Prediction of Cardiorespiratory Compromise on Hospital General Care Units – Are We There Yet?

Ashish Khanna, MD, FCCP, FCCM
The Cleveland Clinic Lerner College of Medicine

October 4, 2018
12:00 pm – 1:00 pm PDT
Moderator

Claire Manneh
Director of Programs
CHPSO, a Division of the Hospital Quality Institute
Housekeeping Items

• All lines will be muted. Raise your hand if you wish to be unmuted.

• A copy of the slides and recording will be available within 1-3 business days

• 1 CE unit will be provided to CHPSO/CHA member hospitals who attend the entire session (12:00 pm - 1:00 pm)
  • Complete the survey by October 11, 2018
  • CE certs will be emailed within 3-5 business days
How to ask a question

You are muted by an Organizer.

Enter a question for staff
Today’s Speaker

Ashish Khanna, MD, FCCP, FCCM
*Cleveland Clinic Lerner College of Medicine*

– Staff Intensivist with the Center for Critical Care
– Assistant Professor of Anesthesiology
Prediction of Cardiorespiratory Compromise on Hospital General Care Units – Are We There Yet?

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Staff Anesthesiologist, Department of General Anesthesiology
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Disclosures

• Medtronic
• La Jolla Pharmaceuticals
Objectives

1. Understand the challenges of predicting cardiorespiratory compromise, and how to address them.
2. Learn potential benefits of continuous monitoring on the general care floor to improve outcomes.
3. Identify who to monitor as well as what and how to monitor.
4. Translate expanded knowledge of cardiorespiratory compromise into improvements in practice and patient monitoring protocols – integrate better in-patient monitoring on the general care floors.
The Scope of the Problem

Hypotension and hypoxemia on the general care floor (GCF) is common, profound, prolonged and cannot be reliably predicted [1,2]

49% of cardiac arrest on GCF had a respiratory cause – higher than ICU [3]

AHRQ rated postoperative respiratory failure as the fourth most common patient safety event [4]

Cardiorespiratory complications are the most common cause of 30-day postoperative mortality [4]

Unplanned ICU admissions may have respiratory indication in 17-47% of cases particularly postoperative pulmonary complications [5-8]
<table>
<thead>
<tr>
<th>Indicator</th>
<th>Description</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Observed Rate per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSI #2</td>
<td>Death Rate on Low-Mortality DRG’s</td>
<td>1,822</td>
<td>5,636,509</td>
<td>0.32</td>
</tr>
<tr>
<td>PSI #4</td>
<td>Death Rate among Surgical Inpatients with Serious Treatable Conditions</td>
<td>22,014</td>
<td>185,587</td>
<td>118.62</td>
</tr>
<tr>
<td></td>
<td>A: DVT</td>
<td>1,258</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>B: Pneumonia</td>
<td>6,151</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>C: Sepsis</td>
<td>5,622</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>D: Cardiac Arrest; shock</td>
<td>7,706</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>E: GI Bleed</td>
<td>1,277</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSI #11</td>
<td>Postoperative Respiratory Failure</td>
<td>22,402</td>
<td>2,228,418</td>
<td>10.05</td>
</tr>
<tr>
<td>PSI #13</td>
<td>Postoperative Sepsis</td>
<td>4,822</td>
<td>501,689</td>
<td>9.61</td>
</tr>
</tbody>
</table>
Results. There was considerable variability between studies in the criteria used for defining respiratory depression and hypotension. The overall mean (95% CI) incidence of respiratory depression of the three analgesic techniques was: 0.3 (0.1–1.3)% using requirement for naloxone as an indicator; 1.1 (0.7–1.7)% using hypoventilation as an indicator; 3.3 (1.4–7.6)% using hypercarbia as an indicator; and 17.0 (10.2–26.9)% using oxygen desaturation as an indicator. For i.m.
Respiratory Depression: Beyond the PACU, before the ICU

Ashish K. Khanna, MD
Staff Intensivist and Anesthesiologist,
Assistant Professor of Anesthesiology,
Center for Critical Care and Departments of General Anesthesiology and OUTCOMES RESEARCH,
Anesthesiology Institute, Cleveland Clinic
khannaa@ccf.org

