Title

Incidence of Opioid-Induced Respiratory Depression in Trauma Patients on the General Care Floor Receiving Patient-Controlled Analgesia or Nurse Administered Intravenous Opioids Monitored by Capnography and Pulse Oximetry: A Prospective, Blinded Obser...

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A dissertation submitted in partial satisfaction of

the requirement for the degree of Doctor of Philosophy in Nursing

by

Susan Joyce Dempsey

2021

ABSTRACT OF THE DISSERTATION

Incidence of Opioid-Induced Respiratory Depression in Trauma Patients on the General Care Floor Receiving Patient-Controlled Analgesia or Nurse Administered Intravenous Opioids Monitored by Capnography and Pulse Oximetry:

A Prospective, Blinded Observational Study

by

Susan Joyce Dempsey

Doctor of Philosophy in Nursing

University of California, Los Angeles

Professor Felicia Schanche Hodge, Committee Chair

Statement of the Problem. Approximately 2.5 million individuals suffer traumatic injuries that demand admission to an acute care hospital. Safe, effective pain management is a priority of care for hospitalized patients receiving opioids for acute trauma-related pain. Opioids remain the primary approach for management of moderate to severe pain. The persistent use of an opioid-only approach to pain management is alarming given that an estimated 0.3% to 46% of hospitalized patients receiving opioids experience serious opioid-related adverse events, such as life-threatening respiratory depression. Opioid-induced respiratory depression (OIRD) among trauma patients hospitalized on general care floors had not been previously described. In this

preliminary analysis the incidence and characteristics of OIRD monitored by continuous capnography and pulse oximetry, as well as, nursing assessment is reported.

Methods. From July through October 2019 patients who presented to the emergency department following traumatic injury and admitted to general care floors were continuously monitored with bedside capnography and pulse oximetry for signs of respiratory depression. The Principal Investigator (PI), an advanced practice registered nurse with expertise in pain management and critical care, also assessed every patient within 5 minutes prior to opioid administration and every 10 minutes for 60 minutes thereafter. The adjusted Wald method was used to calculate the incidence of respiratory depression. STOP-BANG and PRODIGY risk scores were calculated. Time of admission to the ward and time of first OIRD were determined and displayed on a 24-hour radar plot for visual inspection of peak occurrence of events.

Summary of findings. Nineteen patients were admitted for a traumatic injury to a general care floor and underwent continuous monitoring with capnography and pulse oximetry. Indications for admission were orthopedic trauma (n=15), chest trauma (n=3), or abdominal (n=1) trauma. Twelve patients required surgical management. High-risk STOP-BANG and PRODIGY scores were calculated for 5 (26.3%) and 8 (42.1%) patients, respectively. The median duration of monitoring was 7.0 [6.4, 7.4] hours. All patients received intravenous opioids in the emergency department and general care floors. Median morphine equivalents in the emergency department were 17.5 MME (IQR 24) and 18MME (IQR 24) for patients who later experienced $\geq$1 respiratory event on the GCF as compared to those patients who did not experience a respiratory event on the GCF. Median morphine equivalents (MME) on the general care floor were 7 MME (IQR 8) and 7 MME (IQR 3.5) for patients with $\geq$1 respiratory depression event or without, respectively. Respiratory depression was detected in 14 patients

(incidence 71 [95%CI 50.9 – 88.6] cases per 100 patients) with apnea (n=12) and hypoxemia (n=10) the most detected abnormalities and hypopnea (n=5) and low expired end-breath carbon dioxide level (n=4) less common. The median time to first detected OIRD was 108 (24, 275) minutes. Majority of admissions were between 1600 and 2400 (n=9, 64%) and the majority of first OIRD episodes were from 1800 to 2400 (n=9, 64%). 42.8% (n=6) of respiratory events occurred prior to the administration of intravenous or oral opioids on the general care ward. Using the Pasero Opioid-Induced Sedation Scale, sedation was observed in 78% (n=11) of patients. Fifty percent (n=7) of respiratory events were recognized by the PI. No patient received an opioid receptor antagonist (naloxone) or was transferred to a higher level of care.

Conclusion. These findings revealed that respiratory depression detected by bedside capnography and pulse oximetry was common among trauma patients hospitalized on general care floors. Importantly, OIRD typically was first observed early in the hospital course. Furthermore, respiratory depression and apnea were commonly recognized by changes in exhaled carbon dioxide (ETCO2) and oxygen saturation while undetected with nursing assessment. These results offer compelling evidence of the un-met need for continuous monitoring in this patient population.

This dissertation of Susan Joyce Dempsey is approved.

Christopher J. Evans

Elizabeth A. Henneman

Sophie Sokolow

Felicia Schanche Hodge, Committee Chair

University of California, Los Angeles

2021

Dedication

To

Margo McCaffery and Chris Pasero who were the first to recognize and define the nurse's role in identifying and preventing opioid-induced respiratory depression.

The many patients who have experienced unintended opioid-induced sedation and respiratory depression and to the healthcare providers who care for them.

Dr. John C. Liebeskind who was one of the first to recognize that suboptimal pain management can result in negative consequences including immunosuppression and enhanced cancer metastasis.

Most importantly, to my children, Jason and Sarah, who have sacrificed so much so that I could pursue my commitment to making a difference in the care of patients at risk for opioid-related adverse events.

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CHAPTER 1: Introduction and Purpose of the Study

An estimated 89.7% of adults in the United States will experience trauma requiring hospitalization during their lifetime (Connor, Brier, & Price, 2020, Spector, Limcangco, Muller, Pines, & Owens, 2015; Kilpatrick et al., 2013). Safe, effective pain management is a priority of care for hospitalized patients receiving opioids for acute trauma-related pain (Ahmadi et al., 2016; American Society of Anesthesiologists Task Force [ASATF], 2012; Chou et al., 2016; Connor Brier, & Price, 2020; Institute of Medicine [IOM], 2001; Minkowitz, Gruschkus, Shah, & Raju, 2014; The Joint Commission [TJC], 2017).

Pain is an unpleasant sensory, emotional, cognitive and social experience associated with potential or actual tissue damage or described in terms of such damage (Cohen, Quinter, & van Rysewyk, 2018; Merskey et al., 1979; Treede, 2018; Williams & Craig, 2016). Importantly, pain is a subjective experience and is whatever the person experiencing says it, existing whenever the person says it exists (McCaffery, 1968). Pain is common in the inpatient setting with an estimated 20-80% of surgical patients experiencing moderate to severe postoperative pain (Adamson, Lew, Beyzarov, Amara, & Reitan, 2011; Apfelbaum, Chen, Mehta, & Gan, 2003; Chou et al., 2016; Gan, Habib, Miller, White, & Apfelbaum, 2014; Gerbershagen et al., 2013). In a descriptive cross-sectional survey of 424 post-surgical patients within 24 and 72 hours after surgery, 45.5% (n=191) of patients reported moderate to severe pain (Lorentzen, Hermansen, & Botti, 2012). Furthermore, unfortunately, unrelieved pain is also common as demonstrated in a recent study of 300 surgical patients, in which 75% (n=225) of the patients reported ineffective pain management as evidenced by moderate, severe, or extreme pain (Gan et al., 2014). Researchers have reported that 20%–40% of patients suffer severe pain after surgery (Gerbershagen et al., 2013).

Suboptimal management of acute pain can result in physiological and psychological consequences that facilitate negative patient outcomes, delay recovery, decrease satisfaction with the hospital experience, and increase the risk of progression to chronic pain and post-traumatic stress syndrome (PTSD) (Bouman et al., 2014; Chou et al., 2016; Connor, Brier, & Price, 2020; Correll, 2017; Feldmmann-Laufenberg, Kappis, Mauff, Schmidtmann, & Ferner, 2016; Fletcher et al., 2015; Gan, 2017; Gan, Robinson, Oderda, Garimella & Cellini, 2013; Gilron, Vandenkerkhof, Katz, Jian, Rejaei, Shihab, Alston, & Want, 2018; Glare, Aubrey, & Myles, 2019; Kehlet, & Carley, 2017; Katz & Seltzer, 2009; Kehlet, Jensen, & Woolf, 2006; Ledowski, Reimer, Chavez, Kapoor, & Wenk, 2012; Simanski et al., 2014; Wick et al., 2015). Conversely, safe, effective pain management is associated with enhanced recovery, earlier mobility, fewer cardiac and pulmonary complications, shorter hospital length of stay, decreased healthcare costs, and increased patient satisfaction (Danforth et al., 2014; Glowacki, 2015; Harvine & Kao, 2020; Oderda et al., 2013; Perkins & Kehlet, 2000).

A multimodal approach to management of acute pain, using more than one modality that targets different pain pathways or mechanisms of action to achieve effective analgesia while reducing opioid-related adverse events, is an integral component of Enhanced Recovery After Surgery (ERAS) protocols (American Society of Enhanced Recovery, 2017; Chou et al., 2016; Gan et al., 2017; Gustafsson et al., 2020; Harvin & Kao, 2020; Helander et al., 2017; Neugebauer, Wilkinson, Kehlet, & Schug, 2007; Patton et al., 2014; Polomano et al., 2017; Rawlinson, Kang, Evans, & Khanna, 2011; Sullivan, Lyons, Montgomery, & Quinlan-Colwell, 2016; Tan, Law, & Gan, 2015; Tebala et al., 2016). The ERAS protocol has been shown to attain optimal analgesia, minimize opioid-induced adverse events, reduce the surgical stress response, facilitate physiologic function, improve patient outcomes, and decrease length of stay (AHRQ, 2017; Gelinas, 2019; Gustafsson et al., 2020; Hsu et al., 2019; Patton et al., 2014; Wick et al.,

2015). However, multimodal regimes that include medications with sedative properties may increase the risk of respiratory depression. More specifically, the use of gabapentin in multimodal therapy has been reported result in a synergistic impact on respiratory drive and associated with increased rates of respiratory depression among postsurgical patients (odds ration [OR], 1.47 (95% CI, 1.22-1.76: $P < .0001$). (Cavicante, Sprung, Schroeder, & Weingarten, 2017).

Despite the documented efficacy of multimodal analgesia to reduce pain, opioid use, minimize opioid-related adverse events, and enhance recovery (Brindle, Nelson, Lobo, Jian et al., 2018; Ljungqvist, & Gustafsson, 2019; Chou et al., 2016; Gustafsson et al., 2020; Miller et al., 2014; Patton et al., 2014; Wick et al., 2017), opioid-based analgesia remains the primary approach for management of moderate to severe pain in hospitalized patients (Argoff, 2014; ASATF, 2012; Beck, Margolin, Babin, & Russo, 2015; Chou et al., 2016; Dun, Moeschler, Horlocker, Hanssen, & Hebl, 2013; Gan et al., 2014; Gritsenko, Khelemsky, Kaye, Vadivelu, & Urman, 2014; Jahr et al., 2018; Jarzyna et al., 2011; Jungquist et al., 2020; Kehlet & Dahl, 1993; Larsen et al., 2014; Lee et al., 2015; MacIntyre, Loadsman, & Scott, 2011; Oderda, 2012; Overdyk et al., 2016; Pasero & Stannard, 2012; Shafi et al., 2018; Wick et al., 2017). The persistent use of an opioid-only approach to pain management is alarming given that an estimated 0.3% to 46% of hospitalized patients receiving opioids experience serious opioid-related adverse events, such as life-threatening respiratory depression (Canet et al., 2015; Cashman & Dolin, 2004; Dahan, Aarts, & Smith, 2010; Davis et al., 2017; Herzig et al., 2013; Herzig, Rotheberg, Cheung, Ngo, & Marcantonio, 2014; Kessler, Shah, Gruschkus, & Raju, 2013; Rosenfeld et al., 2016; Khanna et al., 2019a; 2019b; Overdyk et al., 2007; Ramachandran et al., 2011; The Joint Commission, 2012).

In a retrospective study of 319,898 surgical patients from over 450 hospitals in a national database, 95% (*n*=303,903) of patients received opioid-based pain management, and 12.2% (*n*=39,116) experienced an opioid-induced adverse event (Oderda, Gan, Johnson, & Robinson, 2013). Similarly, in a retrospective cohort study of 6,285 surgical patients, 99.8% of patients received opioids and 11.5% of those patients experienced an opioid-related event (Minkowitz et al., 2014). In a study of 50 patients undergoing major abdominal surgery, 82% (*n*=41) of the patients who received opioids experienced at least one moderate or severe opioid-induced adverse event (Gan et al., 2004; Kessler, Shah, Gruschkus & Rahu, 2013). More recently, 30 of 92 (30%) patients who received opioids in the post anesthesia recovery unit (PACU) following lower extremity surgery experienced opioid-induced respiratory depression (Galvagno, Brayanov, Williams, & George, 2017).

Among 135,379 hospitalized patients undergoing surgical and endoscopic procedures, 10% (14,386) of patients suffered an opioid-related adverse event which were associated with prolonged length of hospital stay, increased hospital costs, a higher rate of 30-day readmission, and inpatient mortality (Shafi et al., 2018). Opioid-induced sedation and respiratory depression can result in increased morbidity, mortality, length of hospital stay, and healthcare costs (Eckstrand et al., 2009; Fouladpour et al., 2016; Kessler et al., 2013; Jungquist, Willens, Dunwoody, Klingman, & Polomano, 2014; Shafi et al., 2018).

In a recent international, prospective, observational study conducted between April 2017 and April 2018, 1,495 adult patients at 16 sites in the United States of America (USA), Europe, and Asia that expected to receive parenteral opioid therapy were enrolled. Researchers sought to investigate the incidence and risk factors associated with respiratory depression in hospitalized patients receiving parenteral opioids on the general care ward (GCF) monitored by continuous capnography and pulse oximetry (Dempsey, forthcoming; Khanna et al., 2019a; 2019b). An

analysis set included 1,335 enrolled patients who received opioid therapy and started continuous monitoring on the GCF. Results revealed that one or more respiratory depression events were detected in 46% (*n*=614) of the 1,335 patients. Furthermore, researchers derived and validated a novel multivariate risk predication tool.

Opioid-induced respiratory depression has been reported to occur in more than 46% of patients receiving opioids on the general care floor (Cashman & Dolin, 2004; Davis et al., 2017; Dempsey, forthcoming; Dummund, 2013; Fecho, Jackson, Smith & Overdyk, 2009; Jungquist, Smith, Nicely, & Polomano, 2017b; Khanna et al., 2019a; 2019b; Melamed, 2016; McCarter, Shaik, Scarfo, & Thrompson, 2008; Minkowitz et al., 2015; Sun et al., 2015; The Joint Commission, 2012; Weinger & Lee, 2011). However, because opioid-induced respiratory depression is a diagnosis of exclusion, the true incidence is unknown (Dahan et al., 2010). Respiratory compromise or respiratory depression may lead to severe neurologic injury or death (Lee et al., 2015; Morris et al., 2017; Shafi et al., 2018). Unrecognized opioid-induced respiratory depression is described as one of the highest risks to patient safety (ERCI, 2017) and is now the second leading preventable patient safety concern (Respiratory Compromise Institute [RCI], 2017).

Although opioid analgesia can provide effective pain relief, opioids often are associated with preventable serious adverse events (Cashman & Dolin, 2004; Chou et al., 2016; Dahan et al., 2010; Ghelardini, Mannelli, & Bianchi, 2015; Kane-Gill, Rubin, Smithburger, Buckley, & Dasta, 2014; Jarzyna et al., 2011, 2017a; Jungquist et al., 2017a, 2017b; Kehlet, 2009; Lee et al., 2015; MacIntyre et al., 2011; Rafiq, 2014; Solhaug & Molden, 2017; Ramachandran et al., 2011; Shafi et al., 2018; TJC, 2012). Failure to adequately monitor patients receiving opioids has been reported as an important contributing factor to the occurrence of serious opioid-related adverse events (Lee et al., 2015; Stites, Surprise, McNiel, Northrop, & De Ruyter, 2021; TJC, 2012; Koo

& Eikermann, 2011). Essential to prevention of these adverse events is appropriate, systematic monitoring and surveillance of patients receiving opioids for trauma-related pain on the general care ward (Ahmadi et al., 2016; ASATF, 2012; Lam et al., 2017; Lee et al., 2015). The lack of globally accepted monitoring guidelines for the patients receiving opioids increases the risk for poor outcomes related to undetected sedation and *early* respiratory compromise (Ayad, Khanna, Iqbal, & Singla, 2019; Jungquist et al., 2020; RCI, 2017; TJC, 2012).

Background

Outcomes are worse among hospitalized patients who suffer opioid-related adverse events as compared to patients who do not suffer opioid-related adverse events (Herzig et al, 2014; Jungquist et al., 2017; Kessler et al., 2013; Lee, et al., 2015; Oderda, Daid, Evans et al., 2007; Odereda, Gan, Johnson, & Robinson, 2017; Overdyk et al., 2016; Shafi et al., 2018; TJC, 2012). More specifically, surgical patients who experience opioid-related adverse events have a 55% increased hospital length of stay, 47% increased cost of care, 36% increased risk of 30-day readmission, and a 3.4 risk of inpatient mortality (Kessler et al., 2013). Similarly, a study of mortality associated with respiratory compromise among hospitalized Medicare patients revealed that patients with hospital-acquired respiratory compromise had significantly higher mortality (32.7% vs. 27.8%, $p < 0.0001$) during the hospitalization and 30-day discharge period (15.3% vs. 12.9%, $p=0.0001$) as compared to patients admitted with respiratory failure (Lamberti et al., 2017). The fact that 48% of patients who develop hospital-acquired respiratory compromise die during hospitalization or within 30-days following discharge offers compelling evidence of the need for adequate monitoring to identify opioid-induced adverse events *early* and prevent their progression to respiratory failure.

Opioid-related adverse events. All hospitalized patients who receive opioids for acute pain management are at risk for serious opioid-related adverse events (Dahan et al., 2004; Gan et

al., 2007; Jungquist et al., 2020; Lee et al., 2015; Morris et al., 2017; Solhaug & Molden, 2017; Wick et al., 2017). Pharmaocogenetic and inter-individual variability to opioids increase the risk for serious opioid-related adverse events (Solhaug & Molden, 2017; Vieira, Fragoso, Pereira, & Medeiros, 2019). Clearly, safe and effective pain management is a priority of care (Chou et al., 2016). Opioid-related adverse events include nausea, vomiting, constipation, dizziness, ileus, delayed gastric emptying, aspiration pneumonia, dizziness, delirium, hallucinations, cognitive impairment, falls, sedation, and respiratory failure (TJC, 2012; Wick et al., 2017). Sedation and respiratory depression are the most serious of opioid-related adverse events since they can result in respiratory arrest and subsequent cardiopulmonary arrest (Fecho et al., 2009; Jarzyna et al., 2011; Jungquist et al., 2017; Overdyk et al., 2016).

In a study analyzing 3,695 inpatient adverse events, 16% of all events were opioid-related (Davies et al., 2009). Post-surgical respiratory failure is the third cause of preventable death in the United States, preceded only by preventable surgical complications and pressures ulcers, with an incidence of 17.18 per 1,000 patients and accompanying healthcare cost of $1.9 billion in the Medicare population (Healthgrades, 2012). Opioid-induced respiratory failure among post-surgical patients ranges from 0.3% to 46% (Canet et al., 2015; Cashman & Dolin, 2004; Dahan et al., 2010; Herzig et al., 2014; Kessler et al., 2013; Khanna et al., 2019b; Nguyen et al., 2016; Overdyk et al., 2007; Ramachandran et al., 2011; TJC, 2012). Recent evidence suggests that over 20% of post-surgical patients experience prolonged hypoxemia that is severe and often unrecognized (Lee et al., 2015; Sun et al., 2015). Approximately 29% of all reported opioid-related events in The Joint Commission's sentinel event database was the result of inadequate patient monitoring (TJC, 2012). In a recent single-site retrospective review of 57 episodes of opioid-induced respiratory depression, inadequate monitoring was reported as a deficiency in clinical care (Meisenberg, Ness, Rao, Rhule, & Ley, 2017). Inadequate patient monitoring and

surveillance for post-surgical opioid-induced respiratory depression was ranked as the third-highest health hazard and one of the highest ten patient safety concerns for 2017 (ERCI, 2016; 2017). Mortality related to opioid-related adverse events and opioid-induced respiratory failure often occurs within the context of inadequate monitoring (Lam et al., 2017; Lee et al., 2015; Nguyen et al., 2016; Stites et al., 2021; Koo & Eikermann, 2011).

Risk factors for opioid-related adverse events. Risk refers to individual vulnerability for developing a new problem based on pre-existing physiologic conditions, behaviors, or treatment (Morris, et al., 2017). Patient safety is dependent on accurate, timely, and appropriate patient assessment and intervention, which includes an assessment of the risk of preventable opioid-related adverse events (Brant et al., 2018; Jungquist et al., 2017b; Jungquist et al., 2020; Khanna, 2019b; Khelemsky, Kothari, Campbell, & Farnad, 2015; Lee et al., 2015; Pawasauskas, Stevens, Youssef, & Kelley, 2014; Rosenfeld et al., 2016; Weingarten, Herasevich et al., 2015; Weingarten, Warner, & Sprung, 2017).

The constellation of person and treatment-related risk factors influences individual risk for opioid-related adverse events (Gudin, Mogali, Jones, & Comer, 2013; Jarzyna et al., 2011; Jungquist et al., 2020; Lam et al., 2017; Wick et al., 2017). Identification of risk factors and individuals at high risk for opioid-induced respiratory depression is a patient safety imperative and critical to implement effective preventive monitoring and measures (Jarzyna et al., 2011; Jungquist et al., 2017; Khanna et al., 2019; 2019b; Morris et al., 2017; Sadhasivam & Chidambaran, 2012; TJC, 2012).

Person-related risk factors. Person-related risk factors are pre-existing pharmacokinetic, physiologic conditions, or personal behaviors that predispose an individual to opioid-induced sedation and respiratory depression (Nielsen, Olesen, Branford, Christrup, Sato, & Drewes, 2015; Jarzyna et al., 2011; Jungquist et al., 2017a, 2020; Solhang & Molden,

2017; Vieira, Fragoso, Pereira, & Medeiros, 2019). Specific examples of physiologic conditions are increasing age (older than 55 years), poor general state of health (impaired kidney, liver, and functional status); obesity (BMI > 30kg/m^2), obesity hypoventilation syndrome, pre-existing sleep disordered breathing syndromes (e.g., obstructive sleep apnea [OSA]), cardiac or pulmonary comorbidities, and pre-operative opioid tolerance (Broens et al., 2017; Canet et al., 2015; Cauley et al., 2017; Chou et al., 2016; Felhofer, 2013; Fouladpour, Jesudoss, Bolden, Shaman, & Auckle, 2016; Jarzyna et al., 2011; Jungquist, Card, Charchaflieh, Gali, & Yilmaz, 2017; Khelemsky, Kothari, Campbell, & Farnad, 2015; Minkowitz et al., 2014; Opperer et al., 2016; Pawasauskas, Stevens, Youssef, & Kelley, 2014; Ramachandran et al., 2011; Shin et al., 2016; Weingarten et al., 2015; Wickerts, Forsbert, Bouvier, & Jakobsson, 2017). Patients with impaired kidney function, chronic obstructive pulmonary disease, heart failure, sleep-disordered breathing, and obesity are among the groups that are at high risk for opioid-induced adverse events (ASATF, 2012; Fouladpour et al., 2016; Gross et al., 2014; Gross et al., 2018; Jarzyna et al., 2011; Jungquist et al., 2017; Shin et al., 2016; Weingarten et al., 2015). Further, patients with multiple risk factors are at higher risk for opioid-related adverse events and experience higher mean healthcare costs and length of hospitalization (Jarzyna et al., 2011; Khanna 2019b; Minkowitz et al., 2014; Weinger & Lee, 2011).

Personal behaviors such as substance use disorder, such as tobacco, ETOH, or drugs of abuse also increase patient risk for opioid-induced sedation and respiratory depression (Jungquist et al., 2020; Patanwala, Jarzyna, Miller, & Erstad, 2008). In a recent study of 11,317, 958 patients, researchers identified a history of substance use disorder as the strongest predictor of post-operative opioid overdose that could lead to serious opioid-induced

respiratory depression, anoxic brain injury and death (odds ratio = 14.8; 95% confidence interval: 12.7 – 17.2) (Cauley et al., 2017).

Treatment-related factors. Treatment-related factors are pain management-induced events associated with clinical care, pharmacologic management, and are influenced by the clinical setting (Edlund et al., 2014; Jarzyna et al., 2011; Junquist et al., 2017; Pasero & Stannard, 2012). Many treatment-related factors are modifiable through strategies such as vigilance in monitoring and surveillance, implementation of evidence-based policies and procedures that direct practice, education to enhance knowledge and expertise, use of a multi-modal approach to pain management, and appropriate RN staffing levels.

Clinical care risk factors. Clinical care risk factors are related to the type of surgical procedure, patient care, or post-operative adverse events. Site of surgery (head, neck, chest, upper abdominal), prolonged duration of general anesthesia, and use of supplemental oxygen are examples of clinical care risk factors (Jarzyna et al., 2011; Jungquist et al., 2019; Niesters, Mahajan, Aarts, & Dahan, 2013).

Pharmacologic risk factors. Pharmacologic risk factors are the result of inappropriate prescribing and/or administration of opioids or inherent pharmacokinetic and/or pharmacodynamic variability in drug levels and effect among patients (Dahan et al., 2004; Dahan, Overdyk, Smith, Aarts, & Niesters, 2013; Delgado, et al., 2018; Drew, Gordon, Morgan, & Manworren, 2018; Glare, Aubrey, & Myles, 2019; Kim, Nolan, Beaulieu, Shalansky, & Lianping, 2019; Jarzyna et al., 2011; Jungquist et al., 2020; Neuman, Bateman, & Wunsch, 2019; Pasero, Quinlan-Colwell, Rae, Broglio, & Drew, 2016; Meldrum, 2016; Mordecai, Reynolds, Donaldson, & Williams, 2018; York, & Brat, 2018). Continuous opioid infusions, administration of opioids using more than one modality, failure to use equianalgesic dosing as routes and types of drugs change, multiple opioids used simultaneously, and opioid only

analgesia are examples of pharmacologic factors that have been reported to increase patients' risk of opioid-related adverse events (Gudin et al., 2013; Jungquist et al., 2020; Lee et al., 2015; Meisenberg et al., 2017). Co-administration of sedatives, which may potentiate the respiratory depressive events of opioids, leads to twice the risk of cardiopulmonary arrest (Overdyk et al., 2016).

Clinical setting risk factors. The Institute of Medicine reports, "To Err is Human" (2000) and "Crossing the Quality Chasm" (2001), underscore the importance of human and clinical settings or systems, factors that lead to adverse events (IOM, 2001; Kohn, Donaldson, & Corrigan, 2000). Clinical setting risk factors are patient admission to an unmonitored, low acuity-general care ward and circumstances or practices within the hospital environment or culture that influence patient risk (Junquist et al., 2017; Lam et al., 2017; Meinsenberg et al., 2017).

Failure to prevent and failure to recognize opioid-induced respiratory depression early is related to intermittent monitoring strategies and surveillance that result in late recognition of patient deterioration (Henneman, Gawlinski, & Giuliano, 2012; Jungquist et al., 2014; Lynn & Curry, 2011). Safety for patients receiving opioids demands vigilance in monitoring and surveillance. Trauma patients often are placed on low acuity general medical-surgical wards, where assessment and respiratory monitoring are performed intermittently, typically at 4 to 6-hour intervals (ERCI, 2017). Intermittent monitoring and surveillance of sedation, respiratory status, and ventilation increases the risk for undetected respiratory compromise and the delay in appropriate interventions leading to opioid-induced respiratory depression, respiratory failure, anoxic brain injury, or death (Centers for Medicare and Medicaid Services [CMS], 2014; Curry & Jungquist, 2014; ERCI, 2017; Cohen & Smetzer, 2013; Lynn & Curry, 2011). It is imperative for nurses to provide adequate monitoring and surveillance to recognize subtle changes in patient

status and implement appropriate and timely interventions (Clarke & Aiken, 2003; Dresser, 2012; Mitchell & Shortell, 1997).

Inappropriate patient monitoring strategies and surveillance, inadequate RN staffing levels, lack of RN knowledge and expertise, ineffective communication at hand-off during change-of-shift or providers, PCA by proxy, standard order sets that prescribe opioid doses based on pain intensity, and the absence of evidence-based policies and procedures to guide practice are human factors within the culture of the clinical setting that may contribute to serious opioid-induced adverse events (Aiken, Clark, Cheung, Sloan, & Silbur, 2003; Blegen, Vaughn, & Goode, 2001; Christens & Hewitt-Taylor, 2006; Curry & Jungquist, 2014; Estabrooks, Midodzi, Cummings, Ricker, & Giovannetti, 2005; Henneman, Gawlinski, & Giuliano, 2012; Jungquist et al., 2017; Kelly & Vincent, 2011; Pasero, 2014; Pasero, Quinlan-Colwell, Rae, Broglio, & Drew, 2011; Voepel-Lewis, Pechlavanidis, Burke, & Talsma, 2013).

Risk factors and implications for practice. Opioids depress the central nervous system (CNS) which may result in clinically significant opioid-induced respiratory depression, anoxic brain injury, and death (Jarzyna et al., 2011; Jungquist, Karan, & Perlis, 2011; Zedler et al., 2015). Personal and treatment risk factors can negatively influence the ability to safely tolerate opioid exposure, resulting in unintentional overdose and life-threatening opioid-related adverse events (Jungquist et al., 2011; Zedler et al., 2015). The identification of risk factors provides insight into strategies for risk mitigation. However, because many risk factors are not modifiable (e.g., age and gender), the use of risk stratification and predictive models that provide an individual risk score may facilitate risk assessment and provide a basis for developing appropriate monitoring strategies (Blackwell et al., 2020; Canet et al., 2015; Felhofer, 2013; Godet et al., 2017; Gupta et al., 2011a; 2017b; Jarzyna et al., 2011; Jungquist et al., 2020; Khanna et al., 2019a; 2019b; Nguyen et al., 2016).

Opioid-induced sedation. Opioid-induced sedation is a common effect during the initial 24-hours of opioid analgesia, with increases in dosage, and within the first four hours following admission to the general care ward from the PACU (Chou et al., 2016; Epstein, Dexter, Lopez, & Ehrenfeld, 2014; Jungquist et al., 2017; Lee et al., 2015; Pasero, Quinn, Portenoy, McCaffery, & Rizos, 2011; Ramachandran et al., 2011; Rosenfeld et al., 2016; Schmid-Mazzoccoli, Hoffman, Happ, & Devita, 2008; Taylor, Kirton, Staff, & Kozol, 2005; Weingarten et al., 2015; Weingarten et al., 2017; Wickerts et al., 2017). Sedation and somnolence are the most significant precursors of respiratory compromise among patients receiving intravenous (IV) opioids (Grissinger, 2013; Junquist et al., 2019; Lee et al., 2015). Opioid-induced sedation may progress to life-threatening respiratory failure, severe neurological damage, and death (Lee et al., 2015; MacIntyre et al., 2011). Respiratory depression occurs less often than sedation; however, it is the most serious of opioid-related events (Jarzyna et al., 2011; Lee et al., 2015; MacIntyre et al., 2011; Pasero & McCaffery, 2011).

Opioid-induced sedation occurs on a continuum of severity that ranges from full consciousness to complete loss of consciousness (Jarzyna et al., 2011; Jungquist et al., 2020; Martel & Barnett, 2015). Sedation precedes respiratory compromise along this continuum and offers compelling evidence for vigilance in assessment of sedation and reduction in opioid dose if increased sedation is detected in patients receiving opioids (Abou Hammoud et al., 2009; ASATF, 2012; Ghelardini, Di Cesare Mannelli, & Bianchi, 2015; ISMP, 2013; Jarzyna et al., 2011; MacIntyre et al., 2011; Moline, Roberts, & Houser, 2012; Motov, Rosenbaum, Vilke, & Nakajima, 2016; Nisbet & Mooney-Cotter, 2009; Oosten et al., 2011; Pasero, 2009; Smith et al., 2014; Taylor et al., 2005; Taylor, Voytovick, & Kozol, 2003; TJC, 2012; Yamamotova, Fricova, Rokyta, & Slamberova, 2016). In an analysis of the Anesthesia Closed Claims database, 60% of

patients who developed opioid-induced respiratory depression were described as somnolent prior to the event (Lee et al., 2015).

Early recognition of sedation and respiratory compromise provides the opportunity to intervene and prevent decompensation to respiratory depression, failure, or death (Jarzyna et al., 2011; Jungquist et al., 2020; Lee et al., 2015; Maddox, Oglesby, Williams, Fields, & Danello, 2008; Moline et al., 2012; Morris et al., 2017; Pasero, 2009; TJC, 2012). However, a recent study of eight hospitals that volunteered to participate in pilot data collection for the Centers for Medicare and Medicaid Services (CMS) revealed that only 8.4% of patients receiving opioids with IV patient-controlled analgesia (PCA) received monitoring of sedation level, oxygen saturation, and respiratory rate at least every 2.5 hours (Jungquist et al., 2016). Further, only 26.8% of patients were monitored every 4.5 hours.

