Measuring Risk of Respiratory Depression from Opioid Administration on Medical-Surgical Units

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A lthough many healthcare employees would expect the intensive care unit (ICU) to be the most likely place for a cardiorespiratory event to occur, data from a large observational study in Europe found 73% of patients who died in a postoperative cohort of 46,000 patients admitted to a medical-surgical unit (MSU) had never received care in an ICU (Bein et al., 2016). Other research has shown patients’ cardiorespiratory events can happen at any moment, with almost half occurring on an MSU. Cardiac and respiratory monitoring of patients in MSUs is minimal. Generally, patients on MSUs are assumed to be less complex and hemodynamically stable, and do not need additional or continuous monitoring (Khanna et al., 2018).

Respiratory events are a significant burden for hospitals and health systems, and mortality for admitted patients in MSUs has been shown to be remarkably high, with approximately 40% of patients experiencing an acute respiratory event (Andersen et al., 2016). Opioid administration contributes to respiratory depression and respiratory events in hospitalized patients (Jungquist et al., 2019; Jungquist et al., 2017; Lam et al., 2017; Stites et al., 2017; Weingarten et al., 2017). Data show patients who experience opioid-induced respiratory depression (OIRD) encounter a 55% longer length of stay (LOS), 36% increased risk of 30-day readmission, 47% higher cost of care, and 3.4 times the risk of inpatient mortality, making this a significant issue for hospitals and healthcare providers (Jungquist et al., 2019). The need to identify patients at risk for respiratory events is a business imperative for healthcare leaders given the increased focus on patient outcomes and the rising cost of inpatient hospitalization, which ranges from $1,889 to $2,488 per day in the United States (Ellison, 2019). While early recognition systems such as the National Early Warning System (NEWS) are valuable, the availability of monitoring tools to assist medical-surgical nurses in identifying at-risk patients could decrease the risk of serious adverse events, reduce LOS, and improve patient outcomes.

Many institutions use early warning systems to mitigate the risk of serious adverse events in patients on MSUs (Bein et al., 2016). NEWS is a popular tool developed by the National Early Warning System (NEWS) to help identify patients at risk of serious adverse events. However, studies have shown monitoring patients can lead to early detection of respiratory complications and compromise, early activation of the rapid response team, and a reduction in morbidity and mortality (Jungquist et al., 2020; Stites et al., 2017). Resources to support nursing staff in early detection of respiratory events would enable nurses to intervene earlier to improve patient outcomes.

Background

The incidence of opioid-induced respiratory depression (OIRD) was thought to be less than 1%. More recent evidence suggests the incidence of prolonged hypoxemia is greater than 20% in post-surgical patients and may be as high as 37% (Lee et al., 2015; Weingarten et al., 2017). Data show patients who experience OIRD encounter a 55% longer length of stay (LOS), 36% increased risk of 30-day readmission, 47% higher cost of care, and 3.4 times the risk of inpatient mortality, making this a significant issue for hospitals and healthcare providers (Jungquist et al., 2019). The need to identify patients at risk for respiratory events is a business imperative for healthcare leaders given the increased focus on patient outcomes and the rising cost of inpatient hospitalization, which ranges from $1,889 to $2,488 per day in the United States (Ellison, 2019). While early recognition systems such as the National Early Warning System (NEWS) are valuable, the availability of monitoring tools to assist medical-surgical nurses in identifying at-risk patients could decrease the risk of serious adverse events, reduce LOS, and improve patient outcomes.

Patients decompensate in largely unpredictable ways on medical-surgical units. A risk-assessment tool such as PRediction of Opioid-Induced Respiratory Depression in patients monitored by capnoGraphY (PRODIGY) allows nurses to assess patients at risk for respiratory depression and hasten the care provided to patients experiencing opioid-induced respiratory depression.

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National Institutes of Health in the United States and the Royal College of Physicians in Great Britain. This tool monitors physiologic parameters, such as respiratory rate, oxygen saturation, need for supplemental oxygen, temperature, systolic blood pressure, heart rate, and level of consciousness. NEWS helps staff identify clinical deterioration before a life-threatening event but may not sufficiently identify respiratory depression because of opioid administration (Downey et al., 2017).

Opioids are the standard treatment for pain in the hospital setting (Izrailtyan et al., 2018). Patients may receive opioids for postoperative pain or pain related to medical diagnosis without surgical intervention. Opioid use for pain management is a risk factor for respiratory depression (Supe et al., 2017). Data have demonstrated 58% of naloxone administrations occurred within 12 hours postoperatively and 88% occurred within 24 hours (Weingarten et al., 2017). However, 97% of these events were determined to be possibly or probably preventable (Jungquist et al., 2017; Putnam, 2016).