Where should we look for postoperative hypoxemia? The PACU and ICU are two destinations where patients frequently find themselves immediately after surgery. Though many clinicians feel that respiratory depression needs to be addressed most aggressively while in these care areas, I want to argue otherwise. The PACU and ICU are extensively monitored areas. Every vital sign is tracked continuously and every deviation from the norm results in a physician or nursing intervention. While residual anesthetic gases, muscle relaxants, and narcotics may be common offenders their entire hospitalization. And soberingly and rather shockingly, 90% of serious hypoxemic episodes (saturation <90% for ≥1 full hour) were completely missed by nurses conducting routine vital sign monitoring at four-hour intervals.4

Patients continue to decompensate on the regular nursing floor, resulting in emergency medical team activation and transfer to higher levels of care. If repeated hypoxemic insults occur during these unmonitored periods, are we misplacing the emphasis in the respiratory depression story? Knowing how common
Postoperative Hypoxemia Is Common and Persistent: A Prospective Blinded Observational Study

Zhuo Sun, MD,* Daniel I. Sessler, MD,*† Jarrod E. Dalton, PhD,* PJ Devereaux, MD, PhD,†‡ Aram Shahinyan, MD,* Amanda J. Naylor, BA,* Matthew T. Hutcherson, BS,* Patrick S. Finnegan, BA, NREMT-B,* Vikas Tandon, MD,‡ Saeed Darvish-Kazem, MD,‡§ Shaan Chugh, MD,‡ Hussain Alzayer, BSc, MD,‡|| and Andrea Kurz, MD*
Desaturation on Surgical Wards

Minutes hypoxemia per hour

Blinded ward monitoring

≈850 non-cardiac surgical patients

SpO₂ Threshold
- <90%
- <85%
- <80%
- <75%

% With At Least x Hypoxic Minutes per Hour

x = Hypoxic Minutes per Hour
Hypoxemia episodes of varying duration

90% of episodes during which saturation was <90% for ≥ 1 hour were missed!
Hypoxemia is common!

<table>
<thead>
<tr>
<th>SpO2</th>
<th>Duration</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;90%</td>
<td>&gt;10min/hr.</td>
<td>21%</td>
</tr>
<tr>
<td>&lt;90%</td>
<td>&gt;20min/hr.</td>
<td>8%</td>
</tr>
<tr>
<td>&lt;85%</td>
<td>&gt;5min/hr.</td>
<td>8%</td>
</tr>
<tr>
<td>&lt;90%</td>
<td>1 hour</td>
<td>37%</td>
</tr>
</tbody>
</table>

Hypoxemia goes undetected!
Can we predict post operative hypoxemia?
Post-operative Hypoxemia Common Culprits...
Common Culprits...

- Hypoventilation
  - Residual narcotics
  - Residual benzos
  - Residual inhaled anesthetics
  - Residual muscle relaxants

- Sleep Disordered Breathing/Obstructive Sleep Apnea

- V/Q mismatch and Shunt
  - Atelectasis
  - Pulmonary edema

- Surgery –
  Type/Duration ----
  Pain, splinting, abdominal wall binding, abdominal distension

- Age
- Habitus
- Type and Duration of Anesthesia
Risk Factors for Cardiorespiratory Compromise

- E.g. Obesity, comorbidities, advanced-age, sleep disordered breathing/obstructive sleep apnea
- E.g. frequency of vital signs checkups
- E.g. surgery type/duration, type and duration of anesthesia, residual narcotics

Patient Factors

Area of Care Factors

Treatment Factors

PERFECT STORM

Using the STOP-BANG questionnaire to predict hypoxaemia in patients recovering from noncardiac surgery: a prospective cohort analysis

A. K. Khanna\textsuperscript{1,2,3,*}, D. I. Sessler\textsuperscript{2}, Z. Sun\textsuperscript{2,4}, A. J. Naylor\textsuperscript{2}, J. You\textsuperscript{2,5}, B. D. Hesler\textsuperscript{2,6}, A. Kurz\textsuperscript{2,3}, P. J. Devereaux\textsuperscript{7,8,9,10} and L. Saager\textsuperscript{2,3}

