PROMPT™

PONV RESCUE OUTCOMES AFTER AMISULPRIDE TREATMENT

Participation Playbook

for the PROMPT Study

PACE PERIOPERATIVE & ANESTHESIA CARE EXPLORER *powered by ArborMetrix*

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Introduction

Welcome to the PROMPT Study! This playbook will guide prospective sites through the entire enrollment and setup process for participating in the PROMPT Study via the PACE Registry. If you would like to enroll online, please visit prompt.arbormetrix.com.

What is PROMPT?

The PROMPT (**P**ONV **R**escue **O**utcomes after a**M**isul**P**ride **T**reatment) Study is an observational, retrospective, registry-based study that will collect and analyze real-world evidence on the presentation, evaluation, and rescue treatment of post-operative nausea and vomiting.

PROMPT
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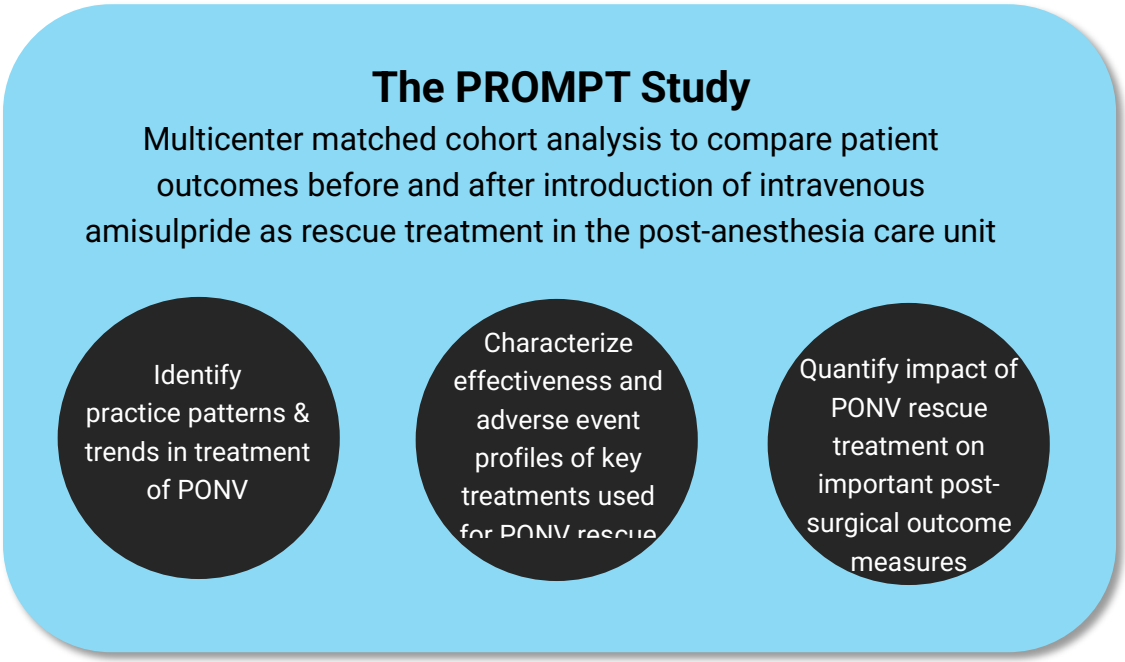
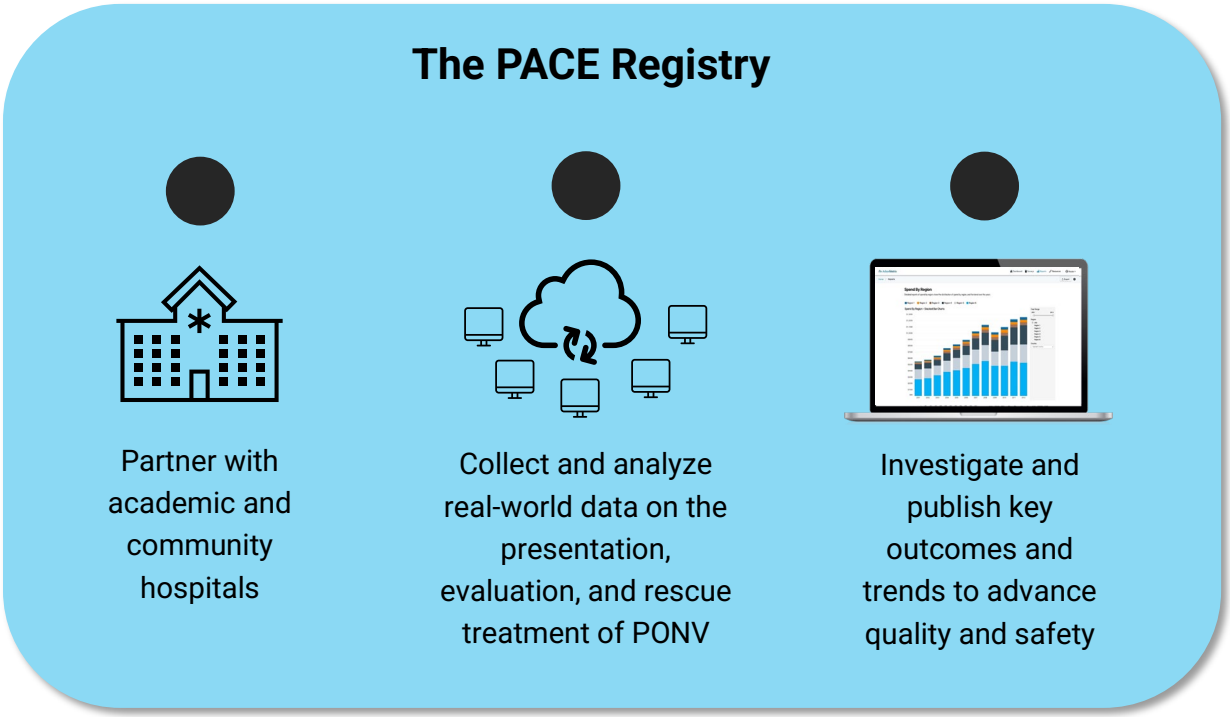


