RETROSPECTIVE APPLICATION OF THE PRODIGY RISK PREDICTION MODEL IN PATIENTS EXPERIENCING POSTOPERATIVE ADVERSE RESPIRATORY EVENTS

by

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Dedication & Acknowledgement

Dedication

To our families and loved ones, you gave us the strength and support to help achieve our goals and aspirations. Without you, this project would not have been completed. To our friends, you gave us joy and laughter when we faced difficult times. Thank you for being present and giving us emotional support. To those friends and family who are no longer with us today, thank you for sharing your courage and wisdom. Without you, we would not be the men we are today.

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Abstract

Background: Postoperative respiratory depression is a major contributor to patient morbidity and mortality. Historically, postoperative opioid-induced respiratory depression (POIRD) has been shown to be difficult to predict, leading to increased patient morbidity and mortality. The *Prediction of Opioid-Induced Respiratory Depression in Patients Monitored by Capnography* (PRODIGY) model is a novel risk prediction tool. It has been shown to be quick and effective for predicting opioid-induced respiratory depression and utilizes five patient characteristics in its scoring system (age, sex, previous opioid use, sleep disordered breathing, and chronic heart failure).

Purpose: This quality improvement project aimed to determine if the PRODIGY risk prediction model would be a valid predictor of POIRD in the adult, inpatient, postsurgical population at a single, large, academic medical center. Additionally, this project aimed to identify timeframes for naloxone administration as well as surgical specialties where naloxone was used more frequently in the postoperative period.

Methods: This quality improvement project consisted of a retrospective chart review of 47 adult, inpatient, postsurgical patients who had received parenteral opioids and naloxone after anesthesia was concluded. PRODIGY risk scores were determined and then subsequently categorized as low-, intermediate-, or high-risk for developing POIRD. Timeframes for naloxone administration were analyzed and a median time was established. Surgical specialties were grouped and analyzed for increased frequency of naloxone administration.

Results: After application of the PRODIGY risk prediction model, 31 (66%) of patients were categorized as high-risk for developing POIRD. Additionally, 42 (89.4%) of 47 total patients were categorized as intermediate- or high-risk for developing POIRD. Only 5 (10.6%) patients were categorized as low-risk. The median timeframe when naloxone was administered after conclusion of anesthesia was 23.4 hours. The surgical specialties with increased incidence of naloxone administration (>10%) were cardiac surgery (17%), general surgery (14.9%), orthopedic surgery (14.9%), endoscopy (14.9%), vascular surgery (10.6%), and neuro-spine surgery (10.6%).

Conclusion: The PRODIGY risk prediction model was effective in predicting POIRD in adult, inpatient, postsurgical patients who had received parenteral opioids and naloxone following anesthesia at this single, large, academic medical center. This risk prediction tool may be utilized preoperatively to identify high-risk patients, establish opioid-sparing anesthetic techniques, and implement appropriate postoperative monitoring (continuous pulse oximetry and capnography). Confirmation that the median timeframe for naloxone administration was within 24 hours after surgery further supports the use of continuous monitoring in high-risk patients for at least 24 hours after anesthesia is concluded.

Key Words: *PRODIGY, opioid-induced respiratory depression, naloxone, postoperative*

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Retrospective Application of the PRODIGY Risk Prediction Model in Patients Experiencing Postoperative Adverse Respiratory Events

The assessment of individuals who are at high-risk for postoperative opioid-induced respiratory depression (POIRD) has been found to promote patient safety and quality patient-centered care outcomes in the postoperative period (Khanna et al, 2020). Patients who have been identified as high-risk for POIRD may require more comprehensive monitoring than postoperative patients who are stable and require standard basic monitoring. Comprehensive monitoring in comparison to standard basic monitoring can include capnography monitoring in addition to continuous pulse-oximetry and frequent vital sign assessments (Lam et al., 2017). Therefore, having an assessment tool that accurately identifies patients who are at high-risk for POIRD is essential in this population. Thus, the purpose of this quality improvement project is to determine if the *Prediction of Opioid-Induced Respiratory Depression in Patients Monitored by Capnography* (PRODIGY) model, developed by Khanna and colleagues (2020), is an accurate risk prediction tool for POIRD. Khanna and colleagues (2020) identified five major risk factors (age, sex, previous opioid use, sleep disordered breathing, and chronic heart failure) used to classify patients as high-risk for developing opioid induced respiratory depression. The PRODIGY risk prediction tool was used in this quality improvement project to determine if postsurgical patients who had suffered an adverse respiratory event would have been categorized as high-risk for developing POIRD. If the PRODIGY risk prediction tool is found to accurately assess individuals at risk for POIRD, evidence to support using this tool with all patient's undergoing surgery is defensible. In addition, identifying patients as high-risk will allow the healthcare team to institute continuous monitoring early in the postoperative period – thus, enhancing patient safety and helping to identify adverse respiratory events before they occur.

Background & Significance

Postoperative respiratory depression is a common cause of morbidity and mortality. According to a publication by the Agency for Healthcare Research and Quality (AHRQ) in 2018, postoperative respiratory failure is regarded as the fourth most common patient safety event. A national registry comprising 13,086 acute respiratory events in US hospitals revealed that in-hospital mortality following an event is roughly 40%, with an estimated incidence of 44,551 events in the year 2012 (Anderson et al., 2016a). A 2015 analysis of 357 closed claims indicated 77% of patients who experienced POIRD either died or suffered severe brain damage. Of the closed claims events analyzed, 97% were deemed preventable with improved monitoring and response (Lee et al., 2015).

Although patients are continuously monitored in the post anesthesia care unit (PACU) following surgery, most patients admitted to the hospital are placed on the general medical unit and undergo monitoring at periodic intervals, typically every four to six hours. Though these patients have been deemed stable and safe for discharge to a general unit, serious cardiac and respiratory events still occur. In the closed claims analysis of postoperative opioid-induced respiratory depression, 13% of events occurred within two hours after discharge from the PACU to the general floor (Lee et al., 2015). The literature indicates postoperative respiratory compromise can exist well beyond the PACU and is most likely to occur in the first 24 hours postoperatively (Ramachandran et al., 2011; Lee et al., 2015; Weingarten et al., 2017; Taylor et al., 2005). During this time, patients are increasingly vulnerable to respiratory depression due to the convergence of multiple factors such as the effects of general anesthesia, optimization of opioid analgesics, sedating antiemetics, and sleep deprivation (Lee et al., 2015). Findings from research studies indicate patients suffering an arrest have abnormal vital signs (heart rate,

respiratory rate, or blood pressure) up to four hours prior (Anderson et al., 2016b). Unfortunately, conventional intermittent monitoring on the general floor may miss significant respiratory depression and hypoxemia. Sun et al. (2015) implemented continuous pulse oximetry monitoring with patients on a general floor following noncardiac surgery and found that 90% of hypoxemic episodes (oxygen saturation less than 90%) lasting longer than one hour were missed by standard monitoring. Interestingly, 21% of patients continuously monitored following non-cardiac surgery experienced hypoxia (oxygen saturation less than 90%) for at least ten minutes per hour for the entire duration of monitoring. Though not all events lead to respiratory arrest, postoperative hypoxemia can negatively impact wound healing and promote other serious complications including brain dysfunction, dysrhythmias, and myocardial ischemia (Sun et al., 2015).

Reported incidences of postoperative opioid-induced respiratory depression (POIRD) range from 0.1 to 23.7%, however, the true incidence is likely unknown based on a lack of a standard definition and varying study measures (Gupta et al., 2018b). In the studies examined by Gupta et al. (2018b), opioid-induced respiratory depression had a wide range of definitions from the use of naloxone, to varying degrees and times for oxygen desaturation and respiratory rates, to sedation and airway obstruction. A recent study by Khanna et al. (2020) demonstrated that when patients receiving opioids are continuously monitored for a median of 24 hours by pulse oximetry and capnography on the general floor, 46% of patients had validated respiratory depression episodes defined by the following: a respiratory rate less than or equal to five breaths for greater than or equal to three minutes, oxygen saturation less than 85% for greater than or equal to three minutes, or an end-tidal carbon dioxide level of less than 15 mmHg or greater than 60 mmHg for greater than or equal to three minutes.

The continued practice of intermittent monitoring on the general medical unit is likely to miss large numbers of opioid-induced respiratory depressive events that have the potential to lead to catastrophic outcomes (Sun et al., 2015; Khanna et al., 2020; Lee et al., 2015). Continuous monitoring of pulse oximetry and capnography on general units has been proposed to enhance early recognition and intervention before serious compromise occurs (Gupta & Edwards, 2018a; Lee, Posner & Domino, 2018). In addition to enhanced monitoring, a better understanding of patient characteristics and risk factors for developing POIRD is necessary. The recent study by Khanna et al. (2020) examined 48 risk factors, which provide a novel risk prediction model (PRODIGY risk prediction model) for opioid-induced respiratory depression. After identifying high-risk individuals utilizing the PRODIGY risk prediction model, healthcare providers can strategize, appropriately triage, and institute continuous monitoring—enhancing the detection of respiratory compromise and patient safety.

The purpose of this quality improvement project was to conduct an electronic medical record retrospective review of surgical patients at a Midwest hospital who had required naloxone administration to identify if the novel PRODIGY risk prediction model would have identified these patients as high-risk, thus indicating the need for continuous monitoring following surgery. According to Khanna and colleagues (2020), utilization of enhanced monitoring in high-risk individuals could lead to early recognition of respiratory compromise and limit the progression of respiratory depression, therefore preventing serious complications. This work aligns with the recommendations of the *Joint Commission Sentinel Event Alert Issue 49: Safe Use of Opioids in Hospitals*, which proposed identification of patients at high risk for opioid-induced respiratory depression (The Joint Commission, 2012). In addition, the purpose of this project aligns with the *Anesthesia Patient Safety Foundation's* perioperative patient safety priority of "preventing,

detecting, and mitigating clinical deterioration in the perioperative period" (Anesthesia Patient Safety Foundation, n.d.).