\textsuperscript{1}Center for Critical Care, \textsuperscript{2}Department of Outcomes Research, \textsuperscript{3}Department of General Anesthesiology, Anesthesiology Institute, Cleveland Clinic, Cleveland, OH, USA, \textsuperscript{4}Anesthesiology and Perioperative Medicine, Georgia Regents University, Augusta, Georgia, USA, \textsuperscript{5}Department of Quantitative Health Sciences, Cleveland, Ohio, USA, \textsuperscript{6}Department of Psychiatry, Rush University, Chicago, IL, USA, \textsuperscript{7}Population Health Research Institute, Hamilton Health Sciences and McMaster University, Hamilton, Canada, \textsuperscript{8}Department of Clinical Epidemiology, \textsuperscript{9}Department of Biostatistics, and \textsuperscript{10}Department of Medicine, McMaster University, Hamilton, Canada

\textsuperscript{*}Corresponding author. E-mail: khanna@ccf.org
Incidence Of Patients With An Average Number Of Minutes Per Hour Of Hypoxemia > X During Monitoring

A. SpO2<95%

B. SpO2<90%

C. SpO2<85%
• Sensitivity Analysis
• Time–Weighted SpO2
Long-Acting Patient-Controlled Opioids Are Not Associated With More Postoperative Hypoxemia Than Short-Acting Patient-Controlled Opioids After Noncardiac Surgery: A Cohort Analysis

Allan W. Belcher, DO,* Ashish K. Khanna, MD,*† Steve Leung, MD,* Amanda J. Naylor, BA,* Matthew T. Hutcherson, BS,* Blanka M. Nguyen, BS,* Natalya Makarova, MS,*‡ Daniel I. Sessler, MD,* PJ. Devereaux, MD, PhD,§|| and Leif Saager, DrMed, MMM¶#
- At 95% threshold, at least 10 min/hour of hypoxemia in 79% of patients
- At 90% threshold, at least 10 min/hour of hypoxemia in 19% of patients
- At 85% threshold, at least 10 min/hour of hypoxemia in 1% of patients
Can we predict post operative hypoxemia?
### Comparison of Risk Models

<table>
<thead>
<tr>
<th>ARISCAT - Overall</th>
<th>Arozullah - Resp failure</th>
<th>Arozullah - Pneumonia</th>
<th>Gupta - Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Age</td>
<td>Age</td>
<td>Age</td>
</tr>
<tr>
<td>Preop SpO2</td>
<td>History of COPD</td>
<td>Dependent functional status</td>
<td>History of COPD</td>
</tr>
<tr>
<td>Resp infection w/in 1 mo</td>
<td>Dependent functional status</td>
<td>History of stroke</td>
<td>Dependent functional status</td>
</tr>
<tr>
<td>Preop hemoglobin &lt;=10</td>
<td>BUN &gt;30</td>
<td>Weight loss &gt;10% in 6mo</td>
<td>ASA class</td>
</tr>
<tr>
<td>Type of surgery</td>
<td>Albumin &lt;3</td>
<td>Impaired sensorium</td>
<td>Preoperative sepsis</td>
</tr>
<tr>
<td>Duration of surgery</td>
<td>Type of surgery</td>
<td>Current smoker within 1yr</td>
<td>Type of surgery</td>
</tr>
<tr>
<td>Emergency procedure</td>
<td>Emergency procedure</td>
<td>Alcohol &gt;2/d past 2 wks</td>
<td>Tumor class</td>
</tr>
</tbody>
</table>

3% of patients develop postop respiratory failure.
25% of these patients die within 30 days.
If We Cannot Predict It, Can We Monitor It?

• Better monitoring?
• Who to monitor?
• What to monitor?
• How to monitor?
Postoperative Opioid-induced Respiratory Depression

A Closed Claims Analysis


Anesthesiology 2015;122:659-65
Opioid Induced Respiratory Depression

- 77% death/severe brain damage
- 88% within 24 hr. post-surgery
- 9% STOP-BANG

✓ 97% preventable – better monitoring and response
✓ 42% - 2hr of last check

- Multiple prescribers
- Non-opioid sedatives
- Inadequate nursing response
Association of Opioids and Sedatives with Increased Risk of In-Hospital Cardiopulmonary Arrest.
Overdyk FJ, Dowling O, Marino J, et. al.