Opioid-induced respiratory compromise. Opioids decrease respiratory drive, alter the normal respiratory rhythm, and disrupt upper airway patency which may lead to hypercarbia and hypoxemia (Dahan et al., 2004; Kiyatkin, 2019; Morris et al., 2017). Respiratory compromise occurs on a continuum of severity from stable to acute respiratory failure (Morris et al., 2017). Acute, critical opioid-induced respiratory depression is characterized by impaired control of breathing as evidenced by hypoventilation (decreased tidal volume and respiratory rate) resulting in hypercarbia and hypoxemia which may lead to respiratory failure, or death, without enhanced monitoring or interventions for reversal (MacIntyre, 2011; Morris et al., 2017; Koo & Eikermann, 2011).

Over 40% of all cardiopulmonary arrests occur on the low acuity general care ward with devastating patient outcomes (Morrison et al., 2017; Perman et al., 2016). An estimated 50% of post-operative Code Blue events are related to opioids (Overdyk, 2010). Monitoring that facilitates early recognition and intervention may prevent the decompensation of respiratory

compromise to potentially fatal respiratory depression or failure (IRSC, 2017). Despite the need for improved monitoring to identify opioid-induced sedation and respiratory compromise early, there are no universally accepted guidelines that direct the method, frequency, or duration of monitoring for hospitalized surgical or trauma patients receiving opioids for acute pain management (Jarzyna et al., 2011; Jungquist et al., 2020).

Monitoring of patients receiving opioids. Safe, optimal pain management demands ongoing reassessment to determine the effectiveness of pain relief and recognize opioid-induced adverse events early. Unfortunately, there is insufficient evidence to direct the optimal method, timing or frequency, and duration of patient monitoring in the low acuity general care setting (Chou et al., 2016). Clearly, patient safety demands ongoing patient monitoring and systematic assessment of sedation and respiratory status using observations and technology to gather measurements for anticipation, detection, and recognition of sedation and respiratory compromise (Jarzyna et al., 2011; Jungquist et al., 2020; Pasero, 2012).

The incidence of respiratory depression in patients receiving opioid analgesia on the general care ward detected by traditional intermittent vital signs monitoring has been defined using various criteria. The criteria are typically derived using arbitrarily assigned thresholds for desaturation, bradypnea, and hypercapnia or hypocapnia, with desaturation typically having the highest incidence of nearly 17%.

Monitoring of patients receiving opioids on the general care ward may include assessment of sedation level, oxygen saturation using pulse oximetry, observation of respiratory rate as evidenced by chest excursion, or end-tidal carbon dioxide using capnography (Jabre et al., 2009; Jarzyna et al., 2011; Jungquist et al., 2020; Mimoz, Benard, Gaucher, Frasca, & Debaene, 2012). The incidence of respiratory depression has been defined using arbitrarily assigned criteria for oxygen desaturation, bradypnea, hypercapnia, or hypercapnia with desaturation

reflecting the highest incidence at nearly 17% (Cashman & Dolin, 2004). Pain management experts suggest that the type, frequency, and duration of monitoring should be based on evaluation of the individual risk profile (person and treatment-related risk factors) coupled with the opioid regime (Jarzyna et al., 2011, Jungquist et al., 2019; Pasero, 2012). However, individual variability and unpredictability in response to opioids demand vigilance in monitoring for all patients, including those not identified as high risk (Weinger & Lee, 2011). Further, appropriate monitoring also requires the interpretation and synthesis of patient data for clinical decision-making (Henneman et al., 2012).

Sedation level. A sedation level that reflects opioid-induced sedation is a clinical endpoint that predicts impending respiratory depression (Dolin & Cashman, 2005). Serial assessment of sedation level is critical in the prevention of opioid-induced respiratory depression as sedation usually precedes respiratory depression (Pasero, 2009; Wells, Pasero, & McCaffery, 2008). Monitoring for opioid-induced sedation requires a serial assessment of alertness and arousability using a valid and reliable sedation scale (Jarzyna et al., 2011; Jungquist et al., 2020; Pasero & McCaffery, 2011; Pasero, 2002; 2009). Opioid-induced sedation may lead to respiratory compromise and progress to respiratory depression with severe neurological damage or death (Lee et al., 2015; MacIntyre et al., 2011).

Sedation occurs on a continuum and typically precedes hypoventilation (elevated arterial carbon dioxide) and opioid-induced respiratory depression (Abou Hammond et al., 2009; Jarzyna et al., 2011; Lee et al., 2015; MacIntyre et al., 2011; Moline et al., 2012; Pasero, 2009; Taylor et al., 2005; Taylor et al., 2003). The fact that sedation occurs on a continuum allows for the transition of a state of light sedation to deep sedation easily and without recognition following the opioid administration. In a closed claims analysis of anesthesia claims, somnolence was reported in 62% of patients before the occurrence of a respiratory depression episodes (Lee et al.,

2015). Therefore, the sedation continuum offers compelling evidence of the importance of vigilance in sedation assessment for patients receiving opioids (Brown et al., 2010; Jarzyna et al., 2011; Lee et al., 2015; Nisbet & Mooney-Cotter, 2009; TJC, 2012). Early recognition of sedation provides the opportunity to implement appropriate care and prevent respiratory compromise or depression (Jarzyna et al., 2011; Jungquist et al., 2020; Lee et al., 2015; Lee et al., 2015; Moline et al., 2012; Pasero, 2009; TJC, 2012).

Respiratory rate and status. Respiratory rate often is measured by observation in patients who are not intubated and requiring mechanical ventilatory assistance (Semler et al., 2013). Although accurate respiratory status assessment is one of the most important components of patient care, researchers have reported that recorded respiratory rates often are inaccurate or omitted (Bianchi et al., 2013; Brabrand, Hallas, Folkestad, Lautrup-Larsen, & Brodersen, 2018; Kellet, Li, Rasool, Green, & Seely, 2011; Latten, Spek, Muris, Cals, & Stassen, 2019; Leuvan & Mitchell, 2008; Mukkamala, Gennings, & Wenzel, 2008; Ronen, Weissbrod, Overdyk, & Ajizian, 2016; Semler et al., 2013; Yang et al., 2017). In a recent prospective, observational study of 368 hospitalized patients, researchers reported that recorded respiratory rates were higher than those directly observed (Semler et al., 2013).

Observation of respiratory rate alone does not necessarily reflect effective ventilation (Pasero, 2009). Adequate evaluation of respiratory status also requires observation of breathing patterns which include chest rise and fall to evaluate the rate, depth, and regularity of respirations (ISMP, 2013). Further, the presence of snoring must be determined as it reflects airway obstruction and increases the risk for opioid-induced respiratory depression (McCaffery & Pasero, 2011; Pasero, 2009).

Pulse oximetry. Pulse oximetry is a commonly-used non-invasive method for the measurement of oxygen saturation (SpO_2). It provides a valuable estimation of oxygenation or the degree of hypoxemia in arterial blood (Lam et al., 2017; Silvilotti et al., 2010; Voepel-Lewis et al., 2013). A recent Cochrane Systematic Review examining the use of pulse oximetry for patient monitoring during the perioperative period with data from five studies comprised of 22,992 subjects revealed that continuous pulse oximetry monitoring enabled detection of hypoxemia and respiratory events; however, monitoring with pulse oximetry did not result in decreased surgical complications or improved care or patient outcomes (Pedersen et al., 2014). Similarly, results from a closed claims analysis of opioid-related adverse events revealed that continuous pulse oximetry monitoring was in use at the time of the event (Lee et al., 2015). Pulse oximetry can lead to inaccurate respiratory status assessment, especially if the patient is receiving supplemental oxygen (Niesters et al., 2013).

Although pulse oximetry detects arterial oxygen saturation accurately, it does not detect early alveolar hypoventilation. Oxygen desaturation lags after hypoventilation and is a late indicator of opioid-induced respiratory depression when the patient is receiving supplemental oxygen (Fu, Downs, Schweiger, Miguel, & Smith, 2004; Jarzyna et al., 2011; Jungquist et al., 2020; Liao et al., 2017; Niesters et al., 2013; Rozario, Sloper, & Sheridan, 2008). Oxygen saturation (SpO_2) can be maintained even in the presence of hypoventilation and respiratory compromise in patients receiving supplemental oxygen, which can result in the delay of recognition and treatment (Chu et al., 2018; Dahan, Douma, Olofsen, & Niesters, 2016, Downs, Schweiger, Miguel, & Smith, 2004; Fu et al., 2004; Jungquist et al., 2020; Lam et al., 2017; Miguel & Smith, 2004; Niesters et al., 2013a; Overdyk, Carter, & Maddox, 2006; Sun et al., 2015). Further, a sleeping patient with opioid-induced hypoventilation or hypoxemia may breathe normally when aroused by the nurse for the application of pulse oximetry (Pasero,

2009; Sun et al., 2015). Therefore, intermittent evaluation of SpO_2, rather than continuous monitoring, may lead the nurse to make inaccurate assumptions about adequate ventilation (Stoelting & Overdyk, 2015).

Capnography. Capnography measures the partial pressure of carbon dioxide in the exhaled breath, referred to as end-tidal carbon dioxide (ETCO2), and can be used to evaluate the effects of opioids on ventilation (Heines, Strauch, Roekaerts, Winkens, & Bergmans, 2013; Kim, Choi, Bank, & Lee, 2016; Wall, Magee, & Campbell, 2017). Measurement of ETCO2 has been reported as an earlier, more sensitive indicator of ventilation and early respiratory compromise as compared to standard monitoring of observation of respiratory rate or SpO_2 using pulse oximetry (Burton, Harrah, Germann, & Dillon, 2006; Carlisle, 2015; Conway, Douglas, & Sutherland, 2016; Kopka et al., 2007; Lee et al., 2015; McCarter et al., 2008; Overdyk et al., 2007; Stites et al., 2021; Waugh, Epps, & Khodneva, 2011; Wadhwa, Gupta, & Vargo, 2019). However, ETCO2 values from capnography in patients with uninstrumented airways are less accurate than in instrumented airways (ETT or LMA) since the nasal cannula may not sample a full tidal breath. There is a lack of research on its use in patients in low acuity general care units, with non-instrumented airways, who receive opioids for trauma-related pain; the majority of studies are of the use of capnography in patients undergoing procedural sedation (Conway et al., 2016; Qadeer, et al., 2009; Wadhwa, Gupta, & Vargo, 2019).

In a blinded, observational study of patients receiving procedural sedation by emergency department physicians administering procedural sedation, results revealed that 33% of cases had an adverse respiratory event (defined as a change in ETCO2 of 10mmHg or greater). Of these cases, 70% were detected by capnography12 to 271 seconds before changes in pulse oximetry or respiratory rate (Burton et al., 2006).

Opioid-induced respiratory compromise will result in hypoventilation and typically precedes hypoxemia, especially in patients receiving supplemental oxygen (Conway et al., 2016). Capnography is more effective than pulse oximetry in providing an early warning of respiratory depression in patients receiving supplemental oxygen (McCarter et al., 2008). In a study of 634 surgical patients receiving patient-controlled analgesia, nine patients (1.5%) suffered respiratory depression as measured by bradynpnea (< 6 breaths per minute). All respiratory depression events (*n*=9) occurred during the initial 24-hours of patient-controlled analgesia, and capnography alerted the nurse to impending respiratory depression while pulse oximetry did not alert the nurse. Furthermore, all patients who suffered opioid-induced respiratory depression were receiving supplemental oxygen (Burton et al., 2006). Similarly, in a small, prospective randomized study of 54 opioid-naïve orthopedic surgical patients receiving opioids on the general care ward, capnography resulted in greater detection of respiratory depression (Hutchison & Rodriguez, 2008).

Evidence reveals that capnography can detect respiratory compromise before changes in SpO_2 and allow for earlier life-saving intervention (Burton, Harrah, Germann, & Dillon, 2006). Therefore, it is conceivable that the use of continuous monitoring of ETCO2 using capnography in patients receiving opioids on the general care ward could be very effective in promptly alerting staff to impending respiratory compromise (Burton et al., 2006; Cacho, Perez-Calle, Barbado, Ojea, & Fernandez-Rodriguez, 2010; Conway, et al., 2016; Deitch, Chudnofsky, Dominici, & Latta, 2010; Maddox, Williams, Oglesby, Butler, & Colclasure, 2006; Waugh et al., 2011). However, a recent systematic review of six randomized trials with 2,524 participants revealed that although monitoring with capnography reduced episodes of hypoxemia with sedation, outcomes were unchanged (Conway et al., 2016). Similarly, a Cochrane Database systematic review of three studies with a total of 1,272 study participants

reported a lack of evidence that capnography with standard monitoring (pulse oximetry, cardiac and blood pressure monitoring) affects the incidence of oxygen desaturation or hypotension among emergency department patients undergoing procedural sedation and analgesia (Wall et al., 2017). The review also reported no difference in airway interventions with the addition of capnography to standard monitoring (Wall et al., 2017). However, there are many possible explanations for the lack of differences found in this review, including that staff may not have been educated on when and how to intervene appropriately. Further, these results may not be applicable for monitoring patients receiving opioids for the treatment of trauma-related pain on the general care ward. Therefore, more research in this area of patient care is needed.

Significance of the Problem

Without appropriate monitoring and surveillance, all patients receiving opioids for acute trauma-related pain are at risk for opioid-induced sedation that may lead to respiratory depression, anoxic brain injury, or death (Barletta, 2012; Lee et al., 2015; MacIntyre et al., 2011; Patanwala et al., 2008; Sun et al., 2015; TJC, 2012).

Although the general care ward is a low acuity medical-surgical inpatient unit, it is the ward where more than half of in-hospital cardiopulmonary arrests occur (Khanna et al., 2020; Perman et al., 2016). Furthermore, more than half of cardiopulmonary arrests are related to opioids, partly, because of their commonality in clinical practice (Overdyk, 2010; Izrailtyan, Qiu, Overdyk, Erslon, & Gan, 2018). Patients with cardiopulmonary arrest on the general care ward can suffer devastating outcomes (Morrison et al., 2013; Perman et al., 2016). Although opioids are capable of providing effective pain management, they also are associated with life-threatening adverse events and potentially fatal outcomes. The most life-threatening opioid-induced events typically cite inadequate monitoring as one of the root causes (TJC, 2012; Koo & Eikermann, 2011).

Opioid-based analgesia remains the primary approach to the management of acute pain. The global use of opioids in clinical practice demands vigilant monitoring to detect opioid-induced sedation so that staff can intervene to prevent its progression to respiratory compromise or respiratory depression. The nurse has a critical role in the prevention of opioid-induced adverse events through the identification of patient risk factors, systematic assessment of sedation level and respiratory status, and appropriate, prompt intervention when increased sedation or respiratory deterioration are detected in patients receiving opioids for trauma-related pain (Chua et al., 2019; Chua et al., 2020; Jungquist et al., 2020).

There is a plethora of research in monitoring patients during procedural or goal-directed sedation. However, studies that describe the method, frequency, and duration of monitoring for patients receiving opioids for acute trauma-related pain are lacking. No study describes and correlates nurse clinical monitoring of sedation and respiratory status (i.e., sedation level and respiratory status) with technology-supported monitoring with capnography (ETCO2) and pulse oximetry (SpO_2) among trauma patients receiving opioids for acute pain management. Furthermore, the incidence of undetected opioid-induced sedation and respiratory depression is not well described. A review of the literature did not identify studies that describe the incidence of opioid-induced respiratory depression in trauma patients receiving patient-controlled analgesia or nurse-administered intravenous opioids on the general care ward.

Purpose of the Study

The primary objective of this prospective, blinded observational study was to correlate nurse monitoring of sedation and respiratory status with technology-supported monitoring (capnography and pulse oximetry) among trauma patients who were administered intravenous opioids for acute pain in both the emergency department and general care ward. Nursing assessment was correlated with capnography and pulse oximetry values to identify opioid-

induced sedation and respiratory depression. The nursing and technology-supported assessments were correlated for their ability to identify opioid-induced sedation and respiratory compromise or respiratory depression. A secondary objective of this study was to identify capnography and pulse oximetry values that correlate with opioid-induced sedation and respiratory compromise or respiratory depression. Furthermore, the temporal distribution of respiratory depression was explored.

Philosophical Underpinnings that Influence the Research

"Knowing is not enough; we must apply. Willing is not enough; we must do."
—von Goethe

Pragmatism is a philosophical view that a concept or theory should be evaluated in its effectiveness of action or "practice" in its consequences or achieving an outcome (Cherryholmes, 1992; Dewey, 1928, 1958; Kloppenberg, 1996; Mounce, 2000). Because pragmatic research is driven by what works in achieving outcomes, this practical-oriented school of thought is appropriate to provide the philosophical underpinnings for research in patient monitoring and surveillance for prevention of *early* recognition of opioid-induced sedation, respiratory compromise or respiratory depression.

Pragmatism as a School of Thought

Pragmatism, a school of thought and theory of truth, was influenced by Charles S. Pierce, Williams James, and John Dewey (Magee, 2001; Popkin & Stroll, 1993). The common element among these theories is the pragmatist maxim as a disciplined method for clarifying concepts through inquiry and identifying practical consequences or outcomes (Popkin & Stroll, 1993).

Charles S Pierce. Charles S. Pierce (1905) introduced pragmatism as a principle of inquiry in search of the meaning of "truth" or knowledge. Pierce believed that the most significant meaning in the search for truth was the experience of the search and the practical or useful application of the outcome (Pierce, 1905). Pierce considered the nature of truth as not

purely within abstract thought or opinion. Rather the belief of truth is independent of opinion and discoverable as a result of active engagement with the world and requires verification with practice or action (Magee, 2001). For Pierce, pragmatism was a method of using scientific inquiry to analyze concepts and their anticipated practical consequences or outcomes (Haack, 2003; Pierce, 1905). More specifically, meaning or truth is dependent on objective observation of the situation and the consequences or outcome as a result of the possible difference in practice (Pierce, 1905). Further, knowledge is an activity and its pursuit is stimulated by the lack of knowledge, need to know, or doubt (Magee, 2001). Sharing of knowledge also was important to Pierce, even if the intended objective was not met. More specifically, the sharing of knowledge ensures that research is not cyclic in that researchers do not repeat the same errors (Haack, 2003).

William James. William James emphasized pragmatism as a theory of truth (Popkin & Stroll, 1993). James proposed a more subjective sense of truth and moved the meaning of truth and scientific observation from the world to the level of the person and sense of experience (James, 1909). His contention was that truth was a summary of the experience in a specific instance. More specifically, the only evidence of truth is that it works in human experience (Popkin & Stroll, 1993). Thus, a belief became true when it was proven to be practical, useful, and helpful in the life of an individual. The central component in the search for truth was in the value of the consequence or outcome to the person or people (Popkin & Stroll, 1993).

The value of "truth" or the desired outcome of prevention or early recognition of opioid-induced respiratory depression is important to nurses, healthcare providers, and patients. Conversely, if research results reveal the inability to prevent or recognize sedation or opioid-induced respiratory depression early, the implications are that the monitoring and assessment have no value. Furthermore, the truth can be revealed in the description of the experience of monitoring as analyzed by the outcomes. Therefore, the knowledge gained from the activities of

this research will be useful and practical in the application of appropriate monitoring strategies in evidence-based clinical practice to improve patient outcomes.

John Dewey. The major tenet of John Dewey is "knowing is doing," and as we "do," we "know" (Popkin & Stroll, 1993). For Dewey, pragmatism was on practical problem-solving and the consequences of action ("doing") (Dewey, 1931). Dewey thought that scientific inquiry was a disciplined, self-critical form of inquiry with a logical structure that could be applied to all forms of inquiry. Further, the impetus for the search for knowledge was related to a sense of perceived difficulty or problem. An inquiry is a dynamic, ongoing process to achieve clarity or meaning of a problem. Dewey argued that reality is not independent of human experience and that a belief is true if it enables the anticipation of future experience. Because knowing involves practice and human experience involves action, knowledge is gained when engaged in action.

Early recognition and intervention to resolve significant patient problems before patient deterioration is a common experience in nursing practice influenced by knowledge and clinical judgment (Benner, 1984, 1985; Benner & Tanner, 1987). Nursing practice is imbedded with knowledge, action in intervening, and experience. More specifically, the identification or early recognition of opioid-induced sedation or respiratory compromise is influenced by nurses' knowledge, expertise, and experience (Dunwoody, Jungquist, Chang et al., 2018; Gaffney, Hatcher, & Milligan, 2016; Henneman & Gawlinski, 2004; Wilkinson, Cauble, & Patel, 2011; Yang et al., 2012). Thus, the nursing practice offers an opportunity to explore the meaning, assumptions, and beliefs of practice by evaluating patient consequences and outcomes

The process of "doing" and "knowing" is cyclical in the nursing practice of patient monitoring and surveillance. More specifically, the nurse needs to have knowledge or "know" the patient, patient risk factors, opioid pharmacokinetics, opioid pharmacodynamics, potential opioid-related adverse events, and be able to interpret and synthesize monitoring data in order to

"do" which is the implementation of appropriate monitoring (Gaffney et al., 2016). Appropriate monitoring is considered "true" in that it works to provide knowledge for early recognition of sedation or opioid-induced respiratory compromise and facilitates appropriate interventions for prevention or reversal (nursing recovery) (see Figure 1.1).

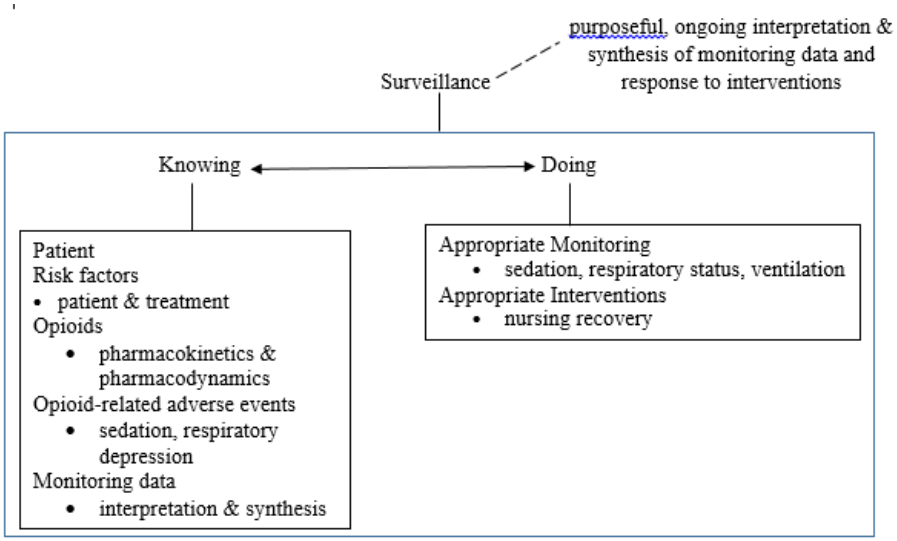

Figure 1.1. Knowing and doing in monitoring and surveillance (Dempsey, 2021).

Researchers have reported that "knowing" the patient as a person and responses to care are integral to the application of skilled clinical judgment (Tanner, Benner, Chesla, & Gordon, 1993). The activity of "knowing" in monitoring and surveillance results in the early recognition of opioid-induced sedation and opioid-induced respiratory compromise needs to be understood so that the knowledge can be shared and practiced to improve overall patient safety and outcomes. The pragmatic notion of consequence and tenets of pragmatism provide a way to explore the potential impact of monitoring strategies on outcomes in patients receiving opioids for post-operative or trauma-related pain.

Tenets of Pragmatism

Pragmatism stems from the Greek word πράγμα (pragma) that means "action" from

which ‘practical’ and ‘practice’ is derived (James, 1907; Weaver & Olson, 2006). Three tenets of pragmatism, “theory of meaning, truth is practical and useful, and knowing is doing,” provide a strong basis for research that is needed for appropriate patient monitoring during opioid analgesia for acute post-operative or trauma-related pain (James, 1907).

Meaning. Within pragmatism, ‘meaning’ is expressed in the practical consequences of the conduct to be recommended or the outcome to be expected (James, 1907; McCready, 2010). A pragmatist seeks to discover a method or theory to solve intellectual and practice problems (Haack, 2003). Vigilant, attentive patient monitoring during opioid analgesia for acute trauma-related pain is both an intellectual and practice problem. It is critical for the nurse to understand opioid pharmacokinetics, central nervous system and respiratory physiology, and apply this knowledge to patient monitoring and surveillance. However, little research has been conducted that links the direct effects of specific nursing interventions on patient outcomes (Douw et al., 2018; Kalliokosi, J., Kyngas, Al-Kokko, & Merilainen, 2019; Osborne et al., 2015; Zambas, 2010; Zambas, Smythe, & Koziol-McLain, 2016).

Truth. Pragmatism contends that “truth” in theories and statements is upheld if situations are described accurately, and experiences are anticipated correctly (Magee, 2001; McCready, 2010). Therefore, “truth is “what works” and “what is practical and useful” (McCready, 2010; Popkin & Stroll, 1993). Nursing is a practice-oriented and outcome-focused discipline that is consistent with pragmatism (Donaldson, 1995; McCready, 2010).

The ability to anticipate and recognize subtle changes in patient status and respond appropriately is a critical nursing skill to prevent patient deterioration (Bliss & Aitken, 2018; Cooper, 2013; DaVita et al., 2010; Rattray et al., 2011). Appropriate patient monitoring will enable the nurse to recognize opioid-induced sedation and respiratory compromise early in clinical practice. Knowledge and monitoring practices that enable accurate detection of sedation

are useful in that they enable the nurse the opportunity to implement effective care to prevent the progression of opioid-related adverse events (Jaryzna et al., 2011). Thus, appropriate monitoring is both practical and useful for safe, effective opioid analgesia.

Pragmatism indicates that there is a desired outcome, with usefulness defined in practice and incorporated into practice (James, 1907; McCready, 2010). “Truth” for this research is that appropriate monitoring will facilitate the early recognition of opioid-induced sedation and provide the opportunity for the nurse to balance aggressive pain management interventions with care to prevent opioid-induced adverse effects and ensure optimal patient outcomes (Jaryzna et al., 2011).

The definition of truth in pragmatism is consistent with the nature of this research in that the outcome is shared with nursing and clinical practice. The research results provides evidence to support “what works” in clinical practice and performing appropriate monitoring for patients receiving opioids. Attentive, appropriate monitoring will facilitate “truth” in the prompt recognition of opioid-induced sedation, allow the ability to decrease the opioid dose, and revise the pain management regime to preserve patient safety. This research supports the practice by formalizing evidence for incorporation into clinical practice; thus, pragmatism is compatible with this research topic (see Figure 1.2).

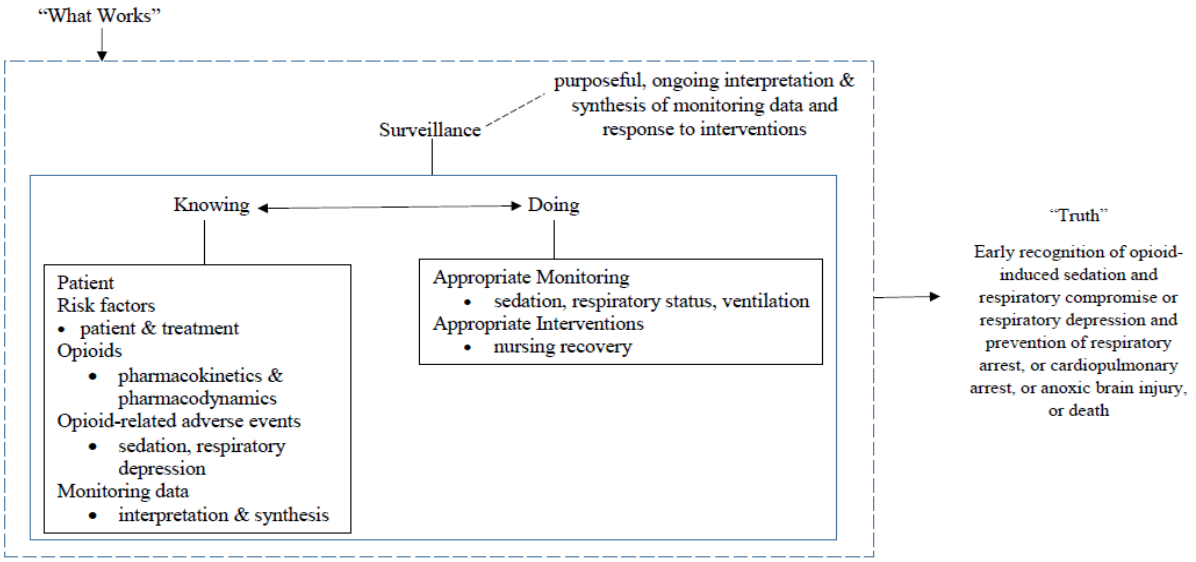

Figure 1.2. "What works" and "truth" in monitoring and surveillance (Dempsey, 2021).

Knowing. Knowing or knowledge within pragmatism is "doing" or a "practical activity" (Magee, 2001; Pierce, 1878). Specific to this premise, researchers are inspired to 'want to know' related to a lack or doubt of knowledge. C. S. Pierce (1878) describes this as "the action of thought is excited by the irritation of doubt." This paucity of knowledge or doubt excites the researcher to evaluate the problem-situation, conduct an inquiry, and consider interventions or methods to solve the error in the situation that results in the problem (Magee, 2001; Pierce, 1878). Congruent with this pragmatic tenet, practice problems or situations inspire research and investigation to more clearly understand the problem and discover or find the knowledge that is useful to answer practice problems. Knowledge generation and application occur in nursing in both practice and research (McCready, 2010). Despite the frequency of opioid-induced sedation and the occurrence of opioid-induced respiratory depression, globally accepted monitoring guidelines of patients receiving opioid analgesia for acute trauma-related pain do not exist (Jaryza et al., 2011; Jungquist et al., 2020).

Furthermore, although there is a plethora of research in the anesthesia literature on goal-

directed sedation, the practice of sedation assessment during opioid pain management is new and the standard of care requires development, as there are no studies to guide practice (Jaryzna et al., 2011; Pasero et al., 2011). Additionally, the impact of nurses' monitoring and surveillance on patient outcomes has not been studied. Further, previous monitoring research has been retrospective and based on documentation and not as real-time observation monitoring. Therefore, the occurrence of opioid-induced events, the paucity of research in determining the most appropriate structures and processes that improve patient outcomes, the absence of research in real-time observation, and lack of global monitoring guidelines to drive practice provided the inspiration to conduct this research.

Within pragmatism, the sharing of knowledge also is important, even if the knowledge generated is inconsistent with the intended outcome. This research aimed to generate knowledge that contributes to the knowledge base of nursing and clinical practice. Sharing of knowledge will facilitate the development of safe, appropriate monitoring and surveillance for patients receiving opioids for acute post-operative pain. The findings from this study will be shared through publications and dissemination of findings at local, national, and international conferences.

Conducting original, scholarly research requires a systematic and rigorous approach (Houghton, Hunter, & Meskell, 2012). The use of pragmatism with its focus on action and outcomes as the philosophical underpinning for this research provides a method to link the need for knowledge (specific aims) with the methodology to generate the knowledge (methods) and translate that knowledge to practice with transformational leadership (Collins et al., 2019; Doane & Varcoe, 2005; Houghton et al., 2012; Weaver & Olson, 2006).

Research Questions and Specific Aims

The research questions and specific aims for this prospective, blinded observational study encompass monitoring and surveillance through the correlation of nurse observations of opioid-induced sedation and respiratory compromise or respiratory depression with capnography and pulse oximetry values as well as a description of the incidence of opioid-induced sedation and respiratory depression.

Research Question 1. What is the incidence of opioid-induced respiratory depression among trauma patients on the general care floor receiving patient-controlled analgesia or nurse administered intravenous opioids during the 60-minute interval following opioid administration as determined by continuous bedside capnography and pulse oximetry as evidenced by:

- Hypopnea (Respiratory rate $\leq$ 8 breaths per minute for $\geq$ 30 seconds duration) or
- Apnea episode (No breath for $\geq$ 30 seconds duration) or
- Hypoxemia (SpO2 $\leq$ 90% for $\geq$ 60 seconds in absence of an abnormal baseline) or
- Low exhaled CO2 (ETCO2 ($\leq$ 15mmHg for $\geq$ 3 minutes duration)

Aim 1. Describe the incidence of opioid-induced respiratory depression among trauma patients on the general care floor receiving patient-controlled analgesia or nurse administered intravenous opioid during the 60-minute interval following opioid administration as determined by continuous bedside capnography and pulse oximetry as evidenced by:

- Hypopnea (Respiratory rate $\leq$ 8 breaths per minute for $\geq$ 30 seconds duration) or
- Apnea (No breath for $\geq$ 30 seconds duration) or
- Hypoxemia (SpO2 $\leq$ 90% for $\geq$ 60 seconds in absence of an abnormal baseline) or
- Low exhaled CO2 (ETCO2 ($\leq$ 15mmHg for $\geq$ 3 minutes duration)

Research Question 2. What is the incidence of opioid-induced respiratory depression

among trauma patients on the general care floor receiving patient-controlled analgesia or nurse administered intravenous opioids during the 60-minute interval following opioid administration as determined by PI nursing monitoring and surveillance as evidenced by:

- Hypopnea (Respiratory rate $\leq$ 8 breaths per minute) or
- Apnea (No observed breath for $\geq$ 30 seconds duration)
- Observation of irregular breathing, snoring, or decreased depth of respirations
- Observation of cyanosis
- Constellation of clinical signs of respiratory depression or the need for resuscitation;
- Observation of respiratory depression that requires intervention within the 60-minute interval after opioid administration; or
- Administration of an opioid receptor antagonist (naloxone);
- Decrease in opioid dose, discontinuation of an opioid, increase in opioid administration frequency interval or change to a different opioid.

