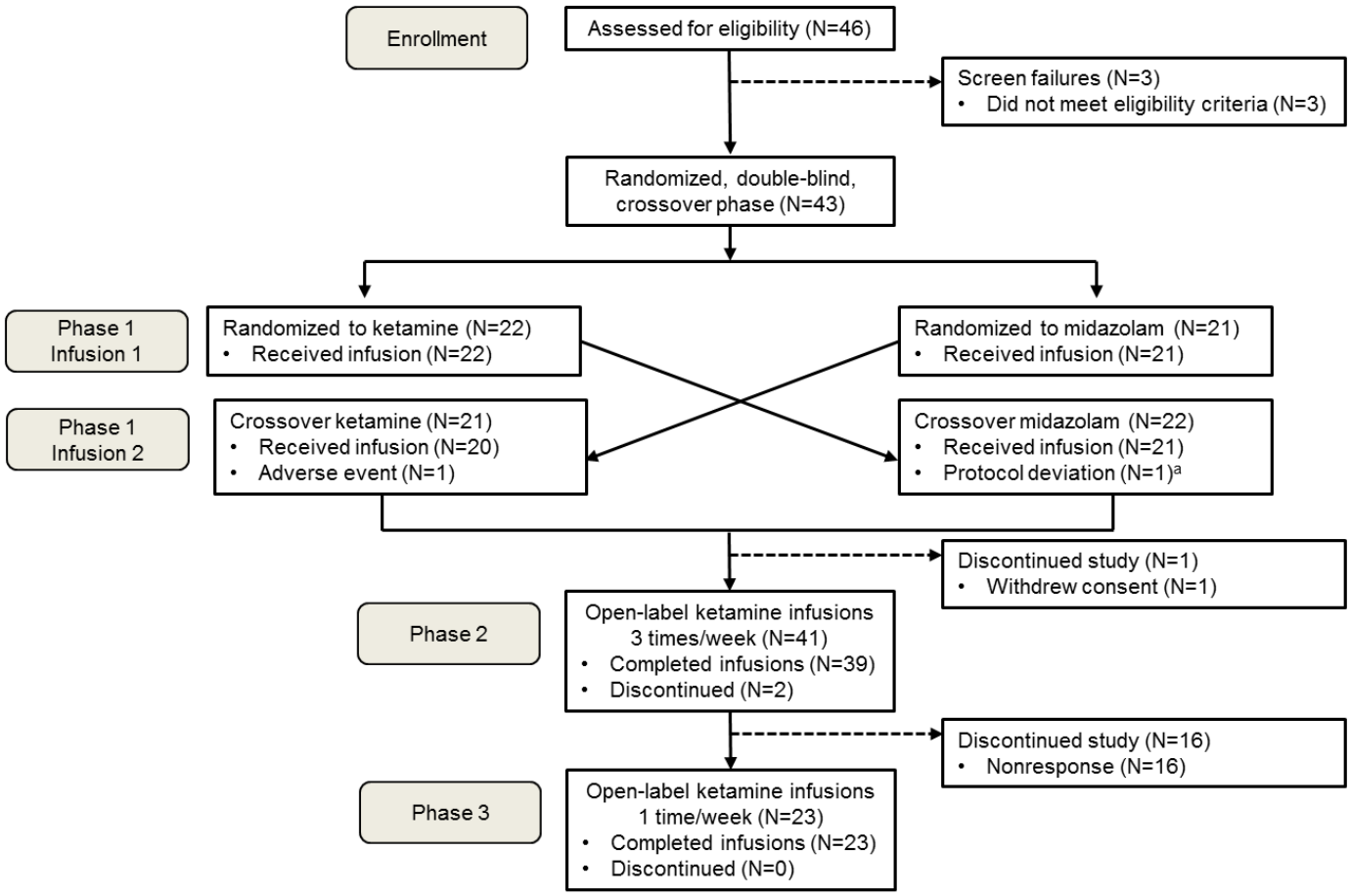
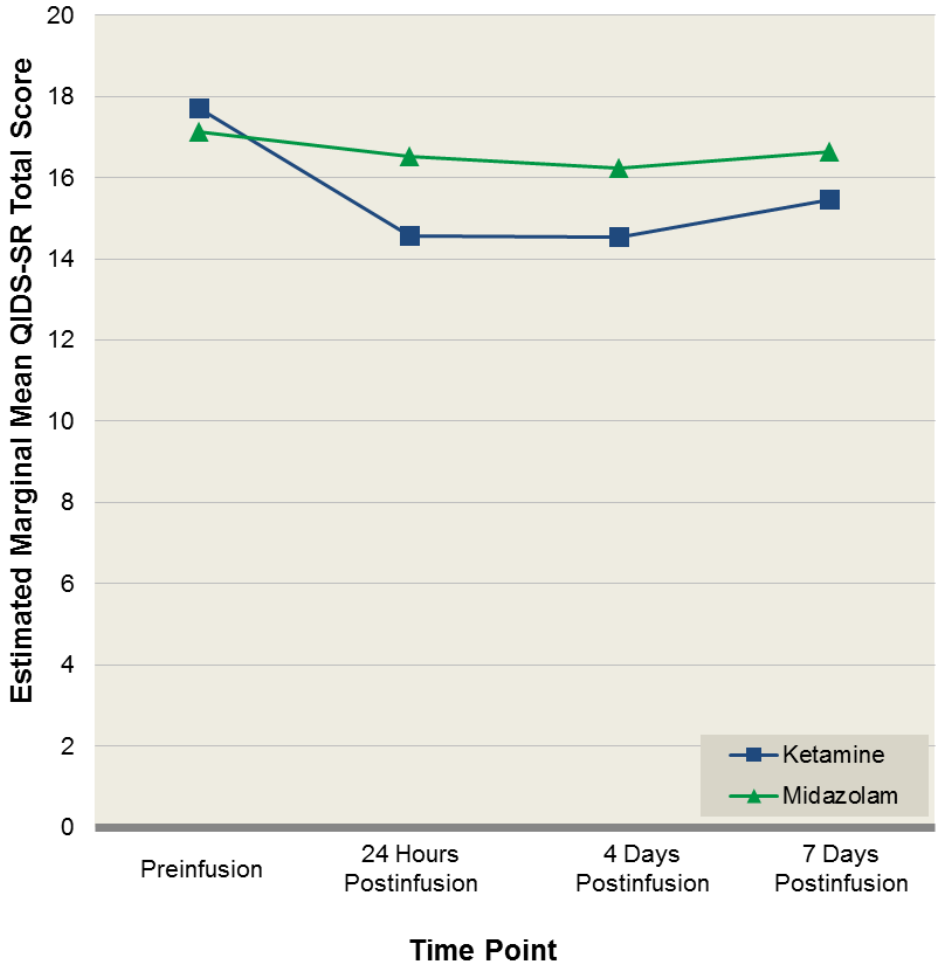
SUPPLEMENTARY MATERIALS

