Protocol ID # 53017
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Title: Nitrous Oxide for Posttraumatic Stress Disorder (PTSD): A Phase IIa Trial

Statistical Methods: Hypothesis Test/Power Analysis

Primary Hypothesis: A one-hour nitrous oxide inhalation session will reduce PTSD within 1 week compared to placebo.
To test the primary hypothesis that nitrous oxide will show efficacy for PTSD, we will regress the 1 week CAPS-5 score on treatment, adjusted for CAPS-5 baseline score. We will incorporate a Kaplan-Meier approach with log-rank test comparing time to drop-out in the two treatment groups as a preliminary analysis.

Power analysis/sample size: Assuming that a change in the CAPS-5 of 12 points represents meaningful improvement in clinical symptoms, using STATA 14 (StataCorp., 2017), we calculate that an expected sample size of 78 completers (39 per group) will provide 80% power to detect a moderate effect size of a difference of 0.6 standard deviations in the change score, allowing a definitive go/no decision. At least 104 participants will be randomized over the 4 years to achieve 78 total sample, accounting for 25% attrition. We note that this estimate is conservative as it does not take into account partial data from non-completers and uses the unrealistic, mathematically worst-case, scenario for mixed effects models in which the intra-individual correlation structure is such that the mixed effects model provides no added information. If the drug does not meet this threshold, it would not be pursued further. On the other hand, if nitrous oxide yields a clinically meaningful change, we would have important data (e.g., an estimated effect size in nitrous oxide vs midazolam and an estimated correlation structure) for a future multi-site Phase 3 confirmatory clinical trial.