Aim 2. Describe the incidence of opioid-induced respiratory depression among trauma patients on the general care floor receiving patient-controlled analgesia and pulse oximetry monitored during the 60-minute interval following opioid administration as determined by PI nursing surveillance and monitoring of:

- Hypopnea (Respiratory rate $\leq$ 8 breaths per minute); or
- Apnea (No observed breath for $\geq$ 30 seconds duration); of
- Observation of irregular breathing, snoring, or decreased depth of respirations or
- Observation of cyanosis; or
- Constellation of clinical signs of respiratory depression or the need for resuscitation or
- Observation of respiratory depression that requires intervention within the 60-minute interval after opioid administration; or

- Administration of an opioid receptor antagonist (naloxone);
- Decrease in opioid dose, discontinuation of an opioid, increase in opioid administration frequency interval or change to a different opioid.

Research Question 3. What is the incidence of opioid-induced respiratory depression among trauma patients on the general care floor receiving patient-controlled analgesia or nurse administered intravenous opioids during the 60-minute interval following opioid administration as determined by continuous bedside capnography and pulse oximetry as compared to the incidence of opioid-induced respiratory depression among trauma patients on the general care floor receiving patient-controlled analgesia or nurse administered intravenous opioids during the 60-minute interval following opioid administration as evidenced by PI nursing assessment of respiratory status?

Aim 3. What is the incidence of opioid-induced sedation among trauma patients on the general care floor receiving patient-controlled analgesia or nurse administered intravenous opioids during the 60-minute interval following opioid administration as determined by continuous bedside capnography and pulse oximetry as compared to the incidence of opioid-induced respiratory depression among trauma patients on the general care floor receiving patient-controlled analgesia or nurse administered intravenous opioids during the 60-minute interval following opioid administration as determined by PI nursing assessment of respiratory status?

Research Question 4. What is the incidence of opioid-induced sedation among trauma patients on the general care floor receiving patient-controlled analgesia or nurse administered intravenous opioids within the 60-minute interval following opioid administration as evidenced by a sedation level of 3 or 4 using the Pasero Opioid-Induced Sedation Scale (POSS)?

Aim 4. Describe the incidence of opioid-induced sedation among trauma patients on the general care floor receiving patient-controlled analgesia or nurse administered intravenous opioids within the 60-minute interval following opioid administration as evidenced by a sedation level of 3 or 4 using the Pasero Opioid-Induced Sedation Scale (POSS).

Research Question 5. What is the temporal distribution of respiratory depression among trauma patients on the general care floor receiving patient-controlled analgesia or nurse administered intravenous opioids within the 60-minute interval following opioid administration as evidenced by continuous bedside capnography and pulse oximetry?

Aim 5. Describe the temporal distribution of respiratory depression among trauma patients on the general care floor receiving patient-controlled analgesia or nurse administered intravenous opioids within the 60-minute interval following opioid administration as evidenced by continuous bedside capnography and pulse oximetry.

Operational Definitions

For the purpose of this study, the following terms are defined:

Monitoring. Monitoring is the process by which the nurse observes, measures, and records serial assessments of sedation and respiratory status (quality, character, rate, and effectiveness) for use in surveillance (Henneman & Gawlinski, 2002; Henneman, Blank, Gawlinski & Henneman, 2006; Henneman et al., 2010; Henneman et al., 2012; Jarzyna et al., 2011; Jungquist et al., 2020). Monitoring is an integral component of surveillance (Henneman et al., 2012; Junquist et al., 2020).

Technology-supported monitoring. The use of technology (capnography or pulse oximetry) in which the nurse observes, measures, and records patient data to enhance monitoring and surveillance. Technology-supported monitoring allows for the continuous surveillance of

physiologic data for the detection of patterns and trends to enhance patient safety (McCloskey Dochterman, & Bulechek, 2004; Jungquist et al., 2020).

Surveillance. Surveillance is a nursing intervention consisting of purposeful and ongoing analysis, interpretation, and synthesis of patient data acquired through monitoring to facilitate appropriate clinical decision-making (Elliot & Coventry, 2012; Henneman et al., 2012; Institute of Medicine, 2004; Orique et al., 2019; Pfrimmer, et al., 2017). Ongoing and accurate surveillance will facilitate the perception of subtle changes in unintended sedation and respiratory status signaling early respiratory deterioration (Hillman et al., 2002; Hillman, 2010; Orique et al., 2019). It is conceivable that surveillance will enable the nurse to anticipate outcomes, make appropriate clinical decision making, and implement early intervention to prevent profession of patient deterioration

Usual care for patients receiving PCA. The usual care for patients receiving PCA at the study site is defined by the Patient Controlled Analgesia Pump – Adolescent/Adult Policy (#12024). Usual care defers as determined by PCA dose only or PCA dose with a continuous opioid infusion.

PCA demand dose only. At the initiation of therapy, vital signs, pain intensity and sedation level using the Richmond Agitation Sedation Scale are monitored and documented every 30 minutes times two at the initiation of therapy followed by assessment and documentation of pain intensity, sedation level, oxygen saturation, respiratory effort and rate every two hours. Respiratory rate is counted for at least 30 seconds and if the rate is less than 12 breaths per minute, or the rhythm is irregular, the rate is counted for 60 seconds.

PCA demand dose with a continuous opioid infusion. At the initiation of therapy, vital signs, pain intensity and sedation level using the Richmond Agitation Sedation Scale are monitored and documented every hour for the first 24 hours followed by assessment and

documentation of pain intensity, sedation level, oxygen saturation, respiratory effort and rate every two hours for the duration of therapy. The patient's respiratory rate is counted for at least 30 seconds and if the rate is less than 12 breaths per minute, or the rhythm is irregular, the rate is counted for 60 seconds.

Pulse oximetry monitoring for patients receiving PCA. Continuous pulse oximetry monitoring is performed for all patients receiving PCA demand dose only or PCA demand dose with a continuous opioid infusion. The pulse oximetry data (oxygen saturation values and waveforms) is assessed intermittently per the assessment method and frequency determined by the PCA method and does not communicate with a nurse notification or central monitoring station.

Usual care for patients receiving nurse-administered intravenous opioids. Usual care for patients who are able to provide a self-report of pain is to assess pain intensity, location, quality, duration, associated symptoms, and the "acceptable level of pain." The components of ongoing reassessment include intensity, location, and response to treatment. Although pain intensity reassessment is a component of usual care, the interval between opioid dose administration and reassessment is based on analgesic modality. A defined time interval for reassessment is not described or defined in the pain management policy of the study site.

Usual care and capnography. Capnography monitoring is usual care for patients undergoing procedural sedation at the study site. Therefore, the study site is familiar with the Medtronic Capnostream20p monitor and ETCO2 sampling line nasal cannula. However, capnography monitoring is not usual care for patients receiving PCA or nurse-administered intravenous opioids.

Opioid-induced sedation. Opioid-induced sedation occurs on a continuum that ranges from full alertness to unresponsiveness and typically precedes opioid-induced respiratory depression (Green & Mason, 2010; Jarzyna et al., 2011; Junquist et al., 2020). Opioid-induced

sedation occurs at increasingly high levels along the sedation continuum and impairs arousal and content processing (Abou Hammond et al., 2009; Brant et al., 2018: Green & Mason, 2010; Jarzyna et al., 2011; Nisbet & Mooney-Cotter, 2009; Pasero & McCaffery, 2011; Young-McCaughan & Miaskowski, 2001a, 2001b). For this study, opioid-induced sedation is defined as observation and assessment of a sedation level of -1, -2, -3, -4, or -5 as measured by the Richmond Agitation Sedation Scale (Sessler et al., 2002) (see Appendix C); a sedation level of 3, 4, 5, or 6 as measured by the Moline-Roberts Pharmacologic Sedation Scale (MRPSS) (see Appendix D) (Moline et al., 2012); or a sedation level 3 or 4 as measured by the Pasero Opioid-Induced Sedation Scale (POSS) (Pasero, 1994) (see Appendix F).

Opioid-induced respiratory depression. Opioid-induced respiratory depression is defined as a decrease in the effectiveness of ventilation after opioid administration (Jarzyna et al., 2011). Opioid-induced respiratory depression is determined by the occurrence of (1) administration of a reversal agent (naloxone) and patient response reveals evidence of reversal of symptoms; or (2) the constellation of clinical signs of sedation (MRPSS level 3-6; POSS level 3 or 4), respiratory arrest, and need for resuscitation; or 3) respiratory rate $\leq$ 8 breaths per minute for $\geq$ 60 seconds; or 4) apnea for $\geq$ 30 seconds; or 5) SpO_2 less than or equal to 90% for $\geq$ 60 seconds in the absence of an abnormal baseline SpO_2; or 6) ETCO2 $\leq$ 15mmHg or $\geq$ 60mmHg for $\geq$ 60 seconds; or 7) observation of opioid-induced respiratory depression (snoring, airway obstruction, or cyanosis) that requires intervention (jaw lift, non-invasive ventilation, or endotracheal intubation) within the 60-minute interval after intravenous opioid administration (Lee et al., 2015).

Gaps in the Literature

Opioid-related adverse events such as sedation and respiratory depression are preventable causes of patient harm (Lee et al., 2015; Maddox & Williams, 2012; Ruscic, Grabitz, Rudolph,

& Eidermann, 2017; Stites et al., 2021). Opioid-induced sedation and respiratory depression can result in increased morbidity, mortality, length of hospital stay, and healthcare costs (Eckstrand et al., 2009; Jungquist et al., 2014; Kessler et al., 2013; Lee et al., 2015).

The effectiveness of continuous respiratory monitoring of trauma patients on the general care ward receiving PCA or nurse-administered intravenous opioids for acute pain has not been described. It is conceivable that continuous respiratory monitoring coupled with nurse surveillance in trauma patients on the general care ward could prevent opioid-induced sedation, respiratory depression, and improve patient safety opioid-related adverse events and subsequent patient harm are preventable (Lee et al., 2015). Unfortunately, a gap exists in both "knowing" (appropriate monitoring) and "doing" (practice) (Lee et al., 2015).

Opioid-based analgesia is commonly used for the management of acute trauma-related pain. Although opioids are capable of providing safe, effective analgesia for most patients, opioid administration may lead to acute respiratory depression in unmonitored, low acuity general care wards.

Although there is a plethora of purposeful, goal-directed research in the anesthesia literature, monitoring and surveillance for unintended opioid-induced sedation and opioid-induced respiratory depression among patients receiving opioids for trauma-related pain is new, and the standard of care requires development as there are no studies to guide current practice (Jarzyna et al., 2020; Lynn & Curry, 2011). Although risk factors are well defined, opioid-induced respiratory depression continues to occur. Therefore, this continued occurrence suggests that the identification of risk factors alone is inadequate to predict which patients will develop opioid-induced sedation and opioid-induced respiratory depression. The literature also does not describe the real-time correlation of nurses' observations of sedation level and respiratory status and correlation with capnography (ETCO2, respiratory rate, IPI) and pulse

oximetry (SpO_2) in trauma patients receiving opioid analgesia (Dempsey et al., 2009; Jarzyna et al., 2011; McIntyre et al., 2011; Nisbet & Mooney-Cotter, 2009). Capnography and pulse oximetry values also have not been correlated with patient deterioration, opioid-induced sedation or respiratory depression. Furthermore, the influence of appropriate monitoring and surveillance on patient outcomes has not been studied (Henneman, 2017).

Significance for Nursing

Opioids can suppress the central respiratory drive (Kiyatkin, 2019). Opioid-induced airway obstruction, respiratory compromise, and respiratory depression with hypoventilation, apnea, and hypoxemia result in increased morbidity and mortality. Researchers have reported that opioid-induced respiratory depression is multifactorial and preventable by assessment, monitoring, surveillance, and appropriate interventions (Lee et al., 2015; TJC, 2012). Early detection of opioid-induced sedation, respiratory compromise, and respiratory depression is critical to allow for the initiation of timely and appropriate interventions (TJC, 2012).

Identification of the trauma patients at risk for opioid-induced respiratory depression would allow for appropriate patient-centered monitoring and surveillance strategies (Cauley et al., 2017; Gordon & Pellino, 2005; Lee et al., 2015; Khanna et al., 2019a; 2019b; Rosenfeld et al., 2016; Taylor et al, 2005; Weingarten, Warner, & Sprung, 2017). Multiple postsurgical patient and treatment-related risk factors for opioid-induced respiratory depression have been described (Cauley et al., 2017; Chung et al., 2015; Chung, Liao, Yegneswaran, Shapiro, & Kang, 2014; Chung et al., 2016; Etches, 1994; Gordon & Pellino, 2005; Khelemsky et al., 2015; Lam et al., 2017; Niesters, Overdyk, Smith, Aarts, & Dahan, 2013; Opperer et al., 2016; Overdyk et al., 2014; Ramachandran et al., 2011; Rosenfeld et al., 2016; Taylor et al., 2005; Weingarten et al., 2017). Individual variation and response to opioids demand accurate risk assessment and comparative effectiveness on monitoring technology and evaluation of patient outcomes.

Alarmingly, OIRD among trauma patients on general care wards has not been previously described. Furthermore, there is no evidence regarding the incidence, frequency, and temporal distribution among trauma patients.

Safe, effective pain management among trauma patients requires careful individual dose adjustment based on appropriate monitoring of pain, sedation, and respiratory status after opioid administration (Drew, Gordon, Morgan, & Manworren, 2018; Chou et al., 2016). Thus, appropriate monitoring and ongoing surveillance are imperative to achieve effective pain management, limit or prevent opioid-induced adverse events, and maintain patient safety (Henneman, 2017; Prgomet et al., 2016). Prevention of unintended sedation and respiratory depression is primarily the responsibility of the nurse (Peet et al., 2018). Nursing surveillance for opioid-induced respiratory depression is critical for early recognition, appropriate clinical decision making, and implementation of (Eckstrand et al., 2009; Nisbet & Mooney-Cotter, 2009; Pasero, 2009; TJC, 2012). Unfortunately, clinical settings or system factors can negatively influence surveillance and the ability of the nurse to perceive and recognize subtle changes in patient status (Gaffney et al., 2016; Henneman, 2017).

Sedation occurs on a continuum of "levels of consciousness and arousability" (Jaryzna et al., 2011; Nisbet & Mooney-Cotter, 2009; Young-McCaughan & Miaskowski, 2001a; 2001b). This continuum offers compelling evidence of the importance of sedation assessment for patients receiving opioids (Jarzyna et al., 2011; Nisbet & Mooney-Cotter, 2009; Pasero, 2009; Zambas, 2010). Early recognition of sedation provides the opportunity to implement appropriate care and prevent the worsening of opioid-induced adverse events such as respiratory compromise, respiratory depression, or cardiopulmonary arrest and death. Despite the importance of sedation assessment, few studies have described the effectiveness of the role of the nurse in sedation assessment and the impact on patient outcomes (Dempsey, 2011; Jaryzna et al., 2011; Young-

McCaughan & Miaskowski, 2001a; 2001b). Assessment must include rate, depth, and quality; however, a standard of practice for respiratory status assessment does not exist (Pasero & Stannard, 2012).

Clinical observation of respiratory status alone is an unreliable indicator of adequate ventilation (Tanaka, Tanaka, & Drover, 2014; Vargo et al., 2002 Zambas, S. I. (2010). SpO_2 monitoring using pulse oximetry is an accepted method of monitoring respiratory function. However, pulse oximetry is a late indicator of apnea, airway obstruction, and hypoventilation, especially when the patient is receiving supplemental oxygen (Dahan et al., 2010; Fu et al., 2004). SpO_2 and respiratory rate are surrogate indicators of ventilation and provide limited information on the opioid effects on ventilation (Cacho et al., 2010; Dahan et al., 2010). ETCO2 monitoring using capnography has been reported as an earlier indicator of a comprised respiratory status than SpO_2 or observed changes in respiratory rate (Burton et al., 2006; Dahan et al., 2010; Lightdale et al., 2006; Qadeer et al., 2009; Overdyk et al., 2007; Silvilotti et al., 2009). Although ETCO2 monitoring is routine during general anesthesia, there is limited information and lack of consensus about the benefits of technology-supported monitoring (pulse oximetry and capnography) in the prevention of opioid-induced respiratory compromise and respiratory depression during opioid analgesia (Jaryzna et al., 2011; Pasero & Stannard, 2012; Waugh et al., 2011). Randomized clinical trials have not been conducted to establish technology-supported monitoring as standard practice in the prevention of opioid-induced respiratory events (Jaryzna et al., 2011; Waugh et al., 2011). Late detections signaled by technology-supported monitoring are often associated with antecedent false alarms and result in a false sense of security by the nurse that could result in a significant delay in recognition of opioid-induced sedation or hypoventilation (Lynn & Curry, 2011). As a result, failure to perform adequate serial assessments may occur because of the reassurance provided by the absence of alarms.

Although few studies have explored the role of the nurse, attentive care patient monitoring, or surveillance of patients receiving opioids medical patients, no studies have described the role of the nurse in preventing and recognizing respiratory depression in the trauma patient on the general care ward (Dempsey, 2011; Henneman, 2017; Jarzyna et al., 2011; Nisbet & Mooney-Cotter, 2009). Although SpO_2 monitoring frequently is used to monitor respiratory status in patients receiving opioids, it is unknown if SpO_2 monitoring is more effective than nursing observation of respiratory status and sedation level because randomized studies do not show a clear effect on patient outcomes.

Monitoring without interpretation and synthesis of data (surveillance) is insufficient and can result in patient deterioration if sedation or opioid-induced respiratory depression is left uninterrupted without the implementation of interventions and nursing recovery (Henneman, 2017).

Challenges exist when studying cognitive and technical processes, such as monitoring and surveillance. Therefore, innovative and multi-dimensional approaches to research must be used. Previous studies of monitoring have been retrospective and real-time observational studies have not been conducted. Studies also have not been conducted that describe the patterns and trends of patient decompensation and correlate continuous nurse observations of sedation level, physiologic parameters (ETCO2, SpO_2, respiratory status, and ventilation) in patients receiving opioids for acute trauma-related pain.

Appropriate monitoring of patients receiving opioids for trauma-related pain is critical for the early recognition of opioid-induced sedation and opioid-induced respiratory depression to maintain patient safety. Despite this recognition and the risk and frequency of serious opioid-related adverse events, globally accepted guidelines to drive monitoring in clinical practice do not exist (Ayad et al., 2019; Jarzyna et al., 2011; Jungquist et al., 2020). Furthermore, the

incidence and temporary distribution among trauma patients who receive opioids in the ED and general ward has not been previously described. The findings from this study provide needed information to assist with the development of evidence-based attentive care, monitoring and surveillance practices for trauma patients receiving opioids for acute pain to facilitate safe, effective pain management.

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CHAPTER 2: Review of the Literature

Effective pain management is a priority for patients hospitalized following trauma (Ahmadi et al., 2016; Chou et al., 2016; Keene, Rea, & Aldington, 2011). Suboptimal management of acute pain is associated with negative physiological and psychological consequences that facilitate negative patient outcomes (Ahmadi et al., 2016; Baratta, Schwenk, & Viscusi, 2015; Chou, et al., 2016; Gordon et al., 2015; Joshi & Ogunnaike, 2005; Kehlet, Jensen, & Woolf, 2006). Safe, optimal pain management goals include reducing the severity of pain intensity, improving function, and preventing opioid-related adverse events (Gordon, et al., 2015; Sinatra, 2010).

Opioid analgesia remains the main pharmacological approach for management of acute moderate to severe pain (Aldington, McQuay, & Moore, 2011; Gausche-Hill et al., 2014; Jarzyna et al., 2011; Keene, Rea, & Aldington, 2011; Pasero, 2009; Phillips et al., 2012; Young-McCaughan & Miaskowski, 2001a; 2001b). In addition to providing effective analgesia, opioids exert central depressant effects on activating and respiratory centers in the brainstem (Morris et al., 2017; Phillips et al., 2012; Ramachandran et al., 2011). Opioids can produce a continuum of adverse effects ranging from opioid-induced sedation to respiratory compromise, and ultimately, if untreated, respiratory arrest and death (Abou Hamoud et al., 2009; Dolin & Cashman, 2005; Morris et al., 2017; Phillips et al., 2012; Ramachandran et al., 2011; Taylor, Voytovich, & Kozol, 2003). Opioid-related adverse events negatively impact patient outcomes through increased morbidity, mortality, length of stay and healthcare costs for post-operative and trauma patients (Jarzyna et al., 2011; Oderda, et al., 2007; Pasero & McCaffery, 2011). All patients receiving opioids for pain management are at risk for opioid-induced sedation that may progress to respiratory compromise and lead to clinically significant opioid-induced respiratory

depression (Jaryzna et al., 2011; MacIntyre, Loadsman, & Scott, 2011; Morris et al., 2017; Pasero, 2009; Young-McCaughan & Miaskowski, 2001a; 2001b).

Prevention, early recognition, and timely appropriate intervention for unintended opioid-induced sedation and respiratory compromise is central to prevent cardiopulmonary arrest and plays a critical role in patient outcomes (Massey, Chaboyer, & Anderson, 2016; Overdyk et al., 2016). Patient and treatment-related factors influence the incidence of opioid-related adverse events (Jarzyna et al., 2011; Jungquist et al., 2017). However, inter-individual variability in response to opioids results in difficulty in the prediction of which patients will develop adverse events and further complicates safe pain management for post-operative or trauma patients on the unmonitored general care ward (Drewes et al., 2013; Henker et al., 2013; Morris et al., 2017; Phillips et al., 2012).

The opioid-induced respiratory compromise also occurs on a continuum of severity from opioid-induced respiratory depression to respiratory failure, cardiopulmonary arrest, and death (Overdyk et al., 2016). The severity of opioid-induced respiratory compromise can escalate, or de-escalate, spontaneously or in response to timely interventions (Morris et al., 2017). It is clear that opioid-induced respiratory depression is preventable with appropriate, vigilant patient monitoring and surveillance (Henneman, 2017; Lee et al., 2015; Overdyk et al., 2016; TJC, 2012). However, there is a paucity of research describing the impact of nursing assessment and technology-supported monitoring on patient safety and outcomes, especially for post-operative and trauma patients on the unmonitored general surgical unit (Davis et al., 2017; Dempsey et al., 2009).

Methodology for Review of the Literature

Monitoring was defined as ongoing, purposeful nurse assessment of sedation level and respiratory status using sedation scales and technology to anticipate, or recognize opioid-induced

sedation, respiratory compromise, or respiratory depression (Abou Hamoud et al., 2009; Jarzyna et al., 2011; Ramachandran et al., 2011). Monitoring using sedation scales, nursing assessment of respiratory rate and status, opioid-induced sedation, pulse oximetry (SpO_2), and end-tidal carbon dioxide (ETCO2) technology was reviewed. The initial population of focus was hospitalized adult patients receiving opioid analgesics for acute trauma-related pain. However, a paucity of evidence related to sedation assessment for patients receiving opioids for acute pain management was retrieved; therefore, the review was extended to include emergency department and hospitalized patients requiring procedural or goal-directed sedation and analgesia.

An extensive review of the literature was conducted to discover relevant studies. Multiple databases, including PubMed, CINAHL PLUS, and Cochrane Library, were searched between 1970 and 2017 for relevant studies. Search strategies combined keywords, synonyms, and subject headings. The MeSH terms included: sedation combined with opioids, opioid-induced sedation, sedation scale, adverse events, prevention, respiratory depression, monitoring, ETCO2, and SpO_2. Only studies involving adult humans published in English were included. Initially, 809 articles were retrieved using the terms of sedation, opioids, sedation scale, adverse events/effects, and monitoring. All study titles and abstracts were scanned to determine relevancy, and focus was given to articles in the subsets of each search identified as original clinical or nursing research. Reference lists of studies selected for inclusion also were scanned for additional relevant studies. Nursing practices with opioid-based and multimodal analgesia in the care of hospitalized patients were examined. A search was conducted for relevant nursing articles in CINAHL; however only one guideline was retrieved using the terms of sedation assessment and opioid.

Opioids and Respiration

Respiration is an essential physiological process that is an intricately controlled rhythmic motor output to maintain blood oxygen (O_2), carbon dioxide (CO_2), and pH (Morris et al., 2017). Opioids induce respiratory depression through stimulation of mu-opioid receptors located in the central nervous system (Bloom et al., 2012; Dahan, Aarts, & Smith, 2010; Montandon, Qin, Ren, Greer, & Horner, 2011; Pattinson, 2008). Opioid-induced respiratory depression is also mediated through inhibition of the pre-Botzinger Complex, a bilateral cluster of neurons in the ventral lateral medulla that is the site for respiratory rhythmogenesis and generation of inspiratory rhythm (Smith et al., 1991).

The constellation of reduced brain arousability (sedation), central depression of respiratory frequency, amplitude and reflex responses, and upper airway dysfunction encompasses opioid-induced respiratory depression (Lalley, Pilowsky, Forster, & Zuperku, 2014; Montandon & Horner, 2014; Pattinson, 2008). Specifically, opioids depress the respiratory rate, alter tidal volume, induce chest wall rigidity, and decrease upper airway patency (Ferguson & Drummond, 2006; Leino, Mildh, Lertola, Seppala, & Kirvela, 1999; Lotsch, Skarke, Schneider, Hummel, & Geisslinger, 2005). Therefore, opioid-induced respiratory depression results in hypoventilation and irregularity in breathing rhythm leading to decreased alveolar ventilation (Morris et al., 2017). Without early recognition and appropriate intervention, hypercarbia and subsequent acidosis ensue as hypoventilation increases in severity (Morris et al., 2017). Consequently, hypoventilation results in hypoxemia related to a decrease in alveolar ventilation. However, the administration of supplemental oxygen may prevent hypoxemia and delay the detection of early opioid-induced respiratory depression (Morris et al., 2017).

Given the ubiquitous use of opioid-based analgesia for trauma-related pain, opioid-induced respiratory depression is a major clinical concern. Therefore, a critical need exists for

individualized and adequate monitoring to ensure recognition of reduced arousability (opioid-induced sedation) and prevent the progression to opioid-induced respiratory depression.

Patient Monitoring

Unintended Opioid-Induced Sedation

Opioids have potent sedative effects that can potentiate their effects on respiration. Opioid-induced sedation is characterized by reduced motor activity, loss of attention, changes in electroencephalogram activity, and depressed arousal (Young-McCaughan & Miaskowski, 2001a; Wang & Teichtahl, 2007).

Unintended opioid-induced sedation is the most important predictor of respiratory depression in the trauma patient receiving opioids for acute pain (Dolin & Cashman, 2005; Grissinger, 2013; Pasero, 2009). Sedation is a common opioid-related adverse effect, especially during the initial 24-hours of opioid analgesia, with increases in dose, or conversion to a different opioid (Badner, Doyle, Smith, & Herrick, 1996; Davis et al., 2017; Gordon & Pellino, 2005; Jarzyna et al., 2011; McPherson, 2008; Paice, 2007; Pasero et al., 2011; Taylor, Kirton, Staff, & Kozol, 2005; TJC, 2012). Opioid-induced sedation is a serious risk to patient safety when it progresses in severity and impairs the level of alertness, arousal, and content processing (Young-McCaughan & Miaskowski, 2001a; 2001b). Life-threatening respiratory depression is less common than opioid-induced sedation and is the most serious of opioid-related adverse event because of the risk for progression to cardiopulmonary arrest and death (Jarzyna et al., 2011; Pasero et al., 2011; Phillips et al., 2012; Ramachandran et al., 2011).

Opioid-induced sedation occurs on a continuum and typically precedes respiratory depression (Jarzyna et al., 2011; Jungquist et al., 2019; Nisbet & Cotter-Mooney, 2009; Pasero, 2009). Less opioid is needed to cause opioid-induced sedation than to cause respiratory depression (Pasero, 2009). Attentive, appropriate assessment of patients receiving opioids is an

important component of safe, effective care; however, no globally accepted practices exist to direct monitoring (Jarzyna et al., 2011). The nurse has a critical role in the prevention of opioid-induced respiratory depression through attentive serial sedation assessment, prompt recognition of opioid-induced sedation, and the provision of care to prevent progression of adverse events using a valid and reliable sedation assessment scale (Considine, 2005; Jarzyna et al., 2011; Needleman, & Hassmiller, 2013; Pasero, 2009; 2013; Wickerstrom, 2008).

One of the most serious opioid-related adverse events is clinically significant, life-threatening opioid-induced respiratory depression (Pasero, 2009; 2013). Opioid-induced sedation typically precedes opioid-induced respiratory depression (Pasero, 2009). Because less opioid is needed to produce sedation than opioid-induced respiratory depression, worsening sedation is an early warning sign and predictor of an opioid-induced respiratory event (Dempsey, 2012; Quinlan-Colwell, Thear, Miller-Baldwin, & Smith, 2017).

Opioid-induced sedation occurs on a continuum and ranges from full alertness and arousability to unresponsiveness (Abou Hammound et al., 2009; American Society of Anesthesiologist [ASA], 2014; Green & Mason, 2010; Gross et al., 2002; Nisbet & Mooney-Cotter, 2009; Jarzyna et al., 2011; Pasero & McCaffery, 2011; Young-McCaughan & Miaskowski, 2001a, 2001b).

Opioid-induced sedation is a common opioid-induced adverse effect, especially during the first 24-hours after initiation of opioid analgesia, with dosage increases and opioid conversion (Jarzyna et al., 2011; Jungquist et al., 2017; Pasero et al., 2011). Sedation can progress to respiratory depression, and early recognition of increasing sedation is critical to prevent life-threatening respiratory depression. Safe and effective pain management is best achieved through opioid dose adjustment based on attentive sedation monitoring, and trending,

as considerable variability exists in individual response to opioids (Dolin & Cashman, 2005; Pesonen et al., 2007).

Few studies have investigated the role of the nurse in sedation assessment for patients receiving opioids for pain management (Jarzyna et al., 2011). The frequency, intensity, and duration of sedation assessment should be based on individual patient risk factors, type of opioid therapy, and response after opioid administration (Dunwoody, Kenzischek, Pasero, Rathmell, & Polomano, 2008; Nisbet & Mooney-Cotter, 2009; Pasero, 2009; Pasero & McCaffery, 2011; Young-McCaughan & Miaskowski, 2001b). Further research about the prevalence of opioid-induced sedation in patients receiving opioids for acute trauma-related pain is needed to establish accepted sedation criteria and validate sedation measurement using valid and reliable sedation scales (Davis et al., 2017; Jarzyna et al., 2011; Young-McCaughan & Miaskowski, 2001b).

A plethora of literature exists about assessment during purposeful, goal-directed sedation in critically ill patients (Jarzyna et al., 2011; Pasero & McCaffery, 2011). However, despite the importance of attentive monitoring to recognize opioid-induced sedation, few researchers have investigated the role of the nurse in sedation assessment and relationship to patient outcomes (Dempsey, 2012; Dempsey et al., 2009; Jarzyna et al., 2011, Nisbet & Mooney-Cotter, 2009). Similarly, limited data exists outside of goal-directed sedation to demonstrate the psychometric properties of sedation scales (Dempsey, 2012; Davis et al., 2017; Jaryza et al., 2011).

Sedation assessment scales. Several valid and reliable scales are used to assess changes in levels of awakeness and arousability to measure sedation (Aldrete & Kroulik, 1070; Aldrete, 1995; Davis et al., 2017; Dunwoody & Jungquist, 2018; Jarzyna et al., 2011; Moline, Roberts, & Houser, 2012; Newton, Pop, & Duvall, 2013; Pasero, 2009; Pasero et al., 2011; Ramsay, Savage, Simpson, & Goodwin, 1974; Rasheed, et al., 2019; Rassin et al., 2007; Rikker & Fraser, 2001; Sessler et al., 2002; Simmons, Riker, Prato, & Fraser, 1999). Goal-directed sedation scales often

are used for sedation assessment regardless of the desired patient outcome. These scales, such as the Richmond Agitation Sedation Scale (RASS) or Ramsey, were developed in the critical care environment to assess purposeful sedation during procedures, facilitate tolerance of the critical care environment, or to effect a change in behavior (Binnekade, Vroom, de Vos, & de Haan, 2006; Brandl et al., 2001; Chernik et al., 1990; De Jonghe et al., 2003; de Lemos, Tweddle, & Chittock, 2000; Devlin et al., 1999; Hogg et al., 2001; Olleveant, Humphris, & Roe, 1998; Olson, Lynn, & Thoyer, 2007; Rassin et al., 2007; Riker, Picard, & Gilles, 1999; Riker, Fraser, Simmons, & Wilkins, 2001; Sessler et al., 2002; Pasero, 2009; Weinert & McFarland, 2004). Goal-directed sedation scales are not recommended for use in patients receiving opioids for pain management when the desired outcome is early recognition of unintended, advancing sedation (Moline et al., 2012; Pasero, 1994; 2009). More specifically, goal-directed sedation scales correlate behaviors, such as anxiety or agitation, to sedation level and complicates sedation assessment. However, anxiety and agitation are not indicators of unintended, advanced opioid-induced sedation (Jaryzna et al., 2011; Pasero, 2002; 2009; 2013). Furthermore, patients may be calm or anxious and sedated (Pasero, 2009). A review of the literature revealed that only the Pasero Opioid-Induced Sedation Scale was designed for patients outside of the intensive care unit receiving opioids for pain management (Pasero, 1994). Despite the significance of serial sedation assessments to recognize opioid-induced sedation, few studies have investigated the effectiveness of sedation assessment on patient outcomes (Dempsey, 2012; Nisbet & Mooney-Cotter, 2009; Pasero, 2002; 2009; 2013).

