Introduction
Naloxone and flumazenil are opioid and benzodiazepine antagonists, respectively, that may be used in episodes of toxicity, especially when life-threatening respiratory depression ensues. However, they have shorter durations of action than most opioid and benzodiazepine agonists, which may lead to recurrent respiratory depression following administration1, especially if benzodiazepines have been used in conjunction with opioids2. Moreover, they are not commonly used outside of high acuity areas of the hospital. A new strategy for educating inpatient pediatric providers administering reversal agents should be deployed to prevent recurrent toxicity and to prepare for vigilant monitoring in appropriate settings.

Case Summary

Case 1
A 5.9 kg, 3 month old male w stridor and suspected laryngotraechomalacia presented for flexible bronchoscopy and bronchoalveolar lavage under moderate sedation. He was a 37 week product of a c-section performed for maternal pre-eclampsia, and was born cyanotic requiring intubation. He was noted to have pneumothorax at birth but was successfully extubated on day of life 1, requiring supplemental oxygen that was weaned before discharge after three days. He also had another hospitalization and recurrent emergency department visits for noisy breathing and retractions for which he was found to have bronchiolitis and laryngomalacia. Intraoperatively, he received IV fentanyl 10mcg and midazolam 1mg but desaturated requiring IV flumazenil 0.59 mg and naloxone 0.06 mg. The pt was found to have moderate to severe laryngomalacia with epiglottic fold swelling but the study was aborted due to desaturations. Pt was discharged home.

Case 2
64 kg 16 yo M w h/o ulcerative colitis reported sharp abdominal pain in the emergency department. He was admitted for further evaluation, and received IV morphine 8 mg and IV hydromorphone 1mg over the course of 6 hours while in the ED and on the general ward. He was evaluated by GI and surgery, and was recommended further observation, given reassuring CT imaging. Six hours after his first dose of opioid, he was unresponsive, diaphoretic, bradypneic and hypoxic. He received IV naloxone 0.4 mg and his symptoms resolved within 10 minutes. He remained on the general ward with IV morphine as needed until 1.5 days later when he was again found unresponsive within an hour of receiving IV morphine 2mg with ketorolac 30 mg, prompting a code blue with IV naloxone 0.4mg and icu admission.

Discussion
Recurrent opioid toxicity is a potential complication in opioid overdose cases in the adult emergency medicine literature, and has been associated with long-acting opioids as opposed to the route of exposure4. The use of reversal agents is uncommon on the general wards compared to post anesthesia care units, emergency departments, and intensive care units. A warning tool to remind of naloxone and flumazenil’s relatively short half-life compared to full agonists may prevent recurrent respiratory depression in pediatric inpatients and help plan for further appropriate monitoring. This may be in the form of text accompanying the computerized orders for these reversal agents, an educational conversation at the time of administration, and/or regular educational sessions.

References