What is the PACE Registry?

PROMPT is a registry-based study that will be managed through the **Perioperative and Anesthesia Care Explorer (PACE).** PACE delivers clinically rich, real-world evidence hospitals can use to understand their outcomes, advance research, and improve patient health after surgery.

PACE PERIOPERATIVE & ANESTHESIA CARE EXPLORER

Data for the PROMPT Study will be collected from de-identified electronic health records into the PACE Registry and compiled and analyzed by an independent data science company, ArborMetrix.



PROMPT Study Overview

Study Design

PROMPT is designed to identify current practice patterns and trends in the treatment of PONV. While there is no predefined hypothesis regarding the magnitude of efficacy or safety of various treatment regimens, they will be compared using established statistical methods for observational studies.

PROMPT will seek to provide insight into pharmacologic treatment for PONV related to clinical and economic outcomes in a real-world environment.

Specifically, PROMPT will examine patients in the PACU who receive amisulpride as a treatment for PONV. PROMPT will compare patient outcomes before (Cohort 1 – Standard of Care rescue anti-emetics) and after implementation of amisulpride as rescue treatment according to the package labeling (Cohort 2 – intravenous amisulpride rescue treatment).

The program design will involve deidentified, retrospective data collection from standard hospital system electronic health records for the duration necessary to collect at least 20,000 individual patient EHRs (at least 10,000 in each Cohort).

Study Sponsor

PROMPT is sponsored by Acacia Pharma.

Target Timeline for Data Collection

The target timeline for baseline data collection for Cohort 1 will attempt to avoid time periods of peak COVID activity due to reduced surgical volume. Data collection will likely commence in the second half of 2021. Ideal data collection per site is 1000 cases for Cohort 1 and 1000 cases for Cohort 2 over a twelve-month time period.

Sites interested in participating should be willing to meet these and other minimum criteria and be able to complete the necessary steps for contracting, data integration and Institutional Review Board approval within 6 months of joining.

