Introduction
Ketamine is a derivative of phencyclidine with properties including NMDA receptor antagonism, analgesia, dissociative anesthesia, sympathomimetic effects, bronchodilation, and reduced risk of respiratory depression. At subanesthetic doses, ketamine may lower pain concentration and are more prone to experiencing adverse effects of the drug.

At our institution, ketamine infusions at sub-anesthetic doses of 0.05-0.15 mg/kg/hr are often used to supplement pain management regimens. Between July 1, 2015, to June 30, 2016, we have used this therapy 287 times to treat 262 different children aged 1-24 with 121 being male and 141 being female, with the goal of reducing both pain scores and narcotic use. Indications for treatment include oncology patients, chronic abdominal pain such as with Crohn’s disease, and major post-surgical patients such as for posterior spinal fusions in adolescent idiopathic scoliosis.

Case Description
Studies describing dosing ranges for sub-anesthetic ketamine infusions are scarce with most studies only describing induction with ketamine. As such, our pain service and inpatient pharmacy dose based on actual body weight rather than ideal body weight. Therefore, overweight patients may experience a greater than expected peak serum concentration and are more prone to experiencing adverse effects of the drug.

Two patients receiving subanesthetic ketamine infusions for oncology pain were noted to have urinary urgency and incontinence after initiation or increase of their ketamine infusion. This adverse effect has not been previously reported at this dosing range. These cases suggest that subanesthetic ketamine infusions may cause side effects that have previously been reported at anesthetic or abuse doses.

Patient 1
The first case is a 23 year old 76 kg African American female with acute myelogenous leukemia admitted for mucositis and back pain. She was initially placed on a morphine PCA, but after multiple increases in her PCA, she was started on a ketamine infusion at 0.1 mg/kg/hr. Over the next 12 hours, she had multiple episodes of new onset urinary incontinence and urgency. Initial evaluation by her primary team was negative and the pain team was notified. Her infusion rate was decreased to 0.05 mg/kg/hr, but symptoms persisted. However, when her infusion was discontinued, her urinary symptoms resolved.

Patient 2
The second case is a 19 year old 112 kg female with ovarian cancer who was admitted for mucositis. As before, the patient was placed on a morphine PCA without adequate control of her pain. She was then started on a ketamine infusion at 0.09 mg/kg/hr. She was continued at this dose for a week with moderate improvement in her pain. Her infusion was increased to 0.13 mg/kg/hr. Within 24 hours, she developed new onset urinary urgency. Causes for her urinary symptoms were investigated and ruled out. Her dose of ketamine was decreased to her initial dose of 0.09 mg/kg/hr. Upon decreasing the dose, her incontinence resolved.

Multimodal Approach to Pain Management
- Acetaminophen
- NSAIDs
- Opioids
- Anticonvulsants
- Local Anesthetics
- Ketamine Infusion

Ketamine Adverse Effects
Complications at Anesthetic Doses (0.5-3.0 mg/kg)
- General psychiatric symptoms
- Positive/negative symptoms of schizophrenia
- Dissociative symptoms
- Intoxication
- Lowered inhibitions with increased mood
- Confusion/Decreased concentration
- Perceptual disturbances – hallucinations
- Light-headedness/Drowsiness
- Headaches
- Nausea
- Diplopia
- Respiratory depression with increased secretions
- Urinary tract Complications – urge incontinence, ulcerative cystitis, dysuria
- Liver toxicity

Discussion
We have presented 2 patients with acute oncology pain that received sub-anesthetic ketamine infusions as part of their multimodal pain regimen that experienced a known side effect of higher doses of ketamine. Despite the benefits of ketamine at low doses, there are no clear guidelines regarding a dosing range for analgesic ketamine infusions. As such, we continue to search for the best dosing strategy that will reduce pain without inducing adverse effects.

References