Nisbet and Mooney-Cotter (2009) conducted a descriptive study to perform reliability and validity testing and performance of three scales sedation scales—the Inova Health System Sedation Scale (ISS), the Richmond Agitation and Sedation Scale (RASS), and the Pasero Opioid-Induced Sedation Scale (POSS). A sample of 96 nurses read several online scenarios,

after which each nurse completed an online survey to assess the sedation level and determine appropriate nursing action and care. Percent agreement was highest for the POSS both for the selection of the sedation level and appropriate nursing intervention (Nisbet & Mooney-Cotter, 2009).

In a more recent study, researchers conducted an exploratory, descriptive study to determine ease of use, applicability, and psychometric testing for inter-rater reliability of the RASS and POSS. Three researchers conducted 252 sedation assessments for 84 critically ill and medical-surgical patients over three study days. Results revealed high reliability of both scales (POSS 0.909; RASS 0.949 by Cronbach's alpha). However, the majority of nurses (76%) rated the POSS easiest to use. Nurses also requested that the POSS be available for use when the desired patient outcome is sedation prevention and the RASS be available for use for goal-directed sedation. Six months after implementation of the POSS for sedation assessment during opioid therapy, there were no occurrences of opioid-induced events requiring reversal agents or transfer to a higher level of care as compared to 43 occurrences in the previous 12-month period (Dempsey, 2012; Dempsey et al., 2009).

In a descriptive study of 86 patients receiving opioids, benzodiazepines, or anesthetic agents using the Moline-Roberts Pharmacologic Sedation Scale, researchers found that routine sedation assessment and trending provided valuable information for early recognition of opioid-induced sedation and appropriate clinical decision-making (Moline et al., 2012).

In a recent multi-center, retrospective study, researchers described the impact of re-education or implementation of the Pasero Opioid-Induced Sedation Scale on the use of naloxone in 212 patients who had received hydromorphone for pain (Davis et al., 2017). However, researchers also evaluated the occurrence of opioid-induced sedation using the Richmond-Agitation-Sedation Scale which is a goal-directed sedation scale. The percentage of

patients requiring naloxone administration and the percentage of patients who suffered opioid-induced sedation (i.e., Pasero Opioid-Induced Scale 3 or 4 or Richmond-Agitation-Sedation Scale -4 or -5) was evaluated. Researchers reported increased recognition of opioid-induced sedation (12.2%; *n*=13) after re-education as compared to recognition of opioid-induced sedation before re-education (3.8%, *n*=4) which was statistically significant ($p = 0.04$). There were no changes in naloxone use.

Findings from these studies support the contention that goal-directed sedation scales are not appropriate for the sedation assessment for patients receiving opioids for pain when the desired patient outcome is early recognition of opioid-induced sedation (Dunwoody & Jungquist, 2020; Pasero, 2009; Pasero & McCaffery, 2011; Smith, 2007). Study results reflect that the nurse has a critical role in the prevention of opioid-induced adverse effects through attentive monitoring and surveillance using a valid and reliable sedation scale that provides a standard quantification of sedation and also directs implementation of appropriate interventions (Dolin & Cashman, 2005; Moline et al., 2012; Pasero, 2009).

Opioid-Induced Respiratory Compromise

The opioid-induced respiratory compromise also occurs on a continuum of severity and reflects a concerning decrease in ventilation effectiveness after opioid administration (Jarzyna et al., 2011; Morris et al., 2017; Nisbet & Mooney-Cotter, 2009). Respiratory compromise represents a constellation of respiratory insufficiency, respiratory depression, respiratory failure, and respiratory arrest (Morris et al., 2017). Identification of patient risk and early recognition of respiratory compromise is essential for the development of appropriate monitoring and surveillance strategies for prevention, *early* identification, and correction of opioid-induced respiratory depression.

Opioid-induced respiratory depression. Respiratory depression is characterized by a decreased respiratory rate resulting in reduced airflow causing a reduction in tidal volume, decreased exhaled carbon dioxide (ETCO2) leading to decreased oxygen intake (Macintyre et al., 2011). Ineffective ventilation leads to decreased blood oxygen levels (hypoxia) and increased carbon dioxide (hypercarbia) (Montadon et al., 2016).

Opioid-induced respiratory depression is characterized by reduced changes in breathing frequency, oxygen saturation (SpO_2), or end-tidal carbon dioxide (ETCO2) (Dahan et al., 2010). However, definitions of respiratory depression differ by practices, researchers, and studies (Catley et al., 1985; Dahan et al., 2010; Ko, Goldstein, & VanDenKerkhof, 2003). In the inpatient setting, severe respiratory depression is considered at a respiratory frequency of less than 8-10/minutes, decreased SpO_2 less than 90%, or ETCO2 less than 30mmHg or greater than 50mm Hg (Dahan et al, 2010; Jarzyna et al., 2011; Wheatley et al., 1990). Severe respiratory depression often is defined as a respiratory rate of fewer than eight breaths per minute with accompanying SpO_2 less than 85% for a period of six minutes (Dahan, 2007; McIntyre et al., 2011). Opioid-induced respiratory depression typically is preceded by opioid-induced sedation (Jaryzna et al., 2011; Junquist, Karan, & Perlis, 2011).

Nurse performance of a comprehensive respiratory status assessment that includes depth and rhythm of respirations, accessory muscles use, and auscultation of breath sounds has been reported as having a positive impact on patient outcomes (Duff et al., 2007; Zambas, Smythe, & Koziol-McLain, 2016). This report offers compelling evidence that nurses can prevent opioid-induced adverse events through the early recognition of unintended advancing sedation that may lead to respiratory depression (Considine, 2005).

Pulse oximetry monitoring (SpO2). Pulse oximetry is a non-invasive method for measuring venous oxygen saturation (SpO2) oxygen to detect hypoxemia (Lam et al., 2017;

Jaryzna et al., 2011; Jungquist et al., 2017). However, SpO2 is an inadequate measurement of opioid-induced sedation and *early* respiratory compromise for patients receiving opioids. Specifically, oxygen saturation is an indirect measurement of oxygenation, however, is not an indicator or measure of hypoventilation (Cacho et al., 2010; Dahan et al., 2010; Fu et al., 2004; Jaryzna et al., 2011; Overdyk, Carter, & Maddow, 2006). Pulse oximetry is a late indicator of hypoventilation in patients with oxygen desaturation (Bergese et al., 2017). Ventilation and oxygenation are separate physiological processes, and ventilatory impairment can occur with adequate oxygenation (Overdyk et al., 2006).

A Cochrane Systematic Review evaluating the role of pulse oximetry in perioperative care revealed that SpO2 monitoring using pulse oximetry detects hypoxemia; however, it does not improve care and patient outcomes (Pedersen et al., 2014). Similarly, in a single randomized, non-blinded study of 1,219 post-operative cardiac surgery patients on a post-surgical ward, researchers reported that continuous SpO2 monitoring with pulse oximetry was not found to be associated with improved patient outcomes, the occurrence of adverse events, or mortality (Ochroch et al., 2006). Furthermore, changes in SpO2 and detection of hypoxemia are delayed when patients are receiving supplemental oxygen (Fu et al., 2004; Overdyk et al., 2006).

In a prospective, descriptive study of 50 patients undergoing colonoscopy, 29 occurrences of disordered breathing were observed in 16 patients (mean 54.4 seconds). Researchers reported that only 38% of episodes of apnea or hypoventilation were recognized by pulse oximetry (Cacho et al., 2010). Furthermore, there was a mean delay of 38.6 seconds of detection of respiratory depression events by pulse oximetry. Two episodes of respiratory compromise were detected by capnography and pulse oximetry simultaneously (Cacho et al., 2010).

In a non-blinded randomized study, researchers compared the effect of continuous pulse oximetry monitoring with standard intermittent monitoring on the rate of ICU transfer from a 33-bed acute postcardiothoracic surgical unit (Ochroch et al., 2006). Study results revealed that continuous monitoring with pulse oximetry did not decrease transfer to the intensive care unit (ICU) as compared to standard intermittent monitoring (6.7% vs. 8.4%) RR. 0.81, 95% CI, 0.54-1.2; *p*=.29, respectively) or mortality (2.3% vs. 2.2%, respectively). However, transfers to the ICU related to pulmonary causes was significantly reduced (8 vs. 0.27; $p = .003$, respectively) among patients monitored with continuous pulse oximetry as compared to standard intermittent monitoring (respectively, 13% vs. 4.2%; RR 0.32; 95% CI, 0.15-0.69; $p = .004$). Although continuous patient monitoring with pulse oximetry did not reduce ICU transfers or mortality, ICU length of stay was shorter, and the cost of overall care was less for patients monitored with continuous pulse oximetry as compared with those monitored with intermittent pulse oximetry. Thus, these results may suggest that continuous monitoring allows for earlier detection of respiratory compromise, earlier intervention, and prevents the worsening of adverse events as compared to standard intermittent monitoring.

In a prospective, historical controlled trial of patients on a 36-bed orthopedic unit, researchers implemented a patient surveillance system using continuous pulse oximetry with nursing notifications when physiologic limits were violated (Taenzer, Pyke, McGrath, & Blike, 2010). The results of this study showed a significant reduction in ICU transfers (5.6 - 1.2 per 1000 patient days; $p = .01$) and rapid response team activation (3.4 -1.2 per 1000 patient days; $P = .02$) with continuous pulse oximetry monitoring as compared to intermittent pulse oximetry monitoring (Taenzer et al., 2010).

Study results indicate that continuous monitoring with pulse oximetry on the general care ward is associated with clinically significant improvement in the detection of oxygen

desaturation as compared to intermittent monitoring. Furthermore, the trend toward fewer ICU transfers with continuous pulse oximetry as compared to intermittent monitoring suggests that changes in patient status are recognized earlier, allow for nursing recovery, and prevent the worsening of the patient deterioration.

In a more recent prospective, observational study of 833 non-cardiac surgery patients in an acute surgical unit, researchers sought to quantify hypoxemia (Sun et al., 2015). Continuous pulse oximetry was initiated on admission to the general surgical unit and continued for up to 48 hours. Clinical nurses were blinded to the continuous pulse oximetry values. Patients also received the usual standard care of intermittent vital sign monitoring every 4 hours (Sun et al., 2015). Study results revealed 21% of patients demonstrated an average of 10 minutes per hour of SpO_2 less than 90% during the length of their hospitalization, and 37% of patients experienced at least one episode of SpO2 less than 90% for one hour. Furthermore, 90% of serious hypoxemic episodes (SpO_2 <90% for ≥1 hour) were undetected (Sun et al., 2015). Results indicated that hypoxemia is common, prolonged, and often undetected on the unmonitored acute surgical unit. Thus, intermittent monitoring underestimates hypoxemia among trauma patients on the general care ward.

Adequate SpO2 monitoring, evaluation of patterns and trends, and accurate documentation are critical in the early recognition of decompensation in patients receiving opioids for post-operative or trauma-related pain (Taenzer, Pyke, Herrick, Dodds, & McGrath, 2014). In a study of 16 patients identified as at high risk for decompensation, researchers compared SpO_2 data collected by continuous pulse oximetry and automated electronic documentation as compared to data collected with intermittent monitoring and manual documentation. Study results revealed that among patients with prolonged desaturations (SpO2 < 90% for >15-minute duration), intermittent pulse oximetry monitoring and manual

documentation of SpO2 values were 6.5% higher as compared to continuous pulse oximetry documentation (p<0.001) and did not reflect the physiologic status of the patient (Taenzer et al., 2014).

Capnography (exhaled end-tidal carbon dioxide) monitoring. Capnography monitoring measures exhaled end-tidal carbon dioxide (ETCO2) and provides an indicator of ventilation (Burton, Harrah, Germann, & Dillon, 2008; Cacho et al., 2010; Deitch, Miner, Chudnofsky, Dominici, & Latta, 2010; Estfan et al., 2007; Saunders, Ersion, & Vargo, 2016). Evidence indicates that capnography is an earlier, more sensitive, and reliable indicator of measure of hypoventilation than pulse oximetry (Burton et al., 2008; Cacho et al., 2010; Carlisle, 2015; Hutchison & Rodriguez, 2008; Lee et al., 2015; McCarter, Shaik, Scarfo, & Thompson, 2008; Overdyk et al., 2007; Tran, Ciarkowski, Wagner, & Stevenson, 2012), therefore, may allow for earlier intervention.

However, most studies of capnography have been conducted during procedural or goal-directed sedation (Beitz et al., 2012; Burton et al., 2008; Deitch et al., 2010; Friedrich-Rust et al., 2014; Klare et al., 2016; Qadeer et al., 2009; Saunders et al., 2016; Sivilotti, Messenter, Vlymen, Dungey, & Murray, 2010; Slagelse, Vilmann, Hornslet, Jorgensen, & Horsted, 2013; van Loon, van Rheineck Leyssius, van Zaane, Denteneer, & Kalkman, 2014; Weaver, 2011) during surgery (Soto, Fu, Vila, & Miguel, 2004) or among intubated patients requiring mechanical ventilation (Walsh, Crotwell, & Restrepo, 2011). Unfortunately, few studies have examined its use in routine clinical care among hospitalized patients receiving opioid-based analgesia.

In an observational study of 178 post-operative patients with continuous capnography and oximetry monitoring, Overdyk et al. (2007) reported frequent episodes of desaturation, 12% and 41% of patients experienced episodes of desaturation (SpO2 <90%) and bradypnea (respiratory frequency <10) with more than a three-minute duration. Additionally, patients

greater than 65 years of age and those with morbid obesity were more likely to experience episodes of oxygen desaturation.

In a recent retrospective study of patients receiving patient-controlled analgesia (PCA), researchers sought to determine the impact of continuous ETCO2 monitoring on the incidence of opioid-induced respiratory depression, as evidenced by rapid response activation (Stites, Surprise, McNeil, Northrop, & De Ruyter, 2021). Results revealed decreased rapid response activation for opioid-induced respiratory depression events (0.02%; *n*=200 events, *n*=93, 412 total patients) after implementation of capnography monitoring as compared to before capnography monitoring (0.04%, *n*=153 events, *n*=34,852 total patients) which was statistically significant ($\chi 2 = 46.246$; df, 1; $p < 0.0001$). The unplanned transfer to a higher level of care related to opioid-induced respiratory depression also was reduced by 79% (pre-implementation *n*=7.6 transfers per month; post-intervention *n*=1.6 transfers per month). When considering the expense of the capnography module and disposable cannula, capnography monitoring resulted in an estimated cost of $9.50 per patient per day. However, because the estimated cost of an opioid-induced respiratory event is reported to be $6,271 per event, capnography monitoring was deemed to be cost-efficient. Study results demonstrate that continuous capnography significantly decreases the incidence of opioid-induced respiratory depression and unplanned transfer to a higher level of care among patients receiving patient-controlled analgesia.

Respiratory rate. Respiratory rate is an important physiological parameter that reflects patient status. Abnormalities in respiratory rate often are an early indicator of acute respiratory compromise (Bergese et al., 2017). Importantly, changes in respiratory rate occur prior to decreases in oxygen saturation, suggesting that respiratory rate may provide an early pragmatic warning of patient decompensation (Barker, Tremper, & Gamel, 1986). Alarmingly, the respiratory rate is often inaccurately measured and inconsistently documented (De Meester,

Bogaert, Clarke, & Bossaert, 2012; Fuhrmann, Lippert, Perner, Ostergaard, 2008; Leuvan & Mitchell, 2008). A mixed-methods retrospective study of 63 patient medical records revealed that respiratory rate documentation was missing within the eight hours of patients who experienced a serious adverse event (De Meester et al., 2012). Failure to recognize changes in the condition of a medical or trauma patient on the general care ward facilitates serious adverse events and negative patient outcomes such as unplanned transfer to the ICU, cardiopulmonary arrest, and increased morbidity and mortality (Churpek et al., 2012; Churpek, Adhikari, & Edelson, 2016; Escobar et al., 2011; Escobar et al., 2008).

Results of an observational study of hospitalized patients on general care medical and surgical wards revealed that one of five patients developed abnormal vital signs. Furthermore, greater than 50% of changes in vital signs were missed by the nursing staff. Patients who developed abnormal vital signs had a three-fold higher 30-day mortality rate (Fuhrmann et al., 2008).

In a retrospective, nested case-control study, researchers sought to determine the best vital sign predictor of cardiac arrest (Churpek et al., 2012). All adult inpatients on the general care ward (n=88) who suffered cardiac arrest within the designated study period were eligible for inclusion. Control subjects (n=352) were all adult inpatients on the general care ward who did not suffer cardiac arrest at the time of the case patient cardiac arrest. Four control subjects were randomly selected and matched to each case patient (4:1). Changes in baseline vital signs were compared between case and control patients. Respiratory rate (AUC 0.72; 95% CI, 0.68-0.78; p=0.002) was reported as one of the most accurate predictors of cardiac arrest.

In a more recent study, researchers compared the accuracy of different methods of modeling trends in vital signs for early recognition of patient deterioration on the GCF (Churpek et al., 2016). Patient admissions (n=269,999) over 5 years were evaluated for the occurrence of

cardiac arrest (*n*=424), transfer to the ICU (*n*=13,188), and death on the general care ward (*n*=2,840). Researchers reported that monitoring of trends in respiratory rate and variability was more accurate in recognition of patient deterioration as compared to monitoring of a discrete respiratory rate. Their results were similar to those of an earlier study that revealed variability in respiratory rate and minimum SpO_2 were independent predictors of patient deterioration (Escobar, LaGuardia, Turk, Ragins, Kipnis, & Draper, 2012).

Respiratory rate is a significant predictor of serious adverse events, patient deterioration, and correlated with in-hospital mortality (Churpek et al., 2012; Churpek et al., 2016; Cretikos, Bellomo, Hillman, Chen, Finfer, & Flabouris, 2008; Escobar et al., 2012; Flenady, Dwyer, & Applegarth, 2017; Goldhill, McNarrry, Mandersloot, & McGinley, 2005). More seriously, a respiratory rate of fewer than six breaths per minute was found to be associated with increased mortality for patients on the general care ward (Buist, Bernard, Nguyen, Moore, & Anderson, 2004). Alarmingly, respiratory rate often is omitted in vital sign assessment, inaccurately measured, and inconsistently documented (Addison, Watson, Mestek, Ochs, Uribe, & Bergese, 2015; Buist et al., 2004; Cretikos et al., 2008; De Meester et al., 2012; Kellett, Li, Rasso, Green, & Seely, 2011; Kyriacos, Jelsma, & Jordan, 2014; McGain et al., 2008; Mok, Wang, & Liaw, 2015; Mukkamala, Gennings, & Wenzel, 2008; Semler et al., 2013). This practice of incomplete and infrequent respiratory rate monitoring for post-operative and trauma patients on the general care ward results in a delay in detection of opioid-related adverse events and patient deterioration.

The detection of patient deterioration remains suboptimal, leading to the development of avoidable serious opioid adverse events (Sun et al., 2020). Early recognition of patient deterioration demands that respiratory rate monitoring and surveillance be performed routinely, accurately measured, interpreted using clinical judgment, and consistently documented to

facilitate effective communication among members of the healthcare team (Cardona-Morrell et al., 2016; De Meester et al., 2012; Fuhrmann et al., 2008; Leuvan & Mitchell, 2008; Ludikhuize, Smorenburg, De Rooij, & De Jonge, 2012; Woolfe Loftus & Smith, 2019). Intermittent monitoring of respiratory rate delays early recognition of patient deterioration as the patient may suffer opioid-induced respiratory depression between monitoring intervals. Therefore, intermittent evaluation of the respiratory rate is inadequate, increases the risk for unrecognized opioid-induced respiratory depression, and delays the implementation of appropriate interventions.

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CHAPTER 3: Theoretical Frameworks

A critical role of the general acute care nurse in caring for the patient experiencing medical or trauma-related pain is appropriate monitoring and surveillance to provide effective pain management, prevent adverse events, and maintain patient safety (IOM, 2004a). Pragmatic research is driven by the desired consequences or outcomes. The theoretical frameworks that provide direction for this research were selected because of their emphasis on clinical practice to achieve desired patient outcomes and maintain patient safety.

A theoretical framework provides the structure to guide research, determine variables, influence data analysis, and is integral to the search for knowledge development (Meleis, 2018). Cyclical integration of theory, research, and practice ensure that the basis for evidence in clinical practice is centered on principles, research processes, and outcomes (Meleis, 2018). Outcome variables in the development, implementation, and evaluation of strategies for appropriate monitoring are enhanced when placed into a framework that portrays their relationships. The theoretical frameworks that provide the theoretical and empirical foundation for this research are, "Pain: A Balance Between Analgesia and Side Effects" (Good, 2017), and "The Near-Miss Model of Nurse's Role in Recovery of Medical Errors" (Henneman, 2017).

Pain: A Balance Between Analgesia and Side Effects

Middle-range theories offer detailed descriptions of situations, provide explanations of outcomes, enhance the wisdom of experiences, and provide direction for action (Meleis, 2018; Peterson & Bredow, 2017). Theory development results from an expectation that theory will clarify or redesign the reality of a situation to achieve an improved consequence or outcome (Dickoff & James, 1968; Dickoff, James, & Widenbach, 1968a; 1968b). Such practice-oriented, useful theories can assist researchers by providing an understanding of the human response to illness, recommending interventions, and explaining practical consequences or outcomes

(Meleis, 2018; Peterson & Bredow, 2017). Middle-range prescriptive theories direct the situations in which the nurse must act to facilitate desired outcomes (Dickoff & James, 1968; Dickoff et al., 1968a; Huth & Moore, 1998; Meleis, 2018).

The middle-range prescriptive theory, "Pain: A balance between analgesia and side effects," provides an ideal theoretical framework consistent with the philosophical underpinnings and nature of this research (see Figure 3.1). More specifically, this theory was developed to achieve a balance between effective pain management and opioid-induced adverse effects in adults experiencing moderate to severe acute post-operative pain (Good, 2017). Furthermore, the deliberate nursing process in monitoring pain and sedation levels is an integral concept of this middle-range theory.

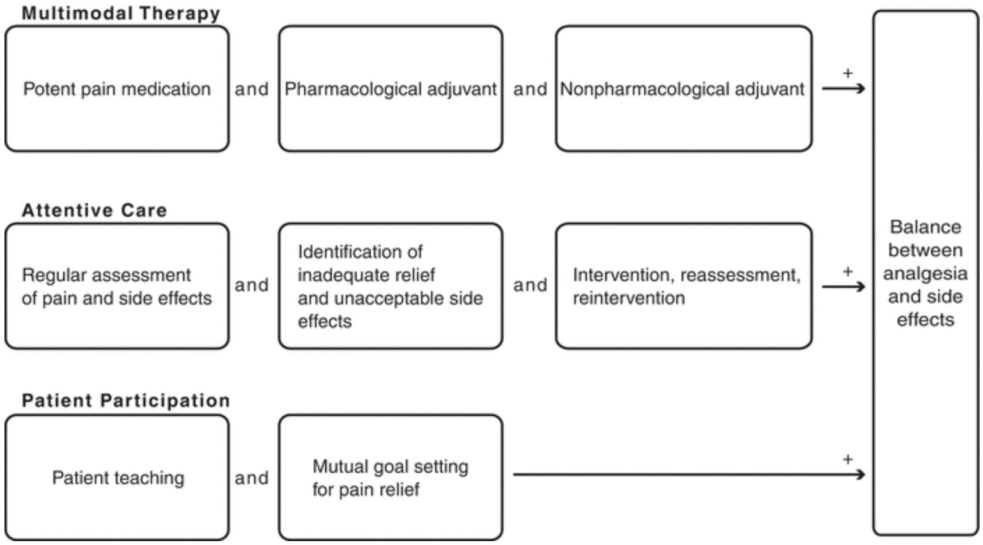

Figure 3.1. Pain: A balance between analgesia and side effects (Good, 2020).

The deliberate nursing process proposes a practical approach in providing attentive nursing care to meet individual patient needs. This process focuses on the nurse's response to patient needs through assessment and validation of observations, perceptions, and interpretation

of physiological and psychosocial events with the patient (Orlando, 1961). Principles of this integrative predictive theory are 'useful' and 'practical' to guide practice, evaluate patient outcomes, and provide theoretical propositions for research (Good, 2017; Good & Moore, 1998).

Middle Range Theory of Pain: A Balance Between Analgesia and Side Effects

Within this theory, acute medical or trauma-related pain is described as a subjective, physiological (sensory) and affective (emotional) phenomenon (Casey & Melzack, 1967; Good, 2017; Good et al., 2001; McCaffery, 1968; Price, McGrath, Rafii, & Buckingham, 1983). Multimodal therapy, attentive care, and patient participation are the three propositions that guide the theory. Concepts are incorporated within each proposition. The outcome of this integrative approach is safe, effective pain management through a balance between analgesia and adverse effects.

Description of the Theory

Marion Good, Ph.D., RN and Shirley Moore, Ph.D., RN developed the "Pain: A Balance Between Analgesia and Side Effects" middle-range theory in 1996 using the Agency for Health Care and Policy for Research (AHCPR) Clinical Practice Guidelines for Pain Management (Acute Pain Management Panel [APMP], 1992). This prescriptive theory intended to provide direction for nurses caring for patients receiving opioids for acute pain. The paradigm of acute pain provided the basis for theory development. Within this paradigm, pain is conceptualized as a subjective experience with a multidimensional nature of physiological, emotional, behavioral, and social, and cultural dimensions (Bond & Simpson, 2006; Bowers & Barrett, 2009; Persson et al., 2008; Vaajoki, Pietila, Kankkunen, & Vehvilainen-Julkunen, 2011). This paradigm is consistent with the intent of the theory for safe, effective pain management, which involves titration of opioid dose determined by pain and sedation assessment and reassessment following administration of opioids (ASPMN & APS, 2004).

The middle range theory, "Pain: A balance between analgesia and side effects," consists of three propositions united in a chain-link, systematic fashion. Summary of propositions is that within acute medical or trauma-related pain, multimodal analgesia, attentive care, and patient and family participation are needed for balanced analgesia to prevent opioid-induced adverse events (Good, 2017). Thus, the theory is constructed as a system of relationships that emphasize attentive care and the role of the nurse in the prevention of opioid-induced respiratory depression through attentive care and the early recognition of unintended, advancing opioid-induced sedation.

The relationship between concepts and the domains of nursing is evident and integral to the theory. The first step in theory development and synthesis was the review of the Agency for Healthcare Policy and Research's (AHCPR) guidelines to identify the content and scope of prescriptive relationships. Second, the theorists used the guidelines to identify metaparadigm concepts that represent prescriptive interventions (nursing care-domains of nursing care and interaction), the problem (pain-domain persons), and the desired outcome (safe, effective pain relief-domain health), within the context of the hospital environment and acute pain experience (domain-environments). The domains of nursing also are evident in each proposition.

"Pain: A balance between analgesia and side effects" is the first integrative, predictive theory of acute pain management (Good, 2017; Peterson & Bredow, 2017). The theory's principles are consistent with current pain management research and can be used to guide research, practice, and education (Good, 2017). Principles of pain physiology, opioid and adjuvant pharmacokinetics, deliberate nursing practice, and patient/family participation are integrated within the theory (Aponte, 2009; Good, 1998; 2017; Good & Moore, 1998; Orlando, 1961; Potter, 2013).

This relevant theory contends that safe, effective pain management requires a balance between opioid and opioid-sparing analgesics in collaboration with nonpharmacological interventions. Furthermore, the nurse has a critical role in the achievement of safe, effective pain management through serial assessments of pain and sedation levels and implementation of appropriate care based on patient monitoring. The three propositions that guide the theory are: 1) multimodal analgesia; 2) attentive care; and 3) patient and family participation (Good, 1998).

Theory Propositions and Concepts

Multimodal analgesia (MMA) (proposition). Multimodal analgesia combines two or more classes of analgesics with varying pharmacodynamics to affect different pain mechanisms (Jaryzna et al., 2020; Pasero, 2003; Pasero, Quinn, Portenoy, McCaffery, & Rizos, 2011; Polomano, Dunwoody, Krenzischek, & Rathmell, 2008; Polomano, Rathmell, Krenzischek, & Dunwoody, 2008; White & Kehlet, 2010). This approach results in reduced opioid consumption and has proven efficacious in acute medical or trauma-related pain management (Jaryzna et al., 2011; Lentschener, Tostivint, White, Gentili, & Ozier, 2007; Smith, 2011). Less opioid consumption results in decreased risk for unintended, opioid-induced sedation that may progress to ventilator impairment and respiratory depression (Gilron, Orr, Tu, Mercer, & Bond, 2009; Kehlet & Dahl, 1993; Marret, Kurdi, Zufferey, & Bonnet, 2005; Mathiesen et al., 2013; Sharma et al., 2013; White & Kehlet, 2010; White, Sacan, Tufanogullari, Eng, Nuangchamnong, & Ogunnaike, 2007). The American Society of Pain Management Nurses' (ASPMN) "Guidelines on Patient Monitoring for Opioid-induced Sedation and Respiratory Depression" purports that nurses should be strong advocates for multimodal pain management regimes (Jaryzna et al., 2011; Jungquist et al., 2017). Using a multimodal approach, the nurse (domain-nursing care) provides pharmacologic and nonpharmacological adjuvants (opioid-sparing) in combination with opioids (potent pain medication).

Potent pain medication (concept within MMA). Potent pain medication signifies the current main approach for pain relief. Despite the efficacy of multimodal analgesia and opioid-sparing strategies, opioids remain the mainstay for acute moderate to severe post-operative pain (Jaryzna et al., 2020). However, an opioid-only approach to analgesia is insufficient to provide comfort and allow function without the occurrence of opioid-induced adverse effects (Kehlet & Dahl, 1993; Smith, 2011).

Pharmacological adjuvant (concept within MMA). Pharmacological adjuvants are classes of medications other than opioids that target different mechanisms of pain (McCaffery & Pasero, 2011). These medications include nonsteroidal anti-inflammatory analgesics (NSAIDs), acetaminophen, anticonvulsants, antidepressants, local anesthetics, and peripheral nerve blockade (Bykov, Bateman, Franklin et al., 2020; Bansal, Saxena, Taneja, & Sareen, 2012; Good, 2017; Jarzyna et al., 2011; Jungquist et al., 2020 Kehlet & Dahl, 1993; Naja, Ziade, El-Rajab, Naccash, & Ayoubi, 2013; Savelloni, Gunter, Lee et al., 2017; Sharma et al., 2013; Smith, 2011).

Nonpharmacological adjuvant *(concept within MMA).* Nonpharmacological adjuvants have demonstrated usefulness for acute medical or trauma-related pain by enhancing and supplementing pharmacological interventions to decrease pain intensity and anxiety (Good, 2017). Such adjuvants may include music, relaxation, and guided imagery (Good, 2017; Good et al., 1999; Pestka, Bee, & Evans, 2010; Roykulcharoen & Good, 2004; Siedlecki & Good, 2006; Vaajoki et al., 2011).

Attentive care *(AC) (proposition).* Attentive care (domains-nursing care, interaction, persons, environment). This proposition has specific application to this research and explains the role of the nurse through a deliberate nursing process based on sedation assessment and patient response after opioid administration (Orlando, 1961; Potter, 2013). It proposes that the nurse

"assess pain and sedation levels, intervene, reassess, and re-intervene to achieve a balance between analgesia and opioid-induced adverse effects" (Good, 2017). Intervention, reassessment after implementation of pain management interventions, and re-intervention by adjusting the opioid or analgesic dose or adding an opioid-sparing, non-sedating analgesic are needed and should continue until effective pain management (comfort) is achieved.

Regular assessment of pain and side effects *(concept within AC).* Nurses have a critical role in the prevention of opioid-induced respiratory compromise and respiratory depression through the regular assessment of pain and sedation levels (Dempsey, 2012; Dempsey, Davidson, Cahill, & Agan, 2009; Dempsey & Wickman, 2018; Good, 2020 Jaryzna et al, 2020; Nisbet & Mooney-Cotter, 2009; Pasero, 2009; TJC, 2012). Regular assessment requires serial observations, using valid and reliable sedation scales, and technologies to facilitate early recognition of opioid-induced sedation, opioid-induced respiratory compromise, and respiratory depression (Jaryzna et al., 2011; Jungquist et al., 2017; Taylor, Kirton, Staff, & Kozol, 2005).

Identification of inadequate relief *and unacceptable side effects (a concept with AC).*
Identification of inadequate pain relief and unacceptable side effects is the desired outcome of serial assessments of pain and sedation using valid and reliable sedation scales and technologies (Jaryzna et al., 2011; Jungquist et al., 2017). This concept offers compelling evidence of the pragmatic 'truth' of this theory as evidenced by its usefulness in practice in the identification of negative physiological consequences of opioid analgesia (James, 1907; Magee, 2001).