<table>
<thead>
<tr>
<th>Opioids/Sedative Use 2007-1012</th>
<th>Cardiac Arrest (n=96,554)</th>
<th>No Cardiac Arrest (n=12,180,137)</th>
<th>Odds Ratio*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both Opioid and Sedative</td>
<td>41.0 %</td>
<td>21.8%</td>
<td>3.47</td>
<td>(3.40, 3.54)</td>
</tr>
<tr>
<td>Opioid only</td>
<td>28.0%</td>
<td>31.4%</td>
<td>1.81</td>
<td>(1.77, 1.85)</td>
</tr>
<tr>
<td>Sedative only</td>
<td>13.8%</td>
<td>14.3%</td>
<td>1.82</td>
<td>(1.78, 1.87)</td>
</tr>
<tr>
<td>Neither Opioid Nor Sedative</td>
<td>17.2%</td>
<td>32.6%</td>
<td>Ref.</td>
<td></td>
</tr>
</tbody>
</table>

“Low Acuity” Patients

<table>
<thead>
<tr>
<th>Cardiac Arrest</th>
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</thead>
<tbody>
<tr>
<td>General Care Floor</td>
</tr>
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</table>
Preventing Respiratory Depression

Daniel I. Sessler, M.D.

LEE et al.¹ evaluated closed malpractice claims related to respiratory depression. They identified 92 closed claims over 20 yr in about a third of covered anesthesiologists, which corresponds very roughly to 14 closed claims per year for all anesthesiologists nationwide among perhaps 75 million cases. Three-quarters of the patients died or were left with severe brain damage; half resulted in settlement payments, with the median being $217,000 (intraquartile range: $50,000 to $604,000). We know that only a small fraction of adverse outcomes results in malpractice claims. It is thus apparent that postoperative respiratory events resulting in death or serious injury occur at a concerning rate.

Most patients whose closed claims resulted from respiratory events were given opioids, nearly half by at least two routes—often prescribed by different physicians, and nearly half had a con-

“It is likely that many catastrophic respiratory events could be prevented by continuous … monitoring. However, major trials are needed to determine what should be monitored and how.”

Case reviewers judged that 97% of claims probably or possibly could have been prevented by better monitoring. More intense conventional monitoring probably is not the answer though. Hypoxemia in postoperative inpatients is common, severe, and prolonged.⁴ Furthermore, even serious and persistent hypoxemia is unrecognized by nurses in 88% of cases (unpublished data, Department of Outcomes Research, Cleveland Clinic, December 2014). That a full quarter of the respiratory events in the series of Lee et al.¹ occurred within 15 min of a nursing evaluation shows how often the current system fails.

So what can we do? Continuous monitoring is perhaps the obvious way to prevent catastrophic postoperative respiratory events. It is tempting to target continuous monitoring to high-risk patients, such as those who have a history of sleep apnea or are obese. The difficulty is that even the best predic-
Manually recorded data were, on an average 6.5% higher than those recorded via automated systems!

*Anesth Analg* 2014;118;326-31
If we cannot predict it, can we monitor it ?

- Better monitoring? YES
- Who to monitor? EVERYONE
- What to monitor?
- How to monitor? CONTINUOUS (AUTOMATED)
<table>
<thead>
<tr>
<th>Advantage</th>
<th>Disadvantage</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noninvasive</td>
<td>Delayed detection of hypoventilation with supplementary O₂&lt;sup&gt;13-17&lt;/sup&gt;</td>
<td>Noninvasive</td>
<td>Increased education needed for interpretation of CO₂ tracing&lt;sup&gt;14,38&lt;/sup&gt;</td>
</tr>
<tr>
<td>Easy to interpret</td>
<td>Hindrance to activities of daily living (attending to personal hygiene, ambulation)&lt;sup&gt;11&lt;/sup&gt;</td>
<td>Early detection of hypoventilation with supplemental O₂&lt;sup&gt;13-17&lt;/sup&gt;</td>
<td>Difficult to capture CO₂ tracing in mouth breathers</td>
</tr>
<tr>
<td>May reduce ICU transfers and rescue team activation&lt;sup&gt;10,22&lt;/sup&gt;</td>
<td>False alarms and alarm fatigue&lt;sup&gt;39&lt;/sup&gt;</td>
<td>Prevent patient harm from respiratory depression&lt;sup&gt;15,16,38&lt;/sup&gt;</td>
<td>Hindrance to ambulation&lt;sup&gt;14,38&lt;/sup&gt;</td>
</tr>
<tr>
<td>Potential for cost savings&lt;sup&gt;22&lt;/sup&gt;</td>
<td>More accurate detection of hypoxemia versus periodic nursing checks&lt;sup&gt;11,12&lt;/sup&gt;</td>
<td>Improves nursing satisfaction&lt;sup&gt;14-16,38&lt;/sup&gt;</td>
<td>Unclear if capnography can be used with CPAP machine&lt;sup&gt;14&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Allows titration of narcotics&lt;sup&gt;15,16&lt;/sup&gt;</td>
<td>False alarms and alarm fatigue&lt;sup&gt;38&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Abbreviations: CPAP, continuous positive airway pressure; ICU, intensive care unit.
Pulse oximetry for perioperative monitoring (Review)

Pedersen T, Nicholson A, Hovhannisyan K, Møller AM, Smith AF, Lewis SR
Pulse Oximetry...

