

Study Title: “Best Practice Alert for Opioid Prescribing” NCT04446975

09/01/2022

Study Protocol and Statistical Analysis Plan

The study is a randomized multiple crossover cluster trial to evaluate a real-time best practice alert embedded into the electronic health record. Our clusters are an academic medical center and three community hospitals, all part of the University of Colorado Health system, which serves both inner-city and rural populations. Primary study subjects are credentialed prescribing providers at each site. Eligible secondary study subjects are postsurgical hospital inpatients who are hospitalized at least one night prior to discharge. There are no exclusion criteria for the prescribing providers. The exclusion criteria for eligible patients is being less than 18 years of age.

During the eight-week periods when prescriber alerts are active, providers that attempt to prescribe higher-than-optimal doses are automatically notified on the order screen with a suggestion for a recommended dose. In the subsequent eight-week period, there is no best practice alert available to trigger. The four hospitals are randomized to the alert starting configuration (ON vs. OFF) in alternating clusters between best practice alert ON and OFF conditions for four eight-week periods, each separated by a four-week washout interval to minimize learning and augment masking. Randomization is implemented, so investigators and data analysts remain masked to the condition designation. While providers are exposed to the alerts during active periods if their prescription triggers a best practice alert, the schedule was not shared with providers or patients.

Baseline characteristics balance is assessed using absolute standardized difference calculated as the difference in means or proportions divided by the pooled standard deviation. An absolute standardized difference > 0.1 was considered to indicate an imbalance. The analysis is conducted at the individual patient level using a modified intention-to-treat strategy. The effect of the best practice alert on opioid prescription at discharge is evaluated using a linear regression model.

We determined that it would be feasible to recruit 1,500 patients per cluster period across four hospitals for four time periods. Although we considered a 33.3% reduction of prescribed opioids a clinically meaningful reduction for prescriptions “exposed” to the best practice alert, we utilized a smaller effect size (11.1% reduction) for the power analysis to incorporate the average effect across all patients. We estimated that the trial would have $>99\%$ power to detect a ratio of geometric means of 0.89 (ON/OFF) for the amount of prescribed opioids or a difference of -0.12 (ON – OFF) on the log-scale, at the 0.05 significance level.