Figure SF1. Participant Flow in a Study of Intravenous Ketamine in Treatment-Resistant Depression



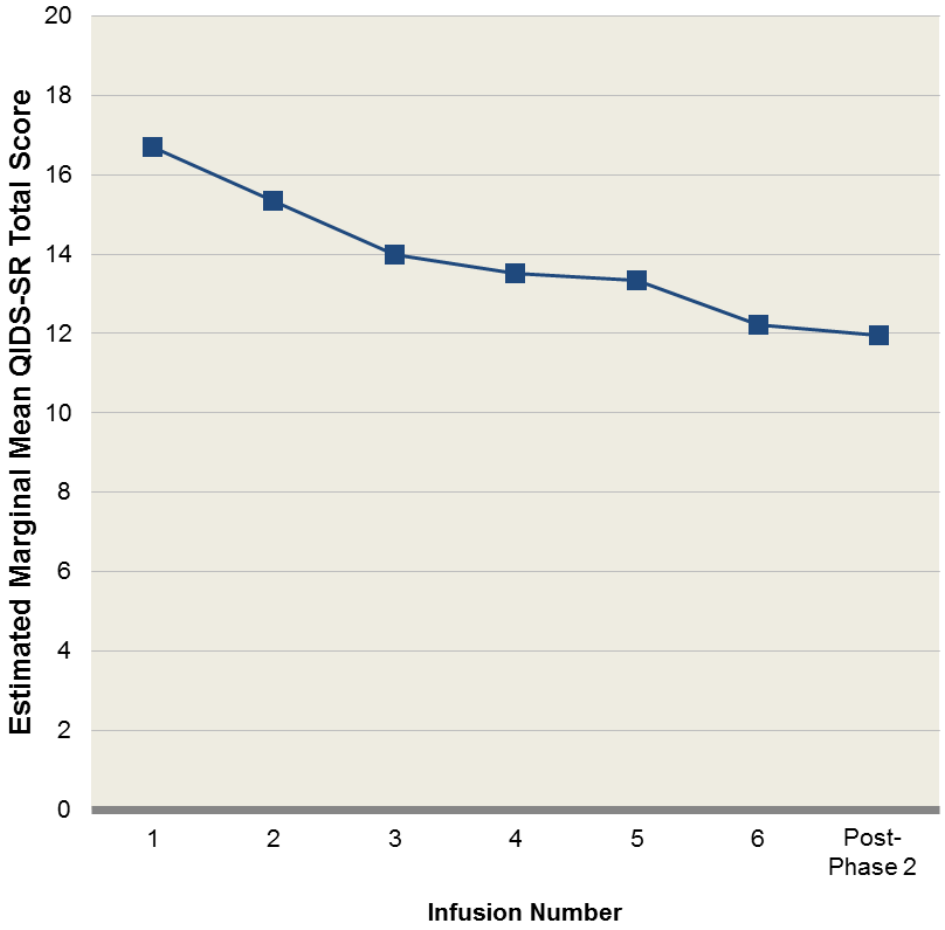
[a] A single study participant received treatment with ketamine prior to enrollment in the study. To maintain study blinding, this individual received a single open-label ketamine infusion during Phase 1 but did not receive the crossover midazolam infusion (considered a protocol deviation). Phase 1 data from this participant was excluded from Phase 1 analysis. The participant completed Phases 2 and 3 of the trial and having received the correct number of ketamine infusions overall, was included in the data analyses for Phases 2 and 3.