- 22,992 participants
- No decrease in-hospital mortality
- No decrease in-hospital stay
- No decrease in transfer to ICU
- No decrease in overall mortality

- Potential increased vigilance and decreased pulmonary complications
Impact of Pulse Oximetry Surveillance on Rescue Events and Intensive Care Unit Transfers

A Before-and-After Concurrency Study

Andreas H. Taenzer, M.D., F.A.A.P.,* Joshua B. Pyke, B.E.,† Susan P. McGrath, Ph.D.,‡ George T. Blike, M.D.§

ABSTRACT

Background: Some preventable deaths in hospitalized patients are due to unrecognized deterioration. There are no publications of studies that have instituted routine patient monitoring postoperatively and analyzed impact on patient outcomes.

Methods: The authors implemented a patient surveillance system based on pulse oximetry with nursing notification of violation of alarm limits via wireless pager. Data were collected for 11 months before and 10 months after implementation of the system. Concurrently, matching outcome data were collected on two other postoperative units. The primary outcomes were rescue events and transfers to the intensive care unit compared before and after monitoring change.

Results: Rescue events decreased from 3.4 (1.89–4.85) to 1.2 (0.53–1.88) per 1,000 patient discharges and intensive care unit transfers from 5.6 (3.7–7.4) to 2.9 (1.4–4.3) per 1,000 patient days.

What We Already Know about This Topic

- Early recognition of deterioration is essential for early intervention to prevent cardiac or respiratory arrest
- Universal surveillance for such early recognition has not been applied to postoperative patients

What This Article Tells Us That Is New

- Implementation of universal surveillance with pulse oximetry was associated with a reduced need for patient rescue and intensive care unit transfers

been to detect deterioration that occurs in the general care setting where the staff is immediately available to intervene
Can Continuous Monitoring Help?

**Continuous Pulse Oximetry and Capnography Monitoring for Postoperative Respiratory Depression and Adverse Events: A Systematic Review and Meta-analysis**

Thach Lam, MD,* Mahesh Nagappa, MD,† Jean Wong, MD,* Mandeep Singh, MD, MSc,* David Wong, MD,* and Frances Chung, MBBS*  
*Anesthesiology 2017;125:2019-2029*
Practice Guidelines for Acute Pain Management in the Perioperative Setting

An Updated Report by the American Society of Anesthesiologists Task Force on Acute Pain Management

Anesthesiology. 2012;116(2):248-273
Practice Guidelines for the Perioperative Management of Patients with Obstructive Sleep Apnea

A Report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea
Preventing Opioid-Induced Postoperative Hypoxemia: No Simple Answer?

Harriet W. Hopf, MD

Long-Acting Patient-Controlled Opioids Are Not Associated With More Postoperative Hypoxemia Than Short-Acting Patient-Controlled Opioids After Noncardiac Surgery: A Cohort Analysis

Allan W. Belcher, DO,* Ashish K. Khanna, MD,*† Steve Leung, MD,* Amanda J. Naylor, BA,* Matthew T. Hutcherson, BS,* Bianka M. Nguyen, BS,* Natalya Makarova, MS,*‡ Daniel I. Sessler, MD,* P.J. Devereaux, MD, PhD,§∥ and Leif Saager, DrMed, MMM¶§
Some answers...

- Multimodal analgesia
- Improved monitoring and feedback
- Continuous capnography
- Continuous pulse oximetry
- Identify risk factors
- Education
- Continuous supplemental oxygen
Future Directions??

- etCO2
- RR
- SpO2
- HR
- ? Blood Pressure
Improved and smarter monitoring for everyone? [1,2,14,15]

**BETTER MONITORING? YES**
Continuous monitoring of capnography and oximetry can provide clinicians with early identification of evolving Respiratory Compromise, allowing for early intervention that may prevent tragic consequences.

