# MEDTRONIC SUMMARY: CLINICAL PAPER

## Medtronic provides the following synopsis of a clinical publication about the PRODIGY trial.

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**TITLE** "Respiratory Depression in Low Acuity Hospital Settings– Seeking Answers from the PRODIGY Trial"

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**JOURNAL** J of Crit Care 2018,
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### KEY TAKEAWAYS:

- The PRODIGY 'Seeking Answers' publication reviews the problem of respiratory compromise in adult patients receiving opioids on the general care floor (GCF) and the methodology that was used in the ongoing PRODIGY trial and planned publications.
  - Opioid-induced respiratory depression (OIRD) is common on the general care floor.
  - Currently, no tool reliably predicts which patients are most likely to experience OIRD in these settings. Multiple key opinion leaders have stated such a tool would be useful.
  - Continuous cardiorespiratory monitoring may be a solution to inform early intervention, mitigating further deterioration.
- PRODIGY is an ongoing trial designed to develop a respiratory depression risk prediction tool and examine the value of continuous capnography and oximetry monitoring.

### BACKGROUND:

- Opioid-induced respiratory depression (OIRD) on the general care floor
  - Mortality within 30 days after surgery is currently the third leading cause of death in the United States. Cardiorespiratory complications are the most common cause of 30-day postoperative mortality.
  - Postoperative respiratory failure is the fourth most common patient safety event.
  - Depending on the definition used, respiratory depression (RD) occurs in up to 17% of postoperative patients.
  - While general care floor patients are low acuity, 41% of in-hospital cardiac arrests occur on the GCF/ward, generally with catastrophic outcomes (adjusted survival rate is 0.106).
  - One study found that 49% of patients on the ward had a respiratory cause of in-hospital cardiac arrest.
- Predicting Risk of OIRD
  - Risk factors for developing RD have been widely studied in post-surgical patients and include age, sleep-disordered breathing, high-risk surgery, previous opioid use and opioid usage during hospitalization, obesity, major organ failure, diabetes, chronic heart failure or other significant cardiac disease, smoking history, and COPD or other significant pulmonary disease.
  - Despite our knowledge of potential risk factors, no standardized tool exists for predicting risk of RD in postoperative patients. The PRODIGY initiative's primary objective is development of an OIRD risk prediction tool.
  - Creation of an OIRD risk prediction tool may help guide clinicians in selecting those that would benefit most from continuous electronic monitoring.

- Continuous Electronic Monitoring
    - Most patients on the GCF are monitored via intermittent vital signs (e.g., every 4 – 8 hours).
    - A study by Sun found that 90% of serious hypoxemic episodes (i.e., SpO2 < 90% for ≥ 1 full hour captured using monitors blinded to nursing) were missed by nurses charting routine vital sign monitoring at four-hour intervals.
    - A review of opioid-related serious events (i.e., deaths and injuries) resulting in litigation found that nearly all (97%) of postoperative opioid-induced RD events on the ward were deemed preventable with better monitoring and response. (Forty-two percent of RD episodes in this analysis occurred within 2 hours of the last nursing check and 16% within 15 minutes[1].) The authors observe that during a spot-check, the patient is awake or awakened and may be instructed to take deep breaths until a satisfactory vital sign is recorded.
    - The inability to predict and detect respiratory compromise suggests improved monitoring may be a solution.
    - Vital signs deteriorate 6–12 hours before cardiac and respiratory arrests occur creating a 'window of opportunity' for early detection and intervention.

- PRODIGY Methodology
    - The PRODIGY initiative is a multicenter, international, prospective study designed to create and validate a risk prediction tool from continuous respiratory monitoring and clinical data that can identify adult patients at greater risk of RD episodes when receiving parenteral opioid therapy on the medical and surgical general care floors/wards.
    - The study will include ~1,650 patients from 16 centers from 7 different countries (US 9, EU 4, Asia 3) allowing potential comparisons across hospitals and geographical regions.
    - The primary outcome of PRODIGY will be RD as detected using 'blinded', non-alarming continuous capnography and oximetry monitoring on the general care floor, defined one or more of the following: etCO2 ≤ 15 or ≥ 60 mmHg for ≥ 3 minutes, RR ≤ 5 breaths for ≥ 3 minutes, SpO2 ≤ 85% for ≥ 3 minutes, apnea episode lasting > 30 seconds, or any respiratory Opioid-Related Adverse Event (rORADE).
    - Secondary outcomes of PRODIGY will include a comparison of RD risk subjects versus no-risk subjects in terms of incidence of adverse events and interventions, healthcare resource utilization, and subject mortality at 30 days.
    - The predictive value of etCO2, RR, SpO2, and the Integrated Pulmonary Index (IPI) will be correlated with the occurrence of RD and ORADE.
    - Data from two-thirds of study participants will be used to derive the risk assessment tool (Derivation Cohort). Data from the remaining third will be used to validate the tool (Internal Validation Cohort).
- PRODIGY Publications
    - The 'seeking answers' paper is the first publication from the trial discussing the importance of this study and the methodology being used.
    - Results from the trial including primary and secondary objectives will be published in subsequent papers to follow.

## **THIS CONCLUDES THE CLINICAL SYNOPSIS OF THIS PUBLICATION**

1. Lee LA, Caplan RA, Stephens LS, et al. Postoperative Opioid-induced Respiratory Depression: A Closed Claims Analysis. Anesthesiology. 2015;122(3):659-665.



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