PRODIGY FAQ

With an eye on driving down healthcare costs through innovation, our objective is to help you alleviate pain, restore health, and extend the life of patients worldwide. Nowhere is this more applicable than for hospitalized patients receiving opioids for acute pain management. It is our goal to apply the full power of technology for improving patient outcomes by empowering you and other clinicians to control patient pain during their hospital recovery, while preventing respiratory compromise that can lead to patient injury and even death.

1. **What is PRODIGY?** PRODIGY is a mnemonic for **P**rediction of **O**pioid-induced respiratory Depression In patients monitored by capnoGraphY. It is a prospective, multi-center, international cohort study to assess the potential for respiratory compromise (RC) risk assessment in patients receiving opioids in the hospital general ward. Respiratory compromise may occur when a combination of risk factors leads to decompensation into respiratory insufficiency, respiratory failure/arrest, and potentially death; enhanced monitoring enabling early identification and intervention might prevent or mitigate decompensation.

2. **Why is PRODIGY important?** Opioid therapy is the gold standard for treatment of post-surgical pain on the ward and more than half of non-surgical (i.e., medical) patients admitted to the hospital are prescribed opioids. Opioid-related adverse drug events (ORADE) significantly increase patient’s hospital length of stay and related costs in post-surgical patients. RC is the leading cause of rescue calls (e.g., rapid response), ICU admissions, and code blues in our hospitals. RC that evolves on the general care floor increases the risk of mortality by 29 times and drives up costs when not recognized and treated early, making it one of the costliest hospital conditions. When indicated, continuous electronic monitoring enables you to recognize and treat RC in its early stages, preventing the downward spiral into respiratory failure and deaths. A study of primary respiratory arrests classified nearly two-thirds (64%) as potentially preventable. A closed-claims analysis (i.e., retrospective review of litigation cases involving injury or death) of patients receiving postoperative opioids found that 97% of cases were preventable by better monitoring and response.

3. **What is the primary objective?** Today, no standardized tool is available to you for assessing risk of developing RC. The primary purpose of this study is to create a risk assessment tool derived from continuous respiratory monitoring and clinical data, so that you can identify patients at increased risk of respiratory compromise episodes when receiving parenteral opioid therapy on the hospital ward. The developed RC risk assessment tool may be used by you and your staff to guide which patients could benefit most from continuous, electronic respiratory monitoring including capnography, respiratory rate, and oximetry for prevention of respiratory failure and/or arrest.

4. **What are secondary objectives?** Based on the quantity and breadth of data collection, there will be many opportunities for secondary analysis and publication. Some of the planned analyses include assessing which subjects develop RC versus those that do not; characterizing the value of etCO2, SpO2, RR and Integrated Pulmonary Index™ algorithm (IPI – an artificial intelligence 1 – 10 index derived from multiple parameters) in predicting RC and opioid-induced
adverse drug events (ORADE); and measuring healthcare utilization costs secondary to RC. After analysis of the data, additional opportunities for further exploration and publication may be identified.

5. **What patient populations were studied?** Consent ing, adult patients receiving parenteral opioid therapy (postop or medical) for pain on the hospital surgical and medical general care floor (aka, wards) were studied. Monitoring and medical record data was collected from approximately 1,500 patients in 16 centers internationally including 9 centers in the US, 4 in Europe, and 3 in Asia. This makes PRODIGY one of the largest studies ever for monitoring patients receiving opioids on the hospital ward.

6. **How were patients monitored and what were the endpoints?** Patients were monitored for 24-48 hours using blinded, non-alarming Medtronic Microstream monitors which will provide etCO2, respiratory rate, SpO2, and PR along with the Integrated Pulmonary Index (IPI) algorithm to identify patients experiencing respiratory compromise. Endpoints include monitor-confirmed RC (i.e., etCO2 ≤ 15 or ≥ 60 mmHg for ≥ 3 minutes, SpO2 ≤ 85% for ≥ 3 minutes, RR ≤ 5 breaths per minute, or an apnea episode lasting > 30 seconds) or any Respiratory Opioid-Related Adverse Drug Event (rORADE).

7. **What risk variables were assessed?** Based on previous studies, primary risk variables to be assessed for prediction of RC include age > 65 years, known or suspected sleep-disordered breathing, high risk surgery, PCA or epidural opioid therapy, obesity, multiple opioid or concurrent CNS/sedating medications, high opioid dosage, major organ failure, diabetes, chronic heart failure or other significant cardiac disease, significant smoking history, and COPD or other significant pulmonary disease (including respiratory events before ward admittance). However, additional data will be collected from the medical record which may result in further examination.

8. **Who are the study investigators?** The study’s steering committee includes Dr Frank Overdyk, Dr Wolfgang Buhre, and Dr Ashish Khanna. The Clinical Event Committee, charged with validating the monitoring data and respiratory events, includes Dr. Luca Brazzi, Dr. Albert Dahan, Dr. Leif Saager, and Dr. Toby Weingarten. In total, approximately 30 highly-esteemed investigators from 3 continents are involved with the study with many additional support personnel.

Medtronic is committed to working with you and clinicians around the world to empower safe, effective pain management for hospitalized patients during their recovery. We believe the results from PRODIGY will take us a significant step forward in the prevention of patient injuries and deaths from opioid-induced respiratory compromise. Through ongoing collaboration on the conditions that matter most to you and your patients, we can go Further, Together.
References

1 Clinical Trials Gov. https://clinicaltrials.gov/ct2/show/NCT02811302
6 Chelluri, L. Preventable In-Hospital Cardiac Arrests—Are We Monitoring the Wrong Organ? Open Journal of Emergency Medicine, 2, 43-45.