**WHO TO MONITOR? EVERYONE**
APSF recommends continuous monitoring for all patients receiving opioid therapy in the postoperative period, especially when supplementary oxygen is administered.

**WHAT TO MONITOR? CARDIORESPIRATORY**
Available evidence has shown that cardiorespiratory compromise is common, goes undetected and is largely unpredictable.

**HOW TO MONITOR? CONTINUOUS (AUTOMATED)**
Continuous monitoring of all patients on the regular floor appears to be the answer to detecting cardiorespiratory compromise early.
The RNF – Real time monitoring!
Trending respiratory vital signs

- **SpO₂**
- **PaCO₂**
- **RR**
- **Ve**

**Onset Potentially Mortal Event** (e.g., Sepsis, CHF, PE)

**Divergence Pattern of SpO₂ and RR**

**First SpO₂ Threshold Warning** (breach - 85)

**Terminal rise of RR due to severe metabolic (lactic) acidosis**
Continuous capnography/oximetry monitoring during PCA

- HR beats/min
- SaO2 %
- "Code Blue"
- RR breaths/min
- ETCO2 mmHg
O2 supplementation may actually worsen things!

Graph showing
- $\text{SpO}_2$ with O2 supplementation
- $\text{SpO}_2$ (room air)
- $\text{PaCO}_2$
- $\text{Ve}$
Continuous capnography/oximetry monitoring during PCA
Pattern identification

- **SpO₂**
- **PaCO₂**
- **Ve**

Apnea Apnea Apnea Apnea

Terminal Apnea (Arousal Failure)

“Lights out Saturation” (Time of “Arousal Failure”)
Resuscitation required after this time.
Pattern identification - OSA
PRediction of Opioid-induced Respiratory Depression In Patients Monitored by capnoGraphY (PRODIGY)

This study is not yet open for participant recruitment. (see Contacts and Locations)

Verified January 2017 by Medtronic - MITG

Sponsor:
Medtronic - MITG

Information provided by (Responsible Party):
Medtronic - MITG

ClinicalTrials.gov Identifier:
NCT02811302

First received: June 21, 2016
Last updated: January 23, 2017
Last verified: January 2017

History of Changes

Full Text View  Tabular View  No Study Results Posted  Disclaimer  How to Read a Study Record
• Increasing concerns over unmonitored mortality and morbidity in patients during opioid therapy for acute pain (postop/medical)\textsuperscript{1,2}

• Need a simple tool to assess risk of developing respiratory compromise

• Study Purpose - Derive and validate an RC risk assessment tool to guide use of Microstream\textsuperscript{TM} monitoring technology (capnography/pulse ox)

• Methodology:
  • Consenting, adult patients receiving parenteral opioid therapy (postop or medical) pain on the hospital ward.
  • Monitored for 24-48 hours using blinded, non-alarming Microstream\textsuperscript{TM} technology
  • Endpoints – Monitor-confirmed RC or Opioid-Related ADE

• 1,650 patients at 16 sites in US (9), EU (4), and Asia (3)

• Assessing 12 high risk variables for prediction rule
  • Collecting data from EMR and Monitors


Respiratory depression in low acuity hospital settings—Seeking answers from the PRODIGY trial

Ashish K. Khanna a,⁎, Frank J. Overdyk b, Christine Greening c, Paola Di Stefano d, Wolfgang F. Buhre e


Fig. 1. Study design flow diagram.

*Including 12 hr nocturnal monitoring up to 2 consecutive nights (when possible)
High Risk Predictor Variables

Risk Prediction Model Development – PRODIGY risk score

- High Risk Variables for Prediction Rule
  - Age > 65 y
  - Known or suspected sleep-disordered breathing (OSA, snoring, etc.)
  - High risk surgery during first 24 hours post-operatively
  - PCA or epidural therapy
  - Obese (BMI >30)
  - Multiple opioid or concurrent CNS/sedating medication
  - High opioid dosage (>30mg oral morphine per day or equivalent)
  - Major organ failure
  - Diabetes
  - Chronic heart failure or other significant cardiac disease
  - Smoke (> 20 packs per year)
  - COPD or other significant pulmonary disease (including respiratory events before ward admittance)
**PRODIGY: Primary Objective**

- Derive and validate a risk assessment tool to identify subjects at risk of having respiratory depression* (RD) while undergoing opioid therapy on the hospital ward.

