposes to delirium (Kalisvaart et al., 2006; Morrison et al., 2003; Vaurio, Sands et al., 2006) with few exceptions (Andersson, Gustafson, & Hallberg, 2001). Other predisposing risk factors include cognitive deficits (Edlund et al., 2001; Kagansky et al., 2004; Kalisvaart et al., 2006), less education (Jones et al., 2006; Vaurio et al, 2006), visual or hearing deficits (Kalisvaart et al., 2006), decreased functional status (Givens, Snaft, & Marcantonio, 2008; Schuurmans, Duursma, Shortridge-Baggett, Clevers, & Pel-Little, 2003), a history of recent falls (Fong et al., 2009; Korc-Grodzicki et al., 2014), intensive care unit admission (Balas et al., 2007), low body mass index (Bjoro, 2008), comorbidities (Leung et al., 2009; Schuurmans et al., 2003), multiple prescription medications (Björkelund et al., 2010; Kagansky et al., 2004) and depression (Kalisvaart et al., 2006). In addition to older age, cognitive impairment at the time of admission is a very strong predictor of postoperative delirium (Bjoro, 2008; Kalisvaart et al., 2006). Despite wide agreement for cognitive impairment as a risk factor, some researchers have concluded that pre-existing cognitive impairment did not significantly impact on the overall risk of delirium (Balas et al., 2007). Interestingly, a descriptive study of 100 patients found hearing impairment to be associated with receiving less pain medication

and may have placed hearing impaired patients at an increased risk for delirium (Robinson et al., 2008).

Precipitating Risk Factors of Postoperative Delirium

Although some predisposing factors can be identified through preoperative screening, factors present at the time of inpatient admission may not be preventable. However, precipitating factors are typically hospital-related factors that contribute to delirium development in patients. Preventive strategies have typically focused on minimizing precipitating factors in patients at high risk for delirium. Many precipitating factors related to postoperative delirium have been identified: urgent or emergent surgery (Andersson et al., 2001, Kalisvaart et al., 2006), a delayed surgery after hip fracture (Edlund et al., 2001), postoperative complications (Edlund et al., 2001), urinary catheters (Inouye & Charpentier, 1996), sleep deprivation (Missildine, Bergstrom, Meininger, Richards, & Foreman, 2010), prolonged duration of preoperative fasting time (Radtke et al., 2010), and poorly controlled pain (Bjoro, 2008, Vaurio et al., 2006).

The type of surgery can also contribute to the development of postoperative delirium. The incidence of postoperative delirium in orthopedic patients has been found to be highest following hip fracture surgery when contrasted to elective surgeries, suggesting that trauma-related surgery is an important risk factor associated with a higher rates of delirium in older adults (Andersson et al., 2001). Major abdominal surgery placed elderly patients at high risk for delirium in approximately half of older patients who developed postoperative delirium. This high risk may be associated with intraoperative blood loss (Olin et al., 2005). A South Korean study that investigated postoperative delirium in older patients following neurosurgical procedures concluded that severe

postoperative pain requiring treatment with opioids was an independent risk factor (Oh, Kim, Chun, & Yi, 2008).

Unrelieved pain following surgery is a precipitating factor of delirium (Morrison et al., 2003; Lynch et al., 1998) that is potentially modifiable or preventable (Leung, 2010). Preoperative delirium in hip fracture patients may develop as a result of severe pain prior to surgery and usually persists into the postoperative period (Bruce, Ritchie, Blizard, Lai, & Raven, 2005). In elective procedures, higher pain levels in patients who developed postoperative delirium was related to longer duration of delirium symptoms (DeCrane et al., 2011). One of the possible precipitating factors to delirium may be uncontrolled postoperative pain (Morrison et al., 2003; Vaurio et al., 2006).

Subsyndromal Delirium in Older Adults

Subsyndromal delirium develops quickly over a few hours or days and represents an acute change in cognitive function that is not directly related to another cognitive disorder (Blazer & Van Nieuwenhuizen, 2012). Subclinical symptoms of delirium may precede or never progress to delirium (Vollmer et al., 2010). Some variation exists in methodology concerning whether subsyndromal delirium is still considered subsyndromal delirium if it does progress to full delirium. For example, some have defined subsyndromal delirium as the presence of one or two core symptoms according to the CAM delirium diagnostic detection tool, without meeting full criteria for a diagnosis of delirium and not associated with delirium (Cole et al., 2013). However, Vollmer et al. (2010) included cases that progressed to full delirium in their definition of subsyndromal delirium. Subsyndromal delirium that is not associated with delirium usually resolves and lasts from 1-3 days up to 133 days (Cole et al., 2013). Adverse outcomes associated with

subsyndromal delirium are costly: increased falls, longterm care admits, and increased length of stay.

Subsyndromal Delirium and Preoperative Risk Factors

Meta-analysis techniques were used to evaluate relevant articles published from 1996 to June 2011 regarding subsyndromal delirium of adults age 60 or older and included 3 out of 12 studies that investigated surgical patients (Cole et al., 2013). Studies included by the researchers in the systematic review were completed with medical patients in acute, longterm and palliative care units, but the majority of the patients were in medical inpatient units. The review's patient combined sample contained 49% with dementia and a median age of 70. Upon close examination of the review by Cole et al. (2012), only one study of surgical patients was included in the six studies used for the risk factor analysis. The sample utilized in the single study of surgical participants focused exclusively on patients who required hip fracture repair. Patients who sustain a hip fracture represent a population with significantly higher morbidity than typical elective orthopedic joint replacement patients. When selecting risk factors for the proposed research, anticipated population characteristics of the sample were identified. In addition to advanced age, cognitive impairment, and functional impairment, Cole et al. (2012) found dementia, increased severity of physical illness, and higher comorbidities significantly increased the risk for subsyndromal delirium. A significant limitation of the review by Cole et al. (2012) was the mixed sample comprised of both medical and surgical patients; only one study consisted of surgical patients who that were included in the risk analysis. There may be important differences may be found in baseline

characteristics between patients who have elective surgical procedures and those patients who have emergent surgery or are hospitalized for medical conditions.

Subsyndromal delirium may have important implications for delirium prevention. In a study that included 250 medical and surgical inpatients aged ≥65 years, Levkoff et al. (1996) found no significant differences in risk factors for subsyndromal delirium and the full syndrome of delirium. In addition, the study found wide agreement that delirium symptoms represent a spectrum of neurobehavioral impairments rather than a condition with distinct clinical profiles and outcomes (Levkoff et al., 1996; Ouimet et al., 2007; Shim & Leung, 2012). However, Skrobik (2009) disagrees that risk factors for delirium and subsyndromal delirium are the same, denying the notion that subsyndromal delirium is a graded step in the spectrum of brain dysfunction severity (Skrobik, 2009). Despite the disagreement regarding subsyndromal delirium as a spectrum disorder, identification of subsyndromal delirium could help achieve early diagnoses and improve patient management. Criterion typically used to identify those older adults at risk for subsyndromal delirium include age, comorbidity burden, cognitive impairment, recent history of a fall, and prolonged preoperative fasting time (Fong et al., 2009, Radtke et al, 2010).

Age. Older age has been identified as a risk factor that predisposes one to delirium (Kalisvaart et al., 2006; Morrison et al., 2003; Vaurio et al., 2006) with a few exceptions (Andersson et al., 2001; De Jonghe et al., 2007). A review of the literature by Fong, Tulebaev, and Inouye (2009) included advancing age (> 65 years) as a nonmodifiable risk factor for delirium. However, age was not associated with subsyndromal delirium in hospitalized older adults on the medical unit (Cole et al., 2003)

but was a risk factor in the Intensive Care Unit (Ceriana, Fanfulla, Mazzacane, Sanroro, & Nava, 2010). Marcantonio, Ta, Duthie, and Resnick (2002) included age as a risk factor for subsyndromal delirium, but with the cutoff at ≥80 years.

Comorbidity burden. Often, patients present for elective surgery with pre-existing conditions. Comorbidity was associated with subsyndromal delirium in medical inpatients (Cole et al. 2003) as well as surgical inpatients (Marcantonio et al., 2002). The Charlson Comorbidity Index (CCI) (Charlson, Pompei, Ales, & MacKenzie, 1987) was used by Cole et al. (2003) to score the level of comorbidity burden present in patients in an investigation into subsyndromal delirium.

Cognitive impairment. Pre-existing cognitive impairment has consistently been associated with delirium (Edlund et al., 2001; Kagansky et al., 2004; Kalisvaart et al., 2006). In addition to older age, cognitive impairment at the time of admission is a very strong predictor of postoperative delirium (Bjoro, 2008; Kalisvaart et al., 2006). The small number of studies available have started to provides early evidence for cognitive impairment as a risk factor for subsyndromal delirium in both medical inpatients (Cole et al., 2011; Levkoff et al., 1996) and surgical inpatients (Marcantonio et al., 2002).

Impaired mobility. Functional status that impairs mobility has been associated with delirium (Fong et al., 2009; Korc-Grodzicki et al., 2014). Furthermore, a history of a fall in the past 6 months is an independent predictor of postoperative delirium, even more than an abnormal Mini-Cog, a dementia screening tool (Korc-Grodzicki et al., 2014).

Preoperative fasting times. Dehydration that can result from prolonged preoperative fasting times can contribute to delirium risk (Levkoff et al., 1996; Popeo, 2011). A prolonged preoperative fasting time is considered a modifiable risk factor for

the development of postoperative delirium (Leung, 2010). Radtke et al. (2010) found the duration of preoperative fasting time was a risk factor for delirium symptoms in the post anesthesia care unit and on the first postoperative day, but did not assess for delirium symptoms beyond the day after surgery.

Recognition of Postoperative Delirium

Delirium is preventable in 40% of cases overall (Inouye, 2006) and in 50% of cases in medical and surgical patients (Inouye et al., 1999a). Early recognition is critical for prompt treatment of underlying etiologies for the prevention of negative outcomes (Vollmer et al., 2010). Possible reasons for under-recognition may be the transient nature of delirium and varied presentations of the subtypes: hypoactive, hyperactive, and mixed. For example, the hypoactive subtype of delirium was seven times more likely to be unrecognized by nurses in patients with advanced age (80 years of age or more), impairment of vision, or underlying dementia (Inouye, Foreman, Mion, Katz, & Cooney, 2001).

Assessment tools are available to assist in the identification of delirium. The most common tool for delirium detection in the literature was developed by Inouye et al. (1990), the Confusion Assessment Method (CAM). The CAM is a standardized tool developed to be used at the bedside by clinicians or by researchers to identify changes in cognition that may be related to delirium quickly and accurately (Waszynski, 2007). Many of the studies mentioned here utilized the CAM measurement tool (e. g., Inouye et al., 2001; Leung et al., 2009; Morrison et al., 2003; Vaurio et al., 2006; Vollmer et al., 2010; Wang, Sands, Vaurio, Mullen, & Leung, 2007). The CAM is sensitive, specific, and reliable for identification of delirium (Inouye et al., 1990).

Standard pain assessment tools may not always be appropriate for older patients with delirium. However, assessment of behavioral indicators of postoperative pain may be utilized. Decker (2009) identified four pain behavior categories that represent either common or subtle expressions of pain. The behavioral indicators of pain in older adults have commonalities with those signaling the presence of delirium (Decker, 2009). Of course, both pain and the presence of delirium require thorough assessments to determine underlying causes and appropriate treatments.

Nurses spend a significant amount of time at the bedside, making frequent contact with patients. Therefore, nurses play a key role in recognition of patient changes in attention, level of consciousness, and cognitive function necessary to identify delirium so early treatment of the underlying etiologies can be initiated (Inouye et al., 2001). However, delirium remains under-recognized in the hospital setting (Inouye et al., 2001).

In a study comparing researcher and nurse assessments of delirium, nurses often missed indications of delirium, especially in high risk patients (Inouye et al., 2001). These findings suggest additional education is needed for nurses regarding the recognition of delirium symptoms as well as the use of assessment instruments.

Postoperative Pain and Risk for Delirium

Pain management may have a greater impact on delirium incidence than patient related risk factors (Vaurio et al., 2006). However, a systematic review that examined the role of postoperative analgesia in delirium and cognitive decline found no evidence to support the etiological impact of opioids on the development of delirium, with the exception of meperidine (Fong, Sands, & Leung, 2006). Some evidence suggests older patients with postoperative delirium have higher self-reported ratings of pain and use

greater amounts of opioid analgesia than non-delirious patients -- when using patient-controlled analgesia, PCA -- (Leung et al., 2009). Postoperative pain in older adults raises the question of how much the opioid medication contributed to symptoms seen in delirium.

Poorly controlled pain has been identified as a precipitating risk factor for postoperative delirium. However, after a review of the available literature, no studies were found that examined the relationship between subsyndromal delirium and postoperative pain. However, previous work has evaluated the relationship between the full syndrome of delirium and postoperative pain. In a prospective study of 477 patients aged ≥50 years who had major elective non-cardiac surgery, higher resting pain scores were significantly associated with increased risk of delirium with an adjusted risk ratio of 1.20 (Lynch et al., 1998). Subsequent studies have demonstrated pain to be associated with increased postoperative delirium (Morrison et al., 2003; Oh et al., 2008; Vaurio et al., 2006). Morrison et al. (2003) found severe pain to place patients at higher risk for delirium in hip fracture patients. Others have further supported the relationship between higher levels of pain and delirium in other surgical patients. For example, Oh, Kim, Chun, and Yi (2008) identified severe pain to be a risk factor for delirium after neurosurgery.

Pain assessment and delirium. Pain assessment in older adults is often challenging. Nurses may assume a confused patient is not able to use a pain intensity rating scale. Although the validity of self-report of pain in older people with moderate and severe dementia has been controversial, self-report is considered the “gold standard” even in the cognitively impaired patient. Research indicates that individuals with mild to

moderate dementia -- even some with severe dementia -- are able to self-report pain (Closs, Barr, & Briggs, 2004; Closs, Barr, Briggs, Cash, & Seers, 2004; Ferrell, Ferrell, & Rivera, 1995; Taylor, Harris, Epps, & Herr, 2005).

The use of pain assessment self-report rating scales in patients with dementia has been validated through testing of several pain measurement tools (Taylor et al., 2005), but there are no validated pain assessment tools that use self-report specifically designed for patients with delirium. A single study investigated the use of a researcher-developed observational pain assessment tool, the Pain Assessment Tool in Confused Older Adults (PATCOA), for patients with delirium (Decker & Perry, 2003). However, the PATCOA has shown poor correlation with self-reported pain (Leong, Chong, & Gibson, 2006). Behavioral pain measures correlate poorly with self-reported pain scores. Behavioral pain scales are not comparable to self-report pain intensity ratings. However, the Pain Assessment in Advanced Dementia (PAINAD) behavioral scale does have ordinality (Leong et al., 2006). The PAINAD should be used cautiously and only as a part of a comprehensive approach to pain management (Ersek, Herr, Neradilek, Buck, & Black, 2010). However, the PAINAD can be useful as a trigger for an analgesic trial in patients unable to self-report pain (Zwakhalen, Van der Steen, & Najim, 2012).

Pain management methods and delirium. Pain management may have a greater impact on delirium incidence than patient-related risk factors (Vaurio et al., 2006). However, a systematic review that examined the role of postoperative analgesia in delirium and cognitive decline found no evidence to support the etiological impact of opioids on the development of delirium, with the exception of meperidine (Fong et al., 2006). Some evidence suggests older patients with postoperative delirium have higher

self-reported pain ratings and use greater amounts of opioid analgesia than non-delirious patients when using patient-controlled analgesia (Leung et al., 2009). The results suggest delirious patients may have been experiencing more pain than the non-delirious patients. Postoperative pain in older adults raises the question of how much the pain and how much the opioid medication contributed to symptoms seen in delirium.

Reducing pain and agitation in the critical care setting may be important to reduce subsyndromal delirium incidence. In a study of Intensive Care Unit patients for whom a protocol was used for sedation and analgesia, subsyndromal delirium was reduced (Skrobik et al., 2010). No other studies were located that specifically examined the relationship between pain management and subsyndromal delirium.

Selection of opioid medication for pain management. Researchers disagree about the role of opioid intake in the development of delirium. Some have concluded the type of opioid, and the cumulative opioid dose does not increase the risk for delirium (Lynch et al., 1998). A systematic review of studies comparing different opioid medications and their relationship to postoperative delirium found no difference among commonly used opioids (morphine, hydromorphone, and fentanyl), with the exception of meperidine (Fong et al., 2009; Morrison et al., 2003). In contrast, Radkte et al. (2010) reported the choice of intraoperative opioid was predictive of delirium in the postoperative period. Meperidine was more often associated with higher incidence of delirium in older adults than morphine and other unspecified opioids in a large clinical trial (Morrison et al., 2003). No conclusive findings were noted regarding the preferred use of one opioid over another other than the avoidance of meperidine.

Dosage of opioid. Inadequate or low doses of opioid analgesics may increase delirium symptoms in older adults. A retrospective study with a matched-group design of 43 medical-surgical patients compared the pharmacological pain interventions for those who developed delirium with those who did not. The researchers found that less pain medication was given to patients who developed delirium by nearly half of the total dosages given to those who did not (Robinson & Vollmer, 2010). Others have found that low doses of postoperative analgesia are associated with a higher risk of delirium (Bjoro, 2008; Morrison et al., 2003). In fact, some researchers have concluded that those patients who had received more analgesia per day following orthopedic surgery had shorter lengths of stay (Morrison, Flanagan, Fischberg, Cintron, & Siu, 2009). Furthermore, other researchers concluded that concern for postoperative delirium should not prevent opioid administration in sufficient doses to reach acceptable levels of comfort (Sieber et al., 2011).

Route of administration. The route of administration of opioid analgesic may have significant implications for delirium in older adults. Some researchers have found a decreased incidence of delirium when oral opioid analgesics are given to older patients in the early postoperative period instead of using alternative routes of administration of opioid analgesics, such as the intravenous route (Vaurio et al, 2006; Wang et al., 2007). Wang, Sands, Mullen, Vaurio, and Leung (2007) found that patients who receive oral analgesics postoperatively are much less likely to develop postoperative cognitive deficits. However, Williams-Russo, Urquhart, Sherrock, and Charleson (1992) found no significant differences in delirium occurrence when they compared patients following bilateral knee replacement who received intravenous analgesic and those who received

epidural analgesia. Other researchers have also failed to detect a difference in the incidence of delirium dependent on analgesic route (Lynch et al., 1998).

Although two studies were identified that found a decreased incidence of delirium with oral opioid analgesics in older postoperative patients (Vaurio et al, 2006; Wang et al., 2007), no studies were identified that investigated the efficacy of around the clock scheduling of oral opioids in the immediate postoperative period for delirium prevention following major surgery. Vaurio et al. (2006) identified decreased incidence of delirium in older non-cardiac surgical patients who were given oral opioids starting on postoperative Day 1 when compared to other pain regimens. Pain at rest and pain with movement was recorded by the researchers; however, the postoperative pain management method was not controlled in the study and measurements of pain and delirium were completed only in the early postoperative period. Similarly, Wang et al. (2007) found that patients who receive oral analgesics postoperatively are much less likely to develop postoperative cognitive deficits. The literature suggests decreased delirium may result when the oral route is used for opioid administration following surgery.

Williams-Russo et al. (1992) compared a sample of 51 consecutive bilateral knee replacement surgery patients for differences in delirium incidence between those who received intravenous analgesic and those who received epidural analgesia and found no significant differences. Other researchers have also failed to detect a difference in the incidence of delirium related to the analgesic route (Lynch et al., 1998).

Delirium Prevention Strategies

Nurses are primarily responsible for providing adequate pain relief to their patients. Pain, as one of the precipitating risk factors for delirium, may be preventable

through quality nursing care that incorporates frequent assessment of pain using self-report (if possible) followed by appropriate analgesia for pain. Identifying patients at risk for delirium before surgery may allow members of the healthcare team to work collaboratively to take measures to minimize exposure to additional risk. Proactive geriatric consultation was an effective strategy to decrease delirium incidence in hospitalized patients with hip fracture (Marcantonio, Flacker, Wright, & Resnick, 2001). Pharmacological treatment with antipsychotic medication in low doses may be an effective measure to treat delirium symptoms in older patients (Markowitz & Narasimhan, 2008). Recommended nonpharmacological methods include orientation, therapeutic activities, and mobility (Fick, Agostini, & Inouye, 2002).

Demographics, Ethnicity and Delirium

Boustani et al. (2010) found no difference in the incidence of delirium between races or ethnicity. Older Americans are at higher risk for delirium. The male gender has been identified as a risk factor for the development of delirium. Men develop delirium twice as often as women with the exception of hip fracture patients, of which 80% are women (Robinson et al., 2008).

Summary

Although delirium research has increased dramatically in recent years, much remains unknown regarding delirium. Both qualitative and quantitative investigations confirm delirium as a significant problem in older adults following major surgery. Pain increases risk for postoperative delirium in older adults, whereas opioid administration in appropriate dosages may not increase delirium. Although postoperative pain is accepted as a precipitating risk factor for delirium, significant gaps exist in evidence regarding

subsyndromal delirium and its relationship to postoperative pain in older adults. Therefore, the purpose of this study was to determine the relationship between subsyndromal delirium and postoperative pain in older adults following major elective orthopedic surgery.

CHAPTER III

METHODS

The purpose of this study was to determine the relationship between subsyndromal delirium and pain in older adults following major elective orthopedic surgery. The specific aims examined in this study were: a) to determine the frequency of delirium symptoms and the frequency distribution of preoperative risk factors, pain intensity ratings and 24 hour opioid intakes of patients age 65 years and older following major elective orthopedic surgery; b) to determine the relationship between delirium symptoms and the preoperative risk factors in older adults following major elective orthopedic surgery; c) to determine the relationship between delirium symptoms and pain intensity ratings controlling for preoperative risk factors in older adults following major elective orthopedic surgery; and, d) to determine the relationship between delirium symptoms and 24 hour opioid intakes controlling for selected preoperative risk factors and pain intensity ratings in older adults following major elective orthopedic surgery. This chapter presents the study design, sample and setting, procedures, tests and measures, data management and analysis, and human subjects protection. Data analyses were discussed separately for each of the study aims.