Finally, this Midwest hospital has recently instituted an "obstructive sleep apnea pilot program" that utilizes electronic medical records to identify patients at high-risk of obstructive sleep apnea. Following notification that the patient is high-risk for obstructive sleep apnea, the health care team institutes continuous pulse-oximetry monitoring. This project theory is similar; however, it is directed specifically at postoperative surgical patients receiving parenteral opioids. Moreover, the PRODIGY risk prediction model incorporates obstructive sleep apnea into its scoring, allowing for a possible merger of the "obstructive sleep apnea pilot program" with this study, pending results of this quality improvement project.

Literature Review

The aim of this literature review was established with the goal of identifying risk factors associated with patients developing POIRD. The online databases of CINAHL (Cumulative Index to Nursing and Allied Health Literature) Complete and PubMed (MEDLINE) were accessed, and specific key words were used to identify eligible research. Key words entered into the databases included "postoperative", "opioid-induced", "respiratory depression", "risk factors", and "contributing factors". Peer-reviewed research that focused on POIRD and was published between 2015 and June 2020 were included in the initial query. Additionally, in order for research to be deemed eligible in the initial review process, it must have been written in the English language, involved adult patients only (eighteen years of age or older), and identified patient characteristics and risk factors associated with POIRD. For the purpose of this integrative review, literature that investigated relationships associated with postoperative respiratory depression *not* related to opioid administration was excluded. In addition to the

database investigation, reference lists of identified literature from the initial search was analyzed. Studies found within reference lists that met the previously mentioned inclusion criteria were selected for initial review and screening.

Once all the available literature was identified, these authors utilized the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram to systematically screen, review, and choose literature that was to be used in this integrative review (Moher et al., 2009). Duplicate records were identified and then subsequently removed. The remaining literature was screened and assessed in order to identify records that did not meet the inclusion criteria. Research that did not meet the specific inclusion criteria was removed. The abstracts of the remaining eligible studies were analyzed by both authors. After abstract review, articles and studies that were deemed ineligible for this integrative review were excluded and reasons for removal were recorded. The remaining records were thoroughly analyzed and read by both authors. If literature still did not satisfy the aim of this review, a discussion between authors occurred, the record was removed, and the reasons for removal were recorded. The remaining records were included in this literature review.

The literature utilized in this review was then synthesized and evaluated by both authors. A total of 249 records were identified using the previously mentioned search criteria. PubMed produced 200 records, CINAHL yielded 47 records, and two records were identified after review of reference lists. After initial review, four duplicate studies were identified and removed from the available list of literature. Abstract and title review was then carried out on the remaining 245 studies. 223 records were removed due to previously mentioned exclusion criteria. Both authors then completed full-text review of the remaining 22 studies. Nine studies were removed after full-text review and thorough discussion between both authors (see Figure 1).

In total, thirteen studies were included in this literature review and pertinent study information was recorded within Appendix A of this paper. Retrospective analysis was used in ten studies (Brant et al., 2018; Weingarten, 2016; Weingarten et al., 2015; Khelemsky et al., 2015; Oderda et al., 2019; Yung et al., 2016; Gonzalez et al., 2016; Lee et al., 2015; Menendez et al., 2015; & Rosenfeld et al., 2016), Jungquist et al. (2017) and Weingarten et al. (2017) presented a literature review, and Gupta et al. (2018b) presented a systematic review. Over 50 risk factors were identified for POIRD in all thirteen studies. For this review, the most prevalent risk factors were identified and recorded in Appendix B. A total of thirteen risk factors appeared most often in the literature, with seven of these factors appearing in five or more studies. According to the literature, the most prevalent risk factors for the development of POIRD was a history of obstructive sleep apnea (OSA), advanced age (referred to as elderly and above the age of 55), having an American Society of Anesthesiologist (ASA) score of three or more, presence of obesity (BMI > 27 kg/m^2), presence of significant comorbidities, concomitant sedative use, and the use of large opioid doses.

Other major risk factors contributing to the development of POIRD identified by the literature was female gender (Brant et al., 2018; Gupta et al., 2018b; & Khelemsky et al., 2015), presence of renal disease (Brant et al, 2018; Gupta et al., 2018b; and Oderda et al., 2019), general surgery (Gupta et al., 2018b; Oderda et al., 2019; & Rosenfeld et al., 2016), opioid dependence or nonopioid drug abuse (Gupta et al., 2018b; Lee et al., 2015; & Menendez et al., 2015), use of patient controlled analgesia (PCA) or epidural infusion (Gupta et al, 2018b; Jungquist et al., 2017; & Rosenfeld et al., 2016), and orthopedic surgery (Gupta et al., 2018b & Rosenfeld et al., 2016). For a complete analysis of risk factors identified for POIRD, refer to Appendix B.

One major consensus among the studies analyzed was the timing of respiratory events in the postoperative period. Seven studies noted the critical time period of 24 hours after surgery as being the most prevalent time for respiratory depression episodes to occur (Gupta et al., 2018b; Jungquist et al., 2017; Weingarten et al., 2017; Khelemsky et al., 2015; Weingarten et al., 2015; Lee et al., 2015; & Rosenfeld et al., 2016).

In summary, one can conclude that there is little consensus regarding what patient characteristics and risk factors place patients at an increased risk of developing POIRD. More than 50 independent risk factors and patient characteristics were identified predisposing patients to developing POIRD. Of these, 13 were identified in multiple sources of literature, and seven were identified in five or more studies. POIRD can lead to devastating negative patient outcomes, with respiratory arrest and death being the most feared. Clinicians must be able to reliably predict which patients are at higher risk for developing POIRD, so that catastrophic outcomes can be avoided and prevented. In addition, preventing POIRD and the associated negative patient outcomes may improve hospital costs associated with adverse postoperative respiratory events. This review revealed a large gap within the literature, with regards to the lack of standardized tools that can help clinicians predict which patients are at increased risk for developing POIRD. Fortunately, Khanna and colleagues (2020) solved this problem with the development of the PRODIGY risk prediction model which utilized five patient risk factors (age, sex, previous opioid use, sleep disordered breathing, and chronic heart failure). These five risk factors are quite similar to the results found in this literature review, further strengthening the findings of the PRODIGY trial. Utilizing this model, practitioners can identify which post-surgical patients will be at the highest risk for developing POIRD. This is an exciting development as this is the first known risk prediction model developed regarding risk factors for

developing opioid induced respiratory depression. The PIs proposed, that by using the PRODIGY risk prediction model, we would be able to retrospectively identify patients who have suffered an adverse respiratory event and be able to categorize them as high-risk for developing POIRD. The risk prediction model could then be utilized for future post-surgical patients. Categorizing patients as high-risk will allow the healthcare team to institute continuous monitoring early in the postoperative period– enhancing patient safety and helping to identify adverse respiratory events before catastrophe occurs.

Evidence-Based Practice Framework

The evidence-based practice framework used in this project involves the Iowa Model. The Iowa Model utilizes evidence-based practice to promote excellence in health care. Using a series of feedback loops, multiphase change can be made in order to improve patient care and promote clinical advancement with the utilization of evidence-based practice (Melnyk & Fineout-Overholt, 2019). This project follows the steps outlined in The Iowa Model (see Figure 2). First, issues and opportunities were identified. Postoperative opioid induced respiratory depression was identified as being a major patient safety issue and new evidence (PRODIGY trial) was identified. A researchable problem was identified, which was determined to be a priority, and a team was formed. All pertinent evidence and literature were synthesized and the quality and strength of the science was evaluated. The PIs determined that sufficient evidence existed, and the project continued onto the next phase and evolved over time. Once data had been collected, the PIs were able to synthesize the results into a formal recommendation and evaluate if findings were appropriate for adoption into actual practice. Finally, the PIs disseminated results to key stakeholders.

If issues arose during any step of this project, re-evaluation took place, and the problems were addressed (feedback loops). This feature of The Iowa Model allowed this project to evolve over time. Furthermore, clinical indicators that were not previously hypothesized and/or emerging trends that were not anticipated were easily integrated into this project. Using The Iowa Model, we were able to systematically implement our findings into clinical practice, improving patient safety, and promoting healthcare excellence.

Project Design & Methodology

A retrospective electronic medical record review design was used in this study. After identification of patients who had suffered opioid-induced respiratory depression postoperatively, defined by naloxone administration, the PIs applied the PRODIGY risk prediction model. Following retrospective scoring of patients meeting inclusion criteria (see participants/population below), the PIs determined if the PRODIGY risk prediction model appropriately categorized patients requiring naloxone for opioid reversal as high-risk.

Setting

The project took place at a large Midwest hospital. The retrospective electronic medical record review was performed on post-surgical patients who met inclusion criteria (see participants/sample section below).

Key Personnel & Stakeholders

Key personnel involved with this project included the Midwest hospital's Nursing Research Review Board and Research Institute; the PIs, project Chair, and CRNA mentor. Key stakeholders include patients, anesthesia providers, healthcare providers in the PACU and general medical units, and nursing leadership.

Participants/Sample

The sample included in this project were adult, postsurgical patients who received parenteral opioids. Inclusion criteria was the following: (1) adults aged 18 years or older, (2) inpatients who have had surgery during the current admission to the hospital, and (3) patients who have received parenteral opioids within 24 hours from the "respiratory event" (naloxone administration). Exclusion criteria was the following: patients who have not had surgery during the admission where naloxone was administered. The Midwest hospital Research Institute members assisted in obtaining the sample by applying the inclusion criteria to the electronic medical record database from April 1, 2021, to February 28, 2022.