In 2012, The Joint Commission released Sentinel Event Alert Issue 49 regarding safe use of opioids in hospitals. This alert was released in response to a review of opioid-related events in the Sentinel Event Database that indicated wrong medication dosage was present in half the events, improper monitoring was present in nearly one-third, and other issues related to medication dosing and interactions were present in 11% of events (Lam et al., 2017; Lee et al., 2015; Sistes et al., 2017). This issue has been retired and incorporated in an R³ report for pain assessment and management standards for hospitals (The Joint Commission, 2017). Per this standard, “Hospital leadership works with its clinical staff to identify and acquire the equipment needed to monitor patients who are at high risk for adverse outcomes from opioid treatment” (p. 4). The Joint Commission, Institute for Safe Medication Practices, and Anesthesia Patient Safety Foundation have identified OIRD as a preventable occurrence; however, the guidelines to prevent OIRD to date are based mainly on consensus rather than evidence. The Joint Commission acknowledged this in the R³ report:

> The most dangerous adverse effect of opioid analgesics is respiratory depression, and monitoring for respiratory depression is sometimes appropriate. However, there are no controlled trials of monitoring to help determine the optimal strategy. Therefore, this decision should be left to the treating clinical team. The leadership team should work with clinician leaders to ensure equipment is available to monitor patients deemed highest risk (e.g., patients with sleep apnea, those receiving continuous intravenous opioids, or those on supplemental oxygen). (p. 4)

Any patient can be at risk for OIRD, defined as hypoventilation with or without oxygen desaturation (Dahan et al., 2010). Vital signs on MSUs often are monitored every 4-8 hours, creating a wide range of time in which a patient's condition could deteriorate (Khanna et al., 2018; Lee et al., 2015; Weingarten et al., 2017). In addition, evidence indicates manual oxygen saturation measurements were 6.5% higher than automatic ones, suggesting the act of performing an assessment increases patient arousal and masks opioid-induced sedation (Weingarten et al., 2017). Early signs of OIRD can be missed with the intermittent monitoring on most MSUs and rousing the patient for spot check assessments may mask respiratory depression. One study found periodic patient monitoring missed more than 90% of prolonged hypoxemia on MSUs (Sun et al., 2015). An analysis of closed anesthetic malpractice claims found the nurse had checked 42% of patients who experienced OIRD within 2 hours of the respiratory depression event. Twelve cases were discovered within 15 minutes of a nursing check, demonstrating respiratory depression can evolve rapidly (Lee et al., 2015).

Another factor that may impact how often a patient is assessed on MSUs is nursing workload. Unlike an ICU where a nurse typically cares for one to two patients, nurses on MSUs care for four or more patients at a time. A study of monitoring practices from analysis of electronic health records at eight hospitals in the United States found significant nonadherence to recommended consensus guidelines (Jungquist et al., 2016). Guidelines suggest assessments at least every 2.5 hours. In this study, 73.2% of patients were not assessed every 2.5 hours and 26.8% were evaluated every 4.5 hours, primarily due to missed sedation assessments. Documentation occurred approximately every 4 hours and more than 60% of patients were missing sedation assessments. Two hospitals demonstrated higher standards for monitoring, but they also were associated with ICUs. The other hospitals likely provided care for these patients on MSUs, which could account for the difficulty adhering to monitoring guidelines. If a nurse on an MSU had more information about a patient's risk for OIRD, interventions could be planned accordingly to improve patient safety and decrease adverse events.

**Physiological Impact of Opioid Administration**

Respiration is the physiological process that enables gas exchange. It is expedited through communication among central neural control (respiratory drive), sensory input systems, lungs, and muscles involved in respiration (Webster & Karan, 2020). The normal respiration process may be impacted when opioids are administered to patients, especially if patients also have an underlying medical condition. Following opioid administration, sedation is common (Jungquist et al., 2016; Lam et al., 2017; Putnam, 2016). Sedation can result
in hypoventilation from airway compromise and reduced respiratory drive (Jungquist et al., 2019). Hypoventilation, or decreased tidal volume, is the first symptom of respiratory depression, resulting in increased carbon dioxide and a fall in oxygen. Monitoring end tidal carbon dioxide (ETCO₂) is an early indicator of ventilation. It may be more effective than oxygen saturation, which is a later indicator, and may be confounded if the patient is on supplemental oxygen (Jungquist et al., 2017; Putnam, 2016; Stites et al., 2017).