Study Design

This prospective study used a correlational design to determine the relationship between subsyndromal delirium and postoperative pain in older adults following major

elective orthopedic surgery. A correlational design is appropriate for the examination of relationships among variables that contribute to an outcome of interest. This study examined whether or not subsyndromal delirium was related to levels of self-reported pain in older adults who underwent major elective orthopedic surgery.

Because pain is an independent risk factor for delirium (Morrison et al., 2003; Vaurio et al., 2006), this study sought to understand the relationship between subsyndromal delirium and postoperative pain. More specifically, the role of postoperative pain levels in predicting subsyndromal delirium was examined. Like delirium, subsyndromal delirium is thought to be multifactorial in nature. Thus, a research investigation that seeks to examine the phenomenon of subsyndromal delirium must consider multiple covariates as potential contributors to the outcome. For this study, Inouye and Charpentier's (1996) multifactorial model for delirium was used as the theoretical framework. Inouye and Charpentier conceptualized delirium as a multifactorial phenomenon resulting from an interaction of predisposing and precipitating factors where risk is increased with each additional risk factor. Multiple regressions were planned to allow for an examination of the impact of postoperative pain on subsyndromal delirium when there are multiple possible covariates.

Sample and Setting

A consecutive sample of older adults scheduled for major elective orthopedic surgery was planned for recruitment to the study. The primary site was a rural hospital in the northwestern region of the United States. The area is a popular retirement destination for older adults - thus contributing to a higher percentage of older adults in the local population than in the national average (United States Census Bureau, 2010). Inclusion

criteria were selected to obtain a sample of individuals who were likely to be at risk for developing delirium symptoms. Preoperative risk factors for subsyndromal delirium identified from the literature included increased number of comorbidities, cognitive status, history of recent fall (within 6 months), and the duration of preoperative fasting times. The hospital selected as a research site typically performed two to three major orthopedic surgeries each week, although not all patients met the eligibility criterion for participants to be 65 years of age or older. The post-surgical unit was a general medical-surgical unit with a specially trained orthopedic nurse designated to oversee the postoperative care of the orthopedic patients each day. Enrollment of participants took place between August 2013 and May 2014.

Inclusion Criteria

Eligible participants were (1) scheduled to undergo major elective orthopedic surgery with an expected length of stay of at least 48 hours; (2) ≥ 65 years of age; and (3) English-speaking. The composition of the sample was more homogenous than anticipated (98% Caucasian, $n = 52$; and, 2% American Indian, $n = 1$) given the proportions of race/ethnicity in the region (92% Caucasian, 3% Hispanic, 3% American Indian, and Others <1% (United States Census Bureau, 2010).

Exclusion Criteria

Participants were excluded if they had (1) pre-existing delirium as determined by preoperative delirium screening using the CAM algorithm at the time of enrollment; or (2) an inability to utilize the Iowa Pain Thermometer pain intensity rating scale. Capability to use the Iowa Pain Thermometer was evaluated preoperatively by way or return demonstration. Successful use of the Iowa Pain Thermometer by potential

participants was evidenced by an ability to state the verbal descriptor from the scale, report a numeric value for pain, or point to the level of pain when asked. Consenting older adults with cognitive impairment were invited to participate in the study if they demonstrated an ability to use the Iowa Pain Thermometer and met the other eligibility criteria. Verbal descriptors were recorded using the corresponding values on the thermometer on the 0-10 scale.

Given the elective nature of this type of surgery and the negligible death rate within the first 3 days following major elective orthopedic surgery, expected loss due to death or attrition was estimated at 5%. Consistent with reports from the clinical research director at a research site in the same geographical region, a typical refusal rate was estimated at 11.8% (Laukes, *Montana Neuroscience Research Institute,* personal communication, March 7, 2013). A power analysis program developed through National Institute of Health funding (Borenstein, Rothstein, Cohen, Schoenfield, & Berlin, 2001, *Power and Precision Version 2: A statistical program for statistical power analysis and confidence intervals*), was used to verify that 53 participants were required for a statistical power of .80 with an alpha of .05 ($\alpha = .05$) and the conventional effect size of 0.30 ($f^2 = 0.30$) (Cohen, Cohen, West, and Aiken, 2003). After accounting for anticipated attrition (5%) and refusal (11.8%), the power analysis indicated that a sample of 62 participants should be recruited for a sample of 53 participants to complete the study. The refusal rate by potential participants was 14.5% ($n = 9$). Following enrollment, two enrolled participants (3.8%, $n = 2$) requested to withdraw for the following reasons: one patient reported he was too ill to continue participate due to severe pain, and the other patient reported uneasiness with the questions used in the cognitive assessment. Both of

the participants who withdrew consented to have their data collected by the researcher up until the time of their withdrawal used for the study.

Procedures

Procedures followed in this study are described in the following section. Procedures for informed consent, sampling and recruitment process, staff training, instruments and measurements, and analysis of data were put in place prior to recruitment of participants.

Informed Consent

At the initial meeting with potential participants, the researcher provided information regarding the purpose of the proposed study, rights of study participants, potential risks and adverse effects, and the duration of study participation. Patient comprehension of the presented information was assessed by the researcher followed by an opportunity for potential participants to have all of their questions answered prior to enrollment in the study. The PI was careful to tell patients that participation in the study was voluntary and that they were free to withdraw at any time. When informed consent was granted, two consent forms were signed by the participant. The participant was given one of the signed consents, and the other consent was kept by the researcher. The consent forms will be kept by the researcher for a time period of four years, as recommended by Erlen (2005). Each partcipant was given a folder that contained the signed consent, contact information for the researcher, an Iowa Pain Thermometer for home use, and instructions related to information to be recorded if discharge occurred prior to the completion of the 72 hour study period.

Sampling and Recruitment Process

A consecutive sample of 62 older adults age 65 or older scheduled for major elective orthopedic surgery were eligible for participation in this study. Figure 2 presents the flow diagram of enrollment of participants into this study. Concerns regarding the introduction of confounding factors and practical considerations of access necessitated narrowing the sample to patients scheduled for elective orthopedic procedures.

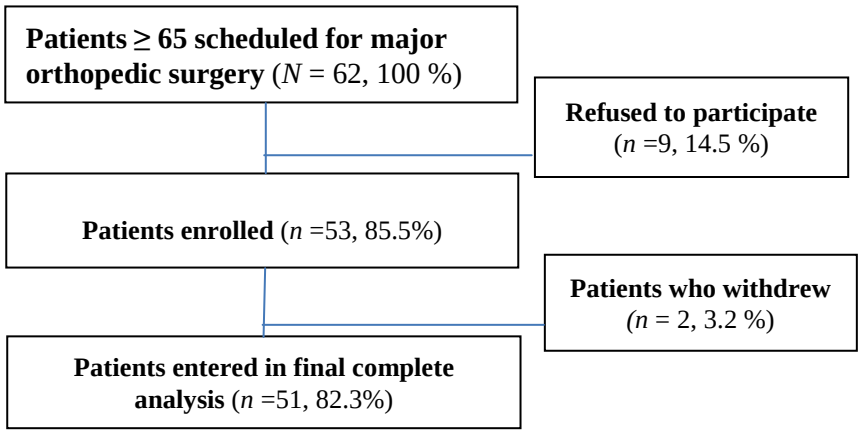
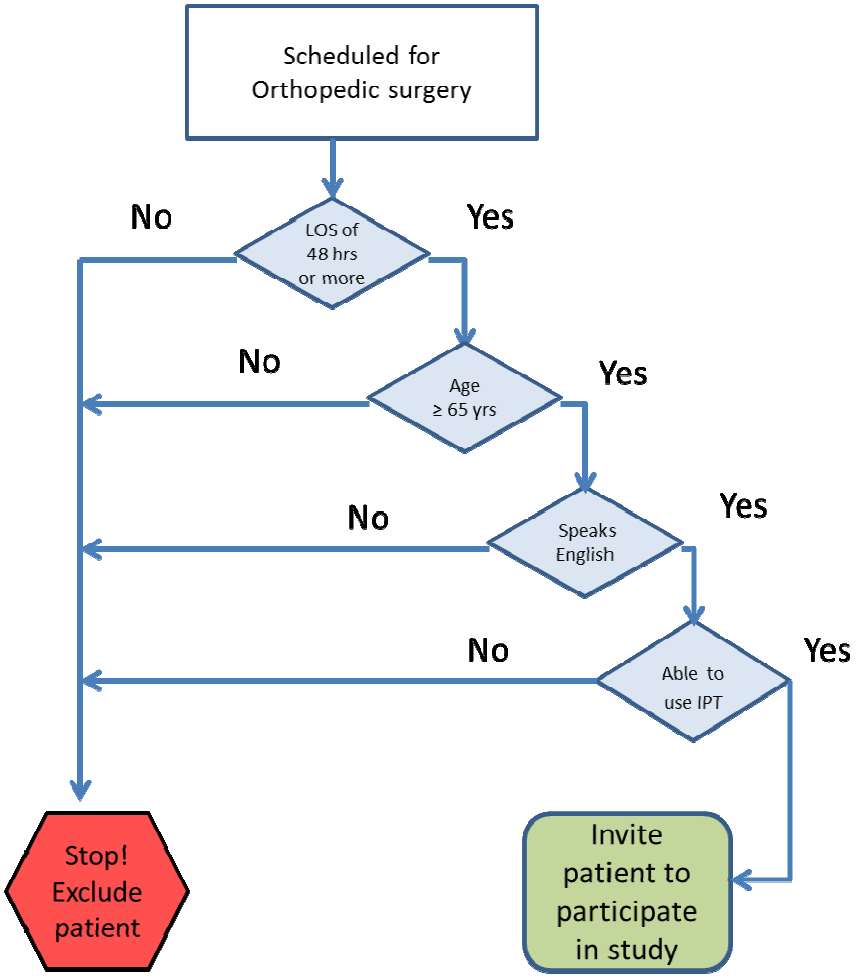


Figure 2. Flowchart of participant enrollment. Percentages reflect portions of the intended study sample size of 62 participants. The prospective consecutive sample included 53 patients who underwent major elective orthopedic surgery with a final sample size of 51 following the withdrawal of 2 participants.

Recruitment. At the time of the preoperative appointment, potentially eligible participants were screened by preoperative nurses according to inclusion and exclusion criteria. Figure 3 presents the algorithm used by the preoperative nurses to identify eligible participants for this study. Patients that met the algorithm criteria were invited to participate in the study. If requested by the patient, the preoperative nurse notified the researcher of the patient's name, phone number, and the date of the planned surgery. An information technology specialist at the research site set up an internal auto-email system from the computerized postoperative assessment to facilitate consistent notification to the

researcher through the in-agency email. The email was triggered by a 'yes' response to the question embedded in the assessment that asked whether the patient was interested in participation in the "pain study". Following notification of a patient interested in participating in the study, the researcher arranged for a time to meet with the patient prior to the scheduled surgical procedure.



LOS= length of stay
IPT= Iowa Pain Thermometer

Figure 3. Eligibility algorithm for study participation. Preoperative nurses used the algorithm to determine eligibility for participation in the study.

Following informed consent, it was necessary to verify each participant's preoperative status. Information was gathered in an interview with each participant. The interview included completion of a demographic questionnaire, a delirium assessment, and a dementia screen. Participants were then instructed in the use of the Iowa Pain Thermometer and asked to rate their pain at rest and with activity.

Demographic information. Demographic information collected at the time of enrollment included age, gender, race/ethnicity, and living arrangement (See Appendix B). In addition, information regarding past medical history, comorbid conditions, recent fall history, and current medications was recorded during the patient interview. In addition, functional status was assessed using the short form of the Barthel Index of Activities of Daily Living (ADL) (Hobart & Thompson, 2001) and scored prior to surgery on the basis of observations and/or self-report from patients and/or proxies at the time of enrollment. The score for Barthel Index is a sum of five ADL items: transfers, bathing, stairs, toilet use, and mobility with a range from 0 (completely dependent) to 5 (completely independent). The Barthel Index has been reported to have excellent reliability and validity and adequate responsiveness to change when measuring physical disability in older patients with musculoskeletal problems (Collin, Wade, Davies, & Horne, 1988).

Delirium, cognitive, and pain assessments. A delirium assessment in conjunction with a cognitive assessment was completed to confirm the participant did not have delirium. In conjunction with the delirium assessment, the researcher used a cognitive assessment/dementia screen. If participants had an abnormal cognitive assessment indicating dementia, the information was recorded as a positive dementia

screen. A positive delirium screen excluded patients from eligibility for the study; whereas a positive dementia screen did not exclude patients. Instruction was given regarding use of the Iowa Pain Thermometer and an assessment of the patient's ability to use the scale was completed. In addition, the participant was asked to use the Iowa Pain Thermometer pain scale to rate their pain.

Early discharge procedures. In anticipation of the possibility of discharge of study participants from the research site prior to completion of the data collection period, an alternative data collection procedure was developed to facilitate continued data collection through the 72 hour period. The alternative procedure required the researcher to conduct a phone interview following the third 24-hour postoperative time period. This follow-up procedure facilitated completion of data collection for 32.3% (n = 17) of the study participants. Telephone assessment of delirium has been effectively used to identify delirium in adults 65 years or older (Marcantonio, Michaels, & Resnick, 1998). As suggested by Marcantonio, Michaels, and Resnick (1998), the Delirium Symptom Interview (DSI) (Albert et al., 1992) was used to elicit specific symptoms of delirium in combination with cognitive testing and was found to have a sensitivity of 1.00 and a specificity of 0 when compared to face-to-face interviews (Marcantonio et al., 1998) (See Appendix C). The phone interview took approximately 15-20 minutes. The information gained from phone interviews was used to complete the CAM diagnostic algorithm in order to detect delirium symptoms. As part of the phone interview, the researcher asked participants to verbally report the Iowa Pain Thermometer pain intensity ratings since their discharge home and what pain medications they had taken since arriving home. Participants received early discharge instructions in study folders given to them at the

time of enrollment. Study folders contained the following information: contact information for the researcher, an Iowa Pain Thermometer, and instructions with a table for the recording pain intensity ratings every 4 hours and the time, dose, and name of pain medications taken. Data were collected by the researcher over the phone on the day following discharge.

Timing of Delirium Assessments

Postoperative delirium typically emerges 24 to 48 hours following surgery and may resolve within 48 hours (Sieber, 2009). Therefore, 3 delirium assessments were completed: 1) at least 24 hours after arrival on the post-surgical unit on the first postoperative day, 2) at least 48 hours after arrival on the post-surgical unit on the second postoperative day, and 3) at least 72 hours after arrival on the post-surgical unit on the third postoperative day. Physician progress notes, nurse report to the researcher, and nursing documentation were reviewed to further identify the presence of delirium symptoms at any time following arrival on the post-surgical unit. The information from the medical record supplemented the daily delirium assessments completed by the researcher in order to capture fluctuating symptoms characteristic of delirium symptoms.

Pain Assessment and Treatment

Nurses were asked to record pain intensity ratings every four hours in the computerized documentation system as part of their routine charting for study participants. Pain intensity ratings recorded by physical therapists or occupational therapists were used to supplement nursing documentation. Nursing documentation and medication administration records were accessed following discharge to collect information regarding pain intensity ratings and opioid intake. Mean pain scores and 24-

hour opioid intake from 0 to 24 hours, 24 to 48 hours, and 48 to 72 hours following arrival on the post-surgical unit -- overall for the 72 hour study period -- were calculated from data in the medical record retrospectively prior to data analysis.

Communication with the Healthcare Team

Notification of the health care team on the day of a participant's surgery occurred according to a protocol developed collaboratively with the research site's orthopedic coordinators. According to the study notification protocol, upon arrival of a study participant on the post-surgical unit following surgery, the health unit clerk ensured the patient's chart was clearly identified as a study participant on both the written and in the computerized chart to alert the health care team. In addition, the orthopedic coordinator placed a placard with the Iowa Pain Thermometer and a notation on the whiteboard in the patient room of the patient's participation in the "Denny Pain Study". The white board in the patient rooms is used by the facility as a tool for communication of important information between various members of the health care team regarding the patient's plan of care.

Staff Training

In preparation for the start of the research investigation, two one-hour educational sessions were held, one for the orthopedic nurse coordinators and another separate session for the preoperative nurses. In addition, one-on-one meetings with the health unit clerks were arranged to describe the procedures related to identification of patients as study participants and their role in facilitating communication of study participation of a patient to the health care team.

All educational sessions included training in the protection of human subjects as well as an overview of the research project. Preoperative nurse education included explanation of the process for study eligibility screening. Each preoperative nurse received a laminated copy of the eligibility algorithm for identification of eligible patients during the routine preoperative appointment. In addition, each preoperative nurse received a typewritten script for use when informing eligible patients of the study opportunity (See Appendix D). Lastly, the researcher explained use of the Iowa Pain Thermometer so that the preoperative nurses could assess patients' ability to use the pain intensity rating scale. Unit nurses were also instructed by the researcher regarding the use of the Iowa Pain Thermometer. A small booklet was prepared and placed at each nursing station at the research site for staff to access information regarding the study and the protocols involved (See Appendix E). In addition, a detailed email was sent to all of the unit nurses with a concise description of the study and the associated protocols. All staff concerns and questions regarding the project were addressed with additional explanations through in-person one-on-one communications.

Throughout the data collection period, daily visits were made to the research site while study participants were in the hospital to complete delirium assessments and passive surveillance. The research site's three orthopedic nurse coordinators assisted with monitoring of staff compliance with study procedures. Ongoing training to new employees or those unfamiliar with study procedures was completed informally by the researcher to new employees or those unfamiliar with study procedures throughout the nine month data collection period.

Tests and Measures

After informed consent was obtained, each participant was screened for dementia using the Mini-Cog (Borson, Scanlan, Brush, Vitaliano, & Dokmak, 2000), and for pre-existing delirium using the Confusion Assessment Method (CAM) (Inouye et al., 1990). Although none of the participants in this study were positive for delirium symptoms at the time of the initial preoperative meeting in this study, had delirium symptoms been detected at the time of enrollment, the participant would have been excluded from participation. A demographic questionnaire was completed at the time of the initial meeting as well. Variables and instruments are described in detail in the following sections. Table 2 summarizes the various instruments -- including variables and their measurement -- and indicates a timeline for data collection.

Delirium Assessment

Postoperative delirium typically emerges 24 to 48 hours following surgery and may resolve within 48 hours, although it may persist for months in some older patients (Sieber, 2009). Delirium assessment was completed initially to screen for pre-existing delirium to determine eligibility for participation in the study and postoperatively on Day 1, 2, and 3 by the PI using the CAM (Inouye et al., 1990). Both the full expression of delirium and subsyndromal delirium were recorded.

The CAM, a diagnostic tool highly sensitive for delirium, was designed for use by non-physician clinicians (Inouye et al., 1990) (See Appendix F). Inouye et al. reported high interobserver reliability for the presence or absence of delirium (κ = .81 – 1.00) and moderate concurrent validity with the Mini-Mental State Exam (κ = 0.64).

Table 2

Study Variables and Instruments

Variables	Indicator or Instrument	Data Source	Level of Measurement	Timing of Measurement
Delirium Assessment				
Delirium Symptoms	Confusion Assessment Method (CAM), shortened version	Patient interview, patient chart, staff interview	Interval	At 24, 48, and 72 hours after patient arrival in post-surgical unit
Pain Treatment and Assessment				
Total 24-hour opioid intake (in milligrams)	Equianalgesic dose of parenteral morphine sulfate for opioid intake over a 24 hour period	Patient chart	Continuous	Post-discharge
Pain intensity ratings	Iowa Pain Thermometer (0-10 scale) (IPT)	Patient interview, pain assessment data from patient chart	Continuous	Every 4 hours for postoperative days 1, 2, and 3
Preoperative Risk Factors				
Comorbidity burden	Charlson Comorbidity Index (CCI)	Patient interview, patient chart	Continuous	Enrollment
Cognitive impairment	Mini-Cog score (0 to 3)	Patient interview	Continuous	Enrollment
Recent fall history	Number of falls in the past 6 months	Patient and family member interview	Continuous	Enrollment
Fasting time	Preoperative fasting duration in hours	Patient report, patient chart	Continuous	Post-discharge
Supplemental instrument				
Delirium assessment	Delirium Symptom Interview (DSI)	Interview of patient and family per phone;	N/A[a]	Supplemented CAM post-discharge to identify symptoms

Note. [a]The Delirium Symptom Interview instrument was used to identify CAM delirium symptoms.

Detection of full delirium requires positive findings of the first two core symptoms (fluctuating course and inattention) on the CAM and at least one of the other two core symptoms (disorganized thinking and altered level of consciousness). The present study used categorization of subsyndromal delirium cases, a positive finding for one of the core symptoms of delirium on the CAM algorithm was designated as

subsyndromal delirium 1 (SSD-1), and those with positive findings for two of the core symptoms of delirium on the CAM were designated as subsyndromal delirium 2 (SSD-2). The core symptoms of delirium included acute onset and fluctuating course, inattention, disorganized thinking, and altered level of consciousness. In this study, if a patient was assessed as having full delirium through delirium assessments performed as part of this study's protocols, a notification was left for the patient's physician.

The CAM has been used in previous studies to detect subsyndromal delirium as well as full delirium (e.g., Cole et al., 2012; & Cole et al., 2011). In this study, the CAM was used to detect the presence of any of the four core delirium symptoms to identify either SSD-1, SSD-2, or full delirium. Each delirium assessment was accompanied by the Mini-Cog cognitive evaluation (See Appendix G) because the performance of the CAM might be compromised if used without cognitive testing (Fong et al., 2009). The delirium symptoms identified using the CAM were not equivalent to an expert clinical diagnosis of delirium.