---

### Primary Objective

- Respiratory Depression Episode
  - etCO2 $\leq 15$ or $\geq 60$ mmHg for $\geq 3$ minutes, or
  - SpO2 $\leq 85\%$ for $\geq 3$ minutes, or
  - RR $\leq 5$ breaths per minute, or
  - Apnea episode lasting $> 30$ seconds, or
  - Any respiratory Opioid-Related Adverse Event (rORADE)

---

*Respiratory depression is a clinical diagnosis made after reviewing monitoring data in conjunction with the clinical data and consistent with accepted pathophysiological mechanisms.*
# PRODIGY: Secondary Objectives

<table>
<thead>
<tr>
<th>Secondary Objectives</th>
<th>Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. To compare subjects that will develop versus not develop RD.</strong></td>
<td>• RD risk versus no-risk subjects compared in terms of:</td>
</tr>
<tr>
<td></td>
<td>• Incidence of respiratory AE’s.</td>
</tr>
<tr>
<td></td>
<td>• Healthcare resource utilization</td>
</tr>
<tr>
<td></td>
<td>• Subject mortality at 30 days.</td>
</tr>
<tr>
<td><strong>2. To characterize the predictive values of etCO$_2$, SpO$_2$, RR and evaluate the value of the Integrated Pulmonary Index (IPI) in predicting RD and ORADE.</strong></td>
<td>• The predictive value (sensitivity, specificity, etc.) of etCO$_2$, SpO$_2$, RR, PR and IPI value’s variations will be correlated with the occurrence of RD and ORADE.</td>
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<tr>
<td><strong>3. To measure healthcare utilization costs during the study period.</strong></td>
<td>• Cost associated with events and actions taken will be estimated retrospectively using standard cost data from different countries.</td>
</tr>
</tbody>
</table>
1-month follow up

• 1-Month Follow Up
  • Visit at 1-Month post enrollment (30 days ±10 days)
  • May be performed by phone (if subject has been discharged)

• 1 Month Follow Up eCRF data collection:
  • Adverse Events
  • Healthcare resource utilization (including hospital length of stay, readmission rate and related primary diagnosis)
Adverse events

• Adverse Events (AE) collected:
  • All AEs with an underlying respiratory cause
  • All adverse device effects (ADE)
  • All Serious Adverse Events (SAE) (including sepsis events or related to opioid therapy)

• Data Collection
  • Date / time of event
  • Diagnosis and description (including confirmation of respiratory nature)
  • Actions taken / treatment (including vital signs, and date and time of rescue related actions when applicable)
  • Assessment of seriousness
  • Relatedness to the event (including opioid therapy or device)
  • Outcome or resolution and date of the resolution
Clinical event committee

• **CEC Composition**
  • Independent CEC consisting of a minimum of three (3) non-Medtronic, non-study investigator clinicians
  • Experienced in evaluating respiratory compromise, respiratory depression, and interpreting continuous monitor data.

• **CEC Members**
  • Dr. Luca Brazzi
  • Dr. Albert Dahan
  • Dr. Leif Saager
  • Dr. Toby Weingarten

• **Responsibilities**
  • Review AE’s to classify the event as respiratory or non-respiratory.
  • Review AE’s to determine the relatedness (including device or opioid therapy).
  • Review RD episodes and classify based on the RD / primary endpoint definition
Prediction Of Cardiorespiratory Compromise On Hospital General Care Units – Are We There Yet?

• Cardiorespiratory decompensation on the GCF remains common and hard to predict
• Continuous, smarter monitoring and early proactive intervention may be preventative
• Who and what to monitor remains a challenge
• Trials such as PRODIGY will aim to answer this critical question
References


Questions?
2018 HQI Annual Conference
October 28-30

Featured Faculty

Vivek Murthy, MD – Former Surgeon General

Allison Massari – Patient experience and compassionate care advocate

Jim Bagian and Yvonne Cagle – former NASA astronauts

Arjun Srinivasan, MD – Associate Director for Healthcare-Associated Infection Prevention Programs at the CDC

Elliott Main, MD – CMQCC, Leading the QI Maternity Workshop with Kim Werkmeister, HQI

More details: [www.hqinstitute.org](http://www.hqinstitute.org)

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