FIGURE SF2. Change in Self-Reported Depression Severity Over Time in Patients with Treatment-Resistant Depression Treated with Single Subanesthetic Infusions of Ketamine and Midazolam using a Randomized, Double-Blind, Crossover Design[a]



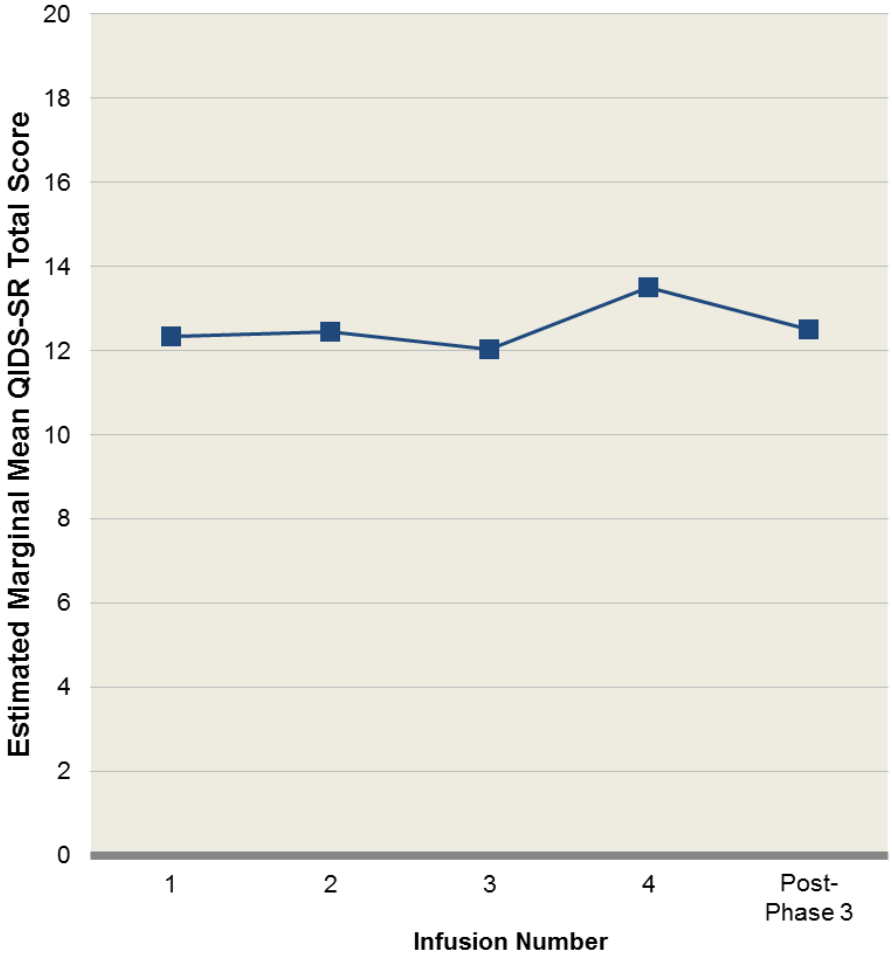
[a] Participants had a significantly larger decrease in self-reported depression severity using the Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR) with ketamine relative to midazolam ($p = 0.03$).