Pain Intensity

Pain intensity ratings were measured using the Iowa Pain Thermometer (IPT), a continuous scale depicted on a diagram of a thermometer with six verbal descriptors (Herr, Spratt, Garand, & Li, 2007). The developers reported reliability of the IPT scale across three scales, the Iowa Pain Scale, the Faces Pain Scale Revised (FPS-R), and the Numeric Rating Scale (NRS). The intraclass correlation of the three scales across single retrospective ratings of worst, least, and average pain ranged from 0.922 to 0.959 ($p<.001$) and high concurrent validity ($r = .78 - .98$). Rationale for selection of the scale for the current study included that the IPT may be preferred by older adults (Li, Herr, &

Chin, 2009) and is excellent for patients with cognitive deficits (Taylor et al., 2005). The version of the IPT used in this study incorporated a 0-10 scale facilitating the collection of pain data from documentation that had been entered into the research site's computerized documentation system (See Appendix H).

Twenty-Four Hour Opioid Intake

Opioid intake totals were calculated for each 24 hour period after surgery following all CAM assessment. The name, amount, and route of medications administered during the three study days were extracted from the patient chart and from post-discharge phone interviews and were recorded on the data collection form. All opioid analgesics were converted to parenteral morphine equivalents in milligrams using an equianalgesic conversion calculator (Kane, 2014). Conversion of opioid doses to an estimated comparable dose of intravenous morphine sulfate was necessary to provide a means for comparison of diverse opioid medications and dosages given. These standardized equivalent doses were then summed to provide a total 24 hour dose for each participant for each of the three 24-hour periods and for the three postoperative days (a 72-hour period).

Preoperative Risk Factors

Comorbidity burden. The Charlson Comorbidity Index (CCI) (Charlson, Pompei, Ales, & MacKenzie, 1987) was used to classify patients by comorbidity burden (See Appendix I). Charlson, Pompei, Ales and MacKenzie (1987) developed the CCI to estimate risk for mortality and the overall burden of comorbid disease. The CCI includes 19 diseases weighted on the basis of the strength of their association with mortality, which is then combined with age to calculate a score (higher scores representing a higher

burden of comorbidity). The CCI is the most extensively studied comorbidity index with correlation coefficients with other comorbidity indexes of over .40 as well as significant correlations with mortality, disability, readmissions, and length of stay (DeGroot, Beckerman, Lankhorst, & Bouter, 2003). Increased CCI scores are associated with increased delirium (Korc-Grodzicki et al., 2014).

Cognitive status. Dementia screening using the Mini-Cog (Borson et al., 2000) was completed at the time of initial assessment as part of baseline demographic information to detect pre-existing cognitive impairment prior to assessment of pre-existing delirium, as recommended by Lemiengre et al. (2006). The Mini-Cog required approximately 3-5 minutes for the researcher to administer. The Mini-Cog has been tested extensively and has high sensitivity (0.99) and very high reliability (r =.97, P <0.001) regardless of educational level of the patient (Doerflinger, 2007). Results from the Mini-Cog indicated either the presence of dementia or no dementia. The presence of dementia significantly increases the risk of the development of delirium (Inouye, 2002). Cognitive status is a non-modifiable predisposing risk factor for subsyndromal delirium (Cole et al., 2012). Positive screens for dementia using the Mini-Cog were not equivalent to an expert clinical diagnosis of dementia.

Recent fall history. A history of a fall in the past 6 months is an independent predictor of postoperative delirium, even more than an abnormal Mini-Cog, a dementia screening tool (Korc-Grodzicki et al., 2014). Participants were asked if they had fallen in the previous 6 months at the time of enrollment. Recent fall history was calculated as the sum of the number of falls a participant had sustained within the previous six months.

Information from the medical record supplemented information from the patient interview to determine if the participant had sustained any recent falls.

Preoperative fasting time. Duration of preoperative fasting time (for liquids or solids in hours) was calculated from the last known time of oral intake to the start time of surgery. If the time of the participant's last oral intake prior to surgery was not known, it was calculated from midnight of the night preceding surgery. Long preoperative fasting times may alter the fluid and electrolyte balance in older surgical patients increasing their risk for postoperative delirium (Radtke et al., 2010).

Demographics

Demographic variables to describe the patient sample include age at the time of the surgical procedure, gender, marital status, residence, and living arrangement. Demographic variables were also potential predisposing risk factors for delirium. Age at the time of the surgical procedure was the number of completed years of life and subsequent months (expressed as a proportion of a year) derived from the date of birth and the date of the planned surgical procedure (for example, 65 years and 6 months, was recorded as 65.5). Living arrangement at the time of enrollment was recorded as follows: lives alone, with spouse, with other relative, with non-relative, with live-in paid caregiver, or in a long-term care facility. Also, specific information regarding the perioperative period was recorded (surgical procedure performed, length of procedure, type of anesthetic, intraoperative medications given, intravenous fluid volume given during the procedure). Preoperative and postoperative laboratory data relevant to delirium risk were extracted from the patient's medical record and recorded (e.g., hemoglobin,

hematocrit, creatinine, blood urea nitrogen, sodium, and potassium), and discharge disposition.

Data Collection Process for Cases of Early Discharge

The use of a supplemental instrument allowed the researcher to gather information needed in order to complete the CAM diagnostic algorithm when participants discharged home prior to the final delirium assessment. The Delirium Symptom Interview (DSI) (Albert et al., 1992) is "an extensive operationalization of the DSM-III criteria" for the diagnosis of delirium (Lindesay, Rockwood, & Macdonald, 2002, p. 17). The DSI was utilized to identify symptoms of delirium on the CAM, but is neither diagnostic nor a severity scale (Marcantonio, Flacker, Michaels, & Resnick, 2000). In this study the DSI was utilized to identify delirium symptoms on the CAM algorithm over the telephone when a participant was discharged prior to completion of the 72-hour study period. The tool is appropriate for assessment over the phone and requires approximately 15-20 minutes to complete. The DSI relies on patient answers to 60 questions as well as 50 supplemental questions for a proxy (caregiver, lay person, or family member) regarding observations of the patient. The DSI has been used with the CAM in previous works to identify symptoms on the CAM algorithm (e.g., Flacker et al., 1998).

Data Analysis and Management

Data analysis strategies are described for management of missing data, estimation of outliers, and evaluation of assumptions for data analysis techniques and evaluation of reliability of data. Data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 17.0. Frequency distributions and explorative techniques were

used to evaluate data for accuracy, evaluate the distribution of missing data, estimation of outliers, and adherence to assumptions of data analysis techniques. The following section will describe how strategies to reduce missing data were implemented.

Missing Data

The amount of missing data for the individual variables varied. While many of the variables did not have missing data, some variables had a small amount of missing data (CAM score, mean pain intensity rating, 24-hour opioid intake). The group mean substitution method was selected to allow for variances among the different surgical procedures represented within the dataset and is more conservative than using prior knowledge to replace missing values (Tabachnick & Fidell, 2011). The replacement method involved inserting a group mean for the missing value based on the surgical procedure. For example, replacement of missing values for a participant who underwent total knee arthroplasty would be replaced with the group mean of the variable for all of the participants who underwent total knee arthroplasty procedures in the study. Group mean substitution for missing values was completed prior to data analyses. The amount of missing data was less than 5% for delirium CAM assessments, 6.3% for pain intensity scores, and 5.7% for 24-hour opioid intakes. Some missing data resulted following the withdrawal of two participants after the first postoperative day. However, both patients agreed to allow continued data collection without additional interviews. Other reasons for missing data included missing pain scores in the nursing documentation and loss to follow-up after early discharge of one participant.

Management of Outliers

Statistical and graphical methods were used to identify outliers. Independent variables were examined utilizing boxplots to identify values outside two standard deviations of the sample mean. Potential outliers were examined for each variable for accuracy. No adjustment for outliers was made to avoid losing meaningful data.

Data Analysis Techniques

Hierarchical regression was selected to analyze the relationship between study variables. Hierarchical regression is a method of multiple regression in which the order predictors are entered into the regression model are determined by the researcher based on previous research (Field, 2009). According to Field (2009), predictors from previous research should be entered into the model first in the order of importance, followed by any new predictors. According to Inouye and Charpentier's (1996) multifactorial model for delirium, risk for delirium increases with each additional risk factor present. Therefore, in order to determine the relationship between delirium symptoms and the independent variables of pain and opioid intake, it was important to account for the influence of other known risk factors for delirium (comorbidities, cognitive status, recent fall history, and preoperative fasting time) in data analyses through the use of hierarchical regression.

Routine pre-analysis screening procedures were used to evaluate normality, linearity, and homoscedasticity. Statistical and graphic methods were used to evaluate the statistical assumptions for linear multiple regression. The mean substitution method was used to replace missing values as described by Tabachnick and Fidell (2007).

In this study, delirium core symptoms (according to the CAM algorithm) were counted from “0” (when no symptoms of delirium were present) to “3” (when 3 or 4 of the four core symptoms of delirium were present). Consistent with Inouye and Charpentier’s multifactorial model, delirium symptoms were assumed to be additive and accumulative in nature for data analysis. The number of core symptoms identified in each CAM assessment (on a scale from 0 to 3) was recorded and utilized for data analysis. With each additional core symptom identified with the CAM, an increase in the number of delirium symptoms present, rather than an increase in severity.

For the primary outcome of subsyndromal delirium, the frequency of delirium symptoms was calculated based on the maximum number of symptoms identified in participants using the CAM algorithm in daily patient interviews. The incidence of SSD-1, SSD-2, and full delirium was calculated for each of the three postoperative days and overall for the 72 hour study period. The frequency distributions of select preoperative risk factors (increased comorbidity burden, cognitive impairment, the presence of a recent fall history, and a longer duration of preoperative fasting time), pain, and opioid intake were evaluated for normalcy and multicollinearity prior to entering the variables into the regressions.

Regression analyses were utilized to determine the relationship between subsyndromal delirium and postoperative pain while accounting for the preoperative risk factors (increased comorbidity burden, cognitive impairment, the presence of a recent fall history, and a longer duration of preoperative fasting time) for each of the three 24-hour periods and for the full 72 hours following surgery. Secondly, regression analyses were

utilized to determine the relationship between subsyndromal delirium and 24-hour opioid intakes while controlling for preoperative risk factors, and pain.

Data collection forms were used by the researcher to enter data into a computerized database for analysis using SPSS, a statistical management system. All data files were stored on the researcher's home computer and were password protected using encryption technology. All files were thoroughly inspected a second time to ensure accuracy. Frequency distributions and explorative techniques were used to identify inconsistencies and impossible values.

An assumption of linear multiple regression is that the outcome will be normally distributed in the population, although not necessarily in the sample (Cohen et al., 2003). For the current study, the population consisted of older adults age 65 and older who undergo major elective orthopedic surgery electively. The model of multiple regression posed by Cohen et al. (2003) that assumes that the dependent variable (subsyndromal delirium) is randomly sampled for each of the predictors was applied in this study. Each of the three 24-hour periods following surgery were analyzed through a separate hierarchical regression analysis. Preoperative risk factors were entered hierarchically (comorbidity score, cognitive score, the number of recent falls, and preoperative fasting time) with the delirium symptoms as the dependent variable. Statistical Package for the Social Sciences (SPSS) software was utilized to facilitate data analysis.

The following aims were examined to determine the relationship between subsyndromal delirium and postoperative pain in older adults who underwent major elective orthopedic surgery and, secondarily, to determine the relationship between subsyndromal delirium and 24-hour opioid intake in older adults who underwent major

elective orthopedic surgery. Data analysis was discussed separately for each of the study specific aims in the following section.

Aim 1. The first aim was to determine the frequency of delirium symptoms and the frequency distribution of preoperative risk factors, pain intensity ratings and 24 hour opioid intakes of patients age 65 years and older following major elective orthopedic surgery. Frequencies were addressed through evaluation of descriptive statistics, including means, medians, and variances for delirium symptoms. Frequency distributions of preoperative risk factors, pain intensity ratings, and 24 hour opioid intake were evaluated for normality through graphical and statistical methods. Significance levels were set at .05 ($\alpha = .05$, 2-tailed).

Aim 2. The second aim was to determine the relationship between delirium symptoms and the preoperative risk factors in older adults following major elective orthopedic surgery. In order to determine the relationship between subsyndromal delirium and the preoperative risk factors, correlational and hierarchical linear regression analyses of preoperative risk factors of participants (comorbidity burden score, cognitive score, number of recent falls, and duration of preoperative fasting time) and delirium symptoms were used to assess the direction and the degree of relationships between the preoperative risk factors and delirium symptoms.

The Charlson Comorbidity Index was used to obtain a comorbidity score and ranges from 0 to 31. To obtain cognitive scores for participants, the Mini-Cog's three-item memory test score completed at the time of enrollment was recorded for each participant. The three item memory component of the Mini-Cog is scored from 0 to 3 with "0" representing demented, and a '3' representing non-demented, a normal finding.

In addition, the other component of the Mini-Cog, the Clock Drawing Task, was recorded for each participant. A score of 0, 1, or 2 with an abnormal Clock Drawing Task indicates the probable finding of dementia. Of the two component tests of the Mini-Cog, the most powerful element is the three-item recall (Borson, et al., 2000). Recent fall history was recorded as the number of falls reported by participants in the past six months.

Aim 3. The third aim was to determine the relationship between delirium symptoms and pain intensity ratings controlling for preoperative risk factors in older adults following major elective orthopedic surgery. To evaluate whether subsyndromal delirium was associated with postoperative pain while accounting for variance associated with preoperative risk factors. Delirium symptoms identified from completion of the CAM at 24 hours following surgery were entered into the regression model as the dependent variable. Preoperative risk factors (comorbidity burden, cognitive status, history of a recent fall, and preoperative fasting time) were entered hierarchically into the multiple (linear) regression equation. Next, mean pain intensity ratings for the first 24-hour period following participant arrival on the post-surgical unit (0 to 24 hours) were entered into the regression model. Regression analyses for the relationship of pain on delirium symptoms were repeated for the second (24 to 48 hours), the third (48 to 72 hours) 24-hour periods, and overall for the entire 72 hour study period.

Aim 4. The fourth aim was to determine the relationship between delirium symptoms and 24 hour opioid intakes controlling for selected preoperative risk factors and pain intensity ratings in older adults following major elective orthopedic surgery. To evaluate whether subsyndromal delirium was associated with 24-hour opioid intake while accounting for variance associated with preoperative risk factors and postoperative pain,

the delirium score from the CAM assessment at 24 hours was entered into the regression model as the dependent variable. To control for the influence of preoperative risk factors (comorbidity burden, cognitive status, history of a recent fall, and preoperative fasting time) on delirium symptoms at 24 hours, they were entered hierarchically into the regression analysis. Next, mean pain intensity rating for 0 to 24 hours (starting at the time of the participant's arrival in the post-surgical unit) was entered into the regression model. Lastly, 24-hour opioid intake for 0 to 24 hours was entered into the regression model. Regression analyses were repeated for the time periods of 24 to 48 hours and from 48 to 72 hours following surgery. An additional analysis was also calculated for the entire 72 hour study period.

The purpose of this prospective study was to determine the relationship between subsyndromal delirium and pain in older adults following major elective orthopedic surgery. The correlational design allowed for the examination of the relationship between delirium symptoms and pain in older adults following major elective orthopedic surgery.

CHAPTER IV

RESULTS

The purpose of this study was to determine the relationship between subsyndromal delirium and pain in older adults following major elective orthopedic surgery. The specific aims examined in this study were: a) to determine the frequency of delirium symptoms and the frequency distribution of preoperative risk factors, pain intensity ratings and 24 hour opioid intakes of patients age 65 years and older following major elective orthopedic surgery; b) to determine the relationship between delirium symptoms and the preoperative risk factors in older adults following major elective orthopedic surgery; c) to determine the relationship between delirium symptoms and pain intensity ratings controlling for preoperative risk factors in older adults following major elective orthopedic surgery; and, d) to determine the relationship between delirium symptoms and 24 hour opioid intakes controlling for selected preoperative risk factors and pain intensity ratings in older adults following major elective orthopedic surgery. This chapter presents study results.

Sample Demographics and Characteristics

A total of 62 older adults were identified as being eligible for the current study according to the eligibility criteria. Detailed information regarding recruitment and enrollment is provided in Chapter 3. Nine participants declined participation in the study when presented with the opportunity by the preoperative nurse (14.1%, $n = 9$).

Sample Demographics

A sample of 53 older adults aged ≥ 65 years who were scheduled for major elective orthopedic surgery agreed to participate in this study. The mean age for the study sample was 73.7 years (*M*=73.7, *SD* = 6.2) with a range of ages of 65 to 90 years. Older adults who declined participation included 9 males (11.3%, *n* = 9) and 2 females (3.2%, *n* = 2). Two participants (3.2) withdrew from the study following the first postoperative day, but agreed to allow continued data collection without additional interviews.

Sample Characteristics

Following admission to the research study hospital located in northwestern part of the United States for major elective orthopedic surgery from August 2013 through May 2014, 53 older adults meeting study criteria were enrolled in this study. Table 3 lists sample demographic characteristics. Gender composition of the sample had a higher percentage of female participants (56.6%, *n* = 30) than male (43.4%, *n* = 23). However, according to United States Census Bureau (2010), the research site's geographical region had a higher percentage of males (42.8%) than females (57.2%). Most of the participants were married (64.2%, *n* = 34) with less than one-fifth of participants in the study living alone (18.9%, *n* = 10).

Table 3

Demographic Characteristics of Older Adults Scheduled for Major Elective Orthopedic Surgery[a]

Characteristic	*n*	%
Gender		
female	30	56.6
male	23	43.4
Housing		
Private rental	2	3.9
Home owner	46	90.2
Long-term care facility	2	3.9
Living arrangement		
Lives alone	10	18.9
With spouse	34	64.1
With other relative	7	13.2
With nonrelative	2	3.8
Marital status		
Single	4	7.5
Married	34	64.2
Widowed	9	17.0
Divorced	5	9.4
Lives with partner	1	2.0

Note. Data were collected at the time of enrollment prior to surgery. [a]*N* = 53.

Older adults often presented for elective surgery with pre-existing co-existing conditions. As part of the preoperative interview for enrollment, information was collected regarding diagnosed chronic conditions on all participants. Although strict medical clearance is often required for major elective orthopedic surgery, participants represented a wide variety of comorbidities reported in Table 4. The most common

conditions reported by participants were hypertension (64.2%, *n* = 34), hypothyroidism (26.4%, *n* = 14), diabetes (22.6%, *n* = 12), and obstructive sleep apnea (20.1%, *n* = 11).

Table 4

Comorbid Conditions in Older Adults Scheduled for Major Elective Orthopedic Surgery[a]

Coexisting Conditions	*n*	%
Anemia	2	3.8
Atrial fibrillation/heart palpitations	4	7.5
Cerebrovascular disease	2	3.8
Congestive heart disease	1	2.0
Chronic obstructive pulmonary disease	6	11.3
Coronary artery disease	3	3.8
Cardiovascular disease (not HTN or CAD)	7	13.2
Dementia	9	17.0
Depression	4	7.5
Diabetes	12	22.6
Hypertension	34	64.2
Hypothyroidism	14	26.4
Obstructive sleep apnea	11	20.4

All of the participants in this study underwent total major elective orthopedic surgery. Total unilateral total knee arthroplasty was the most common procedure performed for participants (34.7%, *n* = 36). Procedures performed on sample participants are reported in Table 5.

Table 5

Orthopedic Procedure Performed and Indication for Surgery in Older Adults[a]

Sample characteristic	*n*	%
Scheduled surgical procedures		
Total knee replacement	35	66.0
Total hip replacement	11	20.8
Bilateral knee replacement	3	5.7
Total shoulder replacement	3	5.7
Total knee revision	1	1.9
Primary diagnosis		
Osteoarthritis	52	98.1
Rheumatoid arthritis	1	1.9

Note. [a]*N* = 53.

The presence of a sensory deficit was identified by the researcher during the initial interview at the time of enrollment or upon review of the medical record following discharge. Sensory loss was recorded based on self-report or documentation in the medical record. Hearing loss was reported by 34% of participants (*n* = 18). Smoking history and the frequency of alcohol use was recorded based on self-report or information in the medical record. In this study, three of the participants reported that they were current smokers (5.7%, *n* = 3), One-fourth (24.5%, *n* = 13) of participants reported daily use of alcohol. Only 5 of the older adult participants reported taking no home meds (9.4%, *n* = 5). Although 30% participants had 1-4 prescribed medications at home prior to surgery, 60.4% of participants (*n* = 32) reported taking five or more medications currently prescribed by their physician. Medications were considered current if they were taking them regularly within the two weeks prior to surgery (See Table 6).

Table 6

Health Related Information for Older Adults Scheduled for Major Elective Orthopedic Surgery[a]

Participant Characteristic[a]	*n*	%
Sensory impairment	30	56.6
Speech	2	3.8
Hearing	18	34.0
Vision	4	7.5
Health-related information		
Current smoker	3	5.7
Alcohol use		
Never	12	22.6
Rare	9	17.0
Occasional	18	34.0
Daily	14	26.4
Number of prescribed home meds		
No home meds	5	9.4
1 – 4 home meds	17	30.2
5 or more home meds	32	60.4

Note. [a]*N* = 53.

Specific Aims

To address the specific aims investigated in this study, the following descriptive and inferential statistical analyses were completed. Results from this study for each of the specific aims for this study are described in the following section.

Specific Aim 1

Aim 1: To determine the frequency of delirium symptoms and the frequency distribution of preoperative risk factors, pain intensity ratings and 24 hour opioid intakes of patients age 65 years and older following major elective orthopedic surgery.

The frequencies and percentages of delirium symptoms among older adults were calculated for each of the three 24 hour periods and for the full 72 hour study period. Delirium scores for participants were scored by the number of the core delirium

symptoms that were detected using the Confusion Assessment Method (CAM) algorithm. Results of daily delirium assessments are reported in Table 7.