Even if healthcare providers and nurses have a strong understanding of how respiration works, knowing when a patient may experience respiratory depression is challenging to predict. However, to improve patient safety and reduce adverse events related to OIRD, early detection is imperative. Detecting OIRD early can decrease rapid response calls and the frequency of patient transfers to higher levels of care (Stites et al., 2017). Nurses can continue to care for patients on an MSU, which may decrease hospital LOS and mitigate other complications associated with longer hospitalization (Jungquist et al., 2020).

The most common method for measuring oxygen saturation has been pulse oximetry using a probe attached to a patient’s finger. The probe detects the percentage of red blood cells saturated with oxygen; oxygen saturation should be 95%-100% while the patient is awake and greater than 92% while the patient is sleeping. Generally, interventions are needed if a patient’s oxygen saturation is below 90% for more than 15 seconds (Jungquist et al., 2019). However, in one review of malpractice suits related to OIRD, data suggested pulse oximetry monitoring alone was insufficient to prevent respiratory depression, given at least one-third of claims indicated pulse oximetry was in use at the time of the respiratory depression event (Lee et al., 2015).

Use of capnography to measure ETCO₂ is a common practice in operating rooms and recovery rooms. More recently, this practice has moved into ICU and MSU settings (Khanna et al., 2018; Stites et al., 2017). The capnography device captures the numeric partial pressure of the maximum value of exhaled breath through the nose or mouth over the previous 20 seconds. The patient wears a cannula under the nose, similar to an oxygen cannula; however, it also has a scoop that extends over the patient’s upper lip to collect data from oral exhalation in mouth breathing. The ETCO₂ numeric value is updated once a second. Normal ETCO₂ is 35-45 mm Hg; clinically relevant levels that may require intervention would be less than 30 or greater than 50 mm Hg lasting more than 15 seconds (Jungquist et al., 2019).

While pulse oximetry and capnography are essential mechanisms to use when monitoring patients for OIRD, not all MSUs have access to the needed devices. If MSUs have only a few capnography devices and not enough to monitor every patient, nurses will need to use clinical judgment to identify patients with the greatest need for the devices. By using a risk-prediction tool, nurses would have objective, validated data to identify patients most at risk for respiratory demise, ensuring they are monitored more closely and scarce resources are allocated appropriately (Jungquist et al., 2020; Jungquist et al., 2017; Khanna et al., 2020; Khanna et al., 2018).

### Risk Assessment Tool for Opioid-Induced Respiratory Depression

A recent clinical trial provided insight into the clinical presentation of OIRD in patients and use of a risk assessment tool to assist in identifying patients at high risk for OIRD (Khanna et al., 2020). Given its relevance to medical-surgical nursing care and managing respiratory depression on MSUs, a description of the trial and its outcomes as well as an explanation of the risk prediction tool are presented.

### Risk Assessment Tool Development

The PRediction of Opioid-Induced Respiratory Depression in patients monitored by capnography (PRODIGY) trial provides nurses and healthcare workers with a risk assessment tool for patients administered opioids (Khanna et al., 2020). PRODIGY was a prospective trial conducted at 16 clinical sites in the United States, Europe, and Asia (see Table 1). Before PRODIGY, a risk assessment tool was not available for MSUs to predict patient risk for OIRD. The instrument was derived using clinical patient data and continuous respiratory monitoring to detect OIRD for patients receiving parenteral opioid therapy. The trial is registered with the U.S. National Library of Medicine (NCT02811302).

Nurses frequently monitor patients’ vital signs and respiratory condition during surgery and immediately after surgery in post-anesthesia care units. However, patients may continue to be at risk for respiratory depression once admitted to MSUs after the immediate recovery period from surgery and anesthesia. Predicting post-surgical respiratory depression in patients is difficult, even with known risk factors (Khanna et al., 2018). A sample of the risk factors includes increasing age, female gender, obstructive sleep apnea, chronic pulmonary or cardiac disease, diabetes, hypertension, neurologic disease, renal disease, and obesity (Gupta et al., 2018). Analysis of patient data and respiratory condition is important, including oxygen saturation and ETCO₂ in patients receiving parenteral opioid medications, especially after surgical intervention when anesthetics have been given.

### PRODIGY Trial

The primary objective of the PRODIGY trial was to derive and validate a risk prediction tool for respiratory depression in patients receiving opioid analgesia in MSUs (Khanna et al., 2020). The tool was created by monitoring continuous pulse oximetry and capnography...
results to identify patients experiencing respiratory depression. Capnography is a validated measurement of respiratory rate and ETCO₂ that captures respiratory depression earlier than pulse oximetry, as CO₂ levels increase before oxygen decreases in response to hypoventilation from OIRD (Stites et al., 2017).