Minimum Requirements for Site Participation

- Estimated surgical volume of approximately 1,000 cases per month
- Routine pre/peri-operative antiemetic prophylaxis
- Standard collection of EMR-appropriate data points (ICD, CPT, SNOMED, others)
- Adequate IT resources to permit timely retrospective data collection
- Adequate research infrastructure to complete the necessary contracting for initiation of study within 3 to 6 months.

Clinical Measures

De-identified data for the PROMPT Study will be retrieved from the Electronic Health Record, Administrative and Practice Management Systems, and the Electronic Anesthesia Record.

The data dictionary for the PROMPT Study contains thousands of data elements describing details related to patients, surgery type, anesthesia type, anesthesia technique, administered medications, adverse events, routine events, and transition times. The data dictionary functions as tool for mapping data retrieved from a hospital to specific clinical metrics that are built upon an analytic engine capable of producing real-time insights from harvested data, and inform the development of the study measures:

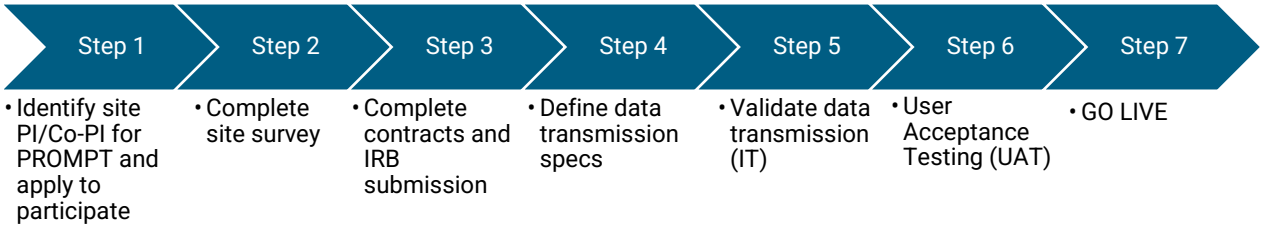
- ✓ PROMPT Study Measure Overview
- ✓ Data Dictionary

Some of the clinical measures that will be viewable in the PROMPT Study include:

- Total Surgical Case Volume
- Demographic Description of the Surgical Patient Population
- Rate of Comorbidities in the Surgical Patient Population
- Rate of History of PONV in the Surgical Patient Population
- Rate of Administration of Prophylactic/Perioperative PONV Medications in the Surgical Patient Population
- Description and Rates of Anesthetic Technique in the Surgical Patient Population
- Perioperative/Postoperative Transition Times in the Surgical Patient Population
- Rate of Occurrences of Delirium/Dysrhythmias/Extrapyramidal Symptoms in the Surgical Patient Population

How to Enroll

Sites can enroll for the PROMPT Study efficiently and securely. The enrollment process includes several key steps:



Step 1: Apply to Participate and Identify Key Personnel

Sites must complete the PROMPT Study Enrollment Form as the initial step to participate in the PROMPT Study. Should there be an independent query (i.e., process NOT initiated by Acacia Medical Affairs personnel), Acacia Medical Affairs follow-up is a requirement to proceed. The initial enrollment form will take 1-2 minutes to complete. Once the enrollment form is received by ArborMetrix, you will receive a welcome email and further instructions regarding next steps, including an additional page of requested information regarding key personnel and site details that will help streamline the onboarding process. Here is a sample of the additional information we will need.

Step 2: Complete Site Discovery Questionnaire

The goal of the site discovery questionnaire is to gather important information regarding your site's EHR system setup and make certain we can gather the necessary data elements from you via an automated data feed from your EHR system directly into the PROMPT Study Registry (PACE). Once you have completed the site discovery questionnaire, a data integration specialist from ArborMetrix will reach out to schedule a meeting with key personnel from your site, including your EHR Vendor contact, IT Support Staff, and the Project Lead.