Table 7

Delirium Scores for Older Adults at 24, 48, and 72 Hours following Major Elective Orthopedic Surgery[b]

	Timing of Postoperative Delirium Assessment					
	At 24 Hours		At 48 Hours		At 72 Hours	
Delirium Score[a]	*n*	%	*n*	%	*n*	%
No Delirium (score=0)	40	75.5	21	39.6	15	28.3
One delirium symptom (score=1)	13	24.5	19	35.8	21	39.6
Two delirium symptoms (score=2)	0	0	10	18.9	7	13.2
Full delirium (score=3)	0	0	3	5.7	10	18.9

Note. [a]Delirium symptoms were identified using the Confusion Assessment Method (CAM). CAM scores were recorded as follows: "0" if no delirium symptoms were present, "1" for one symptom, "2" for two or three symptoms, not meeting criteria for delirium; "3" for 3 or 4 symptoms that meet criteria for full delirium.
[b]$N = 53$.

Subsyndromal delirium with one symptom of delirium (SSD-1) was present in 24.5% ($n = 13$) at the 1st delirium assessment at 24 hours. Three-fourths of the participants (75.5%, $n = 40$) did not have delirium symptoms at 24 hours. None of the participants had subsyndromal delirium with 2 or 3 symptoms (SSD-2) or full delirium at 24 hours after surgery. The presence of delirium symptoms was more common at 48 hours following surgery than at 24 hours. At 48 hours after surgery, SSD-1 was detected in 19 participants (35.8%, $n = 19$) and SSD-2 was detected in 11 participants (18.9%). Full delirium developed in 3 participants (5.7%, $n = 3$) at 48 hours, while 21 participants (39.6%, $n = 21$) did not have any delirium symptoms. At 72 hours following surgery, delirium symptoms continued to be common in older adults with only 15 participants (28.3%, $n = 15$) without at least one delirium symptom. SSD-1 was identified in 21

patients (39.6%, *n* = 21) at 72 hours; whereas, SSD-2 was found to be present in 13.2% (*n* = 7).

Overall incidence of delirium symptoms. Subsyndromal delirium developed in 67.9% of participants on postoperative days 1, 2, or 3 (*n* = 36). Of those participants who developed subsyndromal delirium, 66.7% developed only 1 symptom (SSD-1) (*n* = 24), whereas 33.3% (*n* = 12) developed subsyndromal delirium with 2 symptoms (SSD-2). Full syndromal delirium occurred in 17.0% (*n* = 9). Of the 53 participants, eight did not develop any delirium symptoms on any of the 3 postoperative days (15.1%, *n* = 8). Participants were not evaluated beyond postoperative Day 3. Therefore, follow-up information regarding participant recovery beyond postoperative Day 3 is not available.

The most common core symptom of delirium identified using the CAM algorithm (shortened version) was inattention (*n* = 41), followed by disorganized thinking (*n* = 26). An acute change in mental status with a fluctuating course as a symptom of delirium was less common (*n* = 20) as was a change in a participant's level of consciousness (*n* = 18).

Frequency distribution of preoperative risk factors. The frequency distribution of each preoperative risk factor is described in the following section. The means, standard deviations, and variances of selected preoperative risk factors for subsyndromal delirium (comorbidities, cognitive status, recent fall history, and preoperative fasting time) were recorded for each participant.

Comorbidity burden (CCI score). Using the Charlson Comorbidity Index (CCI), an age-adjusted score of comorbidity burden used to estimate mortality risk was calculated using the age and pre-existing disease burden for each participant then examined using descriptive statistics. The mean of the CCI scores was 3.7 (*SD* = 1.2)

with a variance of 1.5. The age of older adults in the current study ranged from 65 to 90 years, with a mean of 73.7 years (*SD* = 6.24).

Cognitive status. Cognitive status was measured using the Mini-Cog dementia screening tool that was scored from 0 to 3, with lower scores indicating increased cognitive impairment. The mean cognitive score for participants in this study was 2.06 (*M* = 2.1, *SD* = 1.0) with a variance of 1.0, reflecting good memory recall overall. The Mini-Cog screen was positive for dementia in 17% of study participants (*n* = 9). Only two participants had a formal medical diagnosis of dementia in their medical record (see Table 8).

Table 8

Frequency of Dementia in Older Adults Scheduled for Major Elective Orthopedic Surgery[a]

	n	%
No dementia (negative screen)	44	83
Dementia (positive screen)	9	17
Total	53	100

Note. [a]*N* = 53.

Recent fall history. At the time of enrollment, participants were asked whether they had experienced a recent fall within the previous six months, and if so, how many falls they experience during this time. Patient interview were supplemented by information from the medical record for information related to fall history. The study sample included two participants (4%, *n* = 2) with a history of falls within the past 6 months. The mean number of recent falls reported by participants for the six months prior to surgery was 0.2 (*SD* = 0.3) with a variance of 0.1.

Preoperative fasting times. The duration of preoperative fasting times was calculated from the last known time of oral intake, whether it was solid food or liquids. As depicted in Figure 4, the duration ranged from 5.0 to 17.0 hours of fasting with an average of 9.5 hours (M = 9.5, SD = 2.20) with a variance of 4.2. The most frequent preoperative fasting time was 7.5 hours. Patients reported being frequently asked to fast after midnight the night prior to surgery, which seemed to increase fasting times for those patients who had surgery start times later in the day.

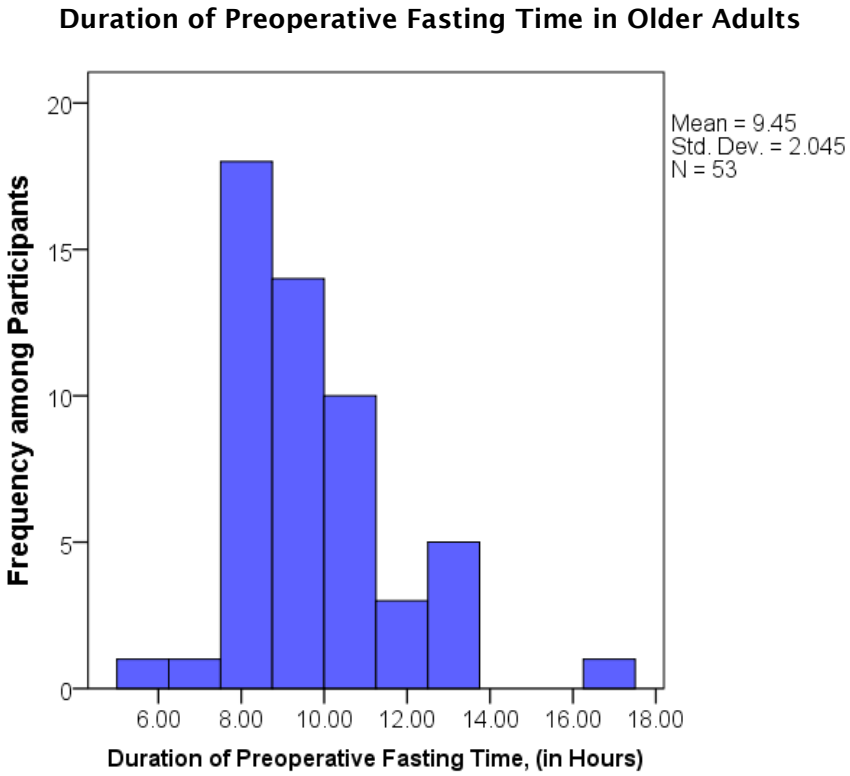


Figure 4. Bar graph showing the frequency distribution of preoperative fasting time duration for older adults. Fasting times were calculated starting from the time of the participant's last known oral intake and ending at the surgery start time (in hours).

Pain intensity. Pain intensity ratings were examined using descriptive statistics and graphic representations of participant data to evaluate overall distribution characteristics. Mean pain intensity ratings were calculated for each of the three consecutive 24 Hour time periods following surgery, and ranged from 0.9 to 6.4 out of 10

with an overall mean pain score was 3.9 out of 10 (*SD* = 1.2) for the 72 Hour study period (See Figure 6). Self-reported pain was higher on average between 48 and 72 hours after surgery (*M* = 4.3, *SD*=1.9) and lowest between 24 and 48 hours (*M* = 3.6, *SD* = 1.9). Descriptive statistics are reported in Table 9.

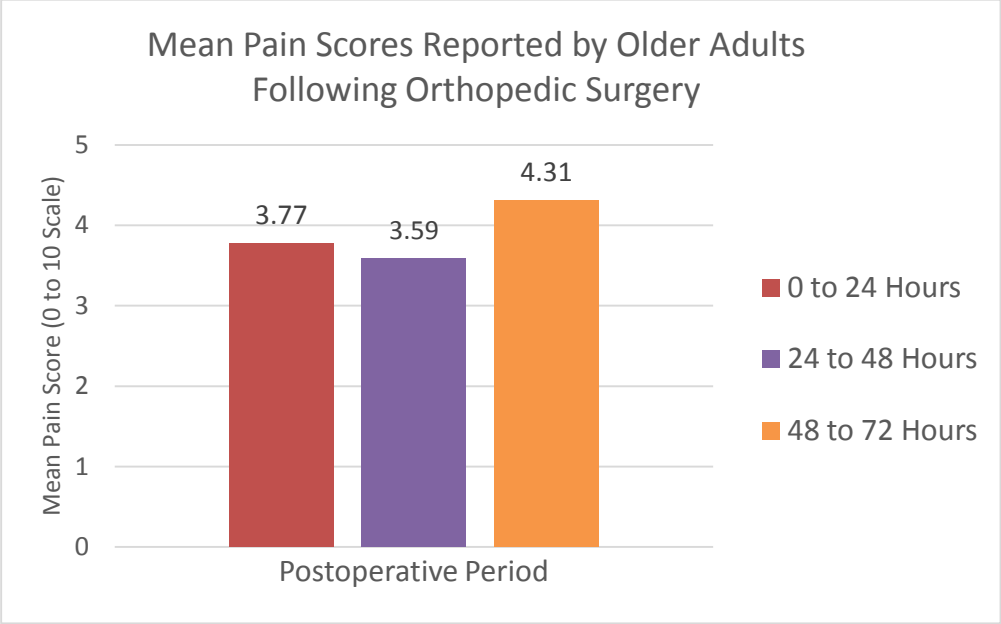


Figure 5. Bar graph showing mean pain scores for older adults for three consecutive 24 hour periods after surgery. Pain scores used in this study started at the time the participant arrived in the post-surgical unit.

Table 9

Descriptive Statistics for Pain Reported by Older Adults Following Major Elective Orthopedic Surgery

Time Period	*M* (*SD*)	Variance
Mean pain ratings[a]		
0 to 24 hours	3.8 (2.0)	5.8
24 to 48 hours	3.6 (1.9)	6.5
48 to 72 hours	4.3 (1.9)	6.7
Overall mean pain rating	3.9 (1.2)	2.7

Note. [a]*N* = 53.

Twenty-four hour opioid intakes. Overall, 24-hour opioid intakes of study participants averaged a morphine sulfate (parenteral) equivalent opioid dose of 24.8 mg (See Figure 7). Descriptive statistics were used to examine total opioid intakes for each of the three 24-hour time periods following surgery as well as for the mean 24-hour opioid intake for the 72-hour study period (See Table 10).

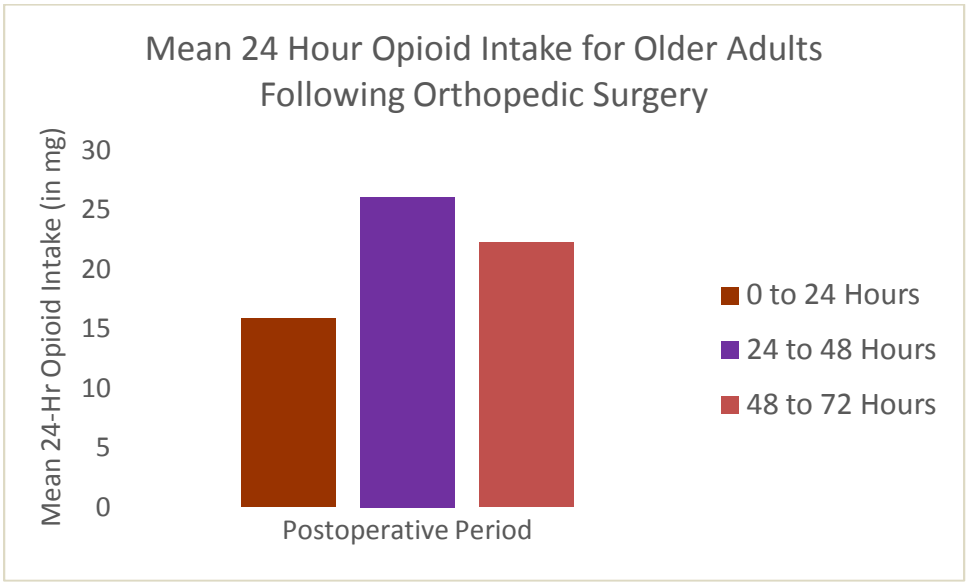


Figure 6. Total 24-hour opioid intake for participants from 0 to 24 hours, 24 to 48 hours, and 48 to 72 hours (*N* = 53). All opioid analgesic doses were converted to morphine sulfate (parenteral) equianalgesic doses to facilitate comparison between participants who were prescribed different opioid analgesic medications.

Table 10

Opioid Intake of Older Adults Following Major Elective Orthopedic Surgery

Opioid Intake[a]	*M* (*SD*)	Variance
0 – 24 hr.	25.9 (15.3)	233.6
24 – 48 hr.	26.1 (15.9)	254.0
48 – 72 hr.	22.3 (13.5)	181.4
Mean 24-hour opioid intake from 0 – 72 hr.	24.8 (12.3)	150.5

Note. Twenty-four hour opioid intakes are reported in IV morphine sulfate-equivalent doses in mg.
[a]*N* = 53.

The average opioid intake was greatest in the 24 to 48 period following surgery (*M* = 26.1 mg). Participants had the lowest amount of opioid intake between 48 and 72 hours following surgery (*M* = 22.3 mg, *SD* = 12.3). On average, participant 24-hour opioid intake was 24.8 mg in estimated equianalgesic morphine sulfate (parenteral) equivalents for the full 72 hour postoperative time period.

Specific Aim 2

*Aim 2: To determine the relationship between delirium symptoms and the preoperative risk factors in older adults following major elective orthopedic surgery***.**

The preoperative risk factors for delirium symptoms used in this correlational study were comorbidities, cognitive status, recent fall history, and preoperative fasting time. Correlations were examined prior to analyses using hierarchical linear regression in order to determine the relationship between delirium symptoms and preoperative risk factors.

Relationship between delirium symptoms and preoperative risk factors. Correlations were examined to identify significant relationships between theoretical preoperative risk factors with delirium symptoms (See Table 11). The relationship between delirium symptoms and each of the preoperative risk factors will be discussed individually in the following section.

Table 11

Correlations of Preoperative Risk Factors and Delirium Symptoms in Older Adults

	Delirium Score					
	At 24 Hours (N = 53)		At 48 Hours (N = 53)		At 72 Hours (N = 53)	
Risk Factor	Pearson *r*	*p*	Pearson *r*	*p*	Pearson *r*	*p*
CCI score	.04	.76	.18	.20	.01	.90
Cognitive score	-.21	.13	-.10	.48	-.08	.55
Fall history[a]	-.11	.45	.37**	.007	.26	.06
Preoperative fasting time	.10	.50	.07	.63	.30*	.03

Note. [a]The number of participant falls that had occurred in the six months prior to enrollment. *$p \leq .05$ level, **$p \leq .01$ level

Comorbidity burden. The Charlson Comorbidity Index score was not related to delirium symptoms in older adult participants (r = .12) between CCI score after surgery. The CCI score averaged 3.6 in participants who developed delirium symptoms (M = 3.6, SD = 1.3, n = 44). Participants with no delirium scored slightly higher than those participants with delirium (M = 3.77, SD = 1.2, n = 22).

Cognitive status. Increased delirium symptoms were not significantly associated with preoperative cognitive impairment for the 72 study period, r = -.13, N = 53, p = .34. Although not significant, cognitive status was negatively related to delirium symptoms at 24 hours following surgery, r = -.21, N = 53, p = .14. Although the negative relationship

persisted, the correlations between cognitive status and delirium symptoms found no significant relationship.

***Recent fall history*.** The number of falls prior to hospital admission (within the past six months) was significantly related with delirium symptoms at 48 hours (r =.37, N = 53, p = .007) and overall for the 72 hour study period (r = .33, N = 53, p = .02). When questioned at the time of enrollment regarding recent falls, two participants reported falling within the past six months.

***Preoperative fasting time*.** An increased duration of preoperative fasting time was associated with significantly increased delirium symptoms at 72 hours (r = .30, N = 53, p = .03) and was a nonsignificant correlate for the 72 hour study period (r = .24, N = 53, p = .09). In order to examine the preoperative risk factor of fasting time more closely, fasting times were grouped into 2-3 hour blocks. When preoperative fasting times for participants were considered in 3 hour blocks with increasing durations, the trend toward increased delirium symptoms with higher fasting time was seen at 48 and 72 hours. A comparison of the number of delirium symptoms for participants who had short, average, long, and extended preoperative fasting times is presented in Table 12.

Table 12

Delirium Symptoms and Durations of Fasting Time in Older Adults

		Delirium Symptoms[b]		
Fasting Duration[a]	% (*n*)	At 24 Hours % (*n*)	At 48 Hours % (*n*)	At 72 Hours % (*n*)
4.0 to 6.9	1.9, (1)	---	100.0 (1)	100.0 (1)
7.0 to 8.9	35.8, (19)	10.5 (2)	52.6 (10)	68.4 (13)
9.0 to 10.9	39.6, (21)	38.1 (8)	52.4 (11)	38.1 (8)
11 or more	22.6, (12)	25.0 (3)	75.0 (9)	91.7 (11)

Note. [a]The duration of preoperative fasting time was calculated from the participant's last known oral intake until the surgery start time, in hours. [b]$N = 53$.

Relationship between delirium symptoms and other select risk factors. In addition to the preoperative risk factors (comorbidity burden, cognitive status, fall history, and fasting time), mean pain scores, and 24-hour opioid intake of participants, other pain related data were recorded as part of retrospective medical record data extraction. The variables of maximal pain, preoperative pain, functional status, and age were examined for their relationship to delirium symptoms. Statistical intercorrelations of study variables were calculated and are presented in Table 13. Preoperative pain reported on the day of surgery and maximal pain reported by participants for each 24 hour period was recorded and examined for association with delirium symptoms. In addition, participant factors recorded at the time of study enrollment included functional status, and age (in years).

Table 13

Intercorrelations of Postoperative Delirium Symptoms, Pain, Opioid Intake, and Other Delirium Risk Factors in Older Adults[a]

Variable		1	2	3	4	5	6	7	8	9	10	11
1.	Mean overall delirium score	1										
2.	Mean pain score (0-72 hr.)	.05	1									
3.	Mean 24-hr opioid intake (0-72 hr.), in mg	.13	.29*	1								
4.	Charlson Comorbidity Index score	.12	-.21	.09	1							
5.	Mini-Cog cognitive score	-.13	-.01	-.22	.28*	1						
6.	Recent fall history (last 6 months)	.33*	-.01	.61**	.46**	-.26	1					
7.	Preoperative fast duration	.24	.13	.06	.01	-.09	.24	1				
8.	Mean delirium score 0-24 hr.	.35**	-.16	-.09	.04	-.21	-.11	.10	1			
9.	Mean delirium score 24-48 hr.	.78**	.10	.10	.18	-.10	.37**	.07	.06	1		
10.	Mean delirium score 48-72 hr.	.84**	.07	.15	.01	-.08	.26	.30*	.06	.41**	1	
11.	Mean pain 1, (0-24 hr.)	-.01	.68**	.02	-.04	.09	.02	.03	.10	.17	-.05	1
12.	Mean pain 2, (24-48 hr.)	.18	.69**	.16-.11	-.06	-.17	-.12	.05	-.08	.22	.14	.33*
13.	Mean pain 3, (48-72 hr.)	-.08	.46**	.36**	-.28**	.04	.08	.16	.05	-.21	.05	-.11
14.	Opioid intake 1, (0-24 hr.), in mg	.10	.24	.81**	.13	-.16	.56**	.09	-.18	.19	.08	.15
15.	Opioid intake 2, (24-48 hr.), in mg	.24	.25	.86**	.17	-.26	.60**	.12	-.02	.24	.17	.02
16.	Opioid intake 3, (48-72 hr.), in mg	-.04	.21	..79**	-.11	.11	.31*	-.08	-.01	-.24	.17	-.14
17.	Maximal pain 1, (0-24 hr.)	.03	.59**	-.07	-.05	.01	.05	.06	-.18	.28*	-.10	.88**
18.	Maximal pain 2, (24-48 hr.)	.24	.69**	.19	-.11	-.10	-.01	.05	-.21	.33*	.20	.34*
19.	Maximal pain 3, (48-72 hr.)	-.10	.31*	.19	-.20	.13	.01	.12	.09	-.24	.01	-.17
20.	Preoperative pain (day of surgery)	.04	.38*	.26	.01	-.14	.21	-.05	-.14	.26	-.11	.49**
21.	Barthel Index for ADLs score	-.04	.01	.09	.18	.10	.04	.16	.15	.09	-.02	-.24
22.	Age, in years	.09	-.11	-.13	.65**	-.32	.11	-.02	.19	.02	.04	-.03

Note. Intercorrelations reported are for continuous variables represented by Pearson's *r* coefficient.
[a]*N* =53; ADL's=Activities of Daily Living.
*p<.05, **p<.01

Table 13 (Cont.)