Project Intervention Plan

The following steps and procedures were performed to complete this quality improvement project. A formal presentation that included the background and significance of opioid-induced respiratory depression, the newly published PRODIGY risk prediction model, and the use of this model to enhance patient safety was given to the Nursing Research Review Board. The evidence-based practice and quality application was then reviewed by the Nursing Research Review Board. The project was deemed quality improvement, thus exempt from IRB approval. In lieu of IRB approval, a Data De-Identification Attestation form (see Appendix C) was completed and access to patient data was granted. The Research Institute was then provided the data collection tool (see below). Patient data was collected using the collection tool from April 1, 2021, to February 28, 2022. Patient data was screened to identify those meeting inclusion criteria. The PRODIGY risk prediction model was then applied to the sample to generate a PRODIGY risk score. This score was then used to categorize each patient as low-, intermediate-, or high-risk for developing POIRD. Finally, descriptive statistics were completed

and analyzed. Recommendations were then made and a plan for further research and interventions was discussed.

Data Collection Instruments

The following is the data collection tool that was utilized by the Research Institute and applied to patient medical records from April 1, 2021, to February 28, 2022:

Data to be Obtained		
Naloxone Administration	Yes	No
Surgery During Current Admission	Yes	No
Parenteral (IV) Opioids Administered w/in 24 hours of Narcan	Yes	No
Age (in years) • < 60 • 60-69 • 70-79 • > 80		
Sex • Male • Female		
Previous Opioid Use • Opioid documented as "home medication" prior to surgery	Yes	No
Sleep Disordered Breathing • OSA Diagnosis or • Use of CPAP	Yes	No
Chronic HF Diagnosis	Yes	No
Date/Time of Event • Determine time from anesthesia stop documentation to naloxone administration		
Surgery Performed		

Procedures for Project Implementation

The PI's presented the findings related to the effectiveness of the PRODIGY risk prediction model to the Midwest hospital's Nursing Research Review Board and to members of the healthcare community during the DNP Project Dissemination Day. Recommendations were made related to the use of the PRODIGY risk prediction tool, incorporation of the tool into the

electronic medical record system (EPIC), and use of automated scoring for triggering enhanced post-operative monitoring and decisions regarding perioperative analgesic strategies.

Potential Barriers

Prior to project implementation, potential barriers were identified. Certain components of the STOP-BANG questionnaire through retrospective chart review was determined to be difficult to extract. The STOP-BANG scoring systems allows practitioners to assess for and diagnose obstructive sleep apnea (OSA). Due to the retrospective nature of this project, it was difficult to extract a STOP-BANG score from patient records. Therefore, the PI's excluded the STOP-BANG questionnaire and utilized documented OSA diagnosis and/or documentation of home CPAP use for the diagnosis of sleep disordered breathing for PRODIGY scoring. This was in accordance with the other qualifiers for "sleep disordered breathing" as defined in the PRODIGY trial. Additionally, the attitudes of the stakeholders regarding the usefulness, ease, and resources to implement the PRODIGY score into an electronic warning in EPIC and to utilize continuous monitoring in those at high-risk of respiratory depression will likely be a barrier to implementation moving forward. Cost of continuous monitoring devices could also lead to implementation barriers.

Ethical Considerations & Risks

To ensure this research was conducted ethically and risks to patients were minimized, the Data De-Identification Attestation form was strictly adhered to. Additionally, all de-identified patient data was electronically stored within the hospital's secure data storage system.

Benefits & Outcomes

The expected benefits following conclusion and dissemination of this quality improvement project are the following: improved safety of high-risk postoperative patients at

this Midwest hospital; decreased resource utilization and cost through limiting un-planned intensive care unit transfers and rapid response activation; and enhanced utilization of multimodal opioid-sparing analgesia techniques. Furthermore, our primary outcomes are to increase awareness of risk factors for development of opioid-induced respiratory depression and to recommend an electronic "best-practice advisory" and/or policy based on a patient's PRODIGY score to promote enhanced monitoring of high-risk patients. Secondary outcomes were to determine the time frame postoperatively when naloxone is most likely to be administered and to determine if opioid-induced respiratory depression is more common in patients undergoing certain types of surgery.

Timeline

The following was this quality improvement project timeline:

Task	8/2020	9/2020	12/2020	8/2021	3/2022	3/2022	4/2022	6/2022	6/2022
Literature Review of POIRD	X								
DNP Project Area of Interest Presentation & Approval (Appendix A)		X							
DNP Project Proposal & Approval			X						
Nursing Research Review Board Application & Presentation				X					
Data De-Identification Attestation Form Signature					X				
Data Collection						X			
Statistical Analysis							X		
Final Report Completion								X	
Dissemination of DNP Project									X

Resources: Proposed Budget and Funding

The resources needed for this quality improvement project included access to the medical record database, provided by the Research Institute. The budget was zero dollars to perform this

retrospective chart review and statistical analysis. A funding plan was not applicable to this study.

Project Implementation

The Research Institute completed data collection for patients undergoing surgery between April 1, 2021, and February 28, 2022. The patient data was screened to identify those meeting inclusion criteria. The PRODIGY risk prediction model was then applied to the sample to generate a PRODIGY risk score. The PRODIGY risk score was determined by five variables: age, sex, previous opioid use, sleep disordered breathing, and chronic heart failure diagnosis. Each variable is assigned a specific point value to obtain a total PRODIGY score that is used to determine level of risk for opioid induced respiratory depression. This score was then used to categorize each patient as low, intermediate, or high-risk for developing POIRD (see Table 1). Finally, descriptive statistics were completed and analyzed.

Table 1
PRODIGY Scoring Table

Risk Factors	Scoring Criteria	Points
Patient Age (years)	<60	= 0 points
	Age 60-69	= 8 points
	Age 70-79	= 12 points
	Age ≥ 80	= 16 points
Sex	Male	= 8 points
	Female	= 0 points
Previous Opioid Use*	Opioid Naïve	= 3 points
	Previous Opioid Use	= 0 points
Sleep Disordered Breathing**	Yes	= 5 points
	No	= 0 points
Chronic Heart Failure	Yes	= 7 points
	No	= 0 points

Note. Low-risk → < 8 points, Intermediate-risk 8-14 points, High-risk → ≥ 15 points
*Opioid Naïve is defined as "no opioids listed in home medications"
**Sleep Disordered breathing is defined as "patient history of OSA or use of CPAP"

Results

From April 1, 2021, to February 28, 2022, there were 46,528 surgical procedures completed. The data collection tool was applied to extract relevant data from these 46,528 procedures. Inclusion criteria was applied to the generated data and a sample size of 47 patients was obtained. Amongst patients receiving naloxone, PRODIGY risk factor variable frequencies were examined (see Table 2).

Table 2
PRODIGY Variable Frequency Table

	Frequency	Percent
Age		
• < 60 years	11	23.4%
• 60-69 years	14	29.8%
• 70-79 years	16	34.0%
• > 80 years	6	12.8%
Sex		
• Female	28	59.6%
• Male	19	40.4%
Previous Opioid Use		
• Yes	9	19.1%
• No	38	80.9%
Sleep Disordered Breathing		
• Yes	9	19.1%
• No	38	80.9%
Chronic HF Diagnosis		
• Yes	13	27.7%
• No	34	72.3%

The PRODIGY risk score was determined for each patient. Five patients (10.6%) were identified as low-risk, 11 patients (23.4%) were identified as intermediate-risk, and 31 patients (66%) were identified as high-risk for developing opioid-induced respiratory depression (Table 3). The minimum PRODIGY score for patients receiving naloxone was 0, while the maximum score was 39 (Table 4). The mean PRODIGY score for patients receiving naloxone was 17.1 and is considered high-risk for developing opioid-induced respiratory depression (Table 4).

Table 3
PRODIGY Risk Scores

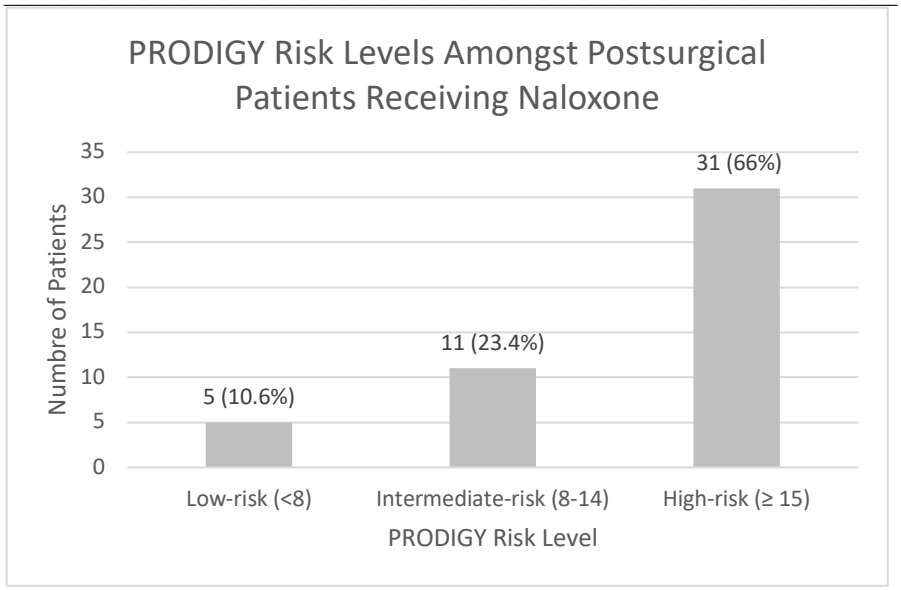

Table 4
PRODIGY Score Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Prodigy Score	47	0.0	39.0	17.1	192.5

The time frame from the anesthesia stop time to naloxone administration was also examined. The minimum time to naloxone administration was 1.4 hours, while the maximum time was 850.1 hours (see Table 5). The median time to naloxone administration was 23.4 hours (see Table 5).