Intervention, reassessment, re-intervention *(a concept with AC).* Regular assessment of pain and sedation using valid and reliable tools refers to the nursing actions to recognize sedation, respiratory compromise, and respiratory depression. This prescriptive theory requires that the nurse prevent and treat opioid-induced adverse effects rather than merely documenting symptoms in the medical record. The use of the Pasero Opioid-Induced Sedation Scale (POSS)

for sedation assessment is consistent with the use of this theory. Specifically, this scale was developed for use only for sedation assessment during the opioid administration process to recognize unintended, advancing sedation (Pasero & McCaffery, 2002). It is easy to understand, incorporates actions based on sedation level, and leads the nurse to make appropriate clinical-decisions (Dempsey, 2012; Dempsey et al., 2009; Dempsey & Wickman, 2018; Nisbet & Mooney-Cotter, 2009; Pasero, 2009; Pasero, Manworren, & McCaffery, 2007; Pasero & McCaffery, 2002).

Patient participation *(PP) (proposition).* Patient and family participation (domains-persons, interaction, health, environment, nursing care) assists patients in their role as active participants in their pain management. Individualized teaching and comfort-function goal setting are integral to the balance between effective pain management and opioid-induced adverse effects.

Patient teaching *(concept within PP).* Teaching should involve the family and include accurate expectations, alternative approaches, pain management regime, the importance of communicating pain to the nurse so that pain management interventions may be implemented, and the importance and frequency of reassessment. Furthermore, patient and family participation in the development of an individualized pain management plan that incorporates the use of nonpharmacological adjuvants (Good, 2017).

Mutual goal setting for goal-directed pain relief *(concept within PP).* The mutual setting of the comfort-goal is important to establish realistic goals for pain relief that are acceptable to the patient (Good, 2020 Pasero, 2004; Pasero & McCaffery, 2002). Establishing comfort-function goals requires that the nurse and patient discuss the relationship between pain relief that will allow the performance of activities of recovery and function (Pasero & McCaffery, 2003; Pasero & McCaffery, 2011). When caring for medical or trauma patients, the

nurse can explain that the appropriate comfort-function goal would allow the use of the incentive spirometer or ambulation (Pasero, 2004). Goal-directed pain relief involves the implementation of individualized interventions, based on patient and treatment-related risk factors, to achieve the comfort-function goal without the occurrence of opioid-induced sedation (e. g., POSS level 3 or 4) or respiratory compromise (Pasero, 2004; Pasero & McCaffery, 2011).

Application of the Theory to Research

Application of theory to research considerations is interwoven in the theoretical framework section and provides an in-depth discussion of the relevance of pain and sedation management to nursing practice particularly for acute moderate to severe medical or trauma-related pain. In summary, this theory is practical, useful, and applicable for this prospective, observational study. Usefulness is specific to the hospitalized adult population who are receiving opioids for acute medical or trauma-related pain management. It also is applicable for early recognition and prevention of opioid-induced adverse effects through the role of the nurse and the deliberate nursing process.

The proposition of attentive care underscores the importance of the nurse in attentive care with monitoring and surveillance of patients receiving opioids for acute post-operative or trauma-related pain. Unintended, advancing opioid-induced sedation occurs on a continuum and typically precedes opioid-induced respiratory depression (Abou Hammoud et al., 2009; Jarzyna et al., 2011; McIntyre et al., 2011; Moline et al., 2012; Pasero, 2009; Taylor et al., 2005; Taylor, Voytovick, & Kozol, 2003). Opioid-induced adverse events are associated with poor patient outcomes and increased mortality (Barletta, 2012; Considine, 2005; Dahan et al., 2010; Davies et al., 2009; Gan, Odera, & Robinson, 2012; Jarzyna et al., 2011; Jungquist et al., 2020 Oderda et al., 2007; TJC, 2012). Nurses play a critical role in the prevention of unintended opioid-induced sedation and respiratory depression through the provision of practical, useful, and attentive care.

(Nisbet & Mooney-Cotter, 2009; Pasero, 2009; TJC, 2012). As pain management becomes increasingly more complex, attentive nursing care is essential to balance analgesia with effective strategies. These strategies are needed to prevent opioid-induced adverse events ensuring early recognition and timely treatments when they do occur (Jaryzna et al., 2011; Jungquist et al., 2020).

The Near-Miss Model of the Nurse's Role in Error Recovery and Prevention of Adverse Events

The "Near-Miss Model of the Nurse's Role in Error Recovery and Prevention of Adverse Events" provides an additional ideal framework that is consistent with the philosophical underpinnings of this research (see Figure 3.2). More specifically, this model was developed to describe how imperfect systems and human factors can precipitate a sequence of events that can lead to patient harm and adverse patient outcomes without adequate defenses and nursing recovery (Henneman, 2017). Furthermore, patient monitoring and surveillance are integral concepts within this model.

The process of surveillance is a practical approach to providing attentive and safe patient-centered care. Surveillance is a purposeful, ongoing intervention in which nurses use cognitive and behavioral processes to monitor, interpret, and intervene on recognized indications of a change in patient status (Dougherty, 1999; Dresser, 2012; Orique et al., 2019; Peet et al., 2019). Principles of this model also are "useful" and "practical" to guide practice, evaluate patient outcomes, and provide theoretical propositions for research (Henneman, 2017).

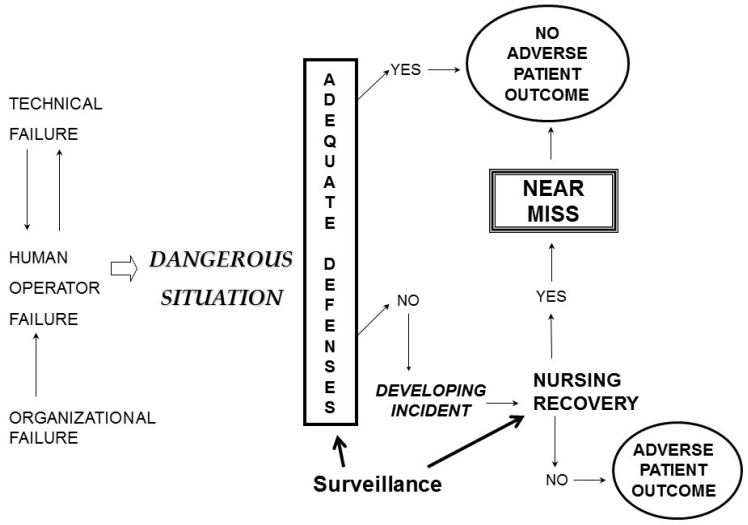

Figure 3.2. Near-miss model of nurse's role in error recovery and prevention of adverse events.

Description of the Model

Elizabeth Henneman, Ph.D., RN, and Anna Gawlinski, Ph.D., RN, described the "Near-Miss Model" in 2004 using the Eindhoven model of the near-miss process which was originally developed for the chemical industry (Henneman, 2017; Henneman & Gawlinski, 2004; van der Schaaf, 1992). This model intends to provide guidance for nurses caring for patients and demonstrate the importance of surveillance and nursing recovery in the prevention of patient harm.

The paradigm of patient safety provided the basis for model development. Within this paradigm, patient safety is conceptualized as a multidimensional construct that is dependent on system effectiveness, human factors, and adequate defenses to ensure safe, patient-centered, effective, timely, and responsive care that is designed to avoid patient harm (Albrecht, 2015; IOM, 2001). This paradigm is consistent with nursing practice for patients receiving opioids, which demands vigilance in monitoring and surveillance for the early recognition of opioid-related adverse events to prevent the progression to opioid-induced respiratory depression, anoxic brain injury, or death.

The overall principles, or propositions, of the model, are applicable for use in clinical practice. The model provides insight into the role of the nurse and nursing practice in identifying, interrupting and correcting dangerous situations to prevent harm and maintain patient safety. The model has four propositions that can be summarized as follows: (1) system failures and flawed human factors can lead to, (2) dangerous situations without, (3) adequate defenses (surveillance) that influence, (4) patient outcomes. Therefore, the model is constructed as a system of relationships that emphasize the role of nursing surveillance in the prevention of opioid-induced respiratory depression through early recognition and implementation of timely, appropriate interventions.

The first step in model development was a review of the Eindhoven Model to identify the content and scope of the relationships and applicability to nursing practice (Henneman & Gawlinski, 2004). Second, the researchers conducted qualitative studies with emergency departmentemergency departments (ED) and critical care nurses to gain insight into the strategies that nurses use in error recovery (Henneman, Blank, Gawlinski, & Henneman, 2006; Henneman, Gawlinski, Blank, Henneman, Jordan, & McKenzie, 2010). Based on the study results, the model was revised to explain the process of nursing strategies in the identification, interruption, and correction of errors to prevent the error from reaching the patient and causing harm. The relationships of propositions and the domains of nursing are evident and integral to the model and represent prescriptive interventions within the nursing metaparadigm (nursing surveillance and recovery–domains of nursing care and interaction), the problem (failures that lead to dangerous situations and developing incidents–domain person and health), and the desired outcome (no adverse patient outcome) within the context of the hospital environment (domain–environment) (Fawcett, 1995; Meleis, 2018).

This relevant model contends that patient safety requires effective surveillance to prevent errors from reaching the patient. Furthermore, the nurse has a critical role in the maintenance of patient safety through appropriate monitoring and surveillance for the early identification, interruption, and correction of opioid-induced sedation and respiratory compromise. The four prepositions that guide the model are (1) system failures, (2) dangerous situations, (3) adequate defenses, and (4) patient outcomes.

Model Propositions and Concepts

Sources of failures (proposition). Human, organizational, and technical failures alone, or together, can trigger high-risk, dangerous situations that can progress to clinically significant life-threatening adverse events and facilitate negative patient outcomes without early recognition and appropriate intervention (Henneman, 2017; van der Schaaf, 1992).

Human failure *(concept within sources of failure).* Nurse characteristics (education, experience, expertise) and organizational failures influence human failure. Human failure is categorized based on cognitive psychology and behavior that is needed to perform the task (Rasmussen, 1990). These three failure categories are skills, rules, and knowledge.

Categories of human failure. Skill-based behaviors are used during routine tasks and do not demand intensive conscious attention or critical thinking but are based more on clinical reasoning (Tanner, 2016). Rule-based behaviors involve the recognition of a familiar problem that requires clinical decision-making. This decision-making is guided by rules learned through training and experience to resolve a predictable situation. Therefore, skill-based and rule-based behaviors are dependent more on clinical reasoning than clinical judgment (Tanner, 2016).

Knowledge-based behaviors occur when the nurse is confronted with a new situation and requires a higher level of cognitive psychology using complex clinical judgment (Tanner, 2016). Clinical judgment requires the ability to recognize subtle changes in patient status, interpret the

meaning of the changes, and intervene timely and appropriately (Chua et al., 2019; Tanner, 2016; van Graan, Williams, & Koen, 2016). Furthermore, clinical judgment requires an understanding of the physiological and pathophysiological aspects of the clinical condition within the illness experience of the patient and family or "knowing" all aspects of the patient (Chua et al., 2019). This hierarchical approach to human failures involves the application of behavioral and cognitive processes and has implications for appropriate monitoring, effective surveillance, and nursing recovery (Aiken et al., 2003; McCloskey Dochterman et al., 2004; IOM, 2004a; Kelly & Vincent, 2011; Kutney-Lee, Lake, & Aiken, 2009; Mattox, 2012; Meyer & Lavin, 2005). Specifically, early recognition and appropriate intervention for the occurrence of opioid-related adverse events relies on higher levels of complex clinical reasoning and clinical judgment to prevent clinically significant opioid-induced respiratory depression (Kutney-Lee et al., 2009; Tanner, 2006; Tanner, Benner, Chesla, & Gordon, 1993).

Organizational failure ***(concept within sources of failure).*** Organizational failures are complex factors within the clinical practice setting that can severely affect how care is delivered within the clinical practice environment. Organization failures that influence human failures include orientation practices for new staff, RN staffing levels, protocols, procedures, clinical pathways, technology, resources, management priorities, and organizational culture. Researchers have reported that the clinical practice environment (underuse of technology, inadequate resources, staffing levels) coupled with nurse characteristics (education, experience, expertise) impacts nursing practice and recovery (Dresser, 2012; Henneman, 2017; Kutney-Lee et al., 2009; Tucker, 2004).

Technical failure ***(concept within organization failure).*** Technical failures occur when technological resources such as software, equipment, monitoring devices, or other patient care

equipment are incorrectly designed, not used according to their indications, and underused or unavailable when needed.

Consequences of the human, organization or technical failures. Human, technical, or organizational failures place the patient in a high-risk and dangerous situation that can progress to serious opioid-related adverse events without adequate defenses to prevent or mitigate the situation. It is clear that human failure is influenced by nurse characteristics (e.g., education, knowledge, experience, and expertise) and the culture within the context of the clinical practice setting, such as staffing adequacy, culture of safety, policies and procedures, monitoring practices, available technology, and professional practice environment (Clarke, 2004; Clarke & Aiken, 2003; Dresser, 2012; Kutney-Lee et al., 2009; Manojlovich & Talsma, 2007; Needleman, Buerhaus, Mattke, Steward, & Zelevinsky, 2002).

Adequate defenses (proposition). Adequate defenses may be internal (physiologic) or external (human or organization) and serve to protect the patient from adverse events (Henneman, 2017). Inadequate human defenses are a threat to patient safety, increase the risk for worsening of the dangerous situation, and facilitation of negative patient outcomes. When defenses are inadequate to reverse or mitigate the dangerous situation, it continues to evolve as a "developing incident." The nurse's ability and capacity to perform appropriate monitoring and surveillance are adequate defenses that facilitate early recognition of a presenting risk (dangerous situation) or evolving incident (Kutney-Lee et al., 2009).

Surveillance ***(concept within adequate defenses).*** Surveillance is recommended as a critical intervention in the early recognition and prevention of adverse events and patient harm (Clarke & Aiken, 2003; Dresser, 2012; Henneman, 2017; Kutney-Lee et al., 2009; Pfrimmer, Johnson, Guthmiller, Lehman, & Rhudy, 2017; Orique, S. G., Despins, L., Wakefield, B. J., Erdelez, S., & Vogelsmeier, A., 2019). Surveillance is the act of purposeful, systematic

monitoring, interpretation, and synthesis of patient data to facilitate appropriate clinical decision-making (Dresser, 2012; Henneman, 2017; Pfrimmer et al., 2017). Ongoing surveillance serves as a defense that can prevent errors from reaching the patient. Surveillance demands that the nurse attends to the patient at the *correct* time and the *correct* sequence to prevent the development or worsening of adverse events. Effective surveillance results in early recognition of subtle changes in the patient's condition. Monitoring is a key component of surveillance in that it provides the patient data for interpretation and synthesis.

Facilitators of surveillance. Examples of structures and processes that support surveillance are checklists, clinical information systems, clinical-decision support systems and alerts, and an organizational culture that supports an interruption-free care delivery system.

Barriers to surveillance. Human and system factors serve as barriers to surveillance. Human factors are a lack of skill-based, rule-based, and knowledge-based behaviors. System factors such as lack of resources, lack of patient and family involvement, and underuse or unavailable technology disrupt care and threaten patient safety.

Nursing recovery *(concept within adequate defenses).* Nursing recovery is a complex process by which the developing incident is recognized, and timely interventions are implemented which limit the incident to a "near-miss" and prevent the progression to an adverse outcome. Recovery consists of three consecutive processes (1) identification, (2) interruption, and (3) correction (Henneman, 2017; Henneman et al., 2006; Henneman et al., 2004; van der Schaaf, 1992).

Nursing recovery requires the knowledge to recognize the error as well as the knowledge, skill, and experience to intervene appropriately and prevent the event from reaching the patient and causing harm (Shoulders, B., Follett, C., & Eason, J., 2014; van der Schaaf, 1992). Conversely, an adverse outcome occurs if the nurse fails to recognize or intervene effectively,

and the error reaches the patient (Henneman et al., 2006; van der Schaaf, 1992). Therefore, the nurse plays a critical role in the prevention of adverse patient outcomes through early recognition and timely, appropriate response and interventions (Henneman et al., 2005).

Dangerous situation (proposition). A dangerous situation is a temporary state of increased or high risk in which the initial human, technical, or organizational failure, however, is without actual consequences (van der Schaaf, 1992). Reversal of a dangerous situation and prevention of serious adverse events is possible with early recognition and implementation of appropriate interventions for recovery.

Developing incident *(concept within dangerous situation).* The developing incident is an evolving adverse event which could result in patient harm is uninterrupted. For example, if monitoring of a patient receiving opioids for medical or trauma-related pain indicates opioid-induced sedation, the patient is at high risk for progression to clinically significant opioid-induced respiratory depression unless the opioid dose is decreased. Therefore, recognition of sedation provides the opportunity to interrupt the pain management regime and correct the opioid-related adverse events to prevent the progression to opioid-induced respiratory depression, anoxic brain injury, or death.

Patient outcome (preposition). Patient outcome is defined as the status of the patient as an intended or unintended result of the interaction between the patient and care provided (Liu, Coalson Avant, Aungsuroch, Zhang, & Jiang, 2014). For this research, the outcome is determined by the presence of an opioid-related adverse event (opioid-induced sedation, respiratory compromise, respiratory depression, respiratory arrest, cardiopulmonary arrest, brain injury, or death) or the absence of an opioid-related adverse event.

Adverse patient outcome (concept within patient outcomes). An adverse outcome is unintended harm suffered by the patient as a result of the care provided as opposed to an outcome caused by the underlying disease or condition (Henneman, 2017; IOM, 2001).

No adverse patient outcome (concept within patient outcomes). No adverse patient outcome infers the provision of "safe" patient care in that the patient did not suffer harm from the care that was intended to help. However, "no adverse patient outcome" does not indicate that an error did not occur. An error of omission or commission could have occurred and been identified, interrupted, and corrected before reaching the patient (nursing recovery). Therefore, because the error to reach does not reach the patient and result in patient harm, "no adverse outcome" occurs.

Near-Miss *(concept within patient outcome).* A "near-miss" is any event or error that had the potential to cause an adverse outcome but does not result in patient harm as a result of early identification, interruption, and reversal or correction.

Application of the Model to Research

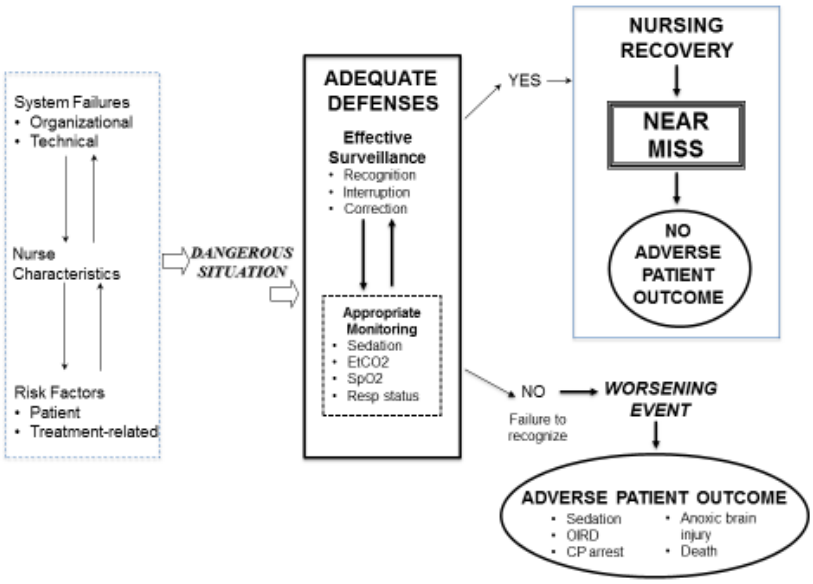

Figure 3.3. Application of near-miss model of nurse's role in error recovery.

This model is useful, practical, and applicable for this prospective, observational study. Patient monitoring and surveillance are critical assessment and intervention practices to ensure patient safety and optimal outcomes in patients receiving opioids for acute medical or trauma-related pain (Kelly & Vincent, 2011). Appropriate monitoring facilitates early recognition of subtle changes in sedation level and respiratory status. However, monitoring alone is insufficient for the prevention of opioid-related adverse events without surveillance. Surveillance is an ongoing process in which the nurse monitors, analyzes monitoring data, and makes clinical decisions based on recognition of changes in patient status (Bulechek, Butcher, Dochterman, & Wagner, 2013; Dougherty, 1999; Dresser, 2012; Henneman et al.,, 2010; Henneman et al., 2012; Kutney-Lee et al., 2009; McCloskey Dochterman & Bulechek, 2004; Pfrimmer et al., 2017).

Safe pain management requires appropriate monitoring and surveillance that is intended to facilitate early recognition of the prompt interventions to interrupt and correct opioid-related adverse events before progression to life-threatening opioid-induced respiratory depression. Appropriate monitoring demands both system effectiveness and nursing practice that is designed to avoid harm to post-operative and trauma patients from the opioid analgesic that is intended to help them.

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CHAPTER 4: Research Design and Procedures

Research Design

This research was a prospective, blinded observational study to describe the incidence of opioid-induced respiratory depression among trauma patients on the general care floor receiving PCA or nurse administered intravenous opioids monitored by continuous bedside surveillance and monitoring. Furthermore, the incidence of opioid-induced respiratory depression as evidenced by continuous bedside capnography and pulse oximetry was compared with the incidence of respiratory depression detected by PI nursing monitoring and surveillance of respiratory status.

Primary endpoint. The primary endpoint of this study was the incidence of respiratory depression, as evidenced by capnography and pulse oximetry values. The incidence of unintended opioid-induced sedation was also a primary endpoint, as evidenced by sedation levels 3 or 4 using the Pasero Opioid-induced Sedation Scale (POSS).

Secondary endpoint. For the secondary endpoint, subjects who developed respiratory depression are compared with those subjects who do not develop opioid-induced respiratory depression in terms of:

- Risk of opioid-induced respiratory depression using the PRODIGY risk assessment tool
- The occurrence of unintended opioid-induced sedation using the POSS
- Actions implemented and outcomes

The findings from this study provide a description and understanding of the relationship and trajectory of sedation, respiratory compromise, and opioid-induced respiratory depression. The outcome of this research also identifies risk factors of medical or trauma patients who develop opioid-induced sedation or opioid-induced respiratory depression as compared to those

medical or trauma patients who do not develop opioid-induced respiratory depression. Furthermore, the influence of nursing assessment and surveillance on early recognition of opioid-related adverse events are elucidated. This understanding can enable the development of appropriate and personalized monitoring practices for patients receiving opioids for acute medical or trauma-related pain to prevent or mitigate opioid-induced respiratory depression, anoxic brain injury, or death.

Study Site

The study setting was the general care wards of a 685-bed Level I Trauma Center, located in the central valley area of California. The medical center has an average of more than 175,000 emergency department visits, 56,000 admissions, and over 7,200 trauma admissions annually.

Study Population

The target study population was hospitalized, adult trauma patients on the general care ward receiving PCA or nurse-administered IV opioids for acute pain. Adult patients of different ethnic backgrounds which offered a diverse study population. The inclusion criteria for all subjects was (1) spontaneously breathing adults 18-89 years of age; (2) receiving PCA or nurse administered IV opioids for medical or trauma-related pain and; (3) admitted to the general care floor from the emergency department.

The language services of the study site was used for prospective or enrolled subjects whose native language is other than English and who cannot speak, read, write, or understand the English language at a level that permits them to interact effectively with healthcare providers per the policy of the study site. The study site's contracted language services who provided foreign language interpretation services either in-person, via computer, video, or telephone.

Exclusion criteria were: (1) less than 18 or greater than 89 years of age; (2) transfer to the general care floor from the ICU; (3) receiving intrathecal or epidural opioids; (4) inability or

unwillingness to wear the ETCO2 sampling line nasal cannula or pulse oximetry sensor; (5) history or diagnosis of a sleep-disordered breathing syndrome; (6) use of CPAP or BIPAP non-invasive ventilation as a home regime; (7) presence of a co-morbidity that impacted respiration or ventilation (e.g., COPD or pulmonary fibrosis); (8) receiving non-invasive ventilation; (9) unwilling or unable to participate or; (10) a member of a vulnerable population such as pregnant women or prisoners. For this study, the population was considered to be two related groups as the same subjects are in both groups and were measured at two separate times (before and after opioid administration).

Sample

A three-month data collection period occurred between July1, 2019, to October 31, 2019. IRB approval was obtained before the data collection process began.

Sampling procedure. All patients who met the inclusion criteria were eligible for study participation during the three-month data collection period.

Sample. A convenience sample of 28 patients were included in the study. One patient was withdrawn by the PI related to a deterioration in clinical status, two patients were withdrawal related to unanticipated discharge prior to completion of the six-hour designated monitoring period; and six patients self-withdrew from the study related to their decision not to wear the ETCO2 sampling line. Therefore, the data from nineteen patients were available for analysis.

Variables

Independent variable. The independent variable was opioid administration. For patients receiving patient-controlled analgesia (PCA), the patient determined the timing for self-administration of the PCA demand ose. For patients receiving nurse-administered IV opioids, the opioid dose and administration was determined by the clinical nurse caring for the patient per

usual practice and care. The independent variable was measured by the administration of the opioid including the specific opioid, dose, route, and time of administration.

Dependent (outcome) variables. The outcome variables were related to the presence (Yes) or absence (No) of hypopnea, opioid-induced respiratory depression (OIRD), or apnea (A), or unintended opioid-induced sedation (OIS), that occurs within the 60-minute interval following intravenous opioid administration and the 6-hour as measured by continuous capnography and pulse oximetry monitoring period and/or the 60-minute interval after intravenous opioid administration. Hypopnea, opioid-induced respiratory depression, apnea, and unintended opioid-induced sedation also were measured by PI nursing monitoring and surveillance.(see Table 4.1).

Table 4.1

Dependent (Outcome) Variables

Outcome Variable	Type
Risk of opioid-induced respiratory depression	Ordinal
Opioid-induced respiratory depression	Categorical
Oxygen desaturation	Categorical
Unintended opioid-induced sedation	Categorical

Risk of opioid-induced respiratory depression. The risk of opioid-induced respiratory depression was determined by the score on the PRODIGY risk assessment tool with categories of low, moderate, and high risk to identify the risk of respiratory depression (Khanna et al., 2018; Khanna et al., Khanna et al., 2020; Khanna et al., 2021). The STOP-BANG questionnaire also was used to determine risk of opioid-induced respiratory depression and is a component of the PROIDGY risk assessment tool.

Opioid-induced respiratory depression by Capnography. The incidence of opioid-induced respiratory depression as determined by continuous bedside capnography and pulse oximetry were measured by data that revealed:

- Hypopnea (Respiratory rate ≤ 8 breaths per minute for ≥ 30 seconds duration) or
- Apnea (No breath for ≥ 30 seconds duration) or
- Hypoxemia (SpO2 ≤ 90% for ≥ 60 seconds in absence of an abnormal baseline) or
- Low exhaled CO2 (ETCO2 (≤ 15mmHg for ≥ 3 minutes duration)

Opioid-induced respiratory depression by PI monitoring and surveillance. The incidence of opioid-induced respiratory depression as determined by PI nursing monitoring and surveillance was determined by the PI assessment of the presence of:

- Hypopnea (Respiratory rate ≤ 8 breaths per minute); or
- Apnea (No observed breath for ≥ 30 seconds duration); or
- Observation of irregular breathing, snoring, or decreased depth of respirations or
- Observation of cyanosis; or
- Constellation of clinical signs of respiratory depression or the need for resuscitation or
- Observation of respiratory depression that requires intervention within the 60-minute interval after opioid administration; or
- Administration of an opioid receptor antagonist (naloxone);
- Decrease in opioid dose, discontinuation of an opioid, increase in opioid administration frequency interval or change to a different opioid.

Unintended opioid-induced sedation as determined by sedation assessment. Sedation was measured as a sedation level of 3 or 4 using the Pasero Opioid-induced Sedation Scale (POSS).

Statistical Analysis

The primary data analysis was performed on all subjects enrolled in the study and included all patient outcomes that occurred during the designated 6-hour continuous capnography and pulse oximetry monitoring period as well as during the 65-minute PI

observation period. Statistical analysis was performed with IBM SPSS Statistics Version 27 (SPSS Inc., Chicago, IL, USA) and MATLAB.

Descriptive statistics was used to report subject characteristics (demographics, co-morbidities, opioids, non-opioid sedation medications, presence of supplemental oxygen, and unit location). This analysis included frequencies and percentages for categorical variables. A 2-tailed Fisher's exact test was used to compare the categorical variables. Adjusted Wald method was used to calculate the incidence of respiratory depression (Field, 2013).

Study Procedures

IRB approval for the study was obtained from the University of California, Los Angeles (UCLA), and was also requested from the study site. The study site was requested to serve as the IRB of record for the UCLA IRB. Because the study involved no more than minimal risk and involved the collection of data through non-invasive methods (capnography, pulse oximetry, and observation) with all study equipment and disposables FDA approved for marketing and commercially available for use, an IRB expedited review was requested.

Study Sponsor and Funding

The PI was the study sponsor. There was no funding for this study. The PI submitted a proposal to the Medtronic External Research Program and requested support of the study through the loan of the two Capnostream35 portable respiratory monitors with accessories (e.g., clamp for IV pole) and consumables (120 ETCO2 adult filter sampling lines; 120 ETCO2 pediatric sampling lines for use with adults if needed; and 120 pulse oximetry sensors). Such support was previously approved by the Medtronic External Research Program for such support and required resubmission following the study site's IRB approval. Thus, the study site did not incur costs for the respiratory monitors, accessories, or consumables.

Subject Identification and Enrollment

The PI requested access to the emergency department (ED) track board. This electronic board is a list of patients with a column that identifies the admission status. The PI scanned the emergency department (ED) track board to identify prospective study subjects. The PI screened the emergency department's electronic medical records of prospective subjects to determine eligibility to participate in the study. To prevent any impact or increase in nurse, physician, or staff workload or workflow, it was necessary for the PI to conduct surveillance of the ED track board to identify and pre-screen prospective subjects to determine study eligibility. The study could not be have been conducted without the PI's ability to screen the ED track board. Therefore, a waiver of subject authorization for pre-screening was approved by the study site IRB.

After communication with the emergency department RN flow coordinator and RN caring for the patient, the PI approached the subject in the emergency department and initiated the informed consent process. If the potential subject agreed to participate in the study, written informed consent was completed.

The PI worked closely with the emergency department RN flow coordinator and conducted routine scanning of the ED track board to determine the approximate time that the patient was anticipated to be admitted to the general care floor. When the ED track board indicated that a room had been assigned to the patient, the PI applied the monitoring equipment (ETCO2 sampling line nasal cannula, pulse oximetry sensor, and capnography monitor) and initiated monitoring. The PI accompanied the patient to the general care ward and provided real-time education to the clinical nurse caring for the patient.

Data Collection and Measures

Each subject was clinically monitored through usual standard methods according to the study site as well as with continuous capnography and pulse oximetry. In order to capture all data, enrolled subjects were connected to capnography using the ETCO2 sampling line (nasal cannula) and to pulse oximetry using the peripheral SpO_2 sensor which was applied to the patient's non-dominant hand index finger (or finger as deemed appropriate as determined by presence of trauma) in the emergency department prior to admission to the general care ward.

Continuous capnography and pulse oximetry monitoring period. For this study, the monitoring period began on admission to the general acute care ward. Continuous capnography and pulse oximetry monitoring occurred for a minimum of six hours after admission to the general care ward to identify the incidence of opioid-induced depression events and allow for the description of capnography and pulse oximetry values that correlated with opioid-induced sedation or respiratory depression.

Blinding the capnography and pulse oximetry waveforms and values. Because capnography is not a component of usual care at the study site, the alarm feature of the capnography and pulse oximetry monitor was "silenced." Only the alarms on the study devices were silenced. Alarms for SpO_2 monitoring that was ordered for the patient was not silenced. The capnography monitor screen was covered to "blind" the waveforms and values.

Rationale for silencing alarms and covering the monitor screen. "Silencing" the alarm features served to "blind" any alarm notification to the PI, clinical nurse, or providers. Furthermore, covering the monitor screen served to "blind" the capnography and pulse oximetry waveforms and values to the PI and prevent potential bias during the observation of sedation and respiratory status before and after opioid administration. The data from the capnography and pulse oximetry monitor was not used for clinical decision making.

PI observation. Each subject was assessed by the PI before and after opioid administration during the six-hour continuous capnography and pulse oximetry monitoring period. Because the hours between 2300-0700 are a high-risk period for opioid-induced respiratory depression, an estimated 50% of subjects were observed by the PI during these hours. The administration of an intravenous opioid was at the request of the patient and not as a research intervention. Within five minutes before intravenous opioid administration, the PI assessed the patient's sedation level using the Pasero Opioid-Induced Sedation Scale (POSS) and respiratory status. Assessment of respiratory status was determined by the rate (observation and manual counting of chest rise and fall for 60 seconds), evaluation of depth, regularity, presence of snoring, or cyanosis. After baseline data assessment, the patient self-administered PCA dose or the clinical nurse administered an intravenous opioid dose. Sedation level and respiratory status assessment were reassessed at 10-minute intervals for 60 minutes after intravenous opioid administration.

