Introduction
- Major depressive disorder (MDD) is a leading cause of disability.
- Most individuals with MDD receiving conventional antidepressants do not achieve full syndromal recovery.
- The dissociative anesthetic and N-Methyl-D-Aspartate (NMDA) receptor antagonist, ketamine, has demonstrated rapid and robust efficacy in adults who have not experienced sufficient syndromal relief following multiple antidepressant treatment trials (i.e., treatment-resistant depression [TRD]).
- The safety and tolerability of long-term ketamine treatment is insufficiently characterized.

Hypothesis
- Intravenous ketamine after repeat dose administration was hypothesized to be safe & tolerable in a real-world outpatient setting providing care to adults with TRD.

Methods
Patients received repeat dose IV ketamine infusions at the Canadian Rapid Treatment Center of Excellence (CRTCE) between July 2018 & December 2019.
- Patients were required to have Stage 2 TRD or higher (i.e., failure of ≥2 antidepressant trials of different classes).
- The Clinician-Administered Dissociative States Scale (CADSS) was used to further characterize current symptoms of dissociation severity.
- Safety was operationalized using transient changes in blood pressure (BP) & heart rate (HR). The pre-infusion, during infusion, post-infusion blood, & 20-min post-infusion BP & HR were each averaged across the 4 infusions & average values were used for analysis.
- Tolerability was operationalized as dissociative symptom severity, as measured by the CADSS (assessed at all four timepoints); tolerability also evaluated treatment-emergent adverse events during infusion and 20 minutes post-infusion.

Results & Conclusions
- Blood pressure significantly increased during infusion, with 44.3% meeting criteria for treatment-emergent hypertension (i.e., blood pressure ≥ 165/100 mmHg).
- 12% of patients exhibiting hypertension required pharmacological intervention (i.e., labetalol 5–30 mg or amlodipine 10 mg).
- Dissociation severity significantly attenuated after the first infusion but plateaued for subsequent infusions.
- The most frequently reported adverse events included drowsiness (56.4%), dizziness (45.2%), dissociation (35.6%), and nausea (13.3%).
- Ketamine was well-tolerated, with less than 5% of patients withdrawing due to tolerability concerns.
- The results from our analysis indicate that ketamine is safe and well tolerated when administered to adults with TRD in a specialized, multidisciplinary, community-based center such as the CRTCE.