Title: RCT of Intraoperative Ketamine vs Saline in Depressive Surgical Patients

Summary:

The Data Studio Workshop brings together a biomedical investigator with a group of experts for an in-depth session to solicit advice about statistical and study design issues that arise while planning or conducting a research project. This week, the investigator(s) will discuss the following project with the group.

This is a single-site, double-blinded, randomized clinical trial (RCT) to evaluate the antidepressant superiority of intravenous (IV) ketamine compared to placebo when administered during surgery to adult patients with symptomatic major depressive disorder. Participants are randomly allocated in a 1:1 ratio to one of two groups: Group A (n=20) will receive a single administration of IV ketamine during surgery. Group B (n=20) will receive IV saline (placebo) during surgery. The study drug will be given after anesthetic induction to ensure participant blinding. Healthcare providers, investigators, and outcomes assessors are also blinded. Our primary outcome measure is the Montgomery-Asberg Depression Rating Scale (MADRS), which is widely used in depression trials. Baseline MADRS scores are obtained from all participants. Post-intervention MADRS scores are collected on post-operative days 1, 2, 3, 5, 7, and 14. Secondary outcomes include the Hospital Anxiety and Depression Scale (HADS), pain scores, opioid use, and hospital length of stay. We have reached three-quarters of our enrollment goal. Data has been collected on these participants. We have blinded data available for review. Our goal is to finalize our statistical analysis plan prior to unblinding of data.

Questions:

1. Which of the following is the most statistically efficient analysis method for our primary outcome?
   (a) Students t-test comparing the difference in depression scores between baseline and a single post-operative timepoint.
   (b) Mixed model for repeated measures (MMRM) using data from all assessed timepoints.

2. Should we consider other methods?

3. If we choose a t-test, which post-operative timepoint is most likely to yield the greatest difference in pre- vs post-operative depression scores between groups?

4. Is it advisable to sum the numeric scores of 2 depression scales (e.g. MADRS+HADS) to report a composite outcome instead?

5. What are the advantages and disadvantages of a composite outcome?

6. How to handle missing data?
Zoom Meeting Information

Join from PC, Mac, Linux, iOS or Android:
https://stanford.zoom.us/j/93839486551?pwd=dEJaWDcyTjNFTUhKR01oNDM1eXdVVT09

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