- ✓ Site Discovery Questionnaire

Step 3: Complete Contracts and Legal Documents

Prior to submitting any data to the PACE Registry for the PROMPT Study, sites must complete the required legal documents:

- ✓ Registry Participation Agreement
- ✓ Business Associate Agreement

ArborMetrix is using Advarra to facilitate a Centralized IRB for the PROMPT study. ArborMetrix will provide the sites with a copy of the exemption ruling from the IRB. Sites will not need to apply for a localized IRB. They can simply enroll to participate and submit data directly to the PROMPT study via the PACE Registry.

Step 4: Define Data Transmission Specifications

Once a site has completed the enrollment documentation, site discovery questionnaire and executed their legal contracts, they can begin the process for data submission. A data integration specialist from ArborMetrix will have already reached out to the program lead at your site to discuss the results of your Site Discovery Questionnaire and answered any further questions. At this point, the site will need to review the following to better understand the data transmission specifications:

- ✓ Data Submission User Guide
- ✓ File Specifications for PROMPT Study
- ✓ SFTP Connection Instructions

ArborMetrix will set up a time to meet with the program lead, EHR vendor, and internal IT support (if applicable) to answer any questions the site has and begin the process of setting up the site for data transfer.

The data specification required to participate in the PROMPT Study is based on the HL7® FHIR® standard for health care data exchange. The sites will need to comply with the specifications to submit data. ArborMetrix has created a template for sites to use with the necessary tab/column names needed. Sites should use this template as a starting point to alleviate setup burden.

During the data integration setup process, ArborMetrix will review with the site the clinical measures that will be populated using the site's data. Understanding what these measures are will be important for the sites, as some of the information is very detailed and will pull from specific areas of the EHR. Without the detailed data, it will be harder to accurately calculate the measures and outcomes. Sites are encouraged to review the PROMPT Study Measure Specifications and Data Dictionary along with the Data Submission Guide to determine if there are any data elements they will not be able to submit to the PROMPT Study.

Minimum Data Elements Requirements

The following is an informal list of data elements that are required to join the PROMPT Study and participate in the PACE Registry. ArborMetrix will help you map the necessary elements required from your system as part of the data specifications testing process.

Data for the PROMPT Study and PACE Registry will be retrieved from the Electronic Health Record, Administrative and Practice Management Systems, and the Electronic Anesthesia Record. Cases to be included in the registry are all adult patients 18 years or older having post-operative nausea and vomiting (PONV) during their PACU stay, regardless of surgery or anesthesia type, etc. All data included in the registry will be deidentified. Comparison of deidentified patient EHRs in Cohort 1 and Cohort 2, including response rates, will be compiled and analyzed by ArborMetrix. Collected data are encrypted and will only be stored electronically in a highly secured database. A sample of the data elements to be collected include (but are not limited to):

- MRN
- Demographic data: gender, age, race
- Past medical history
- Preoperative medication list
- Social history: smoking status, alcohol use, marijuana use
- Family history: nausea, post-operative nausea/vomiting
- Medication administration: preoperative, intraoperative, post-anesthesia care unit, inpatient
- Adverse event documentation: intraoperative, postoperative
- Indication for surgery
- Anesthesia technique: general, regional, neuraxial, monitored anesthesia care
- Transition times: anesthesia start, time in OR, surgery start, surgery end, time out of OR, anesthesia end, time in PACU, time ready for discharge from PACU, time actually discharged from PACU

Step 5: Data Validation

After working with ArborMetrix to develop the data transmission file and working through connectivity, the site will send a sample data extract to ArborMetrix for data and measures validation. This will allow the site and ArborMetrix to develop and refine the pipeline. ArborMetrix will work with the site closely during this process.