Table 5
Time to Naloxone Descriptive Statistics

	N	Minimum (hours)	Maximum (hours)	Mean (hours)	Median (hours)	Std. Deviation (hours)
Time to Naloxone	47	1.4	850.1	111.3	23.4	192.5

Surgery type and naloxone administration were examined in the form of frequencies. The surgery types involved with greater than 10% of naloxone administrations included: cardiac surgery (17%), general surgery (14.9%), orthopedic surgery (14.9%), endoscopy (14.9%), vascular surgery (10.6%), and neuro-spine surgery (10.6%) (Table 6).

Table 6
Surgery Type Frequency Table

	Frequency	Percent
General Surgery	7	14.9%
Neuro-Spine	5	10.6%
Urology	1	2.1%
Orthopedics	7	14.9%
Endoscopy	7	14.9%
Thoracic	2	4.3%
Electrophysiology	3	6.4%
Neurosurgery	1	2.1%
Ear Nose & Throat (ENT)	1	2.1%
Cardiac	8	17.0%
Vascular	5	10.6%

Discussion

The results clearly demonstrate effectiveness of the PRODIGY risk prediction model in identifying patients at risk of opioid-induced respiratory depression. Of the sample population requiring naloxone, a majority of patients (66%) were deemed-high risk for development of opioid-induced respiratory depression. Additionally, the mean PRODIGY score for our sample was 17.1, which corresponds to the high-risk category (15 or greater points). Appropriate separation between participants scoring in the low-, intermediate-, and high-risk categories was demonstrated (low-risk: 5 patients; intermediate-risk: 11 patients; high-risk: 31 patients). As a result of these findings, the PRODIGY score has been deemed an effective predictor of opioid-induced respiratory depression within this sample of adult inpatients receiving parenteral opioids.

The median time from anesthesia stop documentation (end of the anesthesia encounter and patient care transfer to post-operative nursing care) to naloxone administration was 23.4 hours. Similar results in the literature also found the first 24 hours after surgery as the most prevalent time for respiratory depression episodes to occur (Gupta et al., 2018b; Jungquist et al., 2017; Weingarten et al., 2017; Khelemsky et al., 2015; Weingarten et al., 2015; Lee et al., 2015; & Rosenfeld et al., 2016).

Within our sample of patients receiving naloxone, cardiac surgery was the most prevalent surgical type. Other highly prevalent types of surgery included general surgery, orthopedic, endoscopy, vascular, and neuro-spine. These findings, other than endoscopy, mirror the existing literature regarding types of procedures associated with an increased risk of postoperative opioid-induced respiratory depression (Gupta et al., 2018b; Jungquist et al., 2017; Odera et al., 2019; & Rosenfeld et al., 2016). The increased prevalence of endoscopic procedures associated with naloxone requirement at this single institution provides an interesting opportunity for further investigation or root cause analysis in the future.

Another interesting finding was the higher prevalence of females requiring naloxone compared to males despite a male being scored as "higher-risk" (8 points vs. 0 points). Further investigation into this finding by examining a larger sample may be warranted.

Limitations

Multiple limitations of the study exist because of methodology and sampling challenges. Due to the retrospective nature of the project, certain data components were difficult or impossible to obtain. These include: "confirmation of the STOP questions" in the STOP-BANG questionnaire for qualification of sleep disordered breathing; and determination of "no use of opioids in the past medication history" for qualification of opioid naïve. These challenges were

circumvented by excluding the “confirmation of the STOP questions” qualifier for sleep disordered breathing and relying on the other two qualifiers (OSA diagnosis or use of CPAP) for determination within this section of the PRODIGY score. Additionally, “opioid in home medication documentation” was utilized in place of “opioids listed in the past medication history”. These retrospective data collection challenges may have led to lower PRODIGY scores by excluding potential qualifiers in these sections of the model.

Additionally, due to the retrospective design, naloxone administration was used as the indicator of respiratory depression. Although no standard definition of “opioid-induced respiratory depression” exists in the literature, naloxone administration has consistently been used as a measure. However, this differs from the definition of respiratory depression used to develop the PRODIGY model. Moreover, this methodology assumed naloxone was administered for its FDA labeled indication, complete or partial reversal of opioid depression (including respiratory depression), not off label use such as opioid-induced pruritus. As a result, there is potential that study participants may have been included who were not experiencing opioid-induced respiratory depression.

Other limitations involve the narrow inclusion criteria that involved only surgical inpatients, who received naloxone after “anesthesia stop” documentation, and parenteral opioids within 24 hours of naloxone administration. As a result, patients who received naloxone intraoperatively, those who were medical (non-surgical), and those receiving oral opioids were excluded from the study. This limitation restricts the application of the findings to only adult, inpatient, surgical patients, receiving parenteral opioids.

Lastly, although data was extracted on 46,528 surgical procedures, the strict inclusion criteria only led to a sample size of 47 naloxone administrations. This limits the generalizability of the findings.

Recommendations

We recommend use of the PRODIGY risk prediction model preoperatively on all adult inpatients undergoing anesthesia for surgical procedures who will receive parenteral opioids at this single, large, Midwest institution. The PRODIGY risk prediction tool utilizes documented and retrievable information from the electronic medical record (evidenced by retrospective chart review). Therefore, we recommend incorporation of an automated PRODIGY score to be displayed on the pre-operative anesthesia note within the electronic medical record (EPIC). This will alert the anesthesia provider to the level of risk for development of post-operative opioid induced respiratory depression. This information can be used to create a carefully planned, analgesic strategy utilizing opioid sparring techniques and decisions related to the appropriate postoperative monitoring setting. Additionally, for this population of patients, we recommend developing up an automatic best-practice advisory to display on the patient's electronic medical record after the "anesthesia stop" documentation is recorded. The best-practice advisory will state: "Enhanced monitoring in the form of continuous pulse-oximetry and capnography is recommended for the first 24 hours postoperatively in high-risk patients." It is also recommended that a policy be developed to provide enhanced monitoring (continuous pulse oximetry and capnography) for 24 hours postoperatively for all high-risk adult inpatients who will receive parenteral opioids. These recommendations stem from the results of this quality improvement project and are echoed in literature (Gupta & Edwards, 2018a; Lee, Posner &

Domino, 2018; Gupta et al., 2018b; Jungquist et al., 2017; Weingarten et al., 2017; Khelemsky et al., 2015; Weingarten et al., 2015; Lee et al., 2015; & Rosenfeld et al., 2016).

Additionally, we recommend replication of this study utilizing the methods and data collection tool detailed above with a larger time frame for data extraction to increase sample size and to further strengthen the evidence presented. Moreover, we recommend expansion of the study utilizing the methods above to include outpatients, medical (non-surgical patients), and patients receiving oral opioids to determine if the PRODIGY risk prediction model has value outside the population defined in this project.

Recommendations for Sustaining Intervention

It is recommended that the following are performed to apply and sustain the recommended interventions above. First, provide education to healthcare providers about what the PRODIGY risk prediction model is and how it can be utilized to enhance patient safety for high-risk individuals. Second, provide education on capnography monitoring for detection of respiratory depression/obstruction. Third, provide education related to the newly created postoperative monitoring policies. Fourth, screen for adequate policy compliance. Lastly, perform a detailed cost-benefit analysis to provide evidence for creation of a larger number of areas capable of enhanced monitoring (general nursing floor etc.).

Implications for Practice and Career Development

The results of this study have direct and immediately applicable implications for practice. The PRODIGY risk prediction model can be utilized by a healthcare provider to score adult patients who will receive parenteral opioids to determine level of risk of opioid-induced respiratory depression. Depending on risk level, the provider can then plan for the use of non-opioid analgesic strategies to either limit the total dose of opioid needed or avoid opioid usage

altogether to lower respiratory depression risk. Moreover, the provider can plan for an appropriate monitoring location postoperatively with the capability of both continuous pulse oximetry and capnography to allow for early detection and response to respiratory depression. This study highlights the need for the healthcare provider to be able to understand and recognize five risk factors, which in combination, can result in estimation of postoperative opioid-induced respiratory depression risk. Those five risk factors include (patient age, sex, previous opioid use, sleep disordered breathing, and chronic heart failure). Additionally, health care providers need to be well educated and experienced with non-opioid analgesic modalities.

Contribution to Achieving DNP Essentials

Doctor of Nursing Practice (DNP) programs must include curriculum that helps students achieve the *Essentials* of doctoral education. Set forth by the American Association of Colleges of Nursing (AACN), these eight *DNP Essentials* outline the foundational competencies that are core to all advanced nursing practice roles (AACN, 2006). With completion of this DNP project, several *DNP Essentials* were achieved.

Essential I: Scientific Underpinnings for Practice

One core component of Essential I states that the DNP program should prepare the graduate to: use science-based theories and concepts to determine the nature and significance of health and health care delivery phenomena; describe the actions and advanced strategies to enhance, alleviate, and ameliorate health and health care delivery phenomena as appropriate; and evaluate outcomes (AACN, 2006). In addition, Essential I also states that the DNP program prepares the graduate to develop and evaluate new practice approaches based on nursing theories and theories from other disciplines (AACN, 2006). Throughout the development of this DNP project, Essential I was easily achieved. The health care phenomena of POIRD was investigated

and this project aimed to develop a recommendation that could be used clinically in order to alleviate said phenomena. Science-based and nursing-based theories were utilized extensively in development of this project.