Intercorrelations of Delirium Symptoms, Preoperative Factors, Pain, Opioid Intake, and Pain-Related Factors[a]

Variable		12	13	14	15	16	17	18	19	20	21	22
1.	Mean overall delirium score											
2.	Mean pain score (0-72 hrs.)											
3.	Mean 24-hr opioid intake (0-72 hrs.), in mg											
4.	Charlson Comorbidity Index score											
5.	MiniCog cognitive score											
6.	Recent fall history (last 6 months)											
7.	Preoperative fast duration											
8.	Mean delirium score 0-24 hrs.											
9.	Mean delirium score 24-48 hrs.											
10.	Mean delirium score 48-72 hrs.											
11.	Mean pain 1, (0-24 hrs.)											
12.	Mean pain 2, (24-48 hrs.)	1										
13.	Mean pain 3, (48-72 hrs.)	-.03	1									
14.	Opioid intake 1, (0-24 hrs.), in mg	.10	.20	1								
15.	Opioid intake 2, (24-48 hrs.), in mg	.26	.19	.55**	1							
16.	Opioid intake 3, (48-72 hrs.), in mg	.01	.53**	.44**	-.25	1						
17.	Maximal pain 1, (0-24 hrs.)	.29*	-.12	.10	-.04	-.25	1					
18.	Maximal pain 2, (24-48 hrs.)	.88**	.07	.18	.23	.05	.32*	1				
19.	Maximal pain 3, (48-72 hrs.)	-.09	.84**	.06	.37**	-.11	.01	.01	1			
20.	Preoperative pain (day of surgery)	.24	-.02	.14	.29*	.22	.41**	.28	-.22	1		
21.	Barthel Index for ADL's score	.01	.12	.14	.22	-.01	-.23	-.05	.13	-.15	1	
22.	Age, in years	.06	-.23	-.05	-.08	-.22	-.04	-.06	-.19	.03	-.23	1

Note. Intercorrelations reported are for continuous variables represented by Pearson's *r* coefficient.

[a]*N* =53; ADL's=Activities of Daily Living.

*$p<.05$, **$p<.01$

Age and functional status have been reported as important factors in the development of delirium. Age was not related to variation in delirium symptoms (reported in Table 13). Similarly, it was noted that functional status was not significantly related to either delirium symptoms or subsyndromal delirium.

One pain-related variable included in Table 13 is maximal pain, or the maximum pain reported, for each of the 24-Hour periods following surgery. Maximal pain was related to increased delirium symptoms in this study. Maximal pain reported by participants between 0 and 24 hours after surgery was significantly related to increased delirium symptoms at 48 hours, $r = .28$, $N = 53$,$p = .05$.. In addition, the maximal pain score reported by participants between 24 and 48 hours postoperatively was also significantly related to increased delirium symptoms at 48 hours, $r = .33$, $N = 53$, $p = .02$.

Preoperative pain reported by participants in this study on the day of surgery was associated with increased delirium symptoms as a nonsignificant correlate at 48 hours, $r = .26$, $n = 48$, $p = .07$. Participants with higher levels of preoperative pain were significantly associated with increased pain between 0 and 24 hours following surgery, $r = .49$, $n = 48$, $p < .001$, and with increased pain for the entire 72 hour study period, $r = .38$, $n = 48$, $p = .008$.Multiple linear regression was used to test if the preoperative risk factors significantly accounted for a variance in delirium symptoms between 0 and 72 hours. Results of regressions indicated that the four covariates (comorbidities, cognitive status, recent fall history, and preoperative fasting time) entered hierarchically did not account for a significant variance in delirium symptoms, $R^2 = .14$, $F(4, 48) = 1.93$, $p = .12$. The Charlson Comorbidity Score and Mini-Cog cognitive status had very weak negative partial correlations with delirium symptoms. However, participants with a

history of recent falls and longer durations of preoperative fasting had more delirium symptoms (See Table 14). The preoperative risk factors (CCI score, cognitive score, number of recent falls, and preoperative fasting time) did not significantly account for variance among participants in delirium symptoms, $R^2 = .14$, $F(4, 48) = 2.00$, $p = .11$

Table 14

Multiple Linear Regression of Delirium Symptoms[a] *and Preoperative Risk Factors*

Predictor Variables[b]	Partial Correlation	Change in R^2	Cumulative R^2	Beta Coefficients
Recent fall	.26	.11	.11	.29
Preoperative fasting time	.17	.03	.14	.17
Cognitive score	-.05	.00	.14	-.05
Comorbidity score	-.03	.00	.14	-.04
$R^2 = .14$, $F(4, 48) = 1.93$, $p = .12$			Adjusted $R^2 = .07$	

Note. [b]Mean delirium scores calculated from assessments completed at 24, 48, and 72 hours following surgery. [b]$N = 53$.
$^*p \leq .05$; $^{**}p \leq .01$

Specific Aim 3

Aim 3. To determine the relationship between delirium symptoms and pain intensity ratings controlling for preoperative risk factors in older adults following major elective orthopedic surgery.

To evaluate pain intensity, the overall mean pain score for each 24-hour period following surgery was calculated separately and analyzed. In addition, the overall mean pain intensity was calculatedly and examined for its relationship to the mean number of delirium symptoms from CAM algorithm for all three consecutive 24 hour periods after surgery.

Correlations were calculated to determine the relationship between delirium symptoms and postoperative pain in older adults for the three 24-hour study periods (See Table 15). Findings showed that between 0 and 24 hours mean pain scores had a nonsignificant negative correlation with increased delirium symptoms at 24 hours (r = -.26, N = 53, p = .06). However, pain ratings of participants during the second 24 hours following surgery had a nonsignificant positive correlation with delirium symptoms at 48 hours (r = .22, N = 53, p = .11). However, pain from the third 24 hours following surgery was not significantly associated with an increase or a decrease in delirium at 72 hours (r = .05, N = 53, p = .73).

When subsyndromal delirium was considered separately from delirium, mean pain between 0 and 24 hours following surgery was significantly related to subsyndromal delirium on the second postoperative day (r = .33, n = 44, p = .02), whereas mean pain between 48 and 72 hours following surgery was not related to subsyndromal delirium on the third postoperative day, r =-.15, n = 44, p = .34.

Table 15

Relationship between Delirium Symptoms and Mean Pain Scores

Correlated Variables[a]	Pearson *r*	*p*
CAM score on POD 1		
Mean pain from 0 - 24 hr	-.26	.06
CAM score on POD 2		
Mean pain from 0 to 24 hr	.16	.24
Mean pain from 24 – 48 hr	.22	.11
CAM score on POD 3		
Mean pain from 24 – 48 hr	14	.33
Mean pain from 48 – 72 hr	.05	.73

Note. **CAM** = Confusion Assessment Method*;* **POD** = Postoperative Day; [a]N = 53
*$p \leq .05$ **$p \leq .01$

Relationship of pain and delirium symptoms. Following Pearson's correlation for each of the study variables, relationships among delirium symptoms and pain were examined through hierarchical multiple linear regression analyses to evaluate how well pain predicted a change in delirium symptoms for each of the 24 hour postoperative periods. The predictors were the four preoperative risk factors (comorbidity burden, cognitive status, recent fall history, and preoperative fasting time) and pain, while the outcome variable was the number of core delirium symptoms on the CAM algorithm.

Delirium symptoms and pain at 24 hours after surgery. To determine the relationship between delirium symptoms at 24 hours, mean postoperative pain scores between 0 to 24 hours were entered hierarchically into the regression model in the following order: (1) preoperative risk factors (comorbidity score, cognitive score, number of recent falls, and preoperative fasting), and (2) mean pain. Regression results indicated that pain between 0 and 24 hours following surgery was not significantly (p>.05) related to delirium symptoms or subsyndromal delirium at 24 hours following surgery (See Table 16).

Table 16

Hierarchical Regression of Delirium Symptoms at 24 Hours and Pain in Older Adults

Independent Variables[a]	Partial Correlation	R^2 *Change*	Cumulative R^2	Standardized β
Cognitive score	-.21	.04	.04	-.21
Recent fall history	-.20	.04	.08	-.23
Preoperative fasting time	.14	.01	.11	.14
CCI score	.07	.01	.12	.08
Mean pain for 0 -24 hr.	-.24	.03	.15	-.23
R^2 = .15, F(5, 47) = 1.59, p =.18		Adjusted R^2 =.05		

Note. [a]N = 53
*$p \leq .05$; ** $p \leq .01$

Delirium symptoms and pain 48 hours after surgery. Regression results indicated that pain between 24 and 48 hours following surgery was significantly related to increased delirium symptoms at 48 hours following surgery after accounting for the preoperative risk factors of comorbidity, cognitive status, recent fall history, and preoperative fasting time, $F(5, 47) = .2.57$, $p = .04$. A hierarchical regression indicated that 21% of the variance in delirium symptoms can be accounted for by pain and the preoperative risk factors (comorbidity, cognitive status, recent fall history, and preoperative fasting time). The relative contribution of the individual independent variables in predicting delirium symptoms at 48 hours are presented (See Table 17).

Table 17

Hierarchical Regression of Delirium Symptoms at 48 Hours and Pain in Older Adults after Surgery

Independent Variables[a]	Partial Correlation	R^2 *Change*	Cumulative R^2	Standardized **β**
Cognitive score	.06	.00	.04	.06
Recent fall history	.35	.13	.13	.42**
Preoperative fasting time	-.04	.00	.13	-.04
Comorbidity score	.02	.00	.13	.02
Mean pain (24 - 48 hr. post-surgery)	.28	.08	.21	.29*
$R^2 = .21$, $F(5, 47) = 2.57$*, $p = .04$			Adjusted $R^2 = .13$	

Note. [a]$N = 53$
*$p \leq .05$; **$p \leq .01$

When cases of delirium were excluded from the regression, mean pain from 24 to 48 hours was related to subsyndromal delirium after accounting for preoperative risk factors (comorbidity, cognitive status, recent fall history, and preoperative fasting time) on the second postoperative day, although not significantly, $R^2 = .15$, $F(5, 38) = 2.98$, $p =$

.09. In addition, there was a significant positive relationship between subsyndromal delirium at 48 hours and mean pain scores between 0 and 24 hours following surgery, R^2 = .16, $F(5, 38) = 1.65$, $p = .03$.

Delirium symptoms and pain at 72 hours after surgery. The relationship between delirium and pain at 72 hours after surgery was evaluated utilizing hierarchical multiple regression. Variances related to preoperative risk factors (CCI score, cognitive status, recent fall history, and preoperative fasting time) were accounted for in the regression equation. The mean pain score from 48 to 72 hours following surgery was not significantly ($p>.05$) related to increased delirium symptoms at 72 hours (See Table 18). Pain between 48 and 72 hours following surgery was not significantly related to subsyndromal delirium.

Table 18

Hierarchical Regression of Delirium Symptoms and Pain in Older Adults at 72 Hours after Surgery

Independent Variables[a]	Partial Correlation	R^2 *Change*	Cumulative R^2	Standardized β
Cognitive score	-.03	.08	.08	-.03
Recent fall	.23	.01	.09	.27
Preoperative fasting time	.25	.04	.10	.25
Comorbidity score	-.12	.01	.14	-.14
Pain (48 - 72 hr. post-surgery)	-.05	.01	.15	-.05
R^2 = .15, $F(5, 47) = 1.60$, p =.18		Adjusted R^2 =.06		

Note. [a]$N = 53$
$*p \leq .05$; $** p \leq .01$

Delirium symptoms and pain overall for 72 hours after surgery. Mean delirium scores from the 72 hour study period following surgery were not associated with overall mean pain, $r = -.01$, $N = 53$, $p = .94$. See Table 19 for results of the regression that

evaluated the contribution of the overall mean pain on mean delirium symptoms over the 72-Hour study period while accounting for preoperative risk factors (CCI score, cognitive status, history of a recent fall, and preoperative fasting time).The regression results indicated that pain did not contribute either an increase or a decrease in delirium symptoms at 72 hours. In addition, overall mean pain was not significantly related to subsyndromal delirium, R^2 = .10, $F(4, 39)$, p = .53.

Table 19

Hierarchical Regression of Delirium Symptoms and Overall Pain in Older Adults from 0 to 72 Hours after Surgery

Independent Variable[a]	Partial Correlation	Change in R^2	Cumulative R^2	Beta Coefficients
Recent fall	.26	.11	.11	-.03
Preoperative fasting	.17	.03	.14	-.05
Cognitive status	-.05	.00	.14	.29
Comorbidity score	.12	.00	.14	.16
Pain score	.05	.00	.14	.02
R^2 = .14, $F(5, 47)$ = 1.52, p =.20			Adjusted R^2 =.05	

Note. [a]N = 53
*$p \leq .05$; ** $p \leq .01$

Specific Aim 4

Aim 4. To determine the relationship between delirium symptoms and 24 hour opioid intake controlling for selected preoperative risk factors and pain intensity ratings in older adults following major elective orthopedic surgery.

Correlation analyses were performed to determine the relationship between delirium symptoms and 24 hour opioid intake. Each 24 hour period was analyzed separately for each 24-hour time period following surgery. In addition, the relationship between delirium symptoms and mean opioid intake was analyzed for the full 72 hour

study period. Results of the correlation analyses are reported in Table 20. Opioid intake between 24 and 48 hours following surgery had a nonsignificant positive correlation with delirium symptoms at 48 hours, $r = .25$, $N = 53$, $p = .07$.

Table 20

Correlation Between Delirium Symptoms and 24 Hour Opioid Intake[a]

Correlated Variables[b]	*Pearson's r*	*p*
CAM score on POD 1		
Opioid intake from 0 to 24 hr.	-.18	.20
CAM score on POD 2		
Opioid intake from 24 to 48 hr.	.25	.07
CAM score on POD 3		
Opioid intake from 48 to 72 hr.	.15	.28

Note. **CAM** = Confusion Assessment Method*;* **POD** = Postoperative Day; [a]Opioid intake was calculated by converting opioid doses to estimated morphine sulfate equivalent doses using an equianalgesic calculator for each 24 hour period.
[b]$N = 53$
*$p \leq .05$ **$p \leq .01$

Relationship of opioid intake and delirium symptoms. Following Pearson's correlations for each of the study variables, relationships among delirium symptoms and opioid intake were examined to evaluate how well opioid intake predicted a change in delirium symptoms for each of the 24 hour postoperative periods and overall for the 72 hour study period. Hierarchical multiple regressions were also calculated by entering variables in the following order: 1) preoperative risk factors (comorbidity burden, cognitive status, number of recent falls, and preoperative fasting time), 2) mean pain, and 3) 24 hour opioid intake. The predictors were the four preoperative risk factors (comorbidity score, cognitive score, fall history, and preoperative fasting time), mean pain, and opioid intake while the outcome variable was the number of core delirium

symptoms on the CAM algorithm. Results for the overall 72 Hour study period are reported in Table 21.

Table 21

Hierarchical Regression for Delirium Symptoms in Older Adults and Mean Opioid Intake from 0 to 72 Hours after Surgery

Independent Variable[b]	Partial Correlation	R^2 *Change*	*Cumulative* R^2	β Coefficients
Fall history	.26	.11	.11	.39
Preoperative fasting time	.14	.03	.14	.14
Cognitive score	-.07	.00	.14	-.06
Comorbidity Index score	-.05	.00	.15	-.06
Pain score	.06	.00	.15	.06
Mean 24-hour Opioid intake	-.11	.01	.15	-.14
R^2 = .15, $F(6, 46) = 1.34$, $p = .26$			Adjusted R^2 = .04	

Note. [a]Twenty-four hour opioid intake was calculated in morphine sulfate (parenteral) equianalgesic units (in mg) in order facilitate comparison among participants prescribed different opioid medications.
[b]$N = 53$
$*p \leq .05$; $** p \leq .01$

The mean 24-hour opioid intake for all three days (0 to72 hours) after surgery was not significantly related to delirium symptoms ($r = .13$, $N = 53$, $p = .17$).Mean 24 hour opioid intake from the 72 hour study period were not significantly related to delirium symptoms when analyzed in a hierarchical multiple linear regression equation. Opioid intake did not account for a variation in delirium symptoms. over and above the covariates of preoperative risk factors and self-reported pain. When scores from participants who developed delirium were excluded from the hierarchical regression analysis, subsyndromal delirium was not significantly related to mean 24-hour opioid intake for the 72 hour study period, $R^2 = .13$, $F(6,37) = 0.92$, $p = .49$. See Tables 22, 23, and 24 for findings from regression analyses.

Table 22

Hierarchical Regression for Delirium Symptoms and Opioid Intake[a] in Older Adults at 24 Hours after Surgery

Independent Variable[b]	Partial Correlation	R^2 Change	Cumulative R^2	β Coefficients
Fall history	-.12	.01	.01	-.15
Preoperative fasting time	.13	.00	.01	.13
Cognitive status	-.22	.05	.06	-.22
Comorbidity score	.05	.00	.06	.06
Pain score (0 to 24 hr.)	-.22	.02	.08	-.22
Opioid intake (0 to 24 hr.)	-.10	.07	.15	-.11
R^2 = .15, F(6, 46) = 1.38, p = .24			Adjusted R^2 = .04	

Note. [a]Twenty-four hour opioid intake by older adults was calculated in morphine sulfate (parenteral) equianalgesic units (in mg) in order facilitate comparison among participants prescribed different opioid medications.
[b]N = 53
*$p \leq .05$; ** $p \leq .01$

Table 23

Hierarchical Regression for Delirium Symptoms and Opioid Intake in Older Adults at 48 Hours after Surgery[a]

Independent Variable[b]	Partial Correlation	R^2 Change	Cumulative R^2	β Coefficients
Fall history	.36	.01	.01	.52
Preoperative fasting time	-.06	.00	.01	-.05
Cognitive status	.05	.05	.06	.05
CCI score[c]	.00	.00	.06	.00
Pain score (24 to 48 hr.)	.30	.02	.08	.32
Opioid intake (24 to 48 hr.)	-.10	.07	.23	-.14
R^2 = .23, F(6, 46) = 2.22, p = .06			Adjusted R^2 = .12	

Note. [a]Twenty-four hour opioid intake by older adults was calculated in morphine sulfate (parenteral) equianalgesic units (in mg) in order facilitate comparison among participants prescribed different opioid medications. **CCI** = Charlson Comorbidity score
[b]N = 53
*$p \leq .05$; ** $p \leq .01$

Table 24

Hierarchical Regression for Delirium Symptoms and Opioid Intake in Older Adults at 72 Hours after Surgery [a]

Independent Variable[b]	Partial Correlation	R^2 *Change*	*Cumulative* R^2	β Coefficients
Recent fall history	.18	.11	.	.22
Preoperative fasting time	.27	.02	.14	.28
Cognitive score	-.02	.01	.14	-.02
Comorbidity score	-.10	.00	.15	-.12
Mean Pain (48 to 72 hr.)	-.10	.00	.15	-.11
Opioid intake (48 to 72 hr.)	.10	.01	.15	.12
$R^2 = .15$, $F(6, 46) = 1.39$, $p = .24$			Adjusted $R^2 = .04$	

Note. [a]Twenty-four hour opioid intake was calculated in morphine sulfate (parenteral) equianalgesic units (in mg) in order facilitate comparison among participants prescribed different opioid medications.
[b]$N = 53$
$^{*}p \leq .05$; $^{**}p \leq .01$

Summary of Results

Subsyndromal delirium was common in older adults who underwent major elective orthopedic surgery in this study with an overall incidence of 68%. Higher pain levels between 24 and 48 hours following surgery were significantly ($p < .05$) related to increased delirium symptoms at 48 hours after surgery while accounting for the effects of preoperative risk factors, but pain was not significantly ($p > .05$) related to delirium symptoms at 24 hours, 72 hours, or overall for the 72 hour study period. Higher pain levels between 0 and 24 hours following surgery were significantly ($p < .05$) related to subsyndromal on the second day following surgery. The relationship between delirium symptoms and opioid intake was not significant ($p > .05$) on any of the three postoperative days in the study sample. In addition, the maximum pain rating reported by participants between 24 and 48 hours following surgery was significantly related to increased delirium symptoms ($p < .05$). Twenty-four hour opioid intake was not

significantly related to subsyndromal delirium. The purpose of this study was to determine the relationship between subsyndromal delirium and postoperative pain in older adults following orthopedic surgery; secondarily, to determine the relationship between subsyndromal delirium and 24 hour opioid intake in older adults following orthopedic surgery.

CHAPTER V

DISCUSSION

The purpose of this study was to determine the relationship between subsyndromal delirium and pain in older adults following major elective orthopedic surgery. The specific aims examined in this study were: a) to determine the frequency of delirium symptoms and the frequency distribution of preoperative risk factors, pain intensity ratings and 24 hour opioid intakes of patients age 65 years and older following major elective orthopedic surgery; b) to determine the relationship between delirium symptoms and the preoperative risk factors in older adults following major elective orthopedic surgery; c) to determine the relationship between delirium symptoms and pain intensity ratings controlling for preoperative risk factors in older adults following major elective orthopedic surgery; and, d) to determine the relationship between delirium symptoms and 24 hour opioid intakes controlling for selected preoperative risk factors and pain intensity ratings in older adults following major elective orthopedic surgery. The final chapter presents a summary of this study and important conclusions drawn from the data presented in chapter 4. It provides a discussion of the major findings with interpretation of their significance for nursing science, practice and education.

Subsyndromal Delirium and Postoperative Pain

In this study, 35 of 53 or 67.9% (n = 35 of an N of 53) older adults who underwent major elective orthopedic surgery developed subsyndromal delirium on at

least one of the three days following surgery. subsyndromal delirium occurs when core delirium symptoms are present, but are not diagnostic of the syndrome of delirium. According to the Confusion Assessment Method (CAM) diagnostic algorithm (shortened version), delirium is present when the first 2 core symptoms (an acute change in mental status and fluctuating course of abnormal behavior, and inattention) and either the third core symptom (disorganized thinking) or the fourth core symptom (change in the level of consciousness) are present (Inouye, 2003). In addition to previous research that found postoperative pain to be an independent risk factor for the full syndrome of delirium, this study provides evidence for pain as a significant ($p < .05$) risk factor in the development of subsyndromal delirium in older adults following major elective orthopedic surgery. The mean pain scores from the time period of 0 to 24 hours following the participant's arrival in the following surgery unit was significantly ($p < .05$) related to subsyndromal delirium on the second day after surgery. In addition, the findings of this study are consistent with the findings of previous research that found no etiological impact of postoperative administration of opioids on the development of delirium (Fong et al., 2006; Lynch et al., 1998; Morrison et al., 2003), with the exception of meperidine (Morrison et al., 2003). The choice of opioid medication administered to older adults before and during surgery, however, was predictive of postoperative delirium in previous research (Radkte et al., 2010).