Data Recording, Device and Disposables

Subject case report. All subject demographic and assessment data was collected on a confidential Pertinent Medical History case report form.

Sedation level. Sedation level data was recorded by the PI on the PI Observation case report form.

Respiratory status. Respiratory status data was recorded by the PI on the PI Observation case report form.

Capnography and pulse oximetry. Capnostream35 memory data was the source of capnography and pulse oximetry data and the number and duration of opioid-induced respiratory depression events. Memory data was exported to a flash drive memory device. The memory

device was stored at the study site in a secure, locked location accessible only to the PI. Device data were downloaded on a secure server at the study site for review and analysis.

Capnostream35 monitoring system. The Capnostream35 monitoring system consists of a capnography-pulse oximetry monitor, a sampling line for measuring end-tidal carbon dioxide (ETCO2), and a pulse oximetry sensor for measuring peripheral oxygen saturation of arterial hemoglobin (SpO2). This monitoring system used has been approved by the FDA and is commercially available (FDA 510(k); K123690).

Indications for use. The Capnostream35 combined capnography/pulse oximeter monitor and its accessories are intended to provide continuous, non-invasive measurement and monitoring of carbon dioxide concentration of inspired and expired breath (ETCO2), respiratory rate (RR), arterial oxygen saturation (SpO_2), and pulse rate (PR).

Physiologic parameter descriptions are:

1. Exhaled carbon dioxide (ETCO2)—the level of carbon dioxide in the exhaled breath.
2. Fractional inspired carbon dioxide ($FiCO_2$)—the level of carbon dioxide present during inhalation.
3. Respiratory rate (RR)—the total number of breaths per minute.
4. Peripheral oxygen saturation of arterial hemoglobin (SpO_2).
5. Pulse rate (PR)—the pulsatile cycle in beats per minute via pulse oximeter technology.

The monitoring system also provides an Integrated Pulmonary Index™ (IPI) value. The IPI is based on the integration of ETCO2, RR, SpO_2, and PR. The IPI is a single index of ventilation displayed on a scale of 1 to 10, where 10 indicates optimal pulmonary status. An alert is provided for changes in pulmonary status (see Figure 4.1).

Figure 4.1. Capnostream35 monitor.

Setup and calibration. The device was set up prior to the application for each subject according to the manufacturer's instructions for use. Calibration was performed according to the operational manual. Before the start of monitoring for each subject, a "monitoring prep checklist" was completed that ensured accurate and complete setup.

Blinding the data. There was no option on the Capnostream35 Monitor to blackout the monitor or alarm lights. Therefore, one strip of "Velcro-type" tape was placed to the left side of the monitor screen, and one strip of "Velcro-type" tape was placed to the right side of the monitor screen. Black vinyl in a size that completely covered the screen was attached to the "Velcro-type" tape on each side of the screen. "Blackout of the screen "blinded" the capnography and pulse oximetry waveforms as well as the ETCO2, SpO_2, RR, and PR values from the PI. Furthermore, black electrical tape was placed over the alarm lights at the top of the screen to "blackout" and "blind" any alarm alerts. Alarm sounds also were disabled to "blind" the data from the PI.

End-tidal carbon dioxide (ETCO2) sampling line. Each subject was connected to the Capnostream35 Monitor with a single-use, disposable ETCO2 sampling line. The adult or pediatric disposable ETCO2 sampling line can be used as determined by the individual patient preference to facilitate compliance with wearing the nasal cannula.

A sample of the exhaled gases is delivered from the patient (via the cannula) into the monitor for ETCO2 measurement. Supplemental oxygen also may be delivered through the sampling line. If the patient required supplemental oxygen, the oxygen was delivered, assessed, and maintained per usual clinical practice by the clinical nurse and other healthcare providers, caring for the patient.

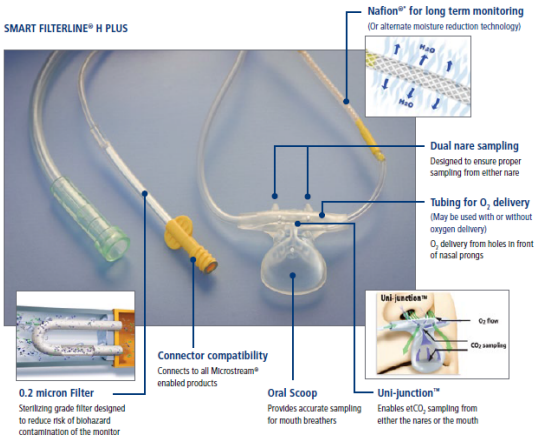

Figure 4.2. ETCO2 adult sampling line (nasal cannula).

Figure 4.3. ETCO2 pediatric sampling line (nasal cannula).

Peripheral oxygen saturation (SpO_2) sensor. Each subject was connected to the Capnostream35 Monitor with a non-invasive SpO_2 single-use, disposable sensor applied to the index finger on the non-dominant hand of the subject or appropriate finger as determined by

individual patient status (see Figure 4.4). Pulse oximetry is a non-invasive method of measuring the amount of hemoglobin saturated with oxygen (SpO_2). Light-emitting diodes (LEDs) emit red and infrared light. Changes in light absorption during the pulsatile cycle determine the SpO_2.

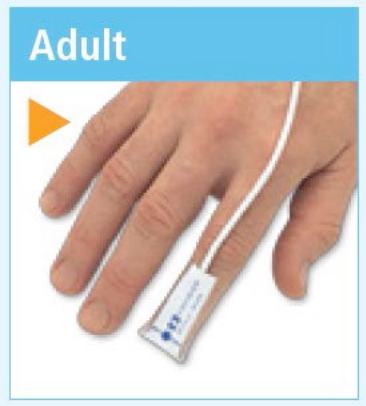

Figure 4.4. SpO_2 sensor.

Prior and Concomitant Medications

Opioids and concomitant medications with sedating actions were documented on the Medications Case Report forms. Medications administered as reversal agents were documented on the Medications Reversal Agents Case Report form.

Collection of medications occurred following the 65-minute monitoring duration to "blind" the PI from any medications that may increase the risk of opioid-induced sedation or respiratory depression and prevent the potential for bias during PI patient assessment.

Protection of Human Subjects

The protection of human subjects was ensured through this study. Subjects of all ethnic minorities were eligible for inclusion in the study. Study subjects include adults 18 to 89 years of age. The PI completed the Collaborative Institutional Training Initiative (CITI Program) requirements for the University of California, Los Angeles (UCLA) and the study site. Institutional Review Board (IRB) approval was obtained from the UCLA and the study site. Expedited review was requested as the collection of data was through non-invasive methods (not

involving general anesthesia or sedation) that are routinely employed in clinical practice. Furthermore, the capnography monitor and disposables used in this study are FDA approved and not experimental. The study commenced after receiving IRB approval.

Informed Consent

Because this study required a review of protected health information, informed consent was obtained. After screening, the PI met with the prospective subject and explained the study and content of the informed consent document. The prospective subject was allowed to ask questions before making a considered decision about whether or not to participate.

Potential Risks

Human subjects in this study include adult patients who were admitted to a general acute floor from the emergency department for a trauma-related condition.

Potential risks. All patients receiving opioids for pain management are at risk for sedation, which may progress to oversedation and lead to life-threatening opioid-induced respiratory depression. The current practice for patients receiving PCA is continuous pulse oximetry and sedation assessment using the Richmond Agitation-Sedation Scale, measurement of respiratory rate by observation of chest rise and fall for 15 seconds and multiplying by four to determine a respiratory rate per minute or for 60 seconds as determined by the discretion of the clinical nurse caring for the patient. The capnography monitoring system and disposables used in this study are FDA approved and commercially available. The monitors and disposables were used in accordance with the manufacturer's instructions for use; therefore, no risks other than the risks typically associated with routine healthcare device usage were anticipated. Risks were minimized by careful assessment by the healthcare team before, during, and after the monitoring phase. Patients also were cared for and monitored according to the usual standard monitoring

practices as defined by the study site. Therefore, no additional risks were associated with participation in the study.

Minimizing risks to confidentiality. The primary investigator assigned each subject a number that was not derived from or related to information about the subject and was not otherwise able to be traced to identify the subject. Following the initial subject number, a second number was randomly assigned to each subject to further ensure patient privacy. A separate data sheet was created, coding each patient initial number and secondary non-specific subject number to record any patient-specific data (i.e., medical record number) for review of any actions that are linked to the patient. The patient-specific data and matching non-specific subject number were file password-secured and stored on a secure study site computer.

The non-specific patient numbering system began with 300. Each subsequent patient was given a number that was one more than the previous patient number. For example, patient one was assigned number 300, and patient two was assigned number 301. Examples of concurrent review of the medical record and data collection of patient information included general care unit type (e.g., medical or trauma); admission diagnosis, patient type (trauma); opioid (drug, dose, frequency, PCA, or nurse administered); concomitant medications with sedating properties; reversal agents administered, sedation level, exhaled end-tidal carbon dioxide (ETCO2), oxygen saturation (SPO2), respiratory rate, pulse rate, and patient demographics (e.g., age, sex [biological as identified by the patient] ethnicity, altitude where patient resided height, weight, BMI, and comorbid conditions).

Immediately following data collection, the completed subject case report forms were placed in a file by the PI. The data recorded from the capnography monitoring system was downloaded on a flash memory drive and was placed in the file with the subject case report

forms. The file containing the subject case report forms and flash memory device were maintained by the PI in a secure, locked cabinet accessible only by the PI.

All identifiers that could be matched to the subject were be destroyed consistent with the conduct of research after completion of data analysis and approval of data analysis and final proposal. The identifiers were destroyed by placement of the data in a confidential shredding bin at the study site.

Risk management protocols for adverse events. The researcher is familiar with the process of adverse events (AE) reporting at the study site. If an adverse event were to occur, the researcher would report it to the IRB, study site supervisor, and Dissertation Chair as soon as possible. Regular meetings with the study site supervisor were conducted to ensure that all individuals involved in the research were informed of how the study was progressing.

Adverse event assessment. In this study, all events with an underlying or potentially underlying respiratory etiology, opioid-induced adverse event, or device monitoring issues were reported as an adverse event. Opioid-related events or respiratory depression occurrences were not considered an adverse event if the subject was asymptomatic, and no intervention was implemented.

Adequacy of protection against risk. The PI explained the study in detail to the patient and clinical nurse prior to the initiation of monitoring.

Potential Benefits

Subjects. Potential benefits to the patients included the early recognition of opioid-induced sedation or respiratory depression during the PI's observation and notification to the clinical nurse to facilitate the prompt implementation of appropriate interventions to prevent the worsening of opioid-induced adverse events. Potential anxiety experienced by the patient was

eliminated when the patient was provided education about the purpose of sedation assessment and continuous capnography with pulse oximetry monitoring to enhance safety.

Generation of knowledge. This study and original research contributes to knowledge about the most valid and reliable practice for the assessment of sedation, ventilation, and oxygenation during PCA or nurse-administered intravenous opioid administration in medical and trauma patients on the general care floor.

A plethora of research exists related to patient monitoring during purposeful sedation in critical care or procedural settings. However, a lack of research exists related to the monitoring of patients receiving opioids for pain management and the prevention of opioid-induced sedation and respiratory events in every patient care setting. This research illuminates the complex interaction of influencing factors in patient assessment, interpretation of assessment, and subsequent nursing actions. The findings from this study help to describe consequences and outcomes of standard practice as compared to continuous monitoring in patients receiving opioids for acute post-operative or trauma-related pain on the general acute care surgical-trauma unit.

Nursing. The clinical nurses caring for the patients who participated in the study benefitted from exposure to a research study in which the results provided data that may drive evidence-based clinical practice changes to facilitate adequate monitoring and influence safe, effective pain management..

Healthcare and patient safety. The healthcare organization benefitted through the conduction of original, scholarly research that will enhance safe and effective pain management and contribute to the advancement of nursing knowledge, and high-level evidence to facilitate the development of universally accepted, patient monitoring practices. Patient safety will be

increased, and the risk of clinically significant opioid-induced respiratory depression will be decreased with patient-centered monitoring with continuous capnography and pulse oximetry.

Risk-Benefit Analysis

The potential risks associated with this study were no more than minimal risk using non-invasive study devices for the following reasons:

1. All devices used in the study were commercially available and used within their intended use.
2. The usual standard of care was followed by the study site for the administration of opioid therapy and patient monitoring.
3. The patient benefited through intermittent observation by the PI, who is an Advanced Practice Nurse (Clinical Nurse Specialist) with expertise and certification in pain management (PGMT-BC).

Summary

Opioid-based analgesia is commonly prescribed for the management of trauma-related pain and often is associated with life-threatening opioid-related adverse events. Intermittent monitoring of oxygenation and ventilation every few hours is inadequate to detect opioid-induced respiratory depression. Although risk factors for opioid-related adverse events are described in the literature, unintended opioid-induced sedation, respiratory compromise, and respiratory depression continue to occur. This indicates that the mere description of risk factors is insufficient to identify characteristics of patients who are at risk for serious opioid-related adverse events. Although guidelines for monitoring have been published, standard monitoring practices do not exist.

This study collected data on patients receiving opioids for trauma-related pain with continuous capnography, pulse oximetry, pulse rate, and respiratory rate. RR Furthermore, PI

observation of sedation level and respiratory status (rate, depth, rhythm, and presence of snoring), allowed a description and understanding of the real-time incidence, trends, and patterns of opioid-induced respiratory depression for which there is no data in the literature. Study results provided data about the incidence of opioid-induced sedation and opioid-induced respiratory depression. This knowledge will enable development of appropriate monitoring and effective surveillance strategies to facilitate safe, effective pain management. Furthermore, this research is foundational for future studies that focus on caring well for this vulnerable patient population.

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CHAPTER 5: Results

Eight-hundred twenty-three trauma patients who presented to the emergency department following a traumatic injury were screened for study eligibility. Twenty-eight trauma patients met inclusion criteria. Nine patients were withdrawn from the study. One patient's condition deteriorated and was excluded from participating; two patients' data were not used for analysis because they did not receive intravenous opioids; six patients withdrew because they decided not to wear the ETCO2 sampling line.

All patients were administered opioids in the emergency department and general care wards. Twelve patients required surgical management. The patients who required surgical management were monitored preoperatively. High-risk STOP-BANG and PRODIGY scores were calculated for 5 (26.3%) and 8 (42.1%) patients, respectively. Baseline characteristics and the respiratory depression are summarized in the Table 5.1. The data set is too small for any meaningful comparisons; thus all p-values are not statistically significant. However, no conclusion can be made about the lack of differences between patients who did or did not have respiratory depression.

Table 5.1

Summary of Baseline Characteristics and Incidence of Respiratory Depression

	Total	**Respiratory depression**	**No respiratory depression**	**P**
	N = 19	**N = 14**	**N=5**	
Baseline characteristics				
Age	40 [32, 60.5]	37.5 [31.5, 61]	42 [40, 59]	0.733
Body mass index, kg/m^2	29.9 [24.4, 32.6]	30.6 [27.0, 33.4]	23.5 [23.4, 32.5]	0.266
Male sex	12 (63.2)	8 (57.1)	4 (80.0)	0.603
White race	16 (84.2)	12 (85.7)	4 (80.0)	>0.999
STOP BANG				0.248
Low risk	7 (36.8)	4 (28.6)	3 (60.0)	
Intermediate risk	7 (36.8)	5 (35.7)	2 (40.0)	
High risk	5 (26.3)	5 (35.7)	0	
PRODIGY Category				0.678
Low risk	5 (26.3)	3 (21.4)	2 (40.0)	
Intermediate risk	6 (31.6)	5 (35.7)	1 (20.0)	
High risk	8 (42.1)	6 (42.9)	2 (40.0)	
Emergency department course				
Duration, hrs	10 [7, 13.5]	9.9 [7.8, 13.2]	11.5 [4.0, 23.0]	>0.999
Opioids, mg IVME	10.5 [4.6, 14.0]	9.3 [5.0, 17.4]	12.6 [1.0, 13.2]	0.578
Intravenous sedation	5 (26.3)	4 (28.6)	1 (20.0)	>0.999
Oral sedation	4 (21.1)	3 (21.4)	1 (20.0)	>0.999
General care ward course				
Opioids, mg IVME	5.7 [4.0, 6.3]	7.7 [6.8, 8.0]	5.3 [3.8, 6.8]	0.266
Gabapentin	3 (15.8)	3 (21.4%)	0	0.53
Supplemental oxygen	4 (21.1)	4 (28.6)	0	0.53

Sample Characteristics

Patient demographics. Demographics are summarized in Table 5.2. Individual patient demographics are described in Appendix A. In the cohort there were 12 (63.15%) males and 7 (36.84%) females with a mean age of 44.1 ± *SD* = 15.90, median age of 40.0 [32.0, 60.5], with a minimum age of 20 and maximum age of 72 years with a range of 52 years. The mode was 35, 40, 20, and 30 years. Demographics are summarized in Table 5.2. Individual patient demographics are described in Appendix A.

Table 5.2

Patient Demographics

Variable	N = 19	%
Sex		
Male	12	63.15%
Female	7	36.84%
Age category		
18-60	14	73.68%
>60-79	5	26.31%
80-89	0	
Race		
American Indian	0	
Asian	0	
African American/Black	1	5.26%
Hispanic/Latino	9	47.36%
Non-Hispanic/Latino	9	47.36%
White	16	84.21%

Comorbid conditions. Patient comorbidities are summarized in Table 5.3. The most common condition was hypertension. Individual patient comorbid conditions are described in Appendix A.

Table 5.3

Comorbid Conditions

Variable	N=19	%
Cardiac Disorders	0	0%
Aortic Aneurysm	0	0%
Aortic Valve Disease	0	0%
Mitral Valve Disease	0	0%
Hypertension w/ medication	9	47%
Pulmonary Hypertension	0	0%
Hepatobiliary Disorder		
Liver	1	5%
Gastrointestinal	0	0%
Immune Disorders		
HIV	1	5%
Cancer	2	11%
Other	2	11%
Infections		
MODS	0	0%
SIRS	1	5%
Sepsis	0	0%
Kidney and Urinary Disorders		
Urinary	0	0%
Kidney dysfunction	1	5%
Kidney failure	0	0%
Metabolic Disorders		
Diabetes Mellitus I	0	0%
Diabetes Mellitus II	2	11%
Musculoskeletal Disorders		
Disc Degeneration	0	0%
Other	0	0%
Pulmonary Disorders		
Asthma	0	0%
COPD (exclusion)	0	0%
Pneumonia	0	0%
Pulmonary embolism	1	5%
Vascular Disorders		
Intracerebral aneurysm	0	0%
Transient ischemic attack	0	0%
Stroke	0	0%

Peripheral vascular disease	0	0%

Types of trauma. Types of trauma are summarized in Table.5.4, with orthopedic trauma the most common injury. Individual patient types of trauma are described in Appendix A.

Table 5.4

Types of Trauma

Trauma type	N = 19	%
Orthopedic	15	78.94%
Chest	3	15.79%
Abdominal	1	5.26%

Types and routes of opioids received in the emergency department. All patients received intravenous opioids in the emergency department. Seventy-nine percent (n=15) of patients received fentanyl, 15.79% of patients (n=3) received hydromorphone, and 63.16% (n=12) received morphine, and 42.11% (n=3). Thirteen patients in the ED also received concomitant oral opioids. Of these patients, 52.63% (n=10) received immediate release oxycodone and 15.79% (n=3) of patients received hydrocodone.

Table 5.5

Opioid Types Administered in the ED

Medication	N = 19	%
fentanyl	15	78.95%
hydromorphone	3	15.79%
morphine	12	63.16%
oxycodone	10	52.63%
hydrocodone	3	15.79%

Number of different opioids administered in the ED. Among patients who were administered opioids in the ED, 31.58% (n=6) were administered 1 opioid, 31.58% (n=6) were

administered 2 different opioids, 26.32% (n=3) were administered 3 opioids, and 10.53% (n=2) were administered 4 different opioids (Table 5.6).

Table 5.6

Number of Different Opioids Per Patient in the ED

Opioid	N = 19	%
opioids 1	6	31.58%
opioids 2	6	31.58%
opioids 3	5	26.32%
opioids 4	2	10.53%

Types of concomitant medications with sedating properties administered in the ED.

Among patients who received opioids and concomitant medications with sedating properties in the emergency department, 15.9% (n=3) received ketamine, 10.53% (n=2) received propofol, 26.32% received IV sedation, 5.26% received IV benzodiazepines, 10.53% (n=2) received gabapentin, 5.26% (n=1) received trazadone, and 21.05% (n=4) received oral sedation (Table 5.7).

Table 5.7

Medications with Sedating Properties Administered in the ED

Medications	N = 19	%
ketamine	3	15.79%
propofol	2	10.53%
IV sedation	5	26.32%
IV benzodiazepines	1	5.26%
gabapentin	2	10.53%
trazadone	1	5.26%
oral sedation	4	21.05%

Types and routes of opioids administered on the general care floor (GCF). All patients received intravenous opioids on the general care floor (Table 5.8). with 32% (n=6) of patients having received fentanyl, 5.3% (n=1) hydromorphone, and 73.68% (n=14) morphine. Twelve patients received oral opioids with 52.63% (n=10) immediate release oxycodone and 10.53% (n=2) hydrocodone.

Table 5.8

Opioid Types Administered on the GCF

Medication	**N = 19**	**%**
fentanyl	6	31.58%
hydromorphone	1	5.26%
morphine	14	73.68%
oxycodone	10	52.63%
hydrocodone	2	10.53%

Number of different opioids administered on the GCF. Thirty-seven percent (n=7) of patients on the GCF received 1 opioid, 52.63% (n=10) received 2 different opioids, and 10.53% (n=2) of patients received 3 different opioids (Table 5.9).

Table 5.9

Number of Different Opioids Per Patient on the GCF

Opioid	**N=19**	**%**
opioid 1	7	36.84%
opioids 2	10	52.63%
opioids 3	2	10.53%

Types of concomitant medications with sedating properties administered on the GCF. Gabapentin was the only concomitant medication administered on the GCF, with 16% (n=3) patients received gabapentin.

Respiratory depression on the GCF. Respiratory depression was detected in 14 patients (incidence 71 [95%CI 50.9 – 88.6] cases per 100 patients). The most common patterns were apnea (n=12) and hypoxemia (n=10) with hypopnea (n=5) and low expired end-tidal carbon dioxide level (n=4) less common (Appendix C).

Time to admission and OIRD. Because the cohort is small, assumptions cannot be made that the variables are normally distributed. Thus, median and quartiles were calculated. Median time for occurrence of the initial respiratory depression episode was 108 [34, 275] minutes after admission to the general care ward. The time between admission from the emergency department and the occurrence of respiratory depression are summarized in Table 5.10.

Table 5.10

Time Interval Between Admission to the General Care Floor and Detection of the First Respiratory Detection Event as Measured in Minutes

Patient	Admit Time	RD Time	Minutes
1	13:00	15:11	131
2	15:42	19:28	226
3	17:24	17:40	16
4	18:36	18:50	14
5	20:12	21:01	49
6	21:40	*	*
7	21:56	23:35	99
8	16:21	22:33	372
9	23:26	23:36	10
10	1:37	2:44	67
11	5:34	*	*
12	16:12	21:51	339
13	22:03	*	*
14	20:21	*	*

15	22:18	*	*
16	5:44	7:41	117
17	7:37	12:28	291
18	16:56	22:12	316
19	21:34	22:45	71

*no respiratory depression

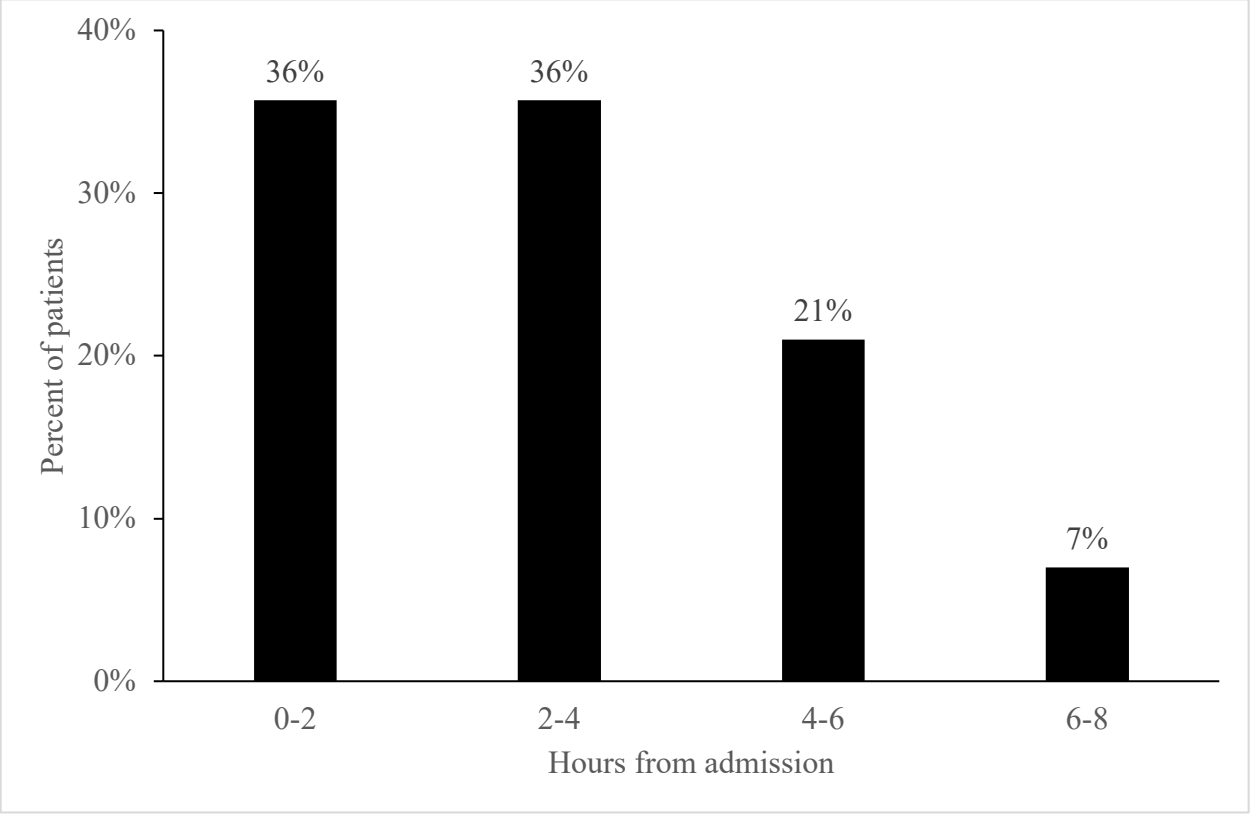

Figure 5.1. Percentage of patients who experienced respiratory depression as calculated in 2-hour intervals after admission to the general care floor.

Monitoring time periods and respiratory depression. If patient monitoring occurred before 24:00 the patient was considered to be monitored during the day. If patient monitoring was continued after 24:00, the patient was considered to be monitored during the night.

Among the 14 patients who suffered respiratory depression, 42.8% (n=6) patients were monitored during the day and 57.1% (n=8) patients were monitored during the night. A Fisher's

exact test determined a two-tailed p value of 0.063 which was considered not clinically significant (Table. 5.9).

Among the 5 patients who did not experienced respiratory depression on the general care floor as measured by continuous capnography and pulse oximetry, 2% (n=1) of patients were monitored during the day and 80% (n=4) were monitored during the night. A Fisher's exact test determined a two-tailed p value of 0.2000 which was considered not statistically significant (Appendix D).

The temporal distributions for time to admission and initial respiratory depression episodes are displayed on a 24-hour radar plot for visual inspection of peak occurrence.

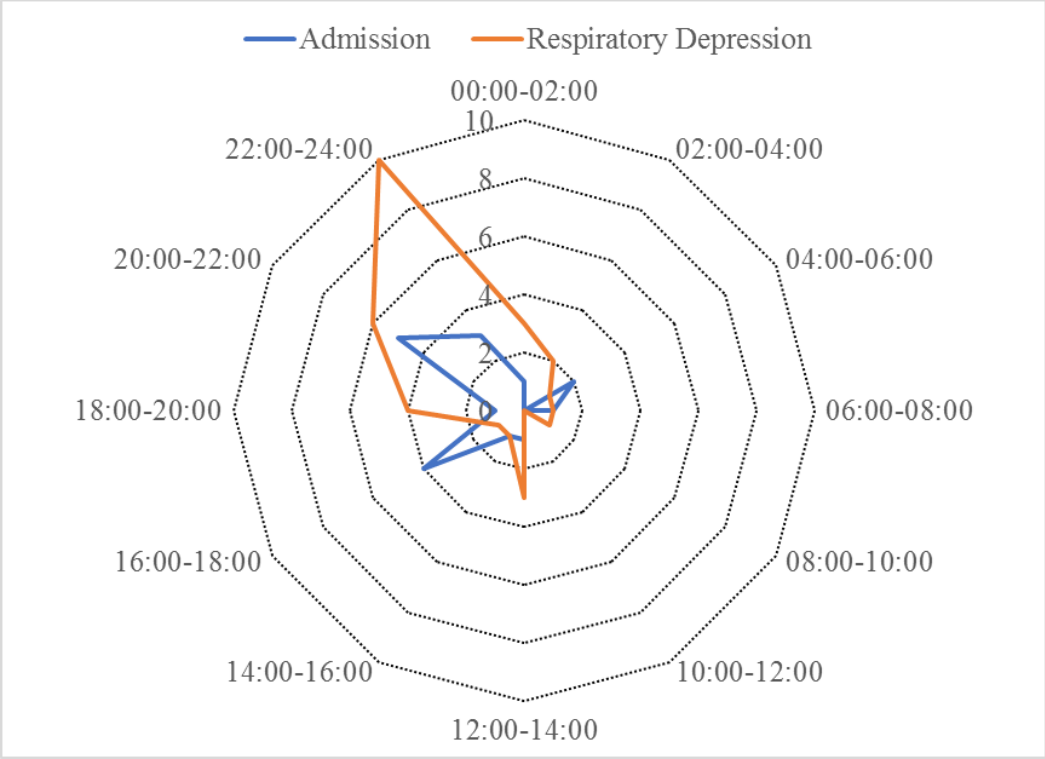

Figure 5.2. Radar plot depicting time on a 24-hour clock and time interval between admission to the general care ward and initial respiratory depression event.

Radar plot interpretation. The blue line on the radar plot represents the time of admission to the general care floor. The orange line represents the initial respiratory depression episode. Spokes on the radar plot depict the time of day on a 24-hour clock. The magnitude of each spoke is the total number of episodes between the previous spoke time and the correct spoke time (e.g., at 2200-2400 is shown the number of episodes that occurred between 20:00-22:00) (Driver et al., 2021).

Visual inspection of the radar plot of all time of admission and respiratory depression episodes revealed that the majority of admissions were between 16:00 and 24:00 (n=9, 64%) and the majority of first OIRD events were from 18:00 to 24:00 [n=9, 64%].

Respiratory depression. Respiratory depression events were determined by evaluation of capnography data. However, the extent of the alarms indicates that the patient experienced at least one apnea episode. Respiratory events are summarized in Table 5.4.

Our findings derived from continuous capnography and pulse oximetry data revealed that 35.7% (n-5) of patients had low exhaled carbon dioxide (ETCO2), 35.5% (n=5) of patients had low respriatory rate (RR), 64% (n=9) of patients had low oxygen saturation (SPO2), 85.7% (n=12) of patients had hypopnea, 85.7% (n=12) of patients had hypoxemia, and 85.7% (n=12) of patients experienced at least one apnea event (Appendix W).