Essential II: Organizational and Systems Leadership for Quality Improvement and Systems Thinking

DNP graduates' practice includes not only direct care but also a focus on the needs of a panel of patients, a target population, a set of populations, or a broad community (AACN, 2006). Two aspects of Essential II that were met with this project include: the DNP program prepares the graduate to ensure accountability for quality of health care and patient safety for populations with whom they work; and use advanced communication skills/processes to lead quality improvement and patient safety initiatives in health care systems (AACN, 2006). This project aimed to improve the health outcomes of future surgical patients who may be at risk for developing opioid-induced respiratory depression. Also, communication with health care system leadership was maintained throughout this entire process, further cementing our initiative for enhanced patient safety outcomes and quality improvement.

Essential VI: Interprofessional Collaboration for Improving Patient and Population Health Outcomes

DNP graduates have preparation in methods of effective team leadership and are prepared to play a central role in establishing interprofessional teams, participating in the work of the team, and assuming leadership of the team when appropriate (AACN, 2006). To improve patient and population health outcomes, DNP graduates must be prepared to: employ effective communication and collaborative skills in the development and implementation of health policy, standards of care, and/or other scholarly products; lead interprofessional teams in the analysis of

complex practice and organizational issues; and employ leadership skills with interprofessional teams to create change in health care (AACN, 2006). With the establishment of this DNP project team, interprofessional collaboration was evident throughout this entire process. Health care system leadership and other interprofessional teams (research) worked together with the DNP project team to achieve the common goal of improving patient outcomes. Additionally, this DNP project team was able to lead in the analysis of a complex practice issue (post-operative opioid-induced respiratory depression), and then develop a recommendation that may improve future patient outcomes.

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Figure 1
PRISMA Flow Diagram

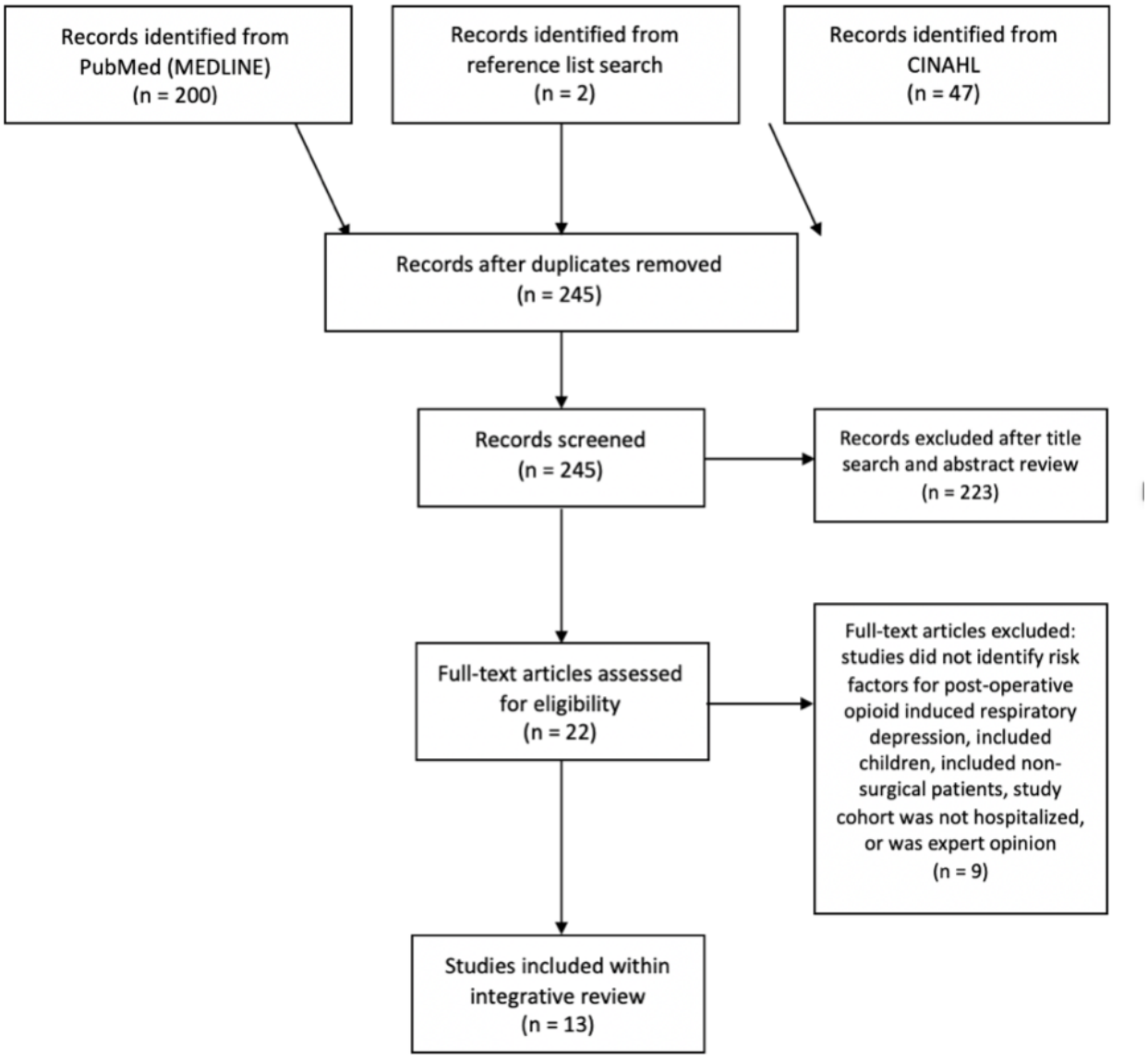
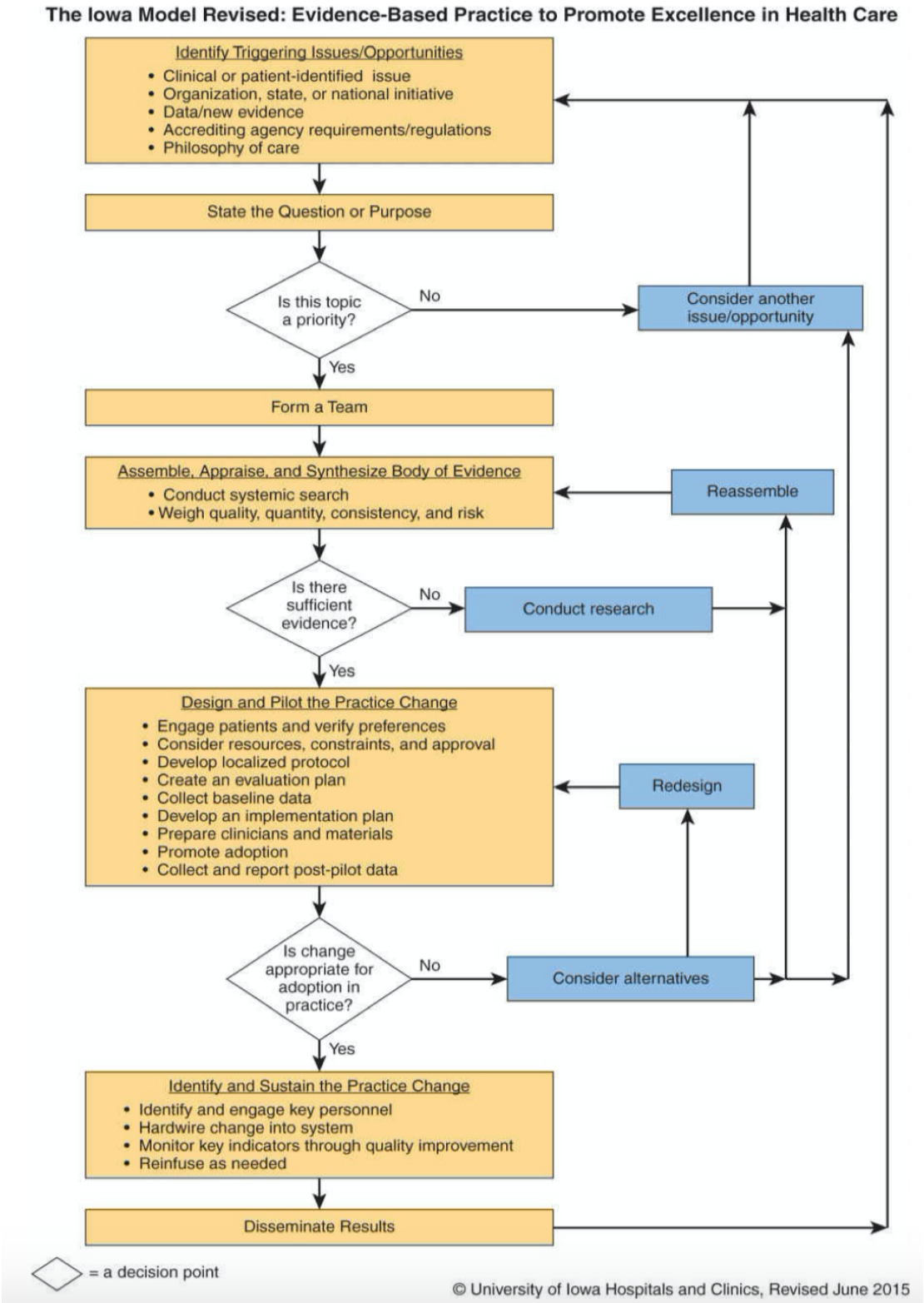