The trial included data from 1,495 patients stratified into three categories according to risk level, determined by the presence of specific characteristics (Khanna et al., 2020). Five factors were associated with risk of respiratory depression among trial patients: patient age (>60), gender (males at greater risk), previous opioid use (opioid naïve at greater risk), sleep-disordered breathing (assessed by the STOP-BANG tool or medical history of obstructive sleep apnea), and chronic heart failure (coexisting disease a greater risk). The three risk levels for respiratory depression are low, intermediate, and high. The tool allows calculation of a risk score for each patient related to personal risk factors (see Figure 1).

**Trial Results and Limitations**

The PRODIGY trial enrolled 1,495 patients, of which 114 patients were excluded due to significant protocol deviations; 1,282 patients completed the 30-day follow up (Khanna et al., 2020). Results identified the effective monitoring time as 24 hours; 655 enrolled patients had at least one index respiratory depression episode during the monitoring period. Of those, 614 were receiving opioids and participating in continuous monitoring. The PRODIGY score stratified patients into risk groups for respiratory depression, with 65% of patients in the high-risk group experiencing at least one episode of respiratory depression, 42% in the intermediate risk group, and 24% in the low-risk group (see Table 2). The majority of alarms identified during the trial were for apnea, low respiratory rate, and low ETCO₂. Low SPO₂ and low ETCO₂ had the highest specificity and apnea had the highest sensitivity. Readmission rates were not impacted by episodes of respiratory depression. However, the mean hospital stay was 3 days longer in patients with at least one episode of respiratory depression, which may impact patient outcomes and an organization’s throughput capabilities directly.

Limitations of the trial by Khanna and colleagues (2020) include lack of information regarding dose and administration route for opioids used during the trial; only the knowledge of a patient’s opioid naïveté was included in the trial. Second, capnography data were subject to artifact and patient adherence. Finally, the trial did not have a control group in place to validate the results. Despite these important limitations, the study demonstrated internal validity of a risk assessment tool for respiratory depression. External validation could not be conducted due to the unavailability of a comparable continuously monitored patient dataset. Instead, bootstrapping (a resampling technique) with stepwise variable selection was used to assess internal validity, along with cross-validation from the multiple sites, as test sets. (Khanna et al., 2020). This tool will assist nurses in assessing patients at high risk for OIRD for interventions to be implemented proactively to improve patient safety.

**Nursing Implications**

While patients commonly receive opioids on MSUs, predicting and detecting respiratory depression are difficult (Belcher et al., 2016; Lam et al., 2017). However, this need is critical to achieving better patient and organizational outcomes, and reducing risk of patient death and expensive litigation (Jungquist et al., 2019; Jungquist et al., 2020; Jungquist et al., 2017). The Joint Commission (2017)
### FIGURE 1.
PRODIGY Risk Prediction Tool

**PATIENT INFORMATION**

<table>
<thead>
<tr>
<th>Name:</th>
<th>Room:</th>
<th>Unique Identifier:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Scoring Criteria</th>
<th>Points</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Age (years)</td>
<td>Age &lt; 60</td>
<td>= 0 pts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age 60–69</td>
<td>= 8 pts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age 70–79</td>
<td>= 12 pts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age ≥ 80</td>
<td>= 16 pts</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>= 8 pts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>= 0 pts</td>
<td></td>
</tr>
<tr>
<td>Previous Opioid Use</td>
<td>Opioid naïve</td>
<td>= 3 pts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Previous opioid use</td>
<td>= 0 pts</td>
<td></td>
</tr>
<tr>
<td>Sleep Disordered Breathing (SDB)</td>
<td>Known SDB or high STOP-BANG score</td>
<td>= 5 pts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No SDB or normal STOP-BANG score</td>
<td>= 0 pts</td>
<td></td>
</tr>
<tr>
<td>Chronic Heart Failure (CHF)</td>
<td>Coexisting CHF</td>
<td>= 7 pts</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No known CHF</td>
<td>= 0 pts</td>
<td></td>
</tr>
</tbody>
</table>

**Total PRODIGY Risk Score**

**PRODIGY Risk Level**

- [ ] Low risk of respiratory depression episodes for less than 8 pts
- [ ] Intermediate risk of respiratory depression episodes for 8–14 pts
- [ ] High risk of respiratory depression episodes for 15 pts or higher