FIGURE SF3. Change in Self-Reported Depression Severity Over Time in Patients with Treatment-Resistant Depression Treated with a Course of Open-Label, Thrice-Weekly Administered Repeated Subanesthetic Infusions of Ketamine[a]



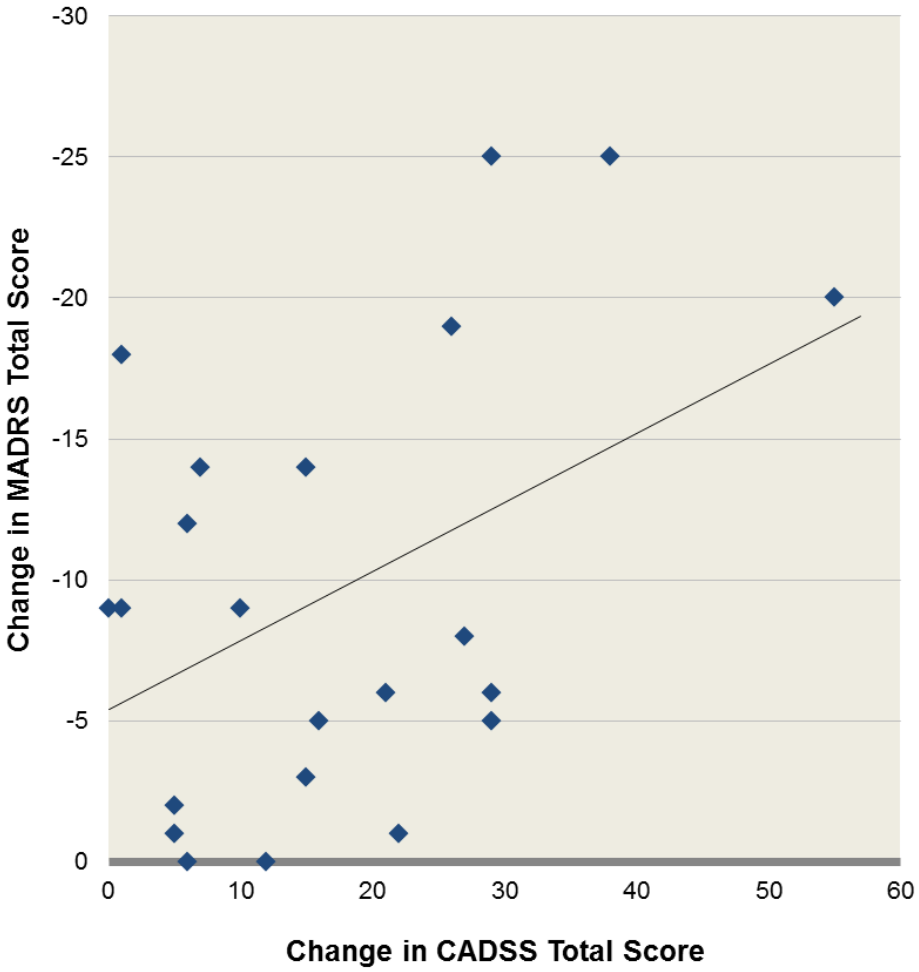
[a] With repeated ketamine infusions, participants had a significant cumulative decrease in self-reported depression severity using the Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR) ($p < 0.001$).

FIGURE SF4. Change in Self-Reported Depression Severity Over Time in Ketamine Responders Treated with Open-Label Weekly Administered Subanesthetic Maintenance Infusions of Ketamine[a]



[a] With weekly maintenance ketamine infusions, participants had no significant change in self-reported depression severity using the Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR; p = 0.30).

FIGURE SF5. Association Between Change in Participants' Dissociative Side Effects and Change in Depression Severity 24 Hours After the Single Ketamine Infusion[a]



[a] Significant negative correlation between participants' change in dissociative side effects during the single ketamine infusion assessed using the Clinician-Administered Dissociative States Scale (CADSS) and their change in depression severity 24 hours postinfusion using the Montgomery-Åsberg Depression Rating Scale (MADRS) (Pearson's r = -0.46; p = 0.03; N = 22).