Figure 2
The Revised Iowa Model



Appendix A

Literature Review Article Summary Table

Author (date)	Study stated purpose	Subjects/setting	Research method/variables/measures	Results	Clinical Implication/ Limitations.
Brant et al., 2018	To determine demographic and clinical characteristics predictive of over sedation and potential opioid-induced respiratory depression (OIRD) in hospitalized patients.	n = 225 patients Single hospital. Inpatients who were over sedated or had respiratory depression, received opioids, receipt of opioid reversal medication that elicited response. Pts excluded: not receiving opioids, received reversal medication in ED, the OR, or in the PACU, or those who received moderate sedation for a procedure. Experimental group of "overly sedated" patients was chosen. n = 75 A control group of "not oversedated" patients was created to compare results. n = 150	Retrospective case-control study. Sample consisted of patients entered into an over sedation database, a quality-improvement tool used at a 304-bed community teaching hospital Binary logistic regression was used	Over sedation and respiratory depression was associated with the following significant predictors: • female sex • untreated sleep apnea • comorbid renal disease, • receipt of long acting oxycodone or as-needed hydromorphone	Limitations: • Operative patients who experienced OIRD were compared with non-surgical patients • Wide confidence intervals were used
Gupta et al., 2018b	To identify risk factors for opioid-induced respiratory depression in the postoperative period.	N = 13 studies 5 retrospective observational 1 retrospective cohort. 3 retrospective case-control	Systematic Review Databases searched Pubmed-Medline, EMBAse, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, PubMed, and Clinicaltrials.gov.	Risk factors for opioid induced respiratory depression: Surgical and Patient Factors: • First 24 hours after surgery • Orthopedic general and transplant surgery • Elderly > 60 years (8/13 studies) • Females (9/13 studies)	"elderly, female sex, presence of OSA, COPD, cardiac disease, diabetes mellitus, neurologic disease, renal disease, obesity, two or more comorbidities, opioid dependence, use of PCA, multiple prescribers, use of 2 or more opioids are significant risk factors for

		1 retrospective closed claim 1 prospective cohort 1 prospective observational 1 retrospective case series	Adult surgical patients only. Postoperative period. Prescribed opioids during hospital stay after surgery. Report of postoperative opioid induced respiratory depression defined by characteristics (RR < 10 and/or O2 sat < 90%, naloxone use, apnea, hypopnea, respiratory failure, excessive sedation, upper airway obstruction. Case reports, editorials, commentaries, reviews, and clinical guidelines excluded.	• ASA 3 and 4 • Opioid dependent • Genetic polymorphism • Smoking > 2 ppd. • History of psychiatric illness, substance abuse, chronic pain. Comorbidities • Diagnosed or suspected OSA • Renal disease • Pulmonary disease (COPD) • Cardiac disease (CHF, arrhythmias, CAD) • Diabetes Mellitus • Obesity (Morbid BMI >40) • Hypertension • Neurologic Disease (stroke, dementia) • Liver disease • 2 or more comorbidities • Opioid dependence Perioperative risk factors: • Concomitant use of sedatives (gabapentin, benzodiazepines) • Continuous PCA infusion • Excessive dose of opioids (>25 mg: morphine equivalents) • Multiple routes of administration • Multiple prescribers • 2 or more opioids • Inadequate monitoring • Hyperoxia • Patient on O2 during respiratory depression. • General Anesthesia > Neuraxial anesthesia • Preoperative gabapentin (>300mg) and sustained release oxycodone (> 10mg)	postoperative opioid induced respiratory depression.” Limitations: • No randomized trials available. • Varying study definitions of opioid induced respiratory depression. (RR < 8-10 per min, SpO2 < 90%, airway obstruction, over sedation, naloxone administration, and respiratory and cardiac arrest.

				• Adverse respiratory events in PACU (hypoventilation, apnea, desaturation, sedation/analgesia mismatch). • Higher dose midazolam (median 5mg; range 2-6mg) with neuraxial block. • Morphine > hydromorphone = fentanyl. Timing: • Majority were reported within 24h post-surgery either in the PACU or ward. Most within first 6h postoperatively. • Reported mostly after orthopedic surgeries. • Thoracic surgery and spinal fusion.	

Jungquist et al., 2017	To review the literature on unintended advancing sedation and respiratory depression associated with opioid administration and present evidence-based recommendations for clinical decision making and patient monitoring.		Evidence Based Practice Literature Review Article	Risk factors for Opioid-Induced respiratory depression:
				• Age > 55
				• Obesity > 30 BMI
				• OSA
				• Obesity hypoventilation syndrome
				  ○ BMI > 30
				  ○ Serum bicarbonate at or below 28 mEq/L.
				• Hx snoring
				• Excessive daytime sleepiness
				• Retrognathia
				• Neck circumference > 17.5”
				• Witnessed apneas
				• Preexisting pulmonary/cardiac disease or dysfunction (COPD, CHF)
				• Multiorgan failure (albumin < 30 g/L, BUN > 30)
					Limitations:
					• No defined search strategy.
					• Many risk factors for development of opioid induced respiratory depression taken from the 2011 “American Society for Pain Management Nursing guidelines for opioid-induced sedation and respiratory depression” by Jarzyna et al.
					• Review includes studies on hospitalized patients not only post-operative patients.

				• Dependent functional status (cannot walk 4 blocks or climb 2 sets of stairs) • Smoker (> 20 pack years) • ASA score of 3-5 • Increased opioid dose requirement and opioid dependence or chronic pain. • First 24hr of opioid therapy • Pain that is controlled after a period of poor control • Prolonged surgery (> 2hr) • Thoracic or other large incisions that may interfere with adequate ventilation. • Concomitant administration of sedating agents (benzodiazepines, or antihistamines) • Large single bolus techniques (single injection neuraxial morphine) • Continuous opioid infusion in opioid-naïve patients. (PCA with basal rate) • Naloxone administration (risk for repeated respiratory depression)	
Weingarten et al., 2017	To describe the temporal pattern of risk of postoperative opioid-induced respiratory failure.	Postoperative surgical patients who received naloxone following PACU discharge. Literature review of the existing evidence regarding the timing of opioid-induced postoperative respiratory failure	Literature review	• 2015 Mayo clinic study in postsurgical patients following PACU discharge: Majority of naloxone administrations occurred within 12hr of PACU dismissal (58%) and 88% occurred within 24hr. • Lee et al., 88% within first 24 hours; 12% within first 2 postoperative hours. • Ramachandran et al., 34% within first 6h, 81% within the first day.	Implications: • First 24 hours is most crucial in the development of respiratory depression following surgery • Continuous monitoring of high-risk patients would be useful in preventing these adverse events • Healthcare staff must be aware of the increased incidence of respiratory depression in the 24 hours following surgery

				• Taylor et al., 56% first 12h postoperative hours; 77% within the first 24h. • Risk of naloxone administration increases during the 4h following PACU discharge.	Limitations: • Only analyzed naloxone administration • Potentially missing a large majority of other adverse respiratory events that occur postoperatively
Weingarten, 2016	To identify characteristics associated with postoperative respiratory depression that required naloxone intervention during phase I recovery following general anesthesia.	Mayo Clinic, Rochester MN Single large academic medical center. A search was done and identified patients who had undergone general anesthesia and received naloxone during phase I of recovery within PACU n =413 events Patients who remained intubated following surgery were excluded from this study	Retrospective case- control Odds ratio, ± SD or median (25^{th} – 75^{th} percentiles) was used for statistical analysis Presurgical variables: • Age • Gender • BMI • ASA score • History of OSA or positive OSA screening Anesthesia and surgical variables: • Type of anesthesia • Duration • Type of anesthetic agent • Use of midazolam, ketamine, and nondepolarizing muscle relaxants (and reversal with neostigmine) • Systemic opioid analgesic use (and doses)	Risk factors shown: • ASA > III • Presence of OSA • Greater intraoperative doses of opioids. Secondary analysis: • Patients who received naloxone in phase I PACU and were discharged to medical floor, were at increased risk for developing adverse events (myocardial infarction, serious pulmonary complications, and death) Anesthesia and surgical variable: • Only greater intraoperative doses of opioids were shown to increase the chances of naloxone administration in phase I PACU • Duration or type of anesthesia, midazolam use, type of agent, or use of ketamine or nondepolarizing agents had no effect	Implications: • Patients with ASA scores of 3 or greater, have a history of OSA, and receive large intraoperative doses of opioids are at increased risk for developing respiratory events in the postoperative period • These patients may require longer recovery times within PACU or require continuous monitoring on the general medical floor Limitations: • Only used naloxone administration in PACU as means of identifying respiratory events • Large portion of events do not require naloxone and this study is missing this subset of patients • Bias with physicians deciding which patients receive naloxone can lead to skewed results and under-reporting
Khelemsky et al., 2015	To characterize the demographics of patients receiving	N = 433 naloxone administrations.	Retrospective cohort study. Single tertiary teaching institution.	Results: • Mean age of 60 years old • Mean BMI 27	Limitations: • Retrospective review.

	postoperative naloxone in the first 72 post-operative hours	Adult population who received naloxone within 72 hours of operative time.	EHR search of almost 450,000 surgical cases between 2001 and 2014 over first 72 postoperative hours at a single urban tertiary teaching institution. Adult patients and organ harvests were excluded.	• 60% were women • Mean ASA score of 3 • Average time of naloxone administration was 21hr post - surgery. • 81% were performed under general anesthesia • 7% were MAC cases • 12% were neuraxial anesthesia. "older, ASA 3, women, overweight but not obese, undergoing general anesthetic, with most cases occurring within first 24 hours"	• Not case control study to identify risk factors just describes a demographic group as well as a time interval. • Reliance upon accurate documentation. • Use of naloxone as sole marker for opioid induced respiratory depression.

Weingarten et al., 2015	To identify patient and procedural characteristics associated with postoperative respiratory depression or sedation requiring naloxone.	N = 134 naloxone administrations.	Retrospective case control design assessing patient and procedural characteristics associated with the requirement of postoperative naloxone administration. At a single large academic tertiary care facility.
			