The overall rate of subsyndromal delirium of 67.9% ($N = 53$) reported in this study is comparable to previous findings in samples of older hospitalized patients who underwent total joint replacement surgery (Liptzin et al., 2005). Diligent pain management may help reduce delirium symptoms in older postoperative patients. The

sample used for this observational study may differ from patients seeking other noncardiac procedures making generalization to other populations inappropriate. However, findings suggest a significant relationship exists between subsyndromal delirium and postoperative pain.

Incidence of Subsyndromal Delirium

In acute care and long-term care settings, incidence rates for subsyndromal delirium reported in the literature ranges from 12% to 68.8% (Bourdel-Marchasson et al., 2004; Ceriana et al., 2010; Cole et al., 2003; Liptzin et al., 2005; Marcantonio et al., 2002; Tan et al., 2008). The incidence of subsyndromal delirium in this study was comparable to the higher incidence rate of 68.8% of subsyndromal delirium reported by Liptzin et al. (2005) in older adults following joint replacement surgeries. Other studies conducted in acute care settings have reported lower incidence rates of subsyndromal delirium among older adults. For example, the incidence of delirium was 46.2% in a mixed sample of medical and surgical patients (Levkoff et al., 1996), 20% in patients with hip fracture (Marcantonio et al., 2002) and 34% in surgical patients following cardiotomy surgery (Tan et al., 2008). Despite the wide range of incidence of delirium symptoms from previous studies, it is clear that delirium symptoms are very common in older adults in the early postoperative period. As Cole (2013) argued, the variation in subsyndromal delirium incidence rates should not be assumed as related to the diagnostic criteria used. Further, some evidence suggests little difference exists in delirium detection despite the use of different sets of validated diagnostic criteria, such as the CAM or the Diagnostic and Statistical Manual for Mental Disorders III or IV (Cole 2012; Voyer, Richard, Doucet, & Carmichael, 2009).

Like delirium, the detection of subsyndromal delirium occurs through the identification of the number of core symptoms present (Cole et al. (2011). Incidence rates for subsyndromal delirium with one symptom of delirium (SSD-1) and subsyndromal delirium with two or three symptoms of delirium not meeting criteria for delirium (SSD-2) are different, with SSD-1 occurring more frequently and SSD-2 having been associated with poorer outcomes (Cole et al., 2013). Very few researchers have reported research findings separately for SSD-1 and SSD-2. Cole et al. (2011) detected SSD-1 in 65.4% and SSD-2 in 26% of longterm care residents who were assessed as negative for delirium prior to the study. The higher rate of SSD-1 (45.2%) versus SSD-2 (20.8%) in the current study is in agreement with the findings reported by Cole et al. (2011).

Incidence rates of delirium have wide variation between studies. In a systematic review, Fong et al. (2006) reported the range of delirium incidence among studies at 10% to 80%. In this study, 18.9% (n=10) of the participants developed full delirium. Of those participants with full delirium, 60% (n = 6) had either 1 or 2 positive findings on one of the CAM assessments prior to the development of full delirium compared to 40% (n = 4) of patients who developed delirium without first exhibiting subclinical delirium symptoms. In this study, participants with one or two delirium symptoms had a 5 times higher risk for progressing to full delirium than those who did not develop subclinical symptoms of delirium supporting the notion that subsyndromal delirium occurs on a spectrum between no delirium and full delirium.

Preoperative Risk Factors and Subsyndromal Delirium in Older Adults

In this study, preoperative risk factors for delirium symptoms for inclusion in data analyses procedures were selected from risk factors repeated in the delirium literature for

older surgical patients. Those risk factors included advanced age (Dasgupta & Dumbrell, 2006; DeCrane et al., 2011), a higher number of comorbidities (Cole et al., 2012; Marcantonio et al., 2002), cognitive impairment (DeCrane et al., 2011; Marcantonio et al., 2002), history of a recent fall (Aizenberg, Sigler, Weizman, & Barak, 2002; Fong et al., 2009), and the duration of preoperative fasting times (Korc-Grodzicki et al., 2014; Radtke et al., 2010). Other risk factors that appear in the literature included increased severity of physical illness.

To determine the relationship between subsyndromal delirium and the preoperative risk factors of comorbidity burden, cognitive status, history of a recent fall, and preoperative fasting time, correlation and regression analyses were conducted. Each preoperative risk factor was discussed as follows in response to relationships to increased delirium symptoms in older adults following elective major orthopedic surgery followed by a discussion of the results of the regression analysis of preoperative risk factors and the outcome of increased delirium symptoms.

Comorbidities. The age-adjusted Charlson Comorbidity Index (CCI) score incorporates age as well as co-occurring conditions into the calculation of a weighted standardized score, with a higher score indicating a greater burden of comorbidity. Mixed results were derived from studies evaluating the role of comorbidities on the development of delirium. For example, some researchers have identified the Charlson Comorbidity Index score as an independent risk factor in hospitalized older adults in medical (Inouye et al., 2007) and surgical patients (Rudolph et al., 2010; Tan et al., 2008), while others have failed to demonstrate a significant relationship between delirium and a patient's level of comorbidity burden (Marcantonio et al., 2002; Neufeld et al., 2013; Velilla et al.,

2012). The age-adjusted Charlson Comorbidity Index was used to determine predictors of postoperative delirium in patients ≥.75 years scheduled for cancer surgery (Korc-Grodzicki et al., 2014) and to identify risk factors for the development of delirium after radical cystectomy (Large et al., 2013). Inouye, Zhang, and Jones (2007) used the Charlson Comorbidity Index to measure baseline characteristics in hospitalized older adults at discharge to determine delirium risk using a Charlson Comorbidity Index cut-off score of 4. In this study, nearly one-half of participants who developed delirium symptoms (n = 23) had a Charlson Comorbidity Index score of 4 or greater (n = 11).

Similarly, previous researchers have identified the Charlson Comorbidity Index score as a predictor of delirium (Korc-Grodzicki et al., 2014; Large et al., 2013). Large et al. (2013) reported a mean Charlson Comorbidity Score as 3.5 for surgical inpatients with delirium and 3.0 for patients without delirium following surgery for a radical cystectomy, usually performed for treatment of bladder cancer. In this study, the average Charlson Comorbidity Score was similar in patients who developed delirium symptoms (M = 3.6) and those who did not (M = 3.8). Differences in comorbidity scores found in this study may reflect differences in the population sampled.

Cognitive impairment. The literature investigating postoperative delirium in older adults identified dementia or cognitive impairment as an important predictor of delirium (Levkoff et al., 1996; Marcantonio et al., 2002; Cole et al., 2003; Cole et al., 2011). In this study, cognitive status was assessed as impaired on the Mini-Cog dementia screening tool in 25% of participants (n = 13), only 15% of those older adults with an abnormal Mini-Cog screen had a formal diagnosis of dementia (n = 2). When broken down by procedure, patients who underwent total hip arthroplasty procedures had the

highest rate of cognitive impairment (36.4%, *n* = 4) compared to patients who underwent other total joint replacement procedures (11.9%, *n* = 5). Because older adults are at highest risk for delirium, it is important to include participants with cognitive impairment in research studies. Lynch et al. (1998) included older adults with cognitive impairment if they had adequate cognitive function to grant informed consent. In this study, older adults with cognitive impairment were invited to participate if they were able to use the Iowa Pain Thermometer.

Cognitive impairment occurred at similar rates in patients who developed SSD-1 (16.7%, *n* = 4) and SSD-2 (18.2%, *n* = 2). Cognitive impairment was somewhat less common in patients who did not develop delirium symptoms (12.5%, *n* = 1). Cognitive impairment has consistently been identified as a risk factor for delirium in the other studies. Marcantonio et al. (1994) developed a predictive model for delirium applicable to noncardiac patients in which one of the three strongest predictors was cognitive impairment, which has been corroborated by a more recent systematic review (Dasgupta & Dumbrell, 2006). In addition, Cole et al. (2003) found dementia to be a strong predictor of subsyndromal delirium in medical patients.

Participants who participated in this study with abnormal preoperative Mini-Cog screens demonstrated the ability to use the Iowa Pain Thermometer at the time of enrollment and in the postoperative period. In addition, patients with cognitive impairment who developed delirium were most often able to continue using the Iowa Pain Thermometer to rate their pain. Nurses caring for older adults with cognitive impairment should be encouraged to attempt self-report for pain assessment in those patients who develop delirium, if possible.

Recent fall history. A history of falls is a nonmodifiable risk factor for delirium (Aizenberg et al., 2002; Korc-Grodzicki, 2014). In this study, 3.8% (n = 2) of the participants had a history of a recent fall (n = 2) and the number of falls within the past six months was an independent risk factor for delirium symptoms in older adults 65 years or older. In a recent investigation with a larger sample (n = 416), Korc-Grodzicki et al. (2014) also found a history of falls to be predictive of postoperative delirium in surgical patients with an age of 75 years and older. Functional status, which may be reflected by a recent history of a fall, has been identified as a risk factor for delirium (Levkoff et al., 1996) but was not related to delirium in this study. Functional status was originally proposed as one of the preoperative risk factors in this study. Upon initial analysis, a significant lack of variability in functional status scores was evident (scores on the Barthel Index for Activities of Daily Living had a mean score of 97.6 out of 100, median of 100, and a mode of 100). However, following a review of the most recent literature, it was noted that a recent fall was an important risk factor for delirium (Fong et al., 2009). Therefore, the decision was made to replace functional status with a history of a recent fall as one of the preoperative risk factor variables entered into the hierarchical regression model.

In this study, the number of falls within the past 6 months was significantly related to increased delirium symptoms at 48 hours after arrival on the post-surgical unit and at 72 hours. After accounting for variances introduced by the other preoperative risk factors (Charlson Comorbidity Index score, Mini-Cog score, and duration of preoperative fasting time), the number of falls within the past six months contributed to a 10.1% increase in delirium symptoms, r = .32, n = 53, p = .008. These findings agree with

previous researchers who have concluded that having a recent fall history placed patients at significant risk for postoperative delirium (Aizenberg et al., 2002; Fong et al., 2009; Korc-Grodzicki et al., 2014). In this study, participants who reported falling in the past six months had an average CCI score of 6.0, which was significantly higher than the average CCI score of 3.6 for those without a recent fall history.

Having a history of a recent fall was a significant correlate with the CCI score, r =.38, N = 53, p=.003. Significance of the correlation coefficient between a recent fall history and CCI score was tested post hoc. Results showed that the correlation between a recent fall history and CCI score differed reliably from zero, $t(51) = -2.93$, p=.005. Therefore, the relationship between a recent fall and the CCI score seems to be mediated by the relationship between the CCI score and other independent variables in the set.

Preoperative fasting time. The time a patient fasts from fluids prior to surgery has been reported as a predictor for early postoperative delirium in older adults in the recovery room and on the first postoperative day (Radtke et al., 2010). In this study, the researcher found that preoperative fasting time may be related to increased delirium symptoms on the third postoperative day, r = .30, N = 53, p = .03, but did not explain an increase in delirium symptoms at 24 hours, r = .10, N = 53, p = .50, or, at 48 hours, r = .07, N = 53, p = .63. Radkte et al. (2010) recommended changes in current practice aimed at reducing certain precipitating risk factors for delirium that include reduction of preoperative fasting times. The findings of this study suggest efforts to reduce preoperative fasting durations may also reduce incidence of subsyndromal delirium.

Relationship between Subsyndromal Delirium and Pain

The average pain intensity rating on the Iowa Pain Thermometer (0 - 10) reported by patients for the study period was 3.9. Patients with SSD-2 reported higher levels of postoperative pain after surgery than either patients with SSD-1 or no delirium symptoms. When each 24 hour period was examined separately, patients with SSD-2 at 48 hours had more pain between 24 and 48 hours following surgery than patients with SSD-1, full delirium, or no delirium symptoms. When stratified by procedure, pain ratings reported by patients who underwent total hip arthroplasty procedures were higher on average than those reported by patients who underwent other total joint replacement procedures.

Previous researchers have labeled pain as a known predictor of delirium (Lynch et al., 1998; Morrison et al., 2003; Leung et al., 2013). In this study, the relationship between subsyndromal delirium and pain intensity was determined by correlations and regressions. Previous studies have found higher levels of pain were predictive of increased delirium incidence (Lynch et al., 1998; Morrison et al., 2003; Oh et al., 2008; Vaurio et al., 2006).

After accounting for the preoperative risk factors (Charlson Comorbidity Index score, cognitive score on the Mini-Cog, number of recent falls, and preoperative fasting time), pain between 24 to 48 hours after surgery accounted for 21% of the variance in delirium symptoms on the second postoperative day. Other researchers have found higher incidences of delirium on postoperative day 2 (Leung et al., 2009; Lynch et al., 1998). Similarly, Leung, Sands, Lim, Tsai, and Kinjo (2013) reported delirium incidence highest on postoperative days 1 and 2, whereas Oh et al. (2008) found significantly higher

incidences of delirium on postoperative day 1. Pain is an important postoperative variable to consider in relation to increased delirium symptoms on the first and second day following surgery when pain experienced by patients is typically at a moderate to severe level. When cases of delirium were excluded, higher levels of pain from between 0 and 24 hours after surgery was significantly related to subsyndromal delirium on the second postoperative day, $R^2 = .16$, $F(5, 38) = 1.65$, $p = .03$. The delay in detection of subsyndromal delirium suggests that the effects of unrelieved pain may not be immediately apparent, but may emerge the following day.

In correlational analyses, the mean pain reported by participants between 24 and 48 hours following surgery was associated with increased delirium symptoms at 48 hours, $r = .22$, $n = 53$, $p = .11$, but did not reach significance. Conversely, pain intensity reported between 0 and 24 hours after surgery was related to decreased delirium symptoms at 24 hours, although the relationship did not reach significance, $r = -.26$, $n = 53$, $p = .06$. As in previous work by Lynch et al (1998), the researcher stratified participant outcomes by procedure to gain insight into the relationship between mean pain ratings and delirium. Findings suggested patients who underwent total hip arthroplasty had higher mean pain levels than patients who underwent total knee arthroplasty, especially on the second day after surgery. This finding differs from findings of Wylde, Rooker, Halliday, and Blom (2011) who found patients who underwent total knee replacement surgery reported more severe pain in the first 3 days after surgery than patients who had total hip replacement surgery. The researchers controlled the pain medication regimen received by patients -- patient-controlled

analgesia with supplemental ibuprofen and tramadol -- and may have contributed to differences in their findings and findings in this study.

Variation in delirium symptoms and pain. Increased pain intensity was related to increased delirium symptoms at 48 hours following arrival in the following surgery unit, but not at 24 or 72 hours. On the second day after surgery, patients may experience more pain due to early mobilization and discontinuation of local anesthetic infusions, if used. In this study, patients with SSD-2 reported more pain after surgery than other patients with no delirium, SSD-1, or full delirium. In addition to having higher levels of pain, patients who developed SSD-2 had a higher baseline comorbidity burden. Overall in the study sample, pain scores and comorbidity score were related, although not significantly, $r = -.21$, $N = 53$, $p = .14$. Pre-existing conditions could contribute to the level of pain experienced following surgery.

Pain levels of participants without delirium. An unexpected finding was that the patients without delirium symptoms had higher levels of pain than patients with subsyndromal delirium or full delirium. Higher levels of postoperative pain reported by individuals who did not develop any delirium symptoms may represent a difference in baseline vulnerability in patients who developed delirium after surgery. According to the multifactorial model for delirium conceptualized by Inouye and Charpentier (1996), those with a very low baseline vulnerability to delirium would be able to withstand higher levels of pain without developing delirium symptoms than those with a higher baseline vulnerability to delirium. In this study, those patients with the highest Charlson Comorbidity Index score were some of the most vulnerable to developing SSD-2 at 48

hours and also had higher mean pain scores between 24 and 48 hours than patients with SSD-1 at 48 hours.

Intraoperative factors and delirium symptoms. Some lingering effects on cognition from anesthesia and on pain from intraoperative medications may continue for 24 hours or longer after surgery. Confounding effects from intraoperative factors could have impacted findings of the first delirium assessment at 24 hours after surgery. By the second delirium assessment at 48 hours after surgery, the effects of the intraoperative factors may have worn off, resulting in opposite directions in effect on delirium symptoms on the 2 days. A large majority of patients in this study had general anesthesia administered for the surgery (n = 52 of an N of 53) and included a variety of postoperative pain regimens depending on the surgeon and patient preference. Marcantonio, Goldman, Orav, Cook, and Lee (1998) concluded intraoperative factors of route of anesthesia and intraoperative hemodynamic complications were not associated with delirium, whereas greater intraoperative blood loss was associated with increased rates of early postoperative delirium. A more recent investigation also found similar results -- intraoperative blood loss of greater than 1,000 milliliters predicted early postoperative delirium (Behrends, DePalma, Sands, & Leung, 2013).

A possible confounder in the study of early postoperative delirium symptoms are delayed cognitive changes that may occur as a result of intraoperative factors and persist longer than was previously thought. In a recent systematic review, researchers who examined the influence of anesthesia on early cognitive changes after elective joint arthroplasty surgery found a possible delayed onset of cognitive changes related to general anesthesia (Zywiel, Prabhu, Perruccio, & Gandhi, 2014). It is possible

intraoperative factors may have influenced cognitive changes that we noted in the early postoperative period.

Relationship between Subsyndromal Delirium and Opioid Intake

The role of opioid administration in delirium etiology remains unclear, except in the case of meperidine, which is related to increased delirium (Fong et al., 2009; Lynch et al., 1998; Sieber et al., 2011). Ongoing heterogeneity exists in the literature regarding the role of opioid dose and delirium symptoms. A general recommendation given by some is to titrate down and reduce doses of opioids given to older adults to reduce subsyndromal delirium rates (Skrobik, 2009), yet research findings of a significant relationship between delirium symptoms and opioid intake have been inconsistent. A clear causal relationship between delirium symptoms and the method of postoperative pain analgesia (DeCrane et al., 2011; Lynch et al., 1998), type of opioid, (with the exception of meperidine) (Morrison et al., 2003), or the total dose of opioid administered (Lynch et al., 1998) has not yet been confirmed.

In this study, pain management regimens for participants varied according to physician preference. Some researchers have found no significant difference in delirium outcomes for patients who have different types of postoperative pain regimens (DeCrane et al., 2011), while other researchers have recommended postoperative that pain regimens avoid morphine and favor oral routes of administration to minimize the cognitive changes in the early postoperative period (Zywiel et al., 2014). In this study, variation in pain regimens among participants may have impacted the seemingly conflicting results for delirium outcomes at 24 and then at 48 hours.

This study found a nonsignificant correlation between opioid intake on the second postoperative day and delirium symptoms at 48 hours, $r = .24$, $N = 53$, $p = .08$. Furthermore, opioid intake was not related to delirium symptoms on the 1st or 2nd day after surgery. However, the relationship did not persist after accounting for the contributions of preoperative risk factors and pain in analysis using a hierarchical linear regression model.

Many nurses assume opioids are the cause of confusion when delirium symptoms develop in older adult patients, which may result in a discontinuation of the opioid (Robinson et al., 2008; Robinson & Vollmer, 2010; Staus, 2011). However, in this study, opioid intake was not significantly associated with either an increase or decrease in delirium symptoms. This finding is consistent with findings of other researchers. In systematic reviews investigating opioid use and cognitive changes, minimal or no change in cognitive function was associated with opioid use (Ersek et al., 2004). In addition, postoperative pain management for older patients using hydromorphone and morphine was not associated with delirium risk following joint replacement surgery (Nandi, Harvey, Saillant, Kazakin, Talmo, & Bono, 2014). Investigations have found that avoiding opioids in older patients following surgery or using very low doses of opioids increases delirium risk in patients who underwent joint replacement surgery (DeCrane et al., 2014) and patient with hip fracture (Sieber et al., 2011). The treatment of pain with appropriate opioids and doses was not associated with increased postoperative confusion in older adults (DeCrane et al., 2014).

Summaries and Conclusions

Implications for Action

Pain is a modifiable precipitating risk factor for delirium symptoms. Previous studies have identified negative outcomes associated with subsyndromal delirium. Therefore, strategies to minimize the modifiable risk factor of postoperative pain are needed. Pain management efforts should include special attention to the first and second day after surgery when patients experience higher levels of pain and have an increased risk for developing delirium symptoms. Given that increases in major elective orthopedic procedures are projected, research is needed to investigate factors that influence nurse decisions when caring for patients with post-surgical pain who develop delirium symptoms in the early postoperative period.

Significance for Nursing Science, Practice and Education

This study contributes to growing evidence regarding the importance of pain management in delirium prevention and treatment strategies. Previously, several studies identified risk factors for subsyndromal delirium in patients following major noncardiac surgery (Liptzin et al., 2005; Marcantonio et al., 2002; Oh et al., 2008), while other investigations focused specifically on the role of pain and pain treatment in the development of delirium (Morrison et al., 2003; Leung et al., 1998; Leung et al., 2013). Prior to this work, evidence in the published literature regarding the relationship between subsyndromal delirium and postoperative pain had not been specifically examined. Additional research is needed to learn how to best integrate assessment for subsyndromal delirium into nursing practice despite the fluctuation of symptoms into daily nursing assessments. With the high frequency of delirium symptoms among older hospitalized

patients, there is a need to investigate the validity of using various pain assessment tools with delirious patients. Additional research is also needed to better understand nurse decisions related to pain management for delirious patients.