Capnography waveform depicting hypopnea evidenced by widely spaced exhaled CO2 patterns

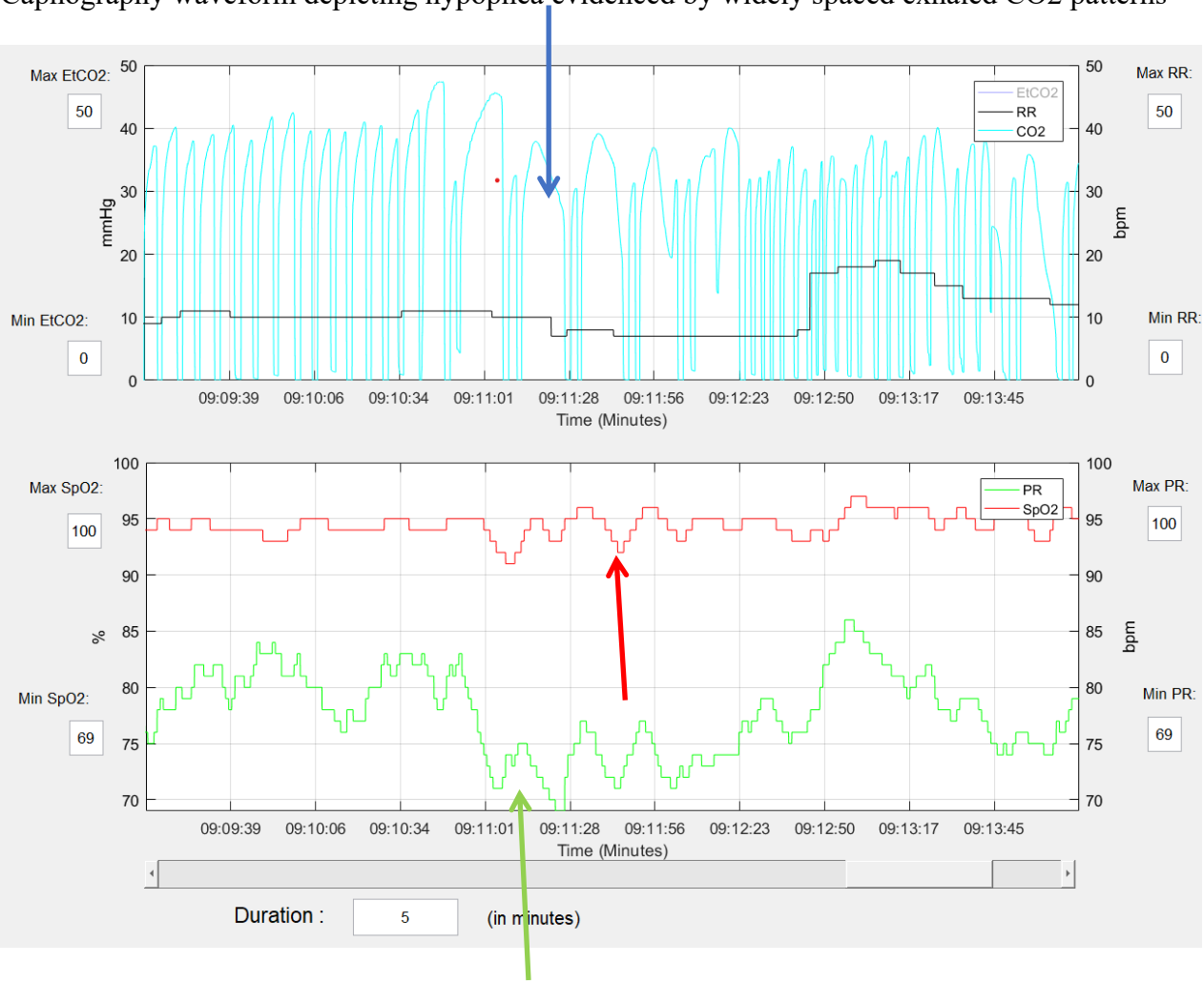

Figure 5.3. Capnography waveform depicting hypopnea as evidenced by the widely spaced carbon dioxide exhalation patterns. The top panel of the capnography waveform displays exhaled carbon dioxide (blue) over time as measured by bedside capnography. The bottom panel displays data from pulse oximetry oxyhemoglobin concentration (red) and heart rate (green).

Figure 5.4. Capnography waveform depicting apnea evidenced by low ETCO2, pattern (blue), oxygen desturation (red), and increased heart rate (green).

The decrease in oxyhemoglobin saturation and increase in heart rate are usually observed during an apneic breathing pattern unless the patient is receiving supplemental oxygen. As previously explained ETCO2 indicates exhaled carbon dioxide; PR, pulse rate; RR, respiratory rate; SPO2 oxyhemoglobin saturation (Driver et al., 2021).

Averages of capnography data. The average of capnography data was calculated for the 60-minute duration after opioid administration. A graph was created to evaluate changes in respiratory status. An example of no change in respiratory within the 60-minute interval following opioid administration is depicted in Figure 5.5.

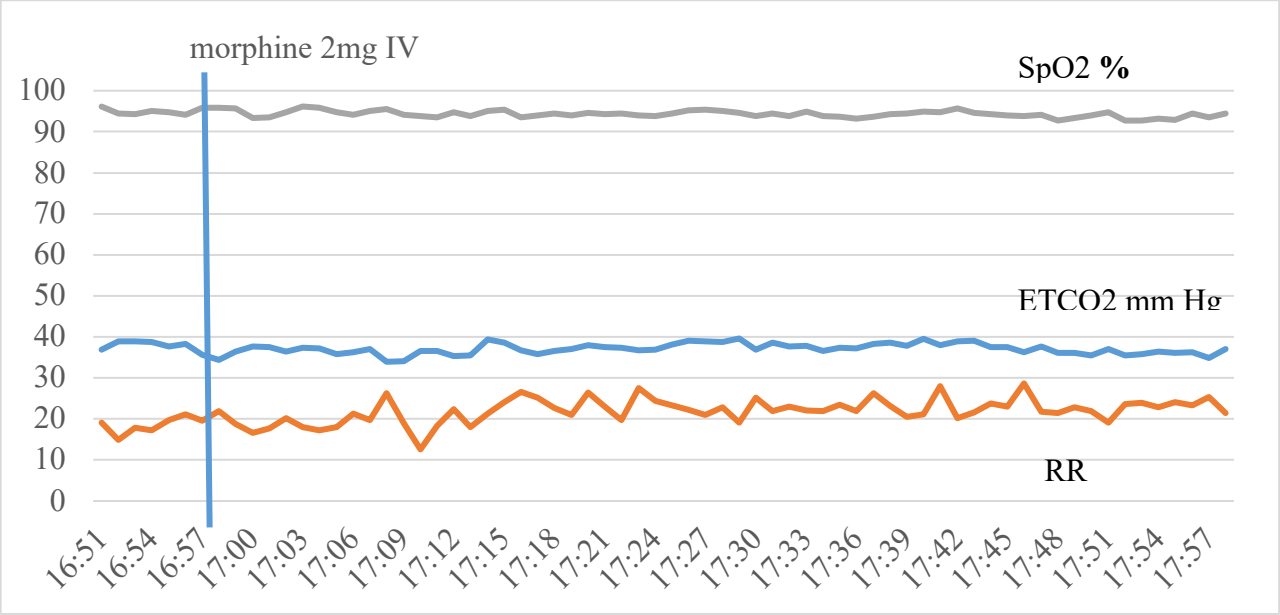

Figure 5.5. Example of no change in respiratory rate, ETCO2, or SPO2 after opioid administration.

Figure 5.6 is that of a 63-year-old female who suffered chest trauma following a fall. Review of the chart depicts a decrease in ETCO2 which reflects hypoventilation. Furthermore, the respiratory rate decreases from 10 breaths per minute to less than 5 breaths per minute over time. The low respiratory rate and low ETCO2 indicates ventilatory insufficiency. The patient was receiving 2 liters of supplemental oxygen and the SPO2 remained unchanged. The PI observed this event and accordingly awakened the patient, stimulated her to breathe, and informed the RN. Vigilant monitoring was recommended and a decrease in opioid dose by 50% was subsequently ordered by the physician.

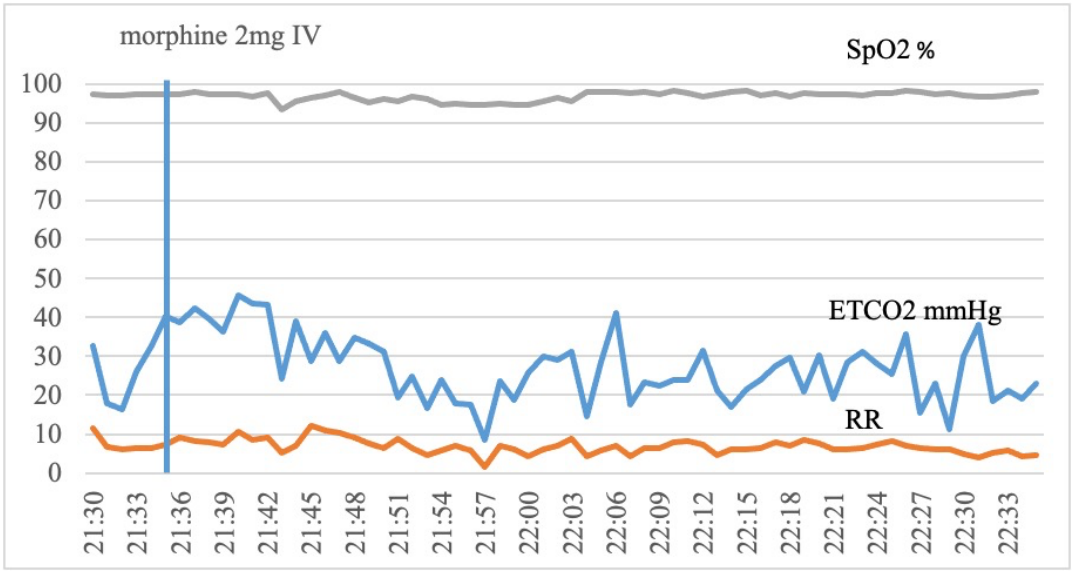

Figure 5.6. Hypoventilation following opioid administration.

Figure 5.7 is of a 41-year-old male who suffered chest trauma following a motor vehicle accident. The capnography data revealed an ETCO2 of 30-40 mmHg and no change in respiratory rate. The patient experienced low oxygen saturation (SPO2 85-88%) despite the receiving of supplemental oxygen. Capnography and pulse oximetry indicated that the patient experienced hypercapnic respiratory depression following opioid administration.

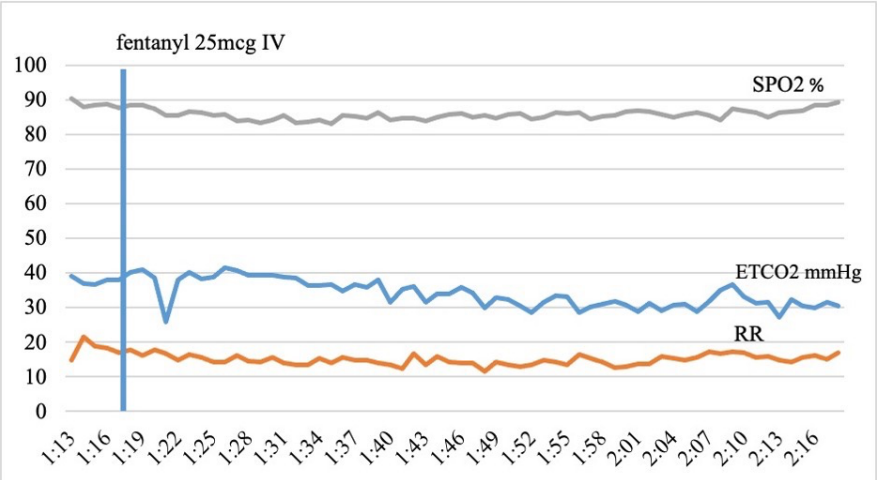

Figure 5.7. 41-year-old male who suffered chest trauma.

Figure 5.8 is that of a 30-year-old male who suffered upper extremity trauma presented following a motorcycle crash.

Capnography data revealed the occurrence of 2 apneic events within the 60-minute interval following the opioid administration and 600mg of gabapentin. The PI observed these events, awakened the patient, stimulated the patient to breath, and informed the RN of the change in patient status.

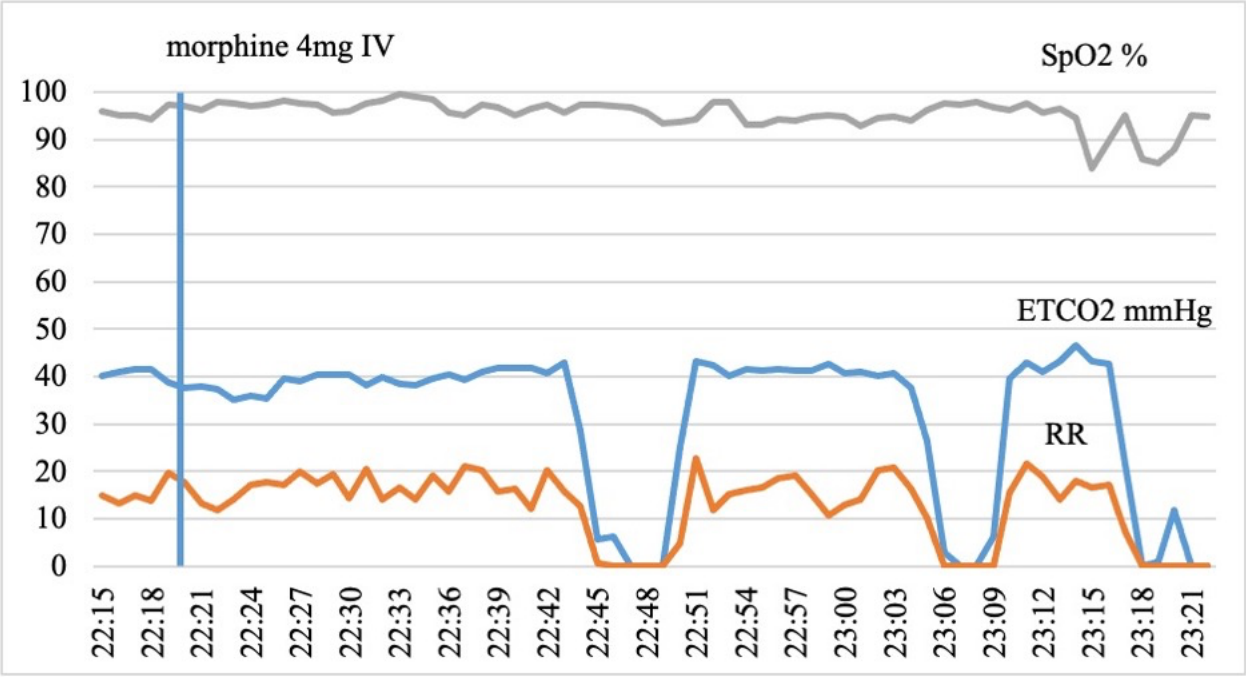

Figure 5.8. Patient 19. Morphine 4mg IV administered at 22:22. ETCO2 and respiratory rate started to decrease at 22:41 and at 22:45 opioid induced apnea occurs. Patient is awakened, stimulated to breath, and exhaled ETCO2 rises. At 23:03 ETCO2 begins to decrease again and apnea occurs. When patient is stimulated to breathe, exhaled ETCO2 begins to rise.

Principle Investigator Observation

Opioid-induced sedation. Using the Pasero Opioid-Induced Sedation Scale (POSS), unintended sedation was observed in 78.5% (n=11) of the 14 patients who experienced respiratory depression. Among the 5 patients who did not experience respiratory depression,

unintended sedation was observed in 80% (n=4). Because unintended sedation is a predictor of respiratory depression, it is conceivable that the patients may have developed respiratory depression if the PI had not detected the sedation and appropriate interventions had not been implemented. The PI notified the bedside nurse of all patients who were observed to have unintended sedation and recommendations were made based on those included in the POSS.

Opioid-induced respiratory depression. The PI recognized 50% (n=7) of respiratory events. The seven respiratory events recognized by the PI also were detected by capnography. It is a possibility that the patients experienced respiratory depression when the PI was not in the room during the time for observation. Furthermore, the general floor nurse was often in the room when the PI arrived for assessment which could explain the rationale of the PI not recognizing more respiratory depression events.

No patient required an opioid-reversal medication (naloxone), experienced a life-threatening adverse respiratory event, or required transfer to a higher level of care. PI assessment of unintended sedation and respiratory depression is summarized in Table 5.11.

Table 5.11

Summary of Respiratory Depression Events

Patient	CAP low RR (N=5)	PI detected low RR (N=4)	CAP RD (N=14)	PI detected RD (N=7)	CAP Apnea > 30 seconds (N=12)	PI detected Apnea > 30 seconds (N=4)	PI detected sedation (POSS) (N=12)
1	No	Yes	Yes	No	Yes	No	No
2	No	No	Yes	No	Yes	Yes	Yes
3	Yes	No	Yes	Yes	Yes	Yes	Yes
4	Yes	No	Yes	Yes	No	Yes	Yes
5	No	No	Yes	No	Yes	Yes	Yes
6	No	No	No	No	No	No	No
7	No	No	Yes	No	No	Yes	Yes
8	No	No	Yes	No	Yes	Yes	Yes
9	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10	No	Yes	Yes	No	Yes	Yes	Yes
11	No	No	Yes	No	No	No	No
12	Yes	No	No	Yes	Yes	No	No
13	No	No	No	No	No	No	No
14	No	No	No	No	No	No	No
15	No	No	No	No	No	No	No
16	No	No	Yes	No	Yes	Yes	Yes
17	No	Yes	Yes	No	Yes	Yes	Yes
18	Yes	No	Yes	Yes	Yes	Yes	Yes
19	No	No	Yes	No	Yes	Yes	Yes

Chapter References

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CHAPTER 6: Discussion

Incidence of Opioid-Induced Respiratory Depression

The incidence of respiratory depression among trauma patients on general care floors prior to surgery had not been previously described. In our study, we used continuous capnography and pulse oximetry monitoring, as well as nursing assessment, to describe the incidence of opioid-induced sedation and respiratory depression among trauma patients who presented to the emergency department and were subsequently admitted to the general care floor. All patients received intravenous opioids in the emergency department and on the general care floor. Our main findings were that undetected sedation, respiratory depression, and apneic events were common among the study patients.

Our first aim was to describe the incidence of opioid-induced respiratory depression in trauma receiving both patient-controlled analgesia (PCA) or nurse administered opioids. However, the balance of patients receiving PCA and nurse administered opioids was unequal in our sample. More specifically, only two of our patients received PCA. One patient's PCA was discontinued within 15 minutes of admission to the general care floor. This resulted in our ability to monitor one patient receiving PCA for the 6-hour monitoring period. The rationale for the lack of patients receiving PCA in our study was related to the concern of the study site that PCA resulted in an increased risk for opioid-induced respiratory depression. This concern resulted in PCA being an uncommon method of pain management at the study site.

Despite only one patient receiving PCA monitored for the 6-hour monitoring period, all patients received intravenous opioids in the emergency department and on the general care floor. Our main findings were that undetected sedation, respiratory depression, and apneic events were common among our study sample.

We used the Capnostream35 respiratory monitor (Medtronic) to collect continuous capnography and pulse oximetry data for a 6-hour duration. Prior to the initiation of capnography and pulse oximetry monitoring, the monitor alarms were silenced, and screen was blinded from the PI and all clinicians. Blinding capnography and pulse oximetry values prevented the use of capnography data for clinical decision making and prevented the potential for PI bias during sedation and respiratory status assessment. Monitoring began on arrival to the general care floor. In an additional attempt to remain objective, the PI did not observe the bedside nurse intermittent spot checks, surveillance, monitoring, performance of usual care, or review bedside nurse documentation.

Using continuous capnography and pulse oximetry data, we calculated the interval between admission to the general care floor and the initial respiratory depression event. Surprisingly, we found that 42.8% (n=6) of patients suffered at least one respiratory event after admission to the general care floor prior to receiving opioids on the general care floor. This finding suggests that opioid administration in the emergency department may negatively impact the respiratory status of patients after admission to the general care floor. We also evaluated the most vulnerable period of time for respiratory depression.

The most vulnerable period for respiratory depression among surgical patients has been reported to be within the initial 24-hours of surgery (Driver et al., 2021; Fisberg et al., 2003; Gupta et al., 2018; Taylor et al., 2005; Khanna et al., 2020; Lee et al., 2015; Ramachandran et al., 2011; Smoker, Kirsopp, & Johnson, 2021). Our results show that this vulnerability is present prior to surgical intervention when opioids analgesics are being administered. Our data showed that the vulnerable period for respiratory depression among our trauma patients on the general care floor was early within the hospital course as evidenced by a median time of 108 minutes [34, 275] minutes after admission from the emergency department. Because oxygen desaturation

lags behind hypoventilation and is a late sign of opioid-induced respiratory depression, we assessed oxygen use and respiratory depression among our patients (Fu et al., 2004; Lam et al., 2017; Laporta et al., 2020; Sun et al., 2015).

Administration of supplemental oxygen has been reported to depress the output of both peripheral and central chemoreceptors and decrease respiratory drive (Dahan, DeGoede, Berkenbosch, & Olievier, 1990; Lambertsen, Hall, Wollman, & Goodman, 1963; Neisters, Mahan, Aarts, & Dahan, 2013). Consistent with these reports, each of our patients who received supplemental oxygen (21.4%, n=4), experienced a respiratory depression event.

Multimodal analgesia is an approach using opioid and nonopioid medications targeting different components of the peripheral and central pain pathways (Cavalcante et al., 2017; Hamrick et al., 2019; Ramierez et al., 2017; Polomano et al., 2017). We reviewed the number, types, and routes of opioids and non-opioid medications with sedating properties the patients received in the emergency department and on the general care floor. Gabapentin often is recommended in ERAS protocols, multimodal pain management regimes, and clinical practice guidelines (Carmichael et al., 2017; Chou et al., 2016; Junquist et al., 2019). Recent research has revealed that gabapentinoids can augment the risk and severity of respiratory depression (Cavalcante et al., 2017; Lee, et al., 2020; Li et al., 2021; Overdyk et al., 2014; Overdyk et al., 2016); Weingarten Njathi, & Wilson, 2015).

In a case-control study of 11,000 patients, undergoing arthroplasty, researchers sought to describe the incidence of postoperative respiratory depression in patients who received gabapentin preoperatively as compared to patients who did not receive gabapentin preoperatively (Weingarten et al., 2015). Results revealed that respiratory depression was increased by 60% among patients who received preoperative gabapentin (odds ratio [OR] 1.60, 95% confidence interval [CI] 1/27, 20.2) with regional anesthesia and an increase of 47% among patients who

received preoperative gabapentin with general anesthesia as compared to patients who did not receive preoperative gabapentin (OR 1.47, 95% CI 1.26, 1.70) (Weingarten et al., 2015). As a result of the serious increased risk of respiratory depression when gabapentinoids are combined with opioids, the United States Food and Drug Administration (FDA) issued a warning that is required in gabapentinoid prescribing information (FDA, 2019).

Among the patients in our study, 100% (n=3) who received gabapentin developed respiratory depression. It is conceivable that the prescribing practice influenced the increased of respiratory depression in these patients. More specifically, the FDA warning recommends that when co-prescribing gabapentinoids with opioids, the initial starting dose should be at the lowest dose (FDA, 2019). Although the lowest dose of gabapentin is 100mg, two of our patients were administered a starting dose of 300mg and 1 patient was administered a single dose of 600mg.

Concerningly, 85.7% (n=12) of patients who experienced a respiratory event on the general care floor had received a combination of different types and routes of opioids in the emergency department and 71.4% (n=10) received a combination on the general care floor.

Among our study, 73.6% (n=14) of patients experienced at least one episode of respiratory depression. Eighty-five percent (n=12) of these patients also experienced at least one episode of apnea. The number of respiratory depression events after admission to the general care floor before opioid administration by the general care bedside nurse coupled with the number of events that occurred after opioid administration on the floor resulted in at least 24 respiratory depression events.

Despite usual care and assessment by the bedside nurse, no episodes of unintended sedation or respiratory depression were identified. We contemplated that because the PI assessed each patient at 10-minute intervals for a 60-minute duration after opioid administration, it was

possible that the bedside nurse unintentionally performed less than usual level of care in patient assessment.

Principle Investigator Patient Assessment

In addition to continuous capnography and pulse oximetry monitoring, the PI assessed the sedation level and respiratory status for every patient within five minutes prior to opioid administration and every 10-minutes thereafter for a 60-minute duration. The Pasero Opioid-Induced Sedation Scale (POSS) was used to assess sedation level. Respiratory rate was measured by the counting the rise and fall of the patient's chest for 60 seconds. The dept and regularity of respirations, as well as, the presence of snoring also was assessed.

Sedation is as the most common precursor of opioid-induced respiratory depression (Jungquist et al., 2017). Despite the importance of sedation assessment, researchers have reported a lack of individualized and vigilant sedation in surveillance, monitoring, and clinical decision making to administer opioids for pain (Jungquist et al., 2016; Pawasauskas, Stevens, Youssef, & Kelley, 2014; Taylor, Kirton, Staff & Kozol, 2005; Weingarten et al., 2015).

Using the Pasero Opioid-Induced Sedation Scale (POSS), the PI observed unintended sedation in 78.9% (n=15) of patients. Among the patients who did not experience a respiratory depression event (n=5), the PI recognized unintended sedation in 80% (n=4) of these patients. The bedside nurse was informed the patient's unacceptable sedation status as evidenced by a sedation level of three (frequently drowsy, arousable, drifts off to sleep during conversation) and recommendations were made for individualized and increased vigilance in monitoring and surveillance as well as a downward adjustment in the opioid dose. Unintended sedation precedes opioid-induced respiratory depression (Jungquist et al., 2019). Therefore, it is clear that these patients may have progressed to respiratory depression without early recognition and

implementation of appropriate interventions to prevent the worsening of opioid-induced adverse events (Jungquist et al., 2017; Rosenfeld et al., 2015).

The PI recommended individualized and vigilant surveillance and monitoring and as well as a downward adjustment in the opioid dose. We determined that the patients who suffered respiratory depression in our study did so because of intervariability in opioid sensitivity and response, such as genetic factors, sex differences, bioavailability, and metabolism in opioids (Dahan et al., 1998; Lotsch et al., 2006; Mauvais-Jarvis et al., 2021; Overdyk et al., 2014; Pattinson, 2008; Sarton et al., 2000).

Respiratory Status Assessment

Current vital sign monitoring on general care floors typically consists of intermittent spot checks every 4-8 hours (Khanna et al., 2019). Intermittent monitoring results in prolonged time intervals between patient surveillance and monitoring. An abnormal respiratory rate can be an important indicator of impending patient deterioration (Vincent et al.,2018). However, in a recent prospective study, researchers sought to determine the adequacy of respiratory rate as an indication of adequate ventilation as compared to transcutaneous ETCO2. Researchers reported a weak correlation (r=0.22) between respiratory rate and ETCO2 (Morimoto et al., 2019).

To assess respiratory status, the PI counted respiratory rate for a 60-second duration and assessed the depth and regularity of respirations, and presence of snoring. Based on this assessment, 50% (n=7) of patients experienced a respiratory depression event as compared to continuous capnography data which detected 14 patient events. This finding supports reports that respiratory rate is an inadequate indicator of ventilatory efficiency and that intermittent spot checks may delay the recognition of patient deterioration (Morimoto et al., 2019).

Limitations

The study site suspended studies that involved direct patient care for over twelve months due to the COVID-19 pandemic, which blocked our ability to enroll patients beyond those enrolled before the pandemic. In addition, our contact with, and enrollment of patients who met inclusion criteria was limited by the fact that the majority of patients were admitted to stepdown and critical care units or underwent immediate surgery. As a result, our sample size is small (n=19) and thus cannot be generalized and comparison cannot be made between patients.

Identification of patients who met inclusion criteria proved difficult. The majority of trauma patients were admitted to stepdown and critical care units or underwent immediate surgery. The constellation of fewer trauma patients admitted to the general care floor and temporary suspending of the study related to the COVID-19 pandemic hindered patient enrollment and sample size.

Nursing Implications

Our data analysis revealed that unintended opioid-induced sedation and respiratory depression are often unrecognized. It is clear that opioids and medications with sedating properties impact the respiratory status of trauma patients on the general care floor. When these medications are administered to trauma patients who are admitted to the general care floor from the emergency department, vigilance and individualized systematic monitoring of sedation and respiratory status are critical to the to the early recognition of unintended sedation and the prevention of life-threatening respiratory depression.

Seventy-two percent (n=10.8) of our patients experienced respiratory depression within the first four hours of their hospital course. This finding suggests that opioids and sedatives administered in the emergency department impacts the respiratory status of trauma patients soon as admission to the general care floor. Therefore, it is recommended that the general care nurse

requests the most recent administration of type, dose, route, and time of opioid administration, as well as, medications with sedating properties during hand-off report with the emergency department nurse. Furthermore, because the amount of opioids, sedatives, and adjunct medications may be too numerous to include in a hand-off report, it is critical that the general care floor nurse review the patient's medication administration record (MAR) for all opioids and sedatives, and adjunct medications received for the duration of time that the patient was in the emergency department.

Based on study findings, it is recommended that the general care floor nurse develop a personalized patient vigilant surveillance and monitoring plan during the first four hours following admission from the emergency department. The frequency of surveillance and monitoring must be based on the patient status and response to opioids and other sedating medication (Le et al., 2020; Overdyk et al., 2016).

Patient risk factors using the PROIDGY risk assessment tool after data collection as one effort to simulate typical nursing practice and prevent PI bias during patient assessment. Using this tool, 78.5 percent (n=11) of patients scored as high or intermediate risk of opioid-induced respiratory depression. Among these patients, 72.7% (n=8) developed respiratory depression. A personalized patient plan must include assessment of patient risk factors for opioid-induced respiratory depression using a research-based and validated risk predication tool (Khanna et al., 2020; Tseregounis & Henry, 2021). However, even with the use of a research-based risk assessment tool, 42.9% (n=6) of patients who scored as low risk experienced respiratory depression. Therefore, the general care floor nurse must consider all patients receiving opioids at risk for opioid-induced respiratory depression and consider patient-level risk factors as well (Tseregounis & Henry, 2021).

Patients experience variable response to opioid drugs (Galer et al., 1992; Glanz et al., 2021; Mauvais-Jarvis et al., 2021). This variable response demands that a personalized patient monitoring plan must be dynamic with revisions to monitoring and surveillance strategies based on patient response after opioid administration, with changes in the type, dose, and frequency of opioids, or the addition of adjunct medications with sedating properties to the pain management plan. An adequate and personalized plan also demands that the general care floor nurse possess knowledge of the action, onset, timing of peak serum concentration and the synergist properties of any medications with opioids (Jungquist et al., 2020).

Our comparison of continuous capnography and pulse oximetry monitoring data with intermittent PI assessment of respiratory status revealed that continuous capnography was more effective in the detection of respiratory depression events monitoring. This important finding offers compelling evidence of the need for continuous monitoring to enhance vigilant nursing monitoring and surveillance.

Using the Pasero Opioid-Induced Sedation Scale (POSS), the PI identified five patients who developed unintended sedation but were not experiencing respiratory depression at the time of assessment. Furthermore, the PI used the recommendations incorporated in the POSS to provide recommendations to the general care floor nurse who subsequently requested a change in the opioid dose from the physician and implemented more vigilant monitoring. Unintended sedation is a predictor of opioid-induced respiratory depression. None of the five patients experienced worsening of opioid-adverse events or progressed to respiratory depression. This finding supports the need for routine, adequate sedation assessment using a valid and reliable sedation assessment scale developed to identify unintended opioid-induced sedation

Conclusion

All patients receiving opioids are at risk for unintended sedation and life-threatening respiratory depression. It is the responsibility of the healthcare team to ensure safe prescribing of opioids based on personalized and patient centered patient risk factors using a valid and reliable risk factor assessment tool. Research results revelated opioids and medications with sedating properties administered in the emergency department may negatively impact the respiratory status of the trauma patient admitted to the general care floor.

Findings also showed that opioid-induced respiratory depression related to the administration of opioids and other sedating drugs is typically experienced early in the hospital course among patients hospitalized for trauma on general care floors. The use of bedside capnography and pulse oximetry was able to detect respiratory depression, mostly apnea and hypoxemia, in the majority of the study sample. It is conceivable, that use of the POSS and implementation of POSS recommendations resulted in the prevention of respiratory depression in at least five patients. Therefore, it is recommended that assessment of level of sedation using the POSS, be conducted before and after opioid administration based on the type, action, and onset of the opioid. Vigilant PI monitoring and surveillance of patients for a 60-minute interval following opioid administration did not detect every opioid-induced respiratory depression event. These results provide compelling evidence to the unmet needs in the quality of care, surveillance, and monitoring for trauma patients on the general care floors receiving opioids.

Implications for Future Research

Future research is needed to study respiratory depression in a larger cohort of trauma patients using continuous pulse oximetry to determine the incidence of hypoxemia in order to assess risk factors using a multi-variable model with a sample size of 100. A retrospective study among trauma patients on general care floors who received naloxone as compared to similar

patients who did not receive naloxone also would yield meaningful data regarding patient risk factors and incidence of respiratory depression. Continuance of this study of research among trauma patients receiving opioids on the general care floor is needed that includes larger sample size so that comparisons can be made between patients and generalizability is possible.

Studies that describe the incidence of concomitant opioids and other drugs with sedating properties administered to patients and the impact on respiratory status, respiratory depression, and death are also needed. Additional research is required that includes methods to continuous and accurately monitor tidal volume and respiratory rate.

Importantly, research is needed that would enable direct communication to the general care floor nurse with technology that would alert the nurse of unintended sedation and impending respiratory depression.

APPENDICES

Appendix A: Patient Demographics

Individual patient demographics, comorbid conditions, type of trauma, risk assessment and occurrence of RD.