			Adult pts who: underwent GA and received naloxone within 48 hours of dismissal from PACU or transfer from the OR to a postsurgical ward or ICU.
				Significant Risk factors:
				• OSA
				• Respiratory events in the PACU (5-fold increase for receiving naloxone after discharge)
				  ○ Hypoventilation
				  ○ Apnea
				  ○ Oxygen desaturation
				• Administration of other sedating medications.
				• Higher doses of opioids following discharge from anesthesia or PACU care.
				• Cardiovascular disease
				• Neurologic disease
				
				Majority of naloxone administrations occurred within first 12 hours (58%) and 82% occurred within first 24 hr.
				
				No correlation between dose of opioid administered during surgery and post anesthesia recovery and dose of administered naloxone.
				
				Did not find that patients who regularly used preoperative opioids to be at an
					Limitations:
					• Patients administered naloxone in the PACU were excluded.
					• Use of naloxone as the marker for opioid-induced respiratory depression. (Misses less severe cases or cases responsive to noninvasive respiratory devices).
					• Study sample involved patients who could have been administered naloxone for sedation without respiratory depression.

				increased risk for naloxone administration. BMI and pulmonary disease not significant risk factors.	
Oderda et al., 2019	To determine the frequency of adverse effects such as respiratory depression and nausea/vomiting in patients treated with intravenous opioids for acute postoperative pain and to identify potential risk factors for and clinical and economic consequences of these effects.	N= 592,127 inpatient stays. Patients were included for analysis if they were 18 years or older, had undergone at least one surgical procedure of interest (cardiothoracic/vascular, general/colorectal, obstetric/gynecologic, orthopedic, or urologic) and received at least one dose of IV morphine, hydromorphone or fentanyl for acute postoperative pain. Patients were excluded if they had pre-existing acute respiratory failure upon admission. Patients with Opioid induced respiratory depression were identified by ICD-CM codes associated with respiratory depression or administration of at least one dose of naloxone. The risk factors examined in this study were age, obesity, respiratory conditions, renal disease, sleep apnea, comorbidity	Retrospective cohort study. Data was collected from the Premier Healthcare Database to evaluate acute care hospital stays during a 1-year study period from 2015 to 2016. The database contained data from over 750 hospitals and health systems in the United States.	Results: • Combined average rate of Opioid induced respiratory depression was 11%. Incidence by procedures: • 3% for OB/GYN procedures • 7% orthopedic procedures • 8% urologic procedures • 12% GEN/Colorectal • 17% CT/VASc procedures. In CT/VASc, GEN/colorectal, and OB/GYN groups: • Age > 85 years significant risk factor In GEN/colorectal and OB/GYN • Age 65-74 years is significant risk factor. Across all surgery groups: • Obesity, respiratory conditions, sleep apnea, and overall comorbidity burden (CCI score) were significant risk factors for opioid induced respiratory depression. GYN/Colorectal and urologic groups: • Renal disease was significant risk factor. Average daily morphine milligram equivalent > 90 mg was associated with opioid induced respiratory depression. Sedative use on day 1 (CT/VASc, GEN/colorectal, and orthopedic) or after day 1 predictive factor across all surgery groups.	Limitations: • Individual patients may have been counted in more than one surgical group since analyses were conducted for individual hospital stays. • Potential for coding errors using ICD codes to identify opioid induced respiratory depression. • Naloxone could have been administered for over sedation and not respiratory depression.

		burden and IV opioid use.			

Yung et al., 2016	To evaluate patterns of naloxone use in hospitalized patients.	n = 124 episodes of naloxone administration (102 unique patients)
		
		Adult hospitalized patients who received naloxone in medical-surgical, telemetry, intermediate care, or obstetrics/gynecology units at a single academic health system. From 2014-2015.
			Retrospective data analysis.
			
			Data was extracted from the EMR. Patient demographics were identified from the history, physical exam, or physician progress notes. Naloxone administration was obtained from the EMR as well as opioids and other concomitant medications. Concomitant CNS depressant medications were included if they were administered up to 24hr prior to naloxone administration.
				Results:
				• 61% were under 65 years old.
				• 55% were female
				• 30% were obese (BMI > 30)
				• 4% had OSA
				• 20% had COPD
				• 17% had surgery within past day.
				• 52% had GFR > 60 ml/min
				• Short acting oral (53%) and IV opioids (44%) were the most commonly administered prior to a naloxone episode.
				• Most common co-administered CNS depressant medications:
				  ○ Antiepileptics 40%
				  ○ Benzodiazepines 25%
				  ○ Antihistamines 9%
				  ○ Muscle relaxants 5%
				• Gabapentin represented 70% of the antiepileptic class and was associated with 28% of naloxone administrations.
					Limitations:
					• Retrospective, relying on data documented in the EMR.
					• Use of naloxone as sole marker of respiratory depression.
					• Involved patients where naloxone was used for excessive sedation in addition to respiratory depression.
					• Did not involve the PACU.
					• Included both medical and surgical patients.
					• Small sample size.

Gonzalez et al, 2016	To evaluate the risk of potential analgesic-related complications after knee arthroscopy using a nationally representative database.	N= 16,567 Medicare patients who underwent knee arthroscopy procedures. Risk of potential analgesic complication within 30- and 90-days following surgery was assessed using ICD-9 diagnosis codes for naloxone exposure, poisoning by opioids, respiratory complications. Studied complications have been reported to be associated with opioid analgesia.	Retrospective database review using 2010-2012 Medicare claims data of patients undergoing knee arthroscopy procedures.	Risk factors for respiratory complications: • Older age (> 80 years relative to those 65-69 years) • Presence of comorbidities (Charlson score > 0) • Lower socioeconomic status • Males	Limitations: • Population selective to only knee arthroscopy procedures. • Long follow up time of 30 to 90 days postoperatively which limits application to immediate post-surgical phase. • Retrospective review reliant on proper documentation and coding.

					• Analysis was restricted to patients age 65 and older only.
Lee et al., 2015	To analyze the Anesthesia Closed Claims Project Database in order to identify clinical characteristics and management factors in malpractice claims associated with post-operative respiratory depression (POIRD). It was hypothesized that trends identified in these claims could guide or reinforce strategies to reduce the potential for opioid-related adverse outcomes.	Anesthesia Closed Claims Project database review from 1990-2009. Claims associated with acute pain management in which damaging events occurred (n = 357) 92 claims met inclusion criteria for possible, probable, or definite respiratory depression (RD)	Retrospective analysis of closed claims (n = 92) Kappa statistic used • 0.40 considered acceptable • 0.75 or higher accepted as excellent agreement beyond chance Definite RD: patient received naloxone and showed evidence of reversal of RD; patient had clear and objective signs of opioid toxicity Probable RD: respiratory rate < 8/min; somnolence; SpO2 < 90% in absence of normal baseline; pinpoint pupils; administration of high dose opioids; qualitative observation of RD that required intervention Possible RD: patient found in cardiopulmonary arrest without another identified cause (pulmonary embolism, neuraxial cardiac events) and with presumed risk for RD Variables: • Types, route of administration, and dose of opioids administered • If sedatives were administered • Number of physicians prescribing opioids and/or sedatives • Timing, monitoring, and nursing assessment • Appropriateness of anesthesia care • Patient characteristics • Gender	Three anesthesiologists independently identified contributory factors for developing RD: • Preoperative diagnosis of OSA • High risk for OSA (3 or more STOP-Bang positive) • More than one opioid modality • More than one physician prescribing opioids or nonopioids sedatives • History of chronic use of opioids • Timing between last nursing check and the RD event Definite RD = 21% of claims Probable RD = 52% of claims Possible RD = 27% of claims • 81% agreement, k = 0.690 55% of these claims resulted in death, and 22% resulted in permanent brain damage Patient factors: • Female: n = 52 (57%) • Obese (BMI of 30 or greater): n = 47 (66%) • ASA status 1 or 2: n = 55 (63%) • Mean age in years: 50± 17.7 • OSA diagnosis or high risk for OSA: 23 (25%) Medication factors: • Nonopioid sedatives were used postoperatively: n = 31 (34%)	Implications: • Obesity, ASA 1-2, OSA diagnosis or high risk for OSA, and being at least 50 years old all can be contributing factors to POIRD • Nonopioid sedatives administered concurrently with opioids can lead to increased incidences of POIRD • Having more than one physician prescribing opioids or sedatives can lead to increased incidences of POIRD • POIRD events occur most frequently within the 1st 24 hours after surgery • Somnolence is a major sign of an impending RD event • Inadequate nursing checks, combined with inadequate or no monitoring at all can lead to increased incidences of POIRD • Monitoring probably or possibly would have prevented these events from occurring 97% of the time • No specific type or route of opioid was identified as a contributing factor of RD; emphasizing the

			• BMI
			• ASA status
			• Age
			• Patient > 50 years old
			• History of chronic opioid use
			• OSA diagnosis
			• High risk of OSA
				• Most common types: phenothiazines and benzodiazepines
				• More than one physician prescribing opioids and/or sedatives: n = 30 (33%)
				• Excessive doses of opioids: n = 15 (16%)
				
				Timing, monitoring, and nursing assessment factors:
				• Timing of RD event: day of surgery - n = 81 (88%), within 2 hours of arrival on floor – n = 12 (13%)
				• Pulse oximetry used during event: n = 30 (33%)
				• No respiratory monitoring: n = 53 (58%)
				• Somnolence before event: n = 56 (62%)
				• Inadequate nursing checks (lack of quality or frequency): n = 28 (31%)
				