Nurses and physicians education regarding the relationship between delirium symptoms, pain, and opioid intake will be necessary to improve both recognition of subsyndromal delirium and pain management for older adults following major elective orthopedic surgery. Delirium prevention efforts that include efforts to prevent moderate to severe pain in older patients may reduce delirium symptoms. Because subsyndromal delirium often goes unrecognized, nurses are encouraged to assess for delirium symptoms using one of the validated delirium assessment tools and report new symptoms detected to facilitate early treatment regardless of whether delirium symptoms meet the criteria for the full syndrome of delirium. Furthermore, nurses are encouraged to assist in delirium prevention through effective management of postoperative pain in older adults using adequate dosages of opioid analgesics to achieve acceptable levels of pain relief. Improvement strategies may include the use of analgesic trials prior to discontinuation of an opioid when delirium symptoms emerge. Although nurses may be reluctant to continue opioid medications if subsyndromal delirium is noted, findings from this study suggest possible causal factors other than opioid intake should also be considered, such as pain. When a patient initially shows signs of delirium, such as inattention, initiating an analgesic trial of the ordered dose of the current opioid analgesic can assist nurses in identifying whether the medication is contributing to the cognitive changes (Darcy, 2006). In an analgesic trial, the ordered opioid analgesic is administered to the patient with a subsequent assessment of the patient for either an improvement or a worsening of

delirium symptoms. The information gained from the analgesic trial is used in the decision regarding continuation or discontinuation of the opioid medication. Physicians are encouraged to allow nurses to try an analgesic trial for older patients when delirium symptoms are detected prior to discontinuing analgesics in sufficient doses for older patients when delirium.

Incorporation of a delirium risk assessments into preoperative and postoperative assessment forms may help with the integration of delirium assessment into daily practice. Educational pre-licensure programs are encouraged to integrate delirium prevention strategies and detection into curriculum. Education may include information regarding the risk factors associated with delirium In addition, information regarding the importance of preventing moderate to severe pain in older patients may help reduce the negative outcomes associated with delirium symptoms.

Appendix A
Acknowledgments

Successful completion of this project was possible only with the strong team of mentors assembled. I want to acknowledge my primary advisor and mentor, Dr. Glenda Lindseth, Professor (University of North Dakota), who spent countless hours guiding me through every step of this journey. In addition, the dissertation team included Dr. Darla Adams, Clinical Associate Professor, College of Nursing and Professional Disciplines and Certified Registered Nurse Anesthetist (University of North Dakota); Dr. Eleanor Yurkovich, Professor Emeritus at the College of Nursing and Professional Disciplines (University of North Dakota); Dr. Jean Shreffler-Grant, Professor (Montana State University); and Dr. Warren Jensen, Director of Aeromedical Research and Flight Surgeon for the University of North Dakota's Odegard School of Aerospace Science.

Appendix B
Demographic Questionnaire

Initial Assessment Form

Study ID _____
Assessment Date: _____
Assessment Time _____
Age: _____Or, ***if >89 years, check here***_____
Gender:
☐ 1. Male
☐ 2. Female

Ethnicity:
☐ 1. Not of Hispanic origin
☐ 2. Hispanic

Race:
☐ 1. White
☐ 2. Black, African American
☐ 3. American Indian or Alaska Native
☐ 4. Asian
☐ 5. Some other race: _____

Scheduled Surgical Procedure (specify) _____
Primary Diagnosis (Please specify) _____
Comorbidities (Check all that apply)
☐ 1. Anemia
☐ 2. Atrial Fibrillation/Heart Palpitations
☐ 3. Cellulitis
☐ 4. Cerebrovascular Disease/TIA
☐ 5. CHF- Congestive Heart Failure
☐ 6. COPD- Chronic Obstructive Disorder
☐ 7. Coronary Artery Disease
☐ 8. CVD- Cardiovascular Disease
☐ 9. Dementia/ Alzheimer's
☐ 10. Depression
☐ 11. Diabetes
☐ 12. FX- Hip
☐ 13. History of falls
☐ 14. HTN- Hypertension
☐ 15. Other

Please specify _____

Payment Source: Please choose all that apply
☐ Medicare
☐ Medicaid
☐ HMO
☐ Private Pay
☐ VA
☐ Other

Other Payment Source _____

Type of Housing
☐ Private Senior Housing
☐ Private Rental Home/Apt
☐ Public Housing
☐ Personal Care/Assistive Living
☐ Nursing Home
☐ Home Owner
☐ Group Home
☐ Other Housing _____

Does patient live alone?

□ No
□ Yes

Living Arrangement: Please choose all that apply.

□ With Spouse
□ With Other Relative
□ With Non Relative
□ With Live-in Paid Caregiver
□ Other

Other Living Arrangement:
_____

Marital Status:

□ Single
□ Married
□ Widowed
□ Divorced
□ Separated
□ Living With Partner

Sensory Impairment(s): Please choose all that apply.

□ Speech
□ Hearing
□ Vision
□ Other: please specify:

_____

Other health-related information:

□ Smoking ___PPD for ___ years
□ Alcohol use: __Rare __Occasional_ Daily__

Regular Home Medications:

Preoperative IPT pain rating: ____/10 _____ (verbal descriptor)

CAM score preop: □ No delirium □ SSD1□ SSD2□ Delirium

CAM score POD#1: □ No delirium □ SSD1□ SSD2□ Delirium

CAM score POD#2: □ No delirium □ SSD1□ SSD2□ Delirium

CAM score POD#3: □ No delirium □ SSD1□ SSD2□ Delirium

Mini-Cog result: □ Abnormal □ Normal

Charlson Comorbidity Index score: _____

Post-Study Data Extraction:

Study ID _____
Assessment Date: _____
Assessment Time _____

Laboratory Data
Preoperative laboratory data:
CBC: Hbg___Hct___
Complete metabolic panel: Sodium___Potassium___BUN___Creatinine___

Postoperative laboratory data:
CBC: Hbg___Hct___POD:___
Complete metabolic panel: Sodium___Potassium___BUN___Creatinine___POD:____

CBC: Hbg___Hct___POD:___
Complete metabolic panel: Sodium___Potassium___BUN___Creatinine___POD:____

Surgery Data
Fasting time to surgery: _____hours Time of last food intake: _____ Time of last fluid intake:____

IV fluids preop:_____mL *Surgery start time:*_____ *EBL:*_____*mL*
Preoperative Medications:
Anesthesia Method: __General __Spinal *Epidural analgesia*:
Yes No
Length of surgery: __ Hours __Minutes *Continuous Local Anesthetic*:
__Hours

Intraoperative Medications:

Medication Data
Scheduled Medications during admission:
Meds: Doses administered: Time: Post-op Day:

PRN Medications during admission:
Meds: Doses administered: Time: Post-op Day:

Study ID_____

Study variables

1. Pain intensity ratings during postoperative period

Time	Pain Ratings POD #1	Time	Pain Ratings POD #2	Time	Pain Ratings POD #3

2. 24 Hour Opioid Intake Data

POD	Opioid #1	Dosage	No. of Doses/24 hours
#1			
#2			
#3			
POD	Opioid #2	Dosage	No. of Doses/24 hours
#1			
#2			
#3			

Indicators of SSD symptoms from staff or chart
(Physician orders, physician progress notes, nurses notes, nursing shift assessments, medication administration record, or verbal report from staff):

1. . *Source:* *POD*:
2. . *Source:* *POD*:
3. . *Source:* *POD*:

Vital Signs
Vital signs on admission: T ___ P ___ R ___ BP ____ O2 sat ___

Vital signs on POD#1: T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___

Vital signs on POD#2: T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___

Vital signs on POD#3: T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___
T ___ P ___ R ___ BP ____ O2 sat ___

Mobilization

Day of Surgery:	__Sat on edge of bed	__Ambulated < 25 feet	__Ambulated > 25 feet
POD #1:	__Sat on edge of bed	__Ambulated < 25 feet	__Ambulated > 25 feet
POD #2:	__Sat on edge of bed	__Ambulated < 25 feet	__Ambulated > 25 feet
POD #3:	__Sat on edge of bed	__Ambulated < 25 feet	__Ambulated > 25 feet

Complications

Infection:___ Pulmonary embolism:___ Air embolism:___
Other:_____

Discharge

Discharge disposition, date and cause of death, if appropriate: _____

Appendix C
Delirium Symptom Interview

Disorientation

1. *Have we met before?*
   1. Correct 2. Incorrect 6. No response 8. Don't Know
2. *Can you tell me what time of day it is now?*
   1. Correct 2. Incorrect 6. No response 8. Don't Know
3. *Can you tell me where you are now?*
   1. Correct 2. Incorrect 6. No response 8. Don't Know
4. *Why were you in the hospital?*
   1. Correct 2. Incorrect 8. Don't Know
5. *During the past day did you think that you weren't really in the hospital?*
   1. NO 2. YES 8. Don't Know
6. *Have you felt confuse at any time during the past day*
   1. NO 2. YES 8. Don't Know

   6a. If yes at what time of day did this confusion bother you the most?
   1. Morning 2. Afternoon 3. Evening 4. Night
   5. Many different times 6. Not Applicable 7. Don't Know

   6b. If yes Did this happen either just before you woke up or just when you were falling asleep?
   1. NO 2. YES 7. Not Applicable 8. Don't Know

   6c. If yes Is this something new that you have experienced since you came to the hospital, or is it something that you experience at home
   1. OLD 2. NEW 7. Not Applicable 8. Don't Know

   6d. During the interview was there evidence of disorientation, for example, the patient first appeared to know that he was the hospital but later indicated that he thought he was elsewhere?
   1. NO 2. YES

Disorientation Score _____
1=Not present
2=present
Present: Scored 2-8 on items #2-5, 6d

Disturbance of Sleep

Now I am going to ask you about your sleep.

7. *Did you have trouble falling asleep last night?*
   1. NO 2. YES 8. Don't Know

   Did you have any problems with your sleep last night, like trouble falling asleep, waking up and having trouble falling back to sleep, waking up to early, being sleepy during the day, or having nightmares that were intense or bothersome.
   1. NO 2. YES 7. Not Applicable 8. Don't Know
   If NO go to #12 If YES go to #7a

   7a. If yes how much difficulty did you have falling asleep last night?
   1. None 2. Some 7. Not Applicable 8. Don't Know

   7b. If yes Is this something new that you have experienced since you case to the hospital, or is it something that you experienced at home?
   1. OLD 2. NEW 7. Not Applicable 8. Don't Know
8. *After you fell asleep, did you wake up and have trouble falling back to sleep?*
   1. NO 2. YES 8. Don't Know

   8a. If Yes how much trouble did you have falling back asleep last night.
   1. None 2. Some 3. A Lot 7. Not Applicable 8. Don't Know

   8b. If yes is this some thing new that you have experienced since you came to the hospital, or is it something that you experience at home?
   1. OLD 2. NEW 7. Not Applicable 8. Don't Know
9. *Did you wake up on your own too early this morning*?
   1. NO 2. YES 8. Don't Know

9a. If yes how difficult did waking up too early this morning cause you?
1. None 2. Some 3. A Lot 7. Not Applicable 8. Don't Know

9b. If yes Is this something new that you have experienced since you came to the hospital, or is this something that you experience at home?
1. OLD 2. NEW 7. Not Applicable 8. Don't Know

10. *Were you sleepy during the day*?
1. NO 2. YES 8. Don't Know

10a. If Yes how much difficulty did being sleepy during the day cause you?
1. None 2. Some 3. A Lot 7. Not Applicable 8. Don't Know

10b. If yes is this something new that you have experienced since you came to the hospital, or is it something that you experience at home?
1. OLD 2. NEW 7. Not Applicable 8. Don't Know

11. *Did you have nightmares or vivid dreams that were intense or bothersome last night*?
1. NO 2. YES 8. Don't Know

11a. If Yes how much difficulty did having these dreams cause you?
1. None 2. Some 3. A Lot 7. Not Applicable 8. Don't Know

11b. If yes is this something new you have experienced since you came to the hospital, or is it something that you experience at home?
1. OLD 2. NEW 7. Not Applicable 8. Don't Know

Disturbance of sleep score: _____
1= Not present
2= Present
Present : Items 7b, 8b, 9b, 10b, 11b

Perceptual Disturbance

12. *Any time during the last day have you experience or imagined seeing, hearing, or feeling things that weren't really there?*
Describe:
1. NO 2. YES

At any time during the last day have you experienced or imagined seeing, hearing, or feeling things that weren't really there, misinterpreted object or sounds ,or seen or heard things that weren't really there?
1. NO 2. YES
If NO go to #16 If YES go to #12a

12a. Saw things?
1. NO 2. YES

12b If Yes how often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently 7. Applicable

12c. Heard thing?
1. NO 2. YES

12d. If yes how often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently 7. Applicable

12e Felt things?
1. NO 2. YES

12f If yes How often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently 7. Applicable

12g. During the interview was there evidence of any of the above hallucinations, for example, patient thought he was at home because the room seemed like home?
Describe:
1. Never 2. Rarely 3. Sometimes 4. Frequantly

13. *I just asked you about things that weren't really there. Now I want to ask you about objects that you have seen or sounds that you have that you may have misinterpreted. For example; sounds that you heard were not what they appeared to be*
1. NO 2. YES

13a. People doing things that they were not really doing?
1. NO 2. YES

13b. If yes how often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently 7. Applicable

13c. Sounds that were not what they seemed to be?
1. NO 2. YES
13d. If yes how often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently 7. Applicable
13e. An object was not what it seemed to be?
1. NO 2. YES
13f. If yes how often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently 7. Applicable
13g. Did you think people were trying to harm you when they weren't?
1. NO 2. YES
13h. If yes how often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently
13i. During the interview, was there evidence of any of the above misperceptions or delusions, for example, patient answered intercom, or thought spot on wall was a surveillance camera?
1. None 2. Rarely 3. Sometimes 4. Frequently

14. *Now, I'd like to ask you whether things that you recognized correctly looked distorted or strange, for example, things looked bigger or smaller than they really were?*
1. NO 2. YES
14a things look smaller?
1. NO 2. YES
14b. If yes how often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently
14c. Things look bigger?
1. NO 2. YES
14d. If yes how often did you have this experience? If yes how often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently
14e. Things were moving that were not really moving?
1. NO 2. YES
14f. If yes how often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently
14g. Things seemed as if they were moving in slow motion?
1. NO 2. YES
14h. If yes how often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently
14i. The patient's body size, shape, or weight looked different from what it is?
1. NO 2. YES
14j. If yes how often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently
14k. Other
Describe:
1. NO 2. YES
14l. If yes how often did you have this experience?
1. Rarely 2. Sometimes 3. Frequently

The following three questions are given whenever there is a YES to any of the perceptual disturbance questions.

14m. If yes for any perceptual disturbance at what time of day did this/these disturbances bother you the most?
1. Morning 2. Afternoon 3. Evening 4. Night
5. Many different times 6. Not Applicable 7. Don't Know
14n. If yes for any perceptual disturbance Did this/these happen either just after you woke up or just when you were falling asleep?
1. NO 2. YES 7. Not Applicable 8. Don't Know
14o. If yes for any perceptual disturbance Is this/these something new that you have experienced since you came to the hospital, or is it something that you experienced at home.
1. OLD 2. NEW 7. Not Applicable

15. During the interview was were evidence of any of the above perceptual distortions, for example patient thought a light was swirling that wasn't?
    1. Never 2. Rarely 3. Sometimes 4. Frequently

Perceptual Disturbance score:
1=Not Present
2= Present
    Present: 2-5 on items #12-15

Disturbance of Consciousness

This is the last group of questions I need to ask you. Some of these may sound unusual, but we ask them of everyone.

16. Can you tell me the days of the week backwards, starting with Saturday? (S, F, TH, W, T, M, S)
    Enter number representing longest correct consecutive series of days.
    9=Refused
17. Can you tell me the months of the year backwards, starting with December?
    (D, N, O, S, A, J, J, M, A, M, F, J)
    Enter number representing longest correct consecutive series of days.
    9=Refused

End of Patient questions

Thank You. Is there anything else you want to tell me, or anything you want ask me?

Observations

18. Did the patient stare into space and appear unaware or his/her environment? If present how much of the time?
    1. Never 2. Rarely 3. Sometimes 4. Most of the time
19. Did the patient talk about something else; change the subject (non-sequitur) or tell a story unrelated to the interview? (Tangential)
    1. NO 2. Mild 3. Moderate 4. Severe
20. Did the patient appear inappropriately distracted by environmental stimuli? For example responded to question asked of roommate? (distractible) If present how much of the time?
    1. Never 2. Rarely 3. Sometimes 4. Most of the time
21. Did the patient show excessive adsorption with ordinary objects in the environment, for example, repetitively fold sheets, or examine the IV tube over and over? (Hypervigilant)
    1. NO 2. Mild 3. Moderate 4. Severe
22. Did the patient have recurring thought that prevented him/her from responding appropriately to the environment, for example, continuously looked for shoes that weren't there? (Persistent Thought)
    1. NO 2. Mild 3. Moderate 4. Severe
23. Did the patient have trouble keeping track of what was being said during the interview, for example fail to follow instructions or answer questions one at a time? (Inattentive)
    1. Never 2. Rarely 3. Sometimes 4. Most of the time
24. Did the Patient appear inappropriately startled by stimuli in the environment?
    1. NO 2. Mild 3. Moderate 4. Severe
25. Did the Patient's level of consciousness fluctuate during the interview, for example, start to respond appropriately and then drift off?
    1. NO 2. Mild 3. Moderate 4. Severe
26. Was the patient
    1. Awake 2. Sleepy 3. Stuporous 4. Comatose

Disturbance of Consciousness Score:
1= Not present
2=Present
    Present: 2-4 on items #18-26

Incoherent Speech

If the patient is non-communicative answer all questions on this page with a code 7 Non Applicable and go to #29

27. Was the patient's speech

27a Unusually limited or sparse?
1. NO 2. Mild 3. Moderate 4. Severe
27b. Unusually slow or halted?
1. NO 2. Mild 3. Moderate 4. Severe
27c Unusually slurred?
1. NO 2. Mild 3. Moderate 4. Severe
27d. Unusually fast or pressured?
1. NO 2. Mild 3. Moderate 4. Severe
27e Unusually loud?
1. NO 2. Mild 3. Moderate 4. Severe
27f Unusually repetitive?
1. NO 2. Mild 3. Moderate 4. Severe
27g. Have speech sounds in the wrong place
1. NO 2. Mild 3. Moderate 4. Severe
27h. Have words or phrases that were disjointed or inappropriate?
1. NO 2. Mild 3. Moderate 4. Severe

28. If present, did the patient's speech fluctuate during the interview, for example, patient spoke normally for a while then sped up.
1. NO 2. YES 7. Not Applicable

Incoherent Speech Score:
1=Not Present
2=Present
Present: Items 27a-h

Level Psychomotor Activity

29. Was there evidence of:
29a. Restlessness
1. NO 2. Mild 3. Moderate 4. Severe
29b. Tremors
1. NO 2. Mild 3. Moderate 4. Severe
29c. Grasping/picking
1. NO 2. Mild 3. Moderate 4. Severe
29d. Increased speed of motor response
1. NO 2. Mild 3. Moderate 4. Severe
29e. Wandering
1. NO 2. Mild 3. Moderate 4. Severe
29f. lethargy and sluggishness
1. NO 2. Mild 3. Moderate 4. Severe
29g. Slowness of motor response
1. NO 2. Mild 3. Moderate 4. Severe
29h. Staring into space
1. NO 2. Mild 3. Moderate 4. Severe

30. If any of the above are present (29a-h) Did the psychomotor activity fluctuate during the interview
1. NO 2. Mild 3. Moderate 4. Severe 7. Not Applicable
30a. During the interview was the patient poseyed, mittened, or otherwise restrained?
1. NO 2. YES 7. Not Applicable

Level Psychomotor Activity Score:
1=Present
2=Present
Present: Items 29a-h

General Behavioral Observations

31. Did the patient show expressions of:

31a. Apathy
1. NO 2. Mild 3. Moderate 4. Severe
31b. Fear

1. NO 2. Mild 3. Moderate 4. Severe

31c. Anger
1. NO 2. Mild 3. Moderate 4. Severe

31d. Euphoria
1. NO 2. Mild 3. Moderate 4. Severe

31e. Irritability
1. NO 2. Mild 3. Moderate 4. Severe

31f. Anxiety
1. NO 2. Mild 3. Moderate 4. Severe

31g. Combativeness
1. NO 2. Mild 3. Moderate 4. Severe

31h. Impatience
1. NO 2. Mild 3. Moderate 4. Severe

31i. Sadness
1. NO 2. Mild 3. Moderate 4. Severe

32. Did the patient do any of the following inappropriately?

32a. Crying
1. NO 2. Mild 3. Moderate 4. Severe

32b. Laughing
1. NO 2. Mild 3. Moderate 4. Severe

32c. Singing
1. NO 2. Mild 3. Moderate 4. Severe

32d. Swearing
1. NO 2. Mild 3. Moderate 4. Severe

32e. Did the patient show emotional liability
1. NO 2. Mild 3. Moderate 4. Severe

Fluctuating Behavior Score
1=Not Present
2=Present

Present: Items 27, 28, 30, 32e

33. Uncooperativeness – resistance, unfriendliness, resentment, and lack of readiness to cooperate with the interviewer. (Rate only on the basis of the patient's attitude and responses to the interviewer and the interview situation. Do not rate on basis of reported resentment or uncooperativeness outside the interview situation.)
1. NO 2. Mild 3. Moderate 4. Severe

34. Patient meets criteria for delirium.
1. NO 2. YES

Note. Adapted from "The Delirium Symptom interview: An interview for the detection of delirium symptoms in hospitalized patients," by M. S. Albert, S. E. Levkoff,, C. Reilly, B. Liptzin, D. Pilgrim, and P. D. Cleary, 1992, *Journal of Geriatric Psychiatry and Neurology.* 5*:* 14-21. Copyright 1992, Sage Publications. Used with permission.

Appendix D
Script for Invitation of Patients to Participate in Research Study

Research Study Opportunity at

North Valley Hospital

With your planned orthopedic surgery, you may be eligible to participate in a pain study being conducted by a doctoral nursing student from the University of North Dakota at our hospital. Whether or not you choose to participate in the study, you will receive the same high quality care you expect here at North Valley Hospital and none of your treatments will be altered. The findings from this study will provide important evidence that may reduce the pain experienced by older adults who undergo major orthopedic surgery.