Step 6: User Acceptance Testing (UAT)

Once a test dataset has been sent to ArborMetrix and validation of the measures is complete, the site will need to complete their own internal testing. Upon approval by all stakeholders, the

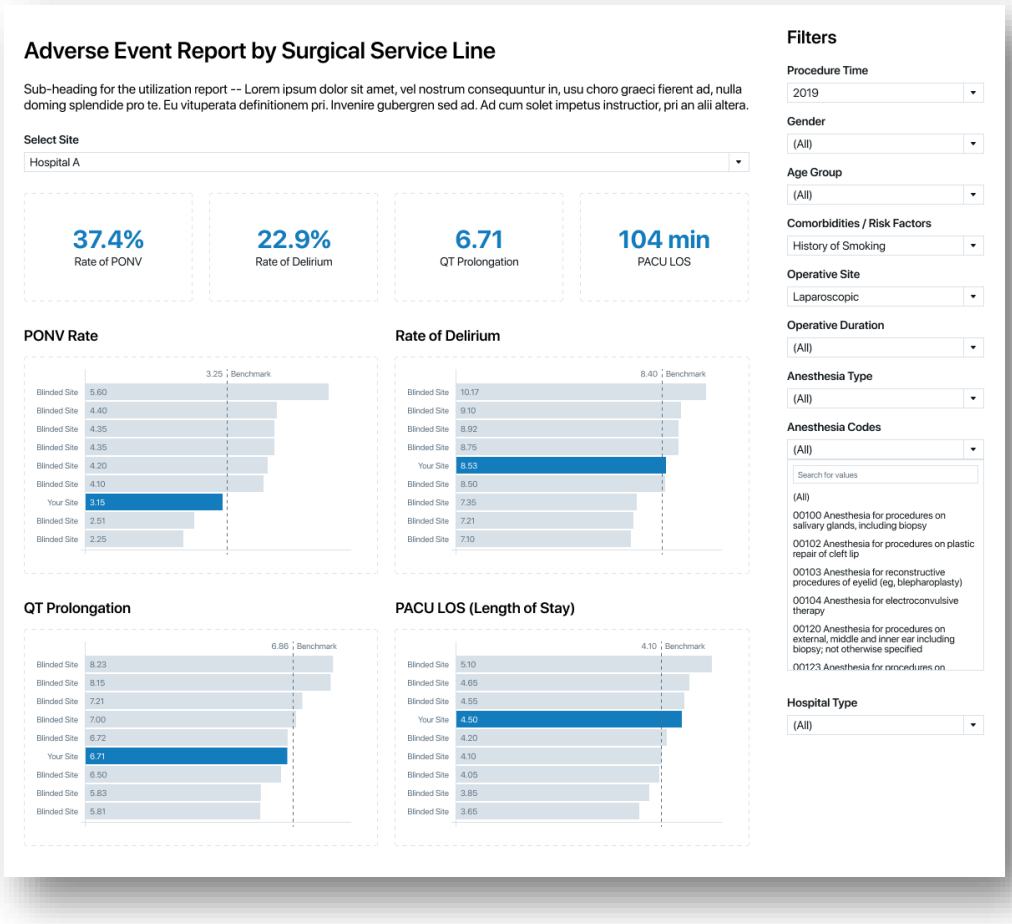
interface will be deployed to production and the site will be considered "live." A regular data submission cadence will be determined based on what works best for the site.

Step 7: GO LIVE: Production Pipeline and Registry Dashboard

Once there is an adequate amount of data to produce a statistically valid comparator, cohort data will be shared. The site will then meet with the program team and Acacia Medical Affairs personnel for the PROMPT Study and will be trained on how to access the PACE Registry, receive access to registry dashboards and understand available reports, benchmarks, etc.

Registry dashboards will be populated by pulling the EHR data provided by the sites and feeding it through an analytic process driven by the PROMPT Study clinical measures. Sites are encouraged to review the entire set of PROMPT Study measure specifications to understand the depth of information the PACE Registry will provide.

Your site will have web-based access to reports for the PROMPT study via the PACE Registry. Below is an example (NOTE: All data in report example are for illustrative purposes only):



After reviewing cohort data, if sites at any point decide they want to publish information based on the data available from the PROMPT study, they can contact their Medical Affairs liaison at Acacia to discuss the steps for publication.

Contact Us

If you have questions regarding the PACE Registry or PROMPT Study, please reach out to prompt@arbormetrix.com.