**DIRECTIONS FOR USE**

1. Enter patient name, room number, and unique identifier.
2. Score the 5 risk factors per the patient’s information. For example, a 64-year-old male, with no previous opioid use, no known SDB, but a diagnosis of CHF would get 8 pts for age (i.e., 60–69 years old), 8 pts for male, and 7 pts for coexisting CHF.
3. Total the points from risk factors. In the example above, 8 pts for male, 8 pts for age and 7 pts for CHF would be 8 + 8 + 7 = 23 pts for the PRODIGY Risk Score.1
4. Determine and check the box for the patient’s risk level by comparing the total pts for the PRODIGY Risk Score to the ranges shown for low/Intermediate/high risk.

Completed by: __________________________________________   Date: __________________________
requires hospitals to have appropriate monitoring protocols in place yet provides no standards for how patient monitoring should be executed. Human and equipment resources may be scarce on MSUs, reinforcing the need for tools to assist with patient risk identification and resource allocation.

Risk-prediction models are one way to determine monitoring needs for patients in MSUs, especially those at high risk for respiratory depression (Jungquist et al., 2017; Khanna et al., 2020; Khanna et al., 2018). The PRODIGY tool is a mechanism to predict which patients would be at higher risk for OIRD or a cardiorespiratory event (Khanna et al., 2020). It assists nurses in determining if capnography is needed for increased monitoring. Identification of high-risk patients correlated to the incidence of respiratory depression events is shown in Table 2. A device that captures capnography, such as the Capnostream™ 20p or 35 portable bedside monitor, is easy to use (Medtronic, n.d.). A specific nasal cannula records CO₂ measurements from the patient’s nose and mouth and from a pulse oximeter placed on a finger. After the CO₂ monitor is plugged into the outlet on the Capnostream, it will engage automatically and start recording. With the PRODIGY Risk Prediction Tool, nurses could identify patients at risk for OIRD earlier in their hospitalization.

The PRODIGY Risk Prediction Tool (see Figure 1) is being built to communicate with multiple electronic health records (EHRs) to facilitate incorporation of this tool into the workflow of MSUs (A. Plihal, personal communication, February 3, 2021). Given nurses’ competing priorities, it is crucial to ensure documentation of all care activities is streamlined within the EHR. Incorporating the risk prediction tool into the EHR may reduce nurses’ time in documenting care. If data from the tool are loaded into the EHR, other healthcare providers, such as physicians, physical therapists, and respiratory therapists, also will have access to the information. This information access provides more opportunities for early intervention to avoid patient deterioration.

Once a patient has been identified at risk for OIRD and a capnography device has been added to the patient’s interventions, nursing staff will be alerted quickly if a patient is decompensating (Khanna et al., 2020). An alarm would be activated to alert nursing staff when levels go above or below normal. Nurses then could intervene to correct the patient’s breathing abnormality, administer medications to reverse sedation, or correct medication dosages as needed.

Patient diagnosis, cardiorespiratory events, opioid usage, and OIRD data should be considered to determine if the PRODIGY risk prediction tool and capnography should be used in a specific MSU (Jungquist et al., 2020; Khanna et al., 2020). Using these data and sharing the PRODIGY risk prediction tool with unit-based shared governance councils provide nurses a voice in their practice related to implementing new tools and technology. Hospital leaders who offer opportunities for nurses to be engaged in institutional decision-making related to new tools and processes have superior quality of care and more positive patient experiences (Kutney-Lee et al., 2016).

**Conclusion**

Patients decompensate in a largely unpredictable way on MSUs (Jungquist et al., 2017; Khanna et al., 2018). A tool such as PRODIGY allows nurses to assess patients at risk for respiratory depression and hasten the care provided to patients experiencing OIRD. The PRODIGY tool assists in identifying which patients may benefit from continuous capnography and pulse oximetry monitoring, allowing early detection of OIRD and helping the nurse intervene with life-saving measures to prevent poor patient outcomes. Use of the tool in conjunction with continuous monitoring could reduce complications during a patient’s hospitalization, prevent transfers to higher levels of care, and avoid lengthy hospital stays. The PRODIGY tool and trial show promise in improving patient safety related to OIRD. By focusing nursing and equipment resources on patients with greatest risk, nurse leaders can prevent more OIRD events, improve patient outcomes, and decrease the burden on hospitals and health systems (Jungquist et al., 2020; Jungquist et al., 2017; Khanna et al., 2020; Khanna et al., 2018). MSN

**REFERENCES**

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