If you are interested in this opportunity, we will contact Ms. Denny so she can contact you to discuss the study in more detail.

If you are interested in this opportunity, you may contact Ms. Denny using the contact information below to learn more about participation in this study.

If you prefer, we will contact Ms. Denny so she can contact you to discuss the study in more detail.

Researcher contact information:

Dawn L. Denny, PhD-c, RN, ONC
(406) 261-0569
University of North Dakota
ddenny@nvhosp.org

Appendix E
Information Regarding the Denny Pain Study

Nursing Research Study at North Valley Hospital Involving Orthopaedic Patients

Researcher: Dawn L. Denny, PhD Candidate (University of North Dakota), RN, ONC; Medical-Surgical RN/Orthopedic Coordinator/Case Manager at North Valley Hospital (Per diem status currently); Advisor: Glenda Lindseth, PhD, RN, FAAN, FADA (University of North Dakota)

Research Title: Subsyndromal Delirium and Postoperative Pain in Older Adults

Research Topic: Subsyndromal Delirium and Postoperative Pain

Approvals: University of North Dakota Institutional Review Board *(expires June 24, 2014)*; North Valley Hospital Senior Leadership Team and Board of Directors *(effective June 25, 2013)*

PURPOSE: To determine the relationship between postoperative pain and subsyndromal delirium in older adults following orthopedic surgery.

RECRUITMENT: Older adults scheduled for elective orthopedic surgery will be screened according to inclusion and exclusion criteria by the preanesthesia testing nurses at the preoperative appointment at the hospital or by phone. The preanesthesia nurse will give potentially eligible participants information regarding the research study. Potential participants will be given written information regarding the study purpose and how to contact the researcher if they choose to participate; or, if preferred, interested patients may ask the preanesthesia testing nurse to contact the researcher who will set up a time to meet prior to surgery to ensure eligibility. Following application of inclusion and

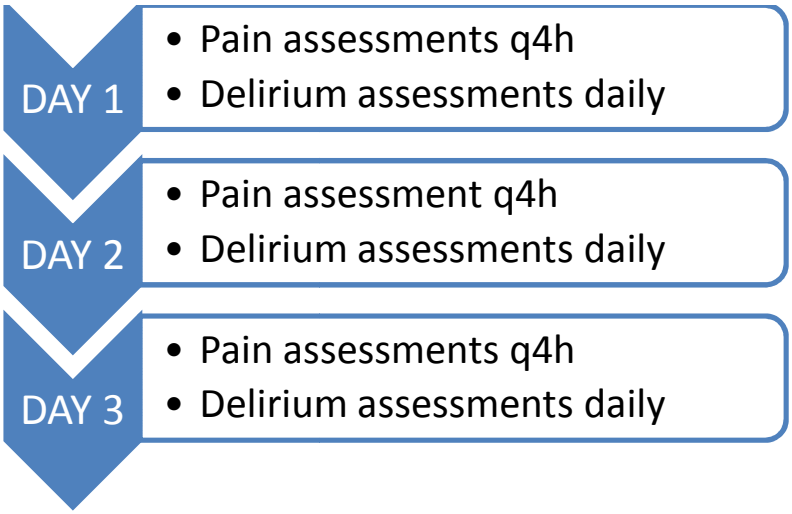
exclusion criteria, eligible patients will be invited by the researcher to participate in the study and informed consent obtained.

INCLUSION AND EXCLUSION CRITERIA: Participants must be (1) scheduled for orthopedic that will require admission to one of two inpatient post-surgical study units; (2) ≥ 65 years of age; (3) English-speaking; and (4) scheduled to undergo elective major orthopedic surgery and expected to have an inpatient stay of at least 48 hours. Participants will be excluded if they have (1) pre-existing delirium; or (2) an inability to utilize the Iowa Pain Thermometer.

SAMPLE SIZE: The researcher plans to enroll 2-3 participants per week over a period of 39 weeks to complete the proposed timeline (Sample size is 115 participants for significance).

STUDY PROCEDURES: The researcher will cooperate with health care personnel so that the provision of care is not delayed or interrupted due to the investigation. Pain assessments will be completed by the nurses using the Iowa Pain Thermometer, a pain intensity rating scale with documented reliability and validity, and thendocumented per the usual hospital procedures. Postoperative data collection by the researcher will occur on POD 1, POD 2, and POD 3 with a chart review to follow. In the case of early discharges, the researcher has made alternative plans for data collection over the telephone in order to collect necessary data for the study.

Data Collection Schematic



Iowa Pain Thermometer

Used with permission, Keela Herr, PhD, RN, FAAN, AGSF, The University of Iowa, College of Nursing.

Contact information:

Dawn L. Denny: ph# 863-9073; cell# 261-0569; email: dawn.denny@my.und.edu

Appendix F
Confusion Assessment Method Worksheet

BOX 1

I. ACUTE ONSET AND FLUCTUATING COURSE

a) Is there evidence of an acute change in mental status from the patient's baseline? O YES NO

b) Did the (abnormal) behavior fluctuate during the day, that is, tend to come and go or increase and decrease in severity? O YES NO

II. INATTENTION

Did the patient have difficulty focusing attention, for example, being easily distractible or having difficulty keeping track of what was being said? O YES NO

BOX 2

III. DISORGANIZED THINKING

Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable, switching from subject to subject? O YES NO

IV. ALTERED LEVEL OF CONSCIOUSNESS

Overall, how would you rate the patient's level of consciousness?

- O Alert (normal)
- O Vigilant (hyperalert)
- O Lethargic (drowsy, easily aroused)
- O Stupor (difficult to arouse)
- O Coma (unarousable)

Do any checks appear in this box? O YES NO

Positive for delirium per CAM (based on above CAM) ? O YES O NO

If all items in Box 1 are checked and at least 1 item in Box 2 is checked a diagnosis of delirium is suggested. They have to have both items 1 and 2 present and either 3 or 4

O NO O YES

Figure 7. The Confusion Assessment Method Worksheet. The worksheet provides a tool for the detection of delirium or subsyndromal delirium. Adapted from "Clarifying Confusion: The Confusion Assessment Method. A New Method for Detection of Delirium," by S. K. Inouye, C. H. vanDyck, C. A. Alessi, S. Balkin, A. P. Siegal, R. I. Horwitz, 1990, *Ann Intern Med*. 113: 941-948. Confusion Assessment Method: Training Manual and Coding Guide, Copyright 2003, Sharon K. Inouye, M.D., MPH. Used with permission

Appendix G
The MiniCog

ADMINISTRATION

The test is administered as follows:

1. Instruct the patient to listen carefully to and remember 3 unrelated words and then to repeat the words.
2. Instruct the patient to draw the face of a clock, either on a blank sheet of paper or on a sheet with the clock circle already drawn on the page. After the patient puts the numbers on the clock face, ask him or her to draw the hands of the clock to read a specific time.
3. Ask the patient to repeat the 3 previously state words.

SCORING

Give 1 point for each recalled word after the clock-drawing test distractor.
Patients recalling none of the three words are classified as demented (Score = 0).
Patients recalling all three words are classified as non-demented (Score = 3)
Patients with intermediate word recall of 1-2 words are classified based on the clock-drawing test (Abnormal = demented; Normal = non-demented)

Note: The clock-drawing test is considered normal if all numbers are present in the correct sequence and position, and the hands readably display the requested time.

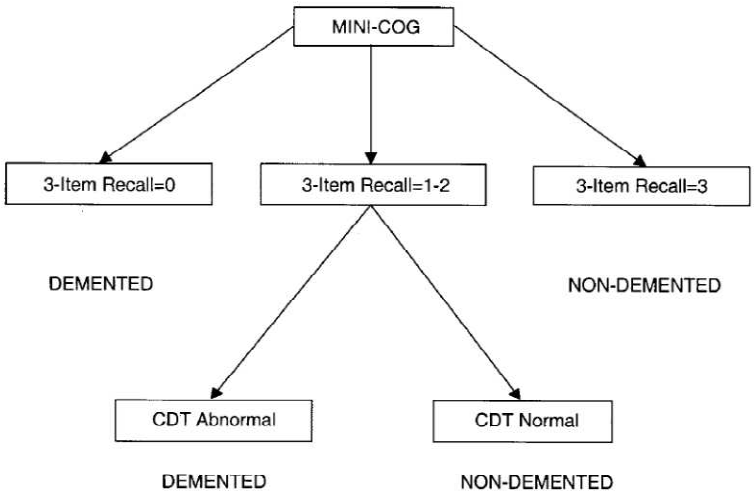


Figure 8. The Mini-Cog. The tool is appropriate for administration by non-physicians and takes approximately 5 minutes to complete. The figure provides a schematic for the determiniation of whether the screen result suggests the patient is demented or non-demented. Adapted from "The Mini-Cog: A cognitive 'vital signs' measure for dementia screening in multi-lingual elderly," by S. Borson, J. Scanlan, M. Brush, P. Vitaliano, and A. Dokmak, 2000, *International Journal of Geriatric Psychiatry*, *15*(11), p. 1024.

Appendix H
Iowa Pain Thermometer

Circle a number on the Pain Thermometer below that best represents the intensity of your pain right now.

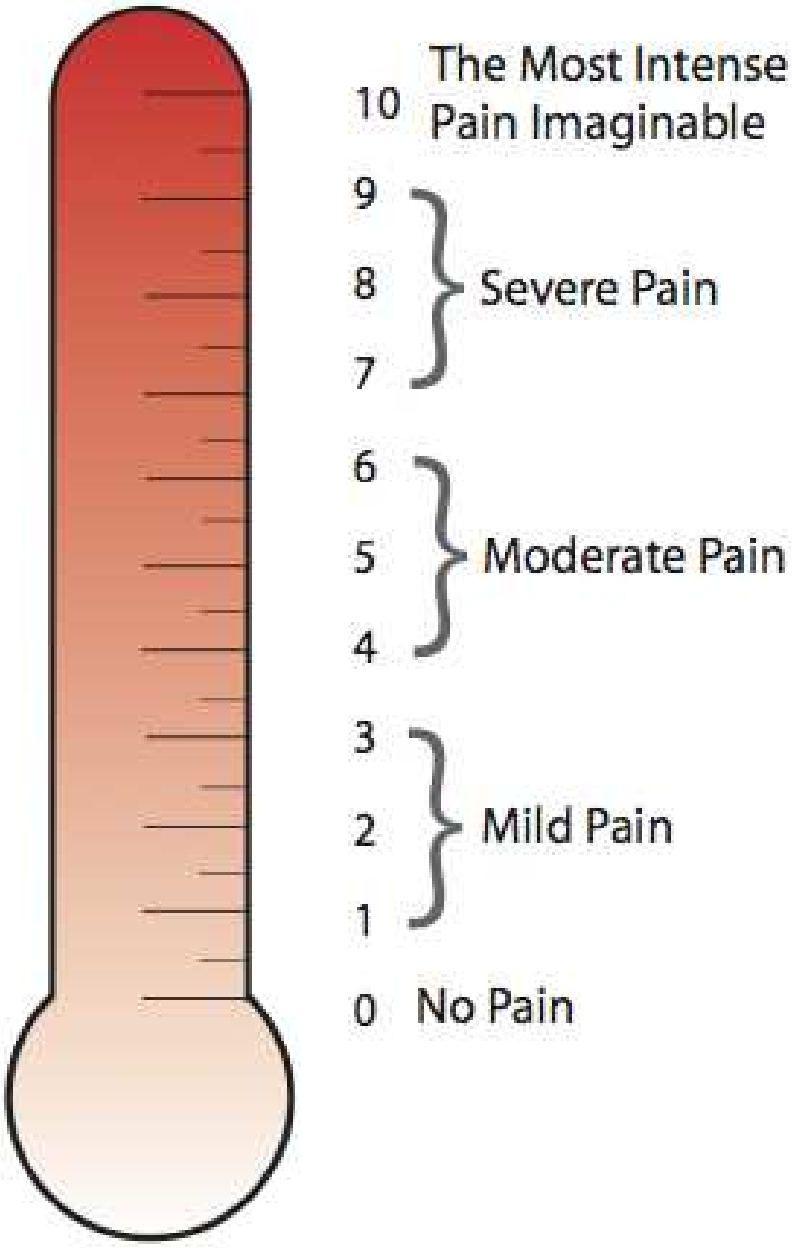


Figure 9. The Iowa Pain Thermometer. The pain intensity rating scale was developed to obtain self-reported pain ratings from older adults with or without cognitive impairment. The "Iowa Pain Thermometer" by Keela Herr, PhD, RN, AGSF, FAAN, College of Nursing, The University of Iowa, Iowa City, IA, USA. Used with permission.

Appendix I
Charlson Comorbidity Index

1. Scoring: Age
    1. Age <40 years: 0 points
    2. Age 41-50 years: 1 points
    3. Age 51-60 years: 2 points
    4. Age 61-70 years: 3 points
    5. Age 71-80 years: 4 points
2. Interpretation
    1. Calculate Charlson Score or Index (i) using assigned weights for diseases
    2. Add Comorbidity score to age score

Assigned weights for diseases	Conditions
1	Myocardial infarct
	Congestive heart failure
	Peripheral vascular disease
	Cerebrovascular disease
	Dementia
	Chronic pulmonary disease
	Connective tissue disease
	Ulcer disease
	Mild liver disease
	Diabetes
2	Hemiplegia
	Moderate or severe renal disease
	Diabetes with end organ damage
	Any tumor
	Leukemia
	Lymphoma
3	Moderate or severe liver disease
6	Metastatic solid tumor
	AIDS

Assigned weights for each condition that a patient has. The total equals the score. Example: chronic pulmonary (1) and lymphoma (2) = total score (3).

Figure 10: The Charlson Comorbidity Index is an index used widely for estimating comorbidity burden and risk of mortality. A score is derived from currently diagnosed conditions and age. Adapted from "A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation," by M. E. Charlson, P., Pompei, K. L., Ales, and C. R. MacKenzie, 1987, *Journal of Chronic Disease, 40*, p. 377.

Appendix J
Protection of Human Subjects

The research facility site was North Valley Hospital in Whitefish, Montana. The small community hospital provides critical-access to a remote area of Montana and includes a total joint replacement program.

The following policy served as the proposed study's procedure regarding human subjects:

1. ***Inclusion of older adults***. Participants for the proposed study were consecutively selected from male and female adults equal to or greater than 65 years of age of any race or ethnicity scheduled for major orthopedic surgery at the research site hospital and who meet eligibility requirements. Children were excluded from the study because the research focus was on the vulnerable population of older adults. Data was collected only from participants who have consented to participate in the investigation. The preanesthesia testing nurse informed potential participants that there was no penalty for withdrawal from the study and that they could do so at any time. The interview was conducted in a private location by the preanesthesia testing nurse.
2. ***Vulnerable participants***. The research study was conducted at a community hospital where patients may be dependent on health care personnel to meet basic needs. In addition, participants included patients with cognitive impairment who met eligibility requirements. Persons with cognitive impairment were included in the study because they represent a group severely impacted by delirium. In this study, consent was obtained from the participant. It was necessary to seek surrogate consent for any study participants.
3. ***Confidentiality***. Deidentified data collection forms were transcribed into computerized data storage with unique random numbers assignments for each participant associated with a key maintained by the PI and kept in a locked file cabinet in the PI's locked home office. Data collection forms were kept in a locked briefcase in the PI's locked home office. The information gathered for data collection was not part of the participant's medical record. Some of the data collected required information contained in the medical record. With the participant's signed consent to release protected health information, data were collected from the medical record to include laboratory testing, doctor orders and progress notes, nursing documentation, medication administration record and medical history to facilitate data analysis. All interviews were conducted in a location and manner that ensures patient privacy. The computer of the primary investigator was password protected and the computer screen was equipped with a privacy screen, a screen saver that begins within 1 minute of non-use, and encryption software for data entry.
4. ***Potential inconveniences or risks to the participants***. The researcher cooperated with health care personnel so that the provision of care was not delayed or interrupted due to the investigation. The researcher completed thorough training concerning the vulnerability of older adults with or without cognitive impairment. Education was provided to nurses who were be assigned to study

participants that emphasized that a participant's condition superceded the use of any of the study protocols if they were in conflict.

5. ***Minority inclusion***. Older adults of any race or ethnicity are eligible to participate in the investigation. All eligible consenting participants will be included in the research study regardless of ethnicity or race.
6. ***Severe adjustment problems*** No cases of adjustment difficulties were reported by participants. If a participant had been identified as having severe adjustment problems, they would have been referred for care. There were no legal or social risks to participants of this study.
7. ***Advantages for the participants***. There were no benefits for participation in this study.
8. ***Risks associated with the study***. No adverse effects from participation in the study were identified. Pain management practices were not altered from standard practices other than the use of the Iowa Pain Thermometer pain intensity rating scale for enrolled participants. The researcher conducted passive surveillance of possible harms associated with the use of the study protocols.
9. ***IRB.*** Approval from the University of North Dakota's Institutional Review Board was obtained prior to the start of the study. In addition, approval from the Board of Directors of the research site was obtained through the procedures of the administrative staff at the facility. The PI completed education in the protection of human subject education prior to the start of the study. The University of North Dakota's Institutional Review Board has received accreditation by the Association for the Accreditation of Human Research Protection Programs, Inc. through a rigorous process.

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CONSENT TO PARTICIPATE IN RESEARCH

Relationship of Confusion and Pain following Surgery in Older Adults

You are invited to participate in a research study sponsored by the University of North Dakota by Dawn Denny (PhD doctoral candidate in Nursing at the University of North Dakota). Your participation in this study is voluntary. Please read the information below, and ask questions about anything you do not understand, before deciding whether or not to participate.

PURPOSE OF THE STUDY

The purpose of this research study is to determine the relationship between mild confusion and pain following surgery. The researcher hopes the knowledge from this study will provide information that can be used to help decrease confusion occurrence after surgery.

PROCEDURES

You are asked to participate in the study because you are scheduled for major orthopedic surgery and are age 65 years or older. If you are willing to join, the investigator will meet with you at a convenient time for you. This meeting will take about 30 minutes. The purpose of the project and details for the study will be explained. The researcher will: help you complete a questionnaire that asks about you and your health history, instruct you on the use of a pain rating scale, and complete a brief test to evaluate memory and how well you are able to care for yourself. You don't need to answer any questions that you would prefer not to answer.

The study will last while you are in the hospital following your surgery for about 3 days. The researcher will be given only names of study participants. No medical information regarding non-participants will be accessed. Only medical records for those participants who have agreed to participate in the study will be reviewed. Whether or not you choose to participate, you will receive pain management according to the usual hospital practices. The researcher will complete daily assessments while you are hospitalized. Assessments will take an estimated 15 minutes and are completed in your hospital room. You may be contacted by the researcher with more questions related to pain and confusion following your

discharge home. I would like to follow up with you by phone after you go home to ask how you are doing.

The doctors will treat you as they usually do. The researcher will be conducting a brief interview with you daily.

POTENTIAL RISKS AND DISCOMFORTS

There are low risks with this study. After the surgery, you may get tired after you answer all the questions. This study does not test any medications or their side effects. We will protect your privacy while you are answering the questions. However, there is a slight risk that personal information may be heard by patients sharing your hospital room. There are no legal risks to be in the study. Referral to a case manager will be made if any significant problems occur as a result of participation in the research study.

WHAT ARE THE BENEFITS OF THIS STUDY?

It is hoped that you or other future patients might benefit from this study because of a better understanding of the relationship of confusion and pain in older adults following surgery. You will not be paid for being in this research study but you can have the results after the study is done if you like.

ALTERNATIVES TO PARTICIPATING IN THIS STUDY

You may choose not to participate in this study, and the researcher will not contact you.

PARTICIPATION AND WITHDRAWAL

If you decide you no longer wish to participate in this study, you are free to quit at any time. However, the information that has been gathered up to that time will be used in the study. This information will not have your name on it. There will be no costs to you for being in this research study.

WITHDRAWAL OF PARTICIPATION BY THE INVESTIGATOR

The investigator may withdraw you from the study if you cannot safely continue, if you can't answer the questions, or if you are transferred to a different area of the hospital, or are transferred to a different hospital.

CONFIDENTIALITY

In order to protect your privacy, your consent form and questionnaires will be held in separate locked files in the researcher's private office. After four years the consent forms and questionnaires will be shredded. This information will not become part of your medical records. Your personal information will not be included on the researcher's worksheets. The researcher will "code" the information by a randomly assigned number that will be known only to the researcher and university officials whose job is to protect your rights in research. Confidentiality of participants will be maintained by the researcher.

NEW FINDINGS

During the course of the study, if any significant new findings are identified, such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation, that might cause you to change your mind about continuing in the study, the researcher will tell you about it and then ask you if you still want to stay in the study. If you choose to stay in the study, you will sign another consent form.

RIGHTS OF RESEARCH PARTICIPANTS/IDENTIFICATION OF INVESTIGATOR

You may choose to stop participating in this study at any time without penalty. You are not waiving any legal claims, rights or remedies because of your being in this research study. If you have questions regarding your rights as a research participant, we ask that you contact the researcher, Dawn L. Denny at (406) 261-0569 or Dr. Glenda Lindseth (Advisor) at (701) 777-4506. If the research causes any injury, treatment will be available including first aid, emergency treatment and follow-up care as needed. You or your medical insurance will need to pay for any such treatment (you will be billed). In the event of a research related injury, if you experience an adverse reaction, or if you have other questions or concerns, please contact the University of North Dakota Institutional Review Board at Phone#: (701) 777-4279, or Fax#: (701) 777-6708.

SIGNATURE OF RESEARCH PARTICIPANT

I have read the information provided above. I have been given an opportunity to ask questions and all of my questions have been answered to my satisfaction. I have been given a copy of this form.

_____

Name of Participant (Please print)

_____ _____-_____

Signature of Participant Date

SIGNATURE OF WITNESS

I have discussed the above points with the participant or, where appropriate, with the participant's legally authorized representative. My signature as witness certifies that the participant signed this consent form in my presence as his/her voluntary act and deed.

_____

Name of Witness (Please print)

_____

Signature of Witness Date

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