Patient demographics , comorbid conditions and risk assessment

Patient	Age	Sex	Ethnicity	Race	Type of Trauma	Opioid Naïve	HTN	Insulin Diabetes Mellitus	CHF	Kidney	STOP Bang RISK	PRODIGY RISK	RD
1	43	Female	Hispanic	White	Ortho	No	Yes	No	No	No	inter**	low	Yes
2	64	Male	Non-Hispanic	White	Chest	Yes	No	No	No	No	inter**	high	Yes
3	63	Female	Hispanic	White	Chest	Yes	Yes	Yes	No	Yes	high	high	Yes
4	35	Female	Hispanic	White	Abd	Yes	No	No	No	No	inter**	low	Yes
5	40	Male	Non-Hispanic	White	Ortho	Yes	No	No	No	No	high	high	Yes
*6	72	Male	Non-Hispanic	White	Ortho	Yes	Yes	No	No	No	inter**	high	No
7	66	Female	Non-Hispanic	White	Ortho	Yes	Yes	No	No	No	inter**	inter**	Yes
8	20	Male	Hispanic	White	Ortho	Yes	No	No	No	No	low	inter**	Yes
9	30	Female	Non-Hispanic	White	Ortho	Yes	No	No	No	No	high	low	Yes
10	33	Male	Hispanic	White	Ortho	Yes	No	No	No	No	low	inter	Yes
11	20	Male	Hispanic	White	Ortho	Yes	No	No	No	No	low	inter**	No
12	31	Male	Hispanic	White	Ortho	Yes	No	No	No	No	low	high	No
*13	59	Female	Non-Hispanic	White	Ortho	Yes	Yes	No	No	No	low	low	No
*14	42	Male	Non-Hispanic	Black	Ortho	Yes	Yes	No	No	No	low	low	No
*15	40	Male	Hispanic	White	Ortho	Yes	No	No	No	No	inter**	high	No
16	58	Female	Non-Hispanic	White	Ortho	Yes	Yes	No	No	No	high	inter**	Yes
17	62	Male	Hispanic	White	Ortho	Yes	No	No	No	No	low	high	yes
18	35	Male	Non-Hispanic	White	Chest	Yes	Yes	No	No	No	high	high	Yes
19	30	Male	Non-Hispanic	White	Ortho	Yes	No	No	No	No	inter**	inter**	Yes

*No RD

**intermediate risk

Appendix B: Types, Routes, and Morphine Equivalents of Opioids

Types, routes, and IV morphine equivalents of opioids received in the emergency department (ED).

Patient	Hours in ED	fentanyl (IV) (mcg)	HM (IV) (mg)	morphine (IV) (mg)	Oxycodone (oral) (mg)	Hydrocodone (IV) (mg)	ED IVME (mg)
1	5.5	0	0	14	10	10	24mg
2	35.75	1250	0	0	15	0	132.5mg
3	13	50	0	4	0	0	4.5mg
4	7.5	0	0	0	0	10	5.7mg
5	13.75	250	0	8	0	0	5mg
6	23	0	0	12	5	0	35.5mg
7	10	75	0	4	0	0	14.5
8	13.3	150	0	0	0	0	11.5mg
9	6.5	100	0	4	10	0	15mg
10	17	175	1	6	20	0	19mg
11	24.25	150	0	6	0	10	41mg
12	8.75	125	0	0	0	0	26mg
13	3.25	100	0	0	0	0	17.5mg
14	11.5	60	0	12	0	0	18mg
15	4	100	0	0	0	0	10mg
16	5	250	1	0	5	0	35mg
17	9.8	0	0	8	0	0	8mg
18	10	75	0	2	5	0	12mg
19	9.75	175	1	4	10	0	34mg

Appendix C: Types and Routes of Medications with Sedation Properties

Types and routes of medications with sedation properties administered in the emergency department (ED).

Patient	Ketamine (IV)	Propofol (IV)	Sedation (IV)	Benzodiazepine (IV)	Gabapentin (Oral)	Trazadone (Oral)	Sedation (Oral)
1	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0
3	0	0	0	0	1	0	1
4	0	0	0	0	0	0	0
5	205	0	1	0	0	0	0
6	0	0	0	0	0	0	0
7	0	0	0	0	0	1	1
8	0	100	1	0	0	0	0
9	80	0	1	0	0	0	0
10	0	0	0	0	0	0	0
11	0	0	0	1	0	0	1
12	0	0	0	0	1	0	1
13	0	300	1	0	0	0	0
14	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0
18	180	0	1	0	0	0	0
19	0	0	0	0	0	0	0

Appendix D: Morphine Equivalents of Opioids

Types, routes, and IV morphine equivalents of opioids received on the general care floor (GCF).

Patient	fentanyl (IV) (mcg)	hydromorphone (IV) (mg)	morphine (IV) (mg)	Oxycodone (oral) (mg)	Hydrocodone (IV) (mg)	GCF IVME (mg)
1	0	0	2	5	0	4.50
2	550	0	0	0	0	55.00
3	0	0	2	0	0	2.00
4	0	0	4	0	5	6.50
5	25	0	0	10	0	7.50
6	0	0	4	5	0	6.50
7	0	0	4	0	0	4.00
8	50	0	4	5	0	11.50
9	50	0	0	0	0	5.00
10	0	0	12	30	0	27.00
11	0	0	4	0	0	4.00
12	50	0	8	5	0	15.50
13	0	0	8	0	0	8.00
14	0	0	4	10	0	9.00
15	0	0	2	10	0	7.00
16	0	0.5	0	0	0	3.75
17	75	0	0	0	10	12.50
18	0	0	2	5	0	4.50
19	0	0	4	10	0	9.00

Appendix E: Patient 1

Patient 1: Opioids and medications with sedating properties received in the *ED and on *GCF. Patient experienced respiratory depression on the GCF.

ED length of stay: 5.5 hours **Admit time: 13:00** **Admit time to RD: 131 minutes**
ED IV Morphine equivalents (IVME): 24.00mg **GCF IVME: 4.5mg**
Monitoring period: 13:00 to 19:47 **Time of RD: 15:11***, 18:39

Patient 1	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	hydrocodone	oral	5mg	once	not documented	7:46	5mg
	morphine	IV	4mg	once	not documented	9:03	4mg
	oxycodone	oral	5mg	6hrs PRN	mod-severe pain	15:10	5mg
	morphine	IV	2mg	once	not documented	16:16	2mg
	morphine	IV	2mg	4hrs PRN	severe pain	20:34	2mg
	morphine	IV	2mg	4hrs PRN	severe pain	0:49	2mg
	morphine	IV	2mg	4hrs PRN	severe pain	5:48	2mg
	oxycodone	oral	5mg	6hr PRN	mod-severe pain	10:42	5mg
	morphine	IV	2mg	4hrs PRN	severe pain	10:42	2mg
General care floor							
	oxycodone	oral	5mg	6hr PRN	mod-severe pain	16:58	5mg
	morphine	IV	2mg	4hr PRN	severe pain	18:27	2mg

*emergency department
**general care floor
***RD prior to IV opioid administration on GCF

Appendix F: Patient 2

Patient 2: Opioids and medications with sedating properties received in the ED and on the GCF. Patient experienced respiratory depression on the GCF.

ED length of stay: 35.75 hours **Admit time: 15:42** **Admit time to RD: 226 minutes**
ED IVME: 132.5mg **GCF IVME: 55.00mg**

Monitoring period: 15:42 to 22:20 **Time of RD: 19:28 and 22:13**

Patient 2	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	fentanyl	PCA	10mcg	10min PRN	not documented	8:30	250mcg*
	fentanyl	PCA	10mcg	10min PRN	not documented	15:15	250mcg*
	oxycodone	oral	5mg	4hrs PRN	mod-severe pain	15:24	5mg
	fentanyl	PCA	10mcg	10min PRN	not documented	19:23	250mcg*
	fentanyl	PCA	10mcg	10min PRN	not documented	7:20	250mcg*
	oxycodone	oral	5mg	4hrs PRN	mod-severe pain	8:48	5mg
	fentanyl	PCA	10mcg	10min PRN	not documented	9:07	250mcg*
	oxycodone	oral	5mg	4hrs PRN	mod-severe pain	14:23	5mg
General care floor							
	fentanyl	PCA	10mcg	10min PRN	not documented	15:42	250mcg*
	fentanyl	PCA	10mcg	10min PRN	not documented	19:24	250mcg*
	fentanyl	PCA	10mcg	10min PRN	not documented	20:29	50mcg**

*fentanyl 250mcg/25mL syringe; fentanyl 250mcg total dose self-administered

**fentanyl 250mcg/25mL syringe: fentanyl 50mcg self-administered during monitoring period

Appendix G: Patient 3

Patient 3: Opioids and medications with sedating properties received in the ED and GCF. Patient experienced respiratory depression on the GCF.

ED length of stay: 13 hours **Admit time: 17:24** **Admit time to RD: 16.00 minutes**
ED IVME: 67.5mg **GCF IVME: 2mg**
Monitoring period: 17:25 to 00:26 **Time of RD: 18:50, 21:43**

Patient 3	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	fentanyl	IV	25mcg	once	not documented	17:21	25mcg
	fentanyl	IV	25mcg	once	not documented	19:52	25mcg
	morphine	PCA	2mg	hr/continuous	not documented	23:13	30mg*
	morphine	PCA	2mg	10min PRN	not documented	23:13	
	morphine	PCA	2mg	hr/continuous	not documented	7:46	30mg
	morphine	PCA	2mg	10min PRN	not documented	7:46	
	morphine	PCA	2mg	hr/continuous	not documented	17:13	0.5mg
	morphine	PCA	2mg	10min PRN	not documented	17:13	2mg
General care floor							
	morphine	PCA	2mg	hr/continous	not documented	17:25	0.5mg**
	morphine	PCA	2mg	10min PRN	not documented	17:25	2mg**
	duloxetine DR	oral	30mg	daily	not documented	18:06	30mg
	sertraline	oral	50mg	daily	not documented	18:06	50mg
	gabapentin	oral	300mg	daily	not documented	18:07	300mg
	morphine	IV	2-4mg	3hrs PRN	***BTP	21:35	2mg
	amitripyline	oral	10mg	nightly	not documented	21:40	10mg

*morphine 30mg/30mL PCA syringe; morphine 30mg total dose self-administered
*morphine 30mg/30mL complete morphine 30mg PCA self-administered
**demand doses of morphine PCA self-administered ***breakthrough pain

Appendix H: Patient 4

Patient 4: Opioids and medications with sedating properties received in the ED and GCF. Patient experienced respiratory depression on the GCF.

ED length of stay: 7.5 hours **Admit time: 17:24** **Admit time to RD: 14.00 minutes**
ED IVME: 5.00mg **GCF IVME: 6.50mg**

Monitoring period: 18:36 to 01:23 **Time of RD: 18:50**

Patient 4	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	hydrocodone	oral	10mg	once	not documented	12:51	10mg
General care floor							
	morphine	IV	2mg	4hrs PRN	mod-severe pain	1838	2mg
	hydrocodone	oral	5mg	once	severe pain	21:30	5mg
	morphine	IV	2mg	4hrs PRN	mod-severe pain	0:11	2mg

Appendix I: Patient 5

Patient 5: Opioids and medications with sedating properties received in the ED and GCF. Patient experienced respiratory depression on the general care floor.

ED length of stay: hours **Admit time: 20:12** **Admit time to RD: 49.00 minutes**
ED IVME: 35.30mg **GCF IVME: 4mg**

Monitoring period: 20:12 to 02:33 **Time of RD: 21:01* and 01:21**

Patient 5	Medication	Route	Dose	Frequency	Rationale	Date Given	Time Given	Dose Received
Emergency department								
	fentanyl	IV	75mcg	once	not documented	8/16/19	6:18	75mcg
	fentanyl	IV	75mcg	once	not documented	8/16/19	9:44	75mcg
	morphine	IV	8mg	once	not documented	8/16/19	10:13	8mg
	oxycodone	oral	5mg	4hrs PRN	mod-severe pain	8/16/19	16:22	5mg
	ketamine	IV	205mg	once	sedation	8/16/19	14:22	205mg
	fentanyl	IV	25-50mcg	1hr PRN	BTP**	8/16/19	17:08	50mcg
	fentanyl	IV	25-50mcg	1hr PRN	BTP**	8/16/19	19:56	50mcg
General care floor								
	oxycodone	oral	5mg	4hrs PRN	mod-severe pain	8/16/19	23:33	5mg
	fentanyl	IV	25-50mg	1hr PRN	BTP**	8/17/19	1:18	25mcg

*RD prior to IV opioid administration on GCF
**breakthrough pain

Appendix J: Patient 6

Patient 6: Opioids and medications with sedating properties received in the ED and GCF. Patient did not experience respiratory depression on the GCF.

ED length of stay: 23.00 **Admit time: 21:40** **Admit time to RD: NA**
ED IVME: 14.50mg **GCF IVME: 8.50mg**

Monitoring period: 21:40 to 04:05 **Time of RD: NA**

Patient 6	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	morphine	IV	4mg	once	not documented	5:07	4mg
	morphine	IV	2mg	4hrs PRN	mod-severe pain	8:25	2mg
	oxycodone	oral	5mg	6hrs PRN	mod-severe pain	9:48	5mg
	morphine	IV	2mg	4hrs PRN	mod-severe pain	12:58	2mg
	morphine	IV	2-4mg	5min PRN	pain	16:46	2mg
	morphine	IV	2-4mg	5min PRN	pain	16:52	2mg
General care floor							
	morphine	IV	2mg	4hrs PRN	mod-severe pain	21:52	2mg
	oxycodone	oral	5mg	6hrs PRN	mod-severe pain	0:41	5mg
	morphine	IV	2mg	4hrs PRN	mod-severe pain	2:19	2mg
	morphine	IV	2mg	4hrs PRN	mod-severe pain	4:05	2mg

Appendix K: Patient 7

Patient 7: Opioids and medications with sedating properties received in the ED and GCF. Patient experienced respiratory depression on the GCF.

ED length of stay: 10 hours **Admit time: 21:56** **Admit time to RD: 99 minutes**
ED IVME: 11.50mg **GCF IVME: 4.00mg**

Monitoring period: 21:56 to 05:12 **Time of RD: 23:35***

Patient 7	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	cyclobenzaprine	oral	10mg	3 times daily	spasms	20:35	10mg
	fentanyl	IV	75mcg	30min PRN	pain	13:55	75mcg
	morphine	IV	2mg	4hrs PRN	mod-severe pain	17:36	2mg
	trazadone	oral	50mg	nightly	not documented	20:36	50mg
	morphine	IV	2mg	4hrs PRN	mod-severe pain	21:41	2mg
General care floor							
	morphine	IV	2mg	once	not documented	0:13	2mg
	morphine	IV	2mg	4hrs PRN	mod-severe pain	4:09	2mg

*RD prior to IV opioid administration on GCF

Appendix L: Patient 8

Patient 8: Opioids and medications with sedating properties received in the ED and GCF. This patient experienced respiratory depression on the GCF.

ED length of stay: 13.30 hours **Admit time: 21:56** **Admit time to RD: 372 minutes**
ED IVME: 15.00mg **GCF IVME: 11.50mg**
Monitoring period: 16:21 to 05:58 **Time of RD: 22:33**

Patient 8	Medication	Route	Dose	Frequency	Rationale	Date Given	Time Given	Dose Received
Emergency department								
	fentanyl	IV	25-50mcg	2hrs PRN	Pain	9/13/19	14:25	50mcg
	propofol	IV	100mg	once	not documented	9/13/19	1456	100mg
	fentanyl	IV	75mcg	once	not documented	9/13/19	14:58	75mcg
	fentanyl	IV	25mcg	once	not documented	9/13/19	15:05	25mcg
General care floor								
	fentanyl	IV	25-50mcg	2hrs PRN	Pain	9/13/19	18:11	50mcg
	oxycodone	oral	5-10mg	4hrs PRN	severe pain	9/13/19	19:06	5mg
	morphine	IV	204mg	6hrs PRN	BTP*	9/13/19	22:02	4mg

*breakthrough pain

Appendix M: Patient 9

Patient 9: Opioids and medications with sedating properties received in the ED and GCF. Patient experienced respiratory depression on the GCF.

ED length of stay: 6.5 hours **Admit time: 23:26** **Admit time to RD: 10 minutes**
ED IVME: 19.00 **GCF IVME: 5.0mg**

Monitoring period: 23:26 to 05:42 **Time of RD: 22:36***

Patient 9	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	fentanyl	IV	50mcg	Code Trauma	not documented	16:53	50mcg
	morphine	IV	4mg	once	not documented	17:36	4mg
	ketamine	IV	80mg	once	sedation	18:57	80mg
	fentanyl	IV	25-50mcg	1hrPRN	*BTP	19:36	50mcg
	oxycodone	oral	10mg	4hrsPRN	mod-severe pain	20:59	10mg
General care floor							
	fentanyl	IV	25-50mcg	1hrPRN	*BTP	4:27	50mcg

*RD prior to IV opioid administration on GCF
**breakthrough pain

Appendix N: Patient 10

Patient 10: Opioids and medications with sedating properties received in the ED and GCF. This patient experienced respiratory depression on the GCF.

ED length of stay: 17 hours **Admit time: 23:26** **Admit time to RD: 67 minutes**
ED IVME: 41.00mg **GCF IVME: 27.00mg**

Monitoring period: 01:37 to 14:25 **Time of RD: 02:44**

Patient 10	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	fentanyl	IV	75mcg	PRN*	Trauma Code	8:27	75mcg
	hydromorphone	IV	1mg	once	not documented	9:29	1mg
	morphine	IV	2-4mg	4hrs PRN	*BTP	11:16	4mg
	fentanyl	IV	100mcg	PRN*	Trauma	11:29	100mcg
	oxycodone	oral	5-10mg	4hrs PRN	severe pain	12:52	10mg
	oxycodone	oral	5-10mg	4hrs PRN	severe pain	17:51	10mg
	morphine	IV	2-4mg	4hrs PRN	*BTP	19:03	2mg
General care floor							
	morphine	IV	2-4mg	4hrs PRN	*BTP	1:36	4mg
	oxycodone	oral	5-10mg	4hrs PRN	severe pain	3:02	10mg
	oxycodone	oral	5-10mg	4hrs PRN	severe pain	7:51	10mg
	morphine	IV	2-4mg	4hrs PRN	*BTP	9:09	4mg
	morphine	IV	4mg	2hrs PRN	*BTP	11:26	4mg
	oxycodone	oral	5-10mg	4hrs PRN	severe pain	12:43	10mg

*breakthrough pain

Appendix O: Patient 11

Patient 11: Opioids and medications with sedating properties received in the ED and GCF. This patient did not experience respiratory depression on the GCF.

ED length of stay: 24.24 hours **Admit time: 5:34** **Admit time to RD: No RD**
ED IVME: 26.00mg **GCF IVME: 4.00mg**

Monitoring period: 05:34 to 14:54 **Time of RD: No RD**

Patient 11	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	fentanyl	IV	75mcg	once	not documented	21:59	75mcg
	hydrocodone	oral	10mg	once	not documented	22:08	10mg
	lorazepam	oral	0.5mg	once	not documented	22:51	0.5mg
	fentanyl	IV	75mcg	once	not documented	23:15	75mcg
	morphine	IV	2-4mg	2hrs PRN	mod-severe pain	1:44	4mg
	morphine	IV	2-4mg	2hrs PRN	mod-severe pain	4:53	2mg
General care floor							
	morphine	IV	2-4mg	2hrs PRN	mod-severe pain	12:00	4mg

Appendix P: Patient 12

Patient 12: Opioids and medications with sedating properties received in the ED and GCF. This patient experienced respiratory depression on the GCF.

ED length of stay: 8.75 hours **Admit time: 16:12** **Admit time to RD: 339 minutes**
ED IVME: 17.50mg **GCF IVME: 15.50mg**

Monitoring period: 16:12 to 23:32 **Time of RD: 21:51**

Patient 12	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	fentanyl	IV	75mcg	once	not documented	6:55	75mcg
	fentanyl	IV	25-50mcg	2hrs PRN	mod-severe pain	12:32	50mcg
	gabapentin	oral	100mg	3 times daily	not documented	12:37	100mg
	oxycodone	oral	5-10mg	4hrs PRN	mod-severe pain	14:46	10mg
General care floor							
	morphine	IV	2-4mg	2hrs PRN	*BTP	18:29	4mg
	fentanyl	IV	25-50-mcg	2hrs PRN	mod-severe pain	19:56	50mcg
	morphine	IV	2-4mg	2hrs PRN	*BTP	21:21	4mg
	oxycodone	oral	5-10mg	4hrs PRN	mod-severe pain	22:39	10mg
	gabapentin	oral	100mg	3 times daily	not documented	22:40	100mg

*breakthrough pain

Appendix Q: Patient 13

Patient 13: Opioids and medications with sedating properties received in the ED and GCF. This patient did not experience respiratory depression on the GCF.

ED length of stay: 3.25 hours **Admit time: 22:03** **Admit time to RD: No RD event**
ED IVME: 10.00mg **GCF IVME: 8.00mg**

Monitoring period: 22:03 to 05:59 **Time of RD: No RD event**

Patient 13	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	fentanyl	IV	50mcg	30min PRN	pain	17:09	50mcg
	fentanyl	IV	50mcg	30min PRN	pain	19:35	50mcg
	propofol	IV	50mg	once	sedation	19:40	50mg
	propofol	IV	250mg	once	sedation	19:48	250mg
General care floor							
	morphine	IV	2-4mg	4hrs PRN	*BTP	22:20	4mg
	morphine	IV	2-4mg	4hrs PRN	*BTP	4:39	4mg

*breakthrough pain

Appendix R: Patient 14

Patient 14: Opioids and medications with sedating properties received in the ED and GCF. This patient did not experience respiratory depression on the GCF.

ED length of stay: 11.50 hours **Admit time: 20:21** **Admit time to RD: No RD event**
ED IVME: 18.00mg **GCF IVME: 9.00mg**

Monitoring period: 20:21 to 02:18 **Time of RD: No RD event**

Patient 14	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	morphine	IV	6mg	once	not documented	14:27	6mg
	fentanyl	IV	60mg	once	not documented	10:13	60mg
	morphine	IV	6mg	once	not documented	17:05	6mg
General care floor							
	morphine	IV	2-4mg	4hrs PRN	severe pain	20:29	4mg
	oxycodone	oral	5-10mg	6hrs PRN	mod-severe pain	23:28	10mg

Appendix S: Patient 15

Patient 15: Opioids and medications with sedating properties received in the ED and GCF. This patient did not experience respiratory depression on the GCF.

ED length of stay: 4.00 hours **Admit time: 20:21** **Admit time to RD: No RD event**
ED IVME: 10.00mg **GCF IVME: 7.00mg**

Monitoring period: 20:48 to 05:25 **Time of RD: No RD event**

Patient 15	Medication	Route	Dose	Frequency	Rationale	Date Given	Time Given	Dose Received
Emergency department								
	fentanyl	IV	50mcg	30min PRN	pain	10/10/19	17:25	50mcg
	fentanyl	IV	50mcg	30min PRN	pain	10/10/19	18:45	50mcg
General care floor	oxycodone	oral	5mg	6hrs PRN	mod-severe pain	10/10/19	20:50	5mg
	morphine	IV	2mg	4hrs PRN	mod-severe pain	10/11/19	1:08	2mg
	oxycodone	oral	5mg	6hrs PRN	mod-severe pain	10/11/19	5:05	5mg

Appendix T: Patient 16

Patient 16: Opioids and medications with sedating properties received in the ED and GCF. This patient experienced respiratory depression on the GCF.

ED length of stay: 4.00 hours **Admit time: 0:544** **Admit time to RD: 117 minutes**
ED IVME: 8.00mg **GCF IVME: 3.75mg**

Monitoring period: 05:44 to 09:16 **Time of RD: *07:41 and 09:08**

Patient 16	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	fentanyl	IV	50mcg	once	not documented	12:58	50mcg
	fentanyl	IV	50mcg	once	not documented	13:38	50mcg
	fentanyl	IV	50mcg	3hrs PRN	pain	14:55	50mcg
	fentanyl	IV	50mcg	3hrs PRN	pain	17:23	50mg
	fentanyl	IV	50mcg	3hrs PRN	pain	19:28	50mcg
	oxycodone	oral	5mg	6hrs PRN	mod-severe pain	21:05	5mg
	hydromorphone	IV	0.5-1mg	3hrs PRN	*BTP	21:06	1mg
General care floor							
	hydromorphone	IV	0.5-1mg	3hrs PRN	*BTP	8:47	0.5mg

*RD prior to IV opioid administration on GCF
*breakthrough pain

Appendix U: Patient 17

Patient 17: Opioids and medications with sedating properties received in the ED and GCF. This patient experienced respiratory depression on the GCF.

ED length of stay: 9.8 hours **Admit time: 07:37** **Admit time to RD: 291 minutes**
ED IVME: 8mg **GCF IVME: 12.50mg**

Monitoring period: 07:37 to 15:06 **Time of RD: 12:28**

Patient 17	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	morphine	IV	4mg	once	not documented	22:25	4mg
	morphine	IV	4mg	once	not documented	5:07	4mg
General care floor	fentanyl	IV	50-75mcg	2hrs PRN	pain	9:29	75mcg
	hydrocodone	oral	5-10mg	6hrs PRN	mod-severe pain	12:41	10mg

Appendix V: Patient 18

Patient 18: Opioids and medications with sedating properties received in the ED and GCF. This patient experienced respiratory depression on the GCF.

ED length of stay: 10 hours **Admit time: 16:56** **Admit time to RD: 17:46**
ED IVME: 12.00mg **GCF IVME: 4.50mg**

Monitoring period: 16:56 to 22:56
Time of RD: 17:50, 19:54, 22:12

Patient 18	Medication	Route	Dose	Frequency	Rationale	Time Given	Dose Received
Emergency department							
	fentanyl	IV	75mcg	Trauma	not documented	7:15	75mcg
	ketamine	IV	180mg	Trauma	procedure	7:24	180mg
	morphine	IV	2mg	4hrs PRN	*BTP	9:45	2mg
	oxycodone	oral	5mg	4hrs PRN	mod-severe pain	10:43	5mg
General care floor	morphine	IV	2mg	4hrs PRN	*BTP	17:27	2mg
	oxycodone	oral	5mg	4hrs PRN	mod-severe pain	19:15	5mg

*breakthrough pain

Appendix W: Patient 19

Patient 19: Opioids and medications with sedating properties received in the ED and GCF. This patient experienced respiratory depression on the GCF.

ED length of stay: 9.75 hours **Admit time: 21:34** **Admit time to RD: 71 minutes**
ED IVME: 34.00mg **GCF IVME: 9.00mg**

Monitoring period: 21:34 to 05:40 **Time of RD: 22:12*, 22:45, 23:07, 00:17**

Patient 19	Medication	Route	Dose	Frequency	Rationale	Date Given	Time Given	Dose Received
Emergency department								
	fentanyl	IV	*Trauma	PRN	not documented	10/18/19	16:05	100mcg
	morphine	IV	4mg	once	not documented	10/18/19	16:44	4mg
	hydromorphone	IV	1mg	once	not documented	10/18/19	17:51	1mg
	fentanyl	IV	75mcg	once	not documented	10/18/19	18:57	75mcg
	oxycodone	oral	10mg	4hrs PRN	mod-severe pain	10/18/19	20:35	10mg
General care floor								
	morphine	IV	2-4mg	4hrs PRN	BTP**	10/18/19	22:22	4mg
	gabapentin	oral	600mg	nightly	not documented	10/18/19	23:40	600mg
	oxycodone	oral	5-10mg	4hrs PRN	mod-severe pain	10/19/19	5:37	10mg

*RD prior to IV opioid administration on GCF
**breakthrough pain

Appendix X: Summary of Respiratory Depression Events

Summary of respiratory depression events

Patient	Low ETCO2	Low ETCO2 (n=5)	Low RR	Low RR (N=5)	Low SPO2	Low SPO2 (N=9)	Hypopena (N=12)	Hypoxemia (N=12)	Apnea > 30 seconds	Apnea (N=12)
1	1280	Yes	0	No	0	No	No	No	120	Yes
2	0	No	0	No	2980	Yes	Yes	Yes	20	Yes
3	0	No	1540	Yes	3280	Yes	Yes	Yes	400	Yes
4	0	No	5680	Yes	2819	Yes	Yes	Yes	0	No
5	0	No	0	No	35162	Yes	Yes	Yes	20	Yes
6	0	No	0	No	0	No	No	No	0	No
7	0	No	0	No	420	Yes	Yes	Yes	0	No
8	0	No	0	No	20	Yes	Yes	Yes	20	Yes
9	1299	Yes	6560	Yes	5220	Yes	Yes	Yes	380	Yes
10	100	Yes	0	No	340	Yes	Yes	Yes	80	Yes
11	0	No	0	No	0	No	No	No	0	No
12	0	No	80	Yes	0	No	No	No	60	Yes
13	0	No	0	No	0	No	No	No	0	No
14	0	No	0	No	0	No	No	No	0	No
15	0	No	0	No	0	No	No	No	0	No
16	0	No	0	No	20	Yes	Yes	Yes	40	Yes
17	280	Yes	0	No	0	No	Yes	Yes	60	Yes
18	0	No	439	Yes	0	No	Yes	Yes	60	Yes
19	0	No	0	No	840	No	Yes	Yes	240	Yes

Appendix Y: Intravenous Opioid Equivalents

Intravenous opioid equivalents received in the emergency department and the general care floor.

Patient	ED IVME (mg)	GCF IVME (mg)	GCF RD (No=0 Yes=1)
1	24.00	4.50	1
2	132.50	55.00	1
3	67.50	2.00	1
4	5.00	6.50	1
5	35.30	4.00	1
6	14.50	8.50	0
7	11.50	4.00	1
8	15.00	27.00	1
9	19.00	5.00	1
10	41.00	27.00	1
11	26.00	8.00	0
12	17.50	9.00	1
13	10.00	7.00	0
14	18.00	7.00	1
15	10.00	7.00	0
16	35.00	3.75	1
17	8.00	12.50	1
18	12.00	4.50	1
19	34.00	9.00	1

Appendix Z: Time Between Admission to GCF and RD Occurrence

Time between admission to GCF and RD occurrence as measured in minutes.

Patient	Admit Time	RD Time	Admit to RD (minutes)
1	13:00	15:11	131
2	15:42	19:28	226
3	17:24	17:40	16
4	18:36	18:50	14
5	20:12	21:01	49
6	21:40	*	*
7	21:56	23:35	99
8	16:21	22:33	372
9	23:26	23:36	10
10	1:37	2:44	67
11	5:34	*	*
12	16:12	21:51	339
13	22:03	*	*
14	20:21	*	*
15	22:18	*	*
16	5:44	7:41	117
17	7:37	12:28	291
18	16:56	22:12	316
19	21:34	22:45	71

*No respiratory depression

Appendix AA: Oxygen Saturation Events

Oxygen saturation (SPO_2) events the number and percentage of high SPO_2, low SpO_2, desaturation, and hypoxemia.

Hypoxemia [(0=No and 1=Yes)]

Patient Number	SpO_2 High	SpO_2 High	SpO_2 Low	SpO_2 Low	DESATUATION EVENT > 4 % for less than 4 min	Hypoxemia (N=10)
1	0	0.00%	0	0.00%	6060	0
2	0	0.00%	2980	0.62%	2201	1
3	0	0.00%	3280	0.65%	1698	1
4	0	0.00%	2819	0.58%	5803	1
5	0	0.00%	35162	7.72%	3778	1
6	0	0.00%	0	0.00%	1240	0
7	0	0.00%	420	0.08%	1580	1
8	0	0.00%	20	0.00%	1080	1
9	0	0.00%	5220	1.16%	8561	1
10	0	0.00%	340	0.04%	1320	1
11	0	0.00%	0	0.00%	240	0
12	0	0.00%	0	0.00%	940	0
13	0	0.00%	0	0.00%	160	0
14	0	0.00%	0	0.00%	880	0
15	0	0.00%	0	0.00%	261	0
16	0	0.00%	20	0.01%	860	1
17	0	0.00%	0	0.00%	640	0
18	0	0.00%	0	0.00%	3302	0
19	0	0.00%	840	0.17%	2479	1

Appendix BB: Respiratory Rate and Depression Events

Respiratory rate and respiratory depression events (No=0, Yes=1)

Patient	RR High	RR Low	Hypopnea (N=5)	No Breath	Respiratory Depression Event (N=14)
1	2640	0	0	1960	1
2	60	0	0	0	1
3	0	1540	1	50720	1
4	0	5680	1	0	1
5	0	0	0	1272	1
6	0	0	0	0	0
7	0	0	0	0	1
8	0	0	0	11640	1
9	0	6560	1	0	1
10	0	0	0	0	1
11	360	0	0	0	0
12	0	80	1	0	1
13	0	0	0	0	0
14	80	0	0	0	0
15	0	0	0	0	0
16	0	0	0	15160	1
17	0	0	0	0	1
18	0	439	1	1140	1
19	0	0	0	53339	1

Appendix CC: Incidence and Time of Apnea Events

The incidence and time of apnea events in seconds (No=0, Yes=1)

Patient	APNEA EVENT > than 10 seconds	APNEA EVENT 10-19 seconds	APNEA EVENT 20-29 seconds	APNEA EVENT >30 seconds	APNEA EVENTS (N=12)
1	240	80	40	120	1
2	180	160	0	20	1
3	3260	2460	400	400	1
4	140	120	20	0	0
5	80	40	20	20	1
6	319	319	0	0	0
7	20	20	0	0	0
8	400	360	20	20	1
9	701	180	141	380	1
10	780	680	20	80	1
11	321	301	20	0	0
12	1600	1380	160	60	1
13	0	0	0	0	0
14	60	40	20	0	0
15	100	100	0	0	0
16	40	0	0	40	1
17	200	140	0	60	1
18	1140	960	120	60	1
19	500	160	100	240	1

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