				Appropriateness of anesthesia care:
				• Less than appropriate: n = 36 (40%)
				• Appropriate: n = 54 (60%)
				• Would better monitoring have prevented the complication:
				  ○ Probably: n = 43 (47%)
				  ○ Possibly: n = 46 (50%)
				  ○ No: n = 3 (3%)
					fact that all opioids carry the risk
					• 55% of these claims resulted in death, and 22% resulted in permanent brain damage
					
					Limitations:
					• Dependence on data that was not designed to collect all relevant information related to RD events
					• Underreporting of factors and unidentified factors are likely
					• These claims are biased towards poorer outcomes
					• Many patients who suffer negative outcomes do not file claims. Very likely that the occurrence of RD after surgery is much higher than described in this small sample size report

Menendez et al., 2015	To characterize the relationship of opioid abuse and dependency with in-hospital postoperative	Encounter data was used using the Nationwide Inpatient Sample (NIS) for 2002 – 2011	Retrospective cross-sectional analysis using multivariate logistic regression models	• Opioid abuse and dependence: increased inpatient mortality and morbidity, respiratory failure, mechanical ventilation, failure to rescue, and pneumonia	Implications: • Patients who abuse and are dependent upon opioid or nonopioids can have an increased likelihood of

	mortality and adverse events, and to identify factors associated with high-risk opioid use in postoperative orthopedic surgery patients	Analysis considered all discharges with a primary procedure code for major orthopedic surgery Patients were excluded if their admission was the source of non-elective surgery (trauma) or if they were transferred from another acute-care hospital	Odds ratio (OD) with 95% confidence intervals (CI) were presented Demographic variables: • Age • Gender • Race/ethnicity (white, black, Hispanic, or unknown) • Primary health insurance (Medicare, Medicaid, private, uninsured, or other) Comorbidity variables: • AIDS and HIV infection • Tobacco use • Alcohol abuse and dependence • Chronic anemia • Depression • Anxiety • Nonopioid drug abuse and dependence In-hospital respiratory adverse events analyzed: • Respiratory failure • Mechanical ventilation • Pneumonia • Pulmonary embolism • Failure to rescue	• Nonopioid abuse and dependence: increased mortality, mechanical ventilation, respiratory failure, pneumonia, and failure to rescue Demographic variables associated with opioid abuse and dependence during the perioperative orthopedic setting: • Decreasing age • Male sex • Black or Hispanic race • Medicaid or Medicare insurance Comorbidities associated with opioid abuse and dependence in order of decreasing magnitude: • Nonopioid drug abuse and dependence • Alcohol abuse and dependence • AIDS/HIV infection • Depression • Tobacco use • Anxiety • Chronic anemia	developing postoperative complications • Younger, male, black or Hispanic, and publicly insured patients are more likely to abuse and be dependent on opioids. Consider these patients to be at high risk for developing adverse events postoperatively • Comorbidities can also increase the likelihood of opioid abuse and dependence. Consider these patients as high risk as well. Limitations: • Only analyzed orthopedic surgery patients who were discharged • Patients who were never discharge (deceased) were not included in this analysis • Missing a massive portion of the post-operative surgical population by only analyzing orthopedics • The analysis data was originally intended for billing purposes. Misclassification can occur

Rosenfeld et al., 2016	To quantitate the incidence of naloxone use and to assess certain patient populations at risk for opioid induced respiratory depression	268 bed tertiary care teaching hospital Patients who experienced a drug-related adverse events, or "sedation events", identified when a patient was administered opioids 24 hours or less prior to naloxone administration Analysis was limited to events on a medical, surgical, or intensive care ward Excluded were cases in the operating room, post anesthesia care unit, procedural areas, or in the emergency department for out-of-hospital overdose	Retrospective record review 445 total events were identified, 194 were excluded due to where the event occurred 251 events included in this analysis • Sedation events were identified, and the following factors were analyzed: o Age o Gender o ASA class o Medical vs. surgical admission o Incidence of patient-controlled analgesia (PCA) o Incidence of post-surgical epidural infusion • Secondary variables identified: o Post-operative time interval when the event occurred o Incidence within specific surgical specialties	Primary variables: • Mean age in years: 63.9 (SD 15.1) • Gender: 52% female • Mean BMI: 28.3 (SD 7.51) • Average ASA class: 2.9 (SD 0.67) • Patients on surgical services: 2 times more likely to receive naloxone vs. medical service (incidences of 3.8/1,000 vs. 2.0/1,000 respectively) • PCA and post-surgical epidural infusion were 3-4 times more likely to have an event (12.1 and 13.1/1,000) – most of these patients were surgical Secondary variables: • Surgical patients experienced events 61% of the time within the first 24 hours post-operatively • 22% of events occurred between 24 and 48 hours post-operatively • General surgical (including transplant) and orthopedic patients were most likely to receive naloxone (5.5 and 4.8/1,000) • Cardiothoracic and gynecologic were more likely to receive naloxone (4.0 and 3.7/1,000) • Urology and otolaryngology were least likely to receive naloxone (1/7 and 1.3/1,000)	Implications: • Surgical patients are at increased risk for opioid-induced respiratory events requiring naloxone administration vs. medical patients • Surgical specialties identified as higher risk were general surgery, orthopedic, cardiothoracic, and gynecologic • 61% of events occurred within the 1st 24 hours post-operatively • Average ASA class of 2.9 shows an increased incidence in opioid-induced respiratory depression events in patients with significant co-morbidities • Patients using PCA or epidural infusions were more likely to have an event • Patients with increased risk factors should receive more intensive monitoring post-operatively, especially within the first 24-48 hours Limitations: • Only analyzed naloxone administration events, likely missing a large proportion of events that did not include naloxone.

n = Participant number; ED = emergency department; OR = operating room; PACU = post-anesthesia care unit; OSA = obstructive sleep apnea, COPD = chronic obstructive pulmonary disease; PCA = patient-controlled analgesia; RR = respiratory rate; BMI = body mass index; ASA = American Association of Anesthesiologists; EHR = electronic health record; MAC = monitored anesthesia care; GA = general anesthesia; ICU = intensive care unit; CT/VASc = cardiothoracic/vascular; CNS = central nervous system

Appendix B

Risk Factors Associated with Postoperative Opioid Induced Respiratory Depression

	Female	OSA	Renal Disease	General Surgery	Elderly *	ASA Score †	Opioid Dependence/ Drug Abuse	Obesity ˆ	Comorbidities ¤	Concomitant Sedative Use	PCA/Epidural Infusion	Large Opioid Doses	Orthopedic Surgery
Brant et al., 2018	X	X	X										
Gupta et al., 2018	X	X	X	X	X	X	X	X	X	X	X	X	X
Jungquist et al., 2017		X			X	X		X	X	X	X	X	
Weingarten et al., 2017													
Weingarten, 2016		X				X						X	
Khelemsky et al., 2015	X				X	X		X					
Weingarten et al., 2015		X							X	X		X	
Odera et al., 2019		X	X	X	X			X	X	X		X	
Yuung et al., 2016								X		X			
Gonzalez et al., 2016					X				X				
Lee et al., 2015		X			X		X	X		X		X	
Menendez et al., 2015							X						
Rosenfeld et al., 2016				X	X	X		X			X		X

ASA = American Society of Anesthesiologists; OSA = obstructive sleep apnea; PCA = patient controlled analgesia

***** = Ages 55 and up (defined differently in studies)
† = ASA score of 3 and above
ˆ = BMI > 27 kg/m^2 (defined differently in studies)
¤ = Presence of any significant comorbidities (cardiovascular, pulmonary, hepatic, neurological, renal)

Appendix C

Beaumont Research Institute
Data De-Identification Attestation: Oakland University Student Researchers

To be completed by the Principal Investigator (PI), Student Study Author(s) and Faculty Advisor:
1. Your IRB application states data for your research will be stored in an approved SharePoint location and NO identifiers will be shared **externally**.
2. Please enter your name (s), the Beaumont study PI, your faculty advisor, and the study title in the boxes below.
3. Submit this document with your Nursing Research Application and your iMedRis submission.

Project PI (Beaumont):	**Andrea Carr**
Study Author(s):	**Brian Nixon & Austin MacDonald**
Faculty Advisor (OU)	**Karen S Dunn, PhD, RN, FGSA**
Study Title:	**Retrospective Application of the PRODIGY Risk Prediction Model in Patients Experiencing Postoperative Adverse Respiratory Events**

The list of identifiers which *must* be removed from the data are:

- Names
- Address (including all geographic subdivisions smaller than a state, including street address, city, county, precinct, zip code, and their equivalent geo-codes, except for the initial three digits of most zip codes)
- All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, and date of death. All ages over 89 and all elements of dates (including year) indicative of age over 89, except that ages over 89 may be aggregated into a single category of "age 90 or older"
- Telephone number
- Fax number
- E-mail address
- Social security number
- Medical record number
- Health plan beneficiary number
- Account number
- Certificate/license number
- Vehicle serial number
- Universal Resource Locators (URLs)
- Device Identifiers and serial numbers
- Internet Protocol (IP) address numbers
- Biometric indicators such as fingerprints or voiceprints
- Full-face photographic images and any comparable images
- Any other uniquely identifying number, characteristic, or code

Data De-Identification Attestation: My signature(s) below attests that **none** of the above listed identifiers are included in the data being used in the above named study, all data will only be stored in a Beaumont approved SharePoint location and no identifiers will be shared externally.
If I have any questions, I can contact the Privacy Department at 877-471-2422 or privacyoffice@beaumont.org

Signature of Student Study Author(s)	3-21-22 Date
Karen S Dunn Karen S Dunn Printed name and Signature of Faculty Advisor(s)	School of Nursing / OU Department

Form Date 03/17/2022