Data supplement for Hien et al.,Project Harmony: A Meta-Analysis With Individual Patient Data on Behavioral and Pharmacologic Trials for Comorbid Posttraumatic Stress and Alcohol and Other Drug Use Disorders. Am J Psychiatry (doi: 10.1176/appi.ajp.22010071)

**CONTENTS**

## 1. Acronyms and Effect Size Color Codes

| Acronym | Description |
|---------|-------------|
| PPI | Participating Principal Investigator |
| IDA | Integrative Data Analysis |
| MNLFA | Moderated Nonlinear Factor Analysis |
| IPTWs | Inverse Probability of Treatment Weights |
| DIF | Differential Item Functioning |
| SEM | Structural Equation Modeling |
| IML | Interactive Matrix Language (SAS) |
| CE | Comparative Effectiveness |
| ES | Effect Size |
| RP | Relapse Prevention |
| COPE | Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure |
| TAU | Treatment-as-Usual |
| SS | Seeking Safety |
| LCL | Lower Confidence Limit |
| UCL | Upped Confidence Limit |
| AMCG | Active Monitoring Control Group |
| MI | Motivational Interviewing |
| CBT | Cognitive Behavioral Therapy |
| CPT | Cognitive Processing Therapy |
| PE | Prolonged Exposure |
| TIPSS | Treatment of Integrated Posttraumatic Stress and Substance Use |
| TARGET | Trauma Adaptive Recovery Group Education and Therapy |
| EMDR | Eye Movement Desensitization and Reprocessing |
| MET | Motivational Enhancement Therapy |
|  |  |

| Effect Size Color Codes | |
|---|---|
| 🟩 | Focal Treatment is Superior; Statistically Significant at p<.05 and ES > |.20| |
| 🟩 | Focal Treatment is Superior; Not Statistically Significant at p<.05 but ES > |.20| |
| 🟧 | Focal Treatment is Inferior; Not Statistically Significant at p<.05 but ES > |.20| |
| 🟥 | Focal Treatment is Inferior; Statistically Significant at p<.05 and ES > |.20| |

## 2. Systematic Search Strategy

We conducted a systematic search of PSYCINFO and MEDLINE, that built on recent systematic reviews of PTSD/AOD treatments at the time of submission of the grant application (1995-2017). This involved replicating the search terms, criteria, and parameters employed by

the other systematic reviews. This process yielded the 21 studies identified previously by these reviews plus an additional 64 studies that were newly published beyond the systematic reviews. Studies were considered for inclusion in *Project Harmony* if they met the following eligibility criteria: (1) psychological and/or pharmacological intervention targeting either PTSD symptoms, AOD symptoms or both; (2) collected measures of PTSD and AOD outcomes, targeting one or both of the disorders (at pre- and post-treatment); (3) PTSD/AOD adult sample defined as individuals (a) ages 18 and above, (b) with a current diagnosis of an AOD (i.e., alcohol and other drug abuse or dependence in *DSM-IV*, substance use disorder in *DSM-5*), and (c) a current diagnosis of full or subthreshold PTSD (*DSM-IV or DSM-5*). This study was reviewed and approved by the Institutional Review Boards (IRB) of RTI International and Rutgers University (Institutions for *Project Harmony*'s principal investigators).

To combat the "file drawer effect" (i.e., unpublished data from either completed, in progress or under submission studies), we searched Clinicaltrials.gov for registered trials meeting the aforementioned criteria, yielding 163 studies. In total, across all searches prior to the funding of *Project Harmony* in June 2018, as well as searches after the project was funded and PPIs making our group aware of other studies that were ongoing that had not been published (i.e., "word of mouth"), 248 non-overlapping studies were identified, from which 55 studies met criteria for inclusion. Of these 55 studies, 6 were single-arm trials identified for use in other analyses excluding the primary outcomes paper. Participating principal investigators (PPIs; principal investigators of the identified studies) identified prior to the project being funded provided a good-faith letter of agreement for deidentified raw data access to the identified datasets to *Project Harmony*. After retrieval and preliminary examination, PPIs for eligible studies were contacted for confirmation of eligibility criteria as well as additional study-level information (e.g., treatment retention rates, measure availability, fidelity measurement process). We acquired data for 36 trials (1–34); two datasets were unpublished.

### 3.  <u>Overview of Dataset Types</u>

Three types of datasets were made available to *Project Harmony* by PPIs. The primary type of data (28 of the 35 studies) were individual-level observations, with item-level data for indicators of PTSD (i.e., symptoms), alcohol use severity and drug use severity. The item-level data for PTSD, alcohol use severity, and drug use severity were used in estimating latent factor scores under the Integrative Data Analysis (IDA) framework. The IDA framework (35,36) is an empirical data harmonization procedure that is grounded in the principles of advanced forms of factor analysis (FA) and item response theory (IRT) that allow for scale score estimation of latent constructs that take into account cross-study differences in measurement. A more extensive description of IDA is provided later in this Appendix, with additional pedagogical descriptions of IDA found in (36,37). The second type of data that were provided were individual-level observations with total scores for PTSD and AOD outcomes; in these studies (5 of 35), the original items were no longer available. The final data type was aggregated summaries (i.e., means/correlations/standard deviation) on the item-level data for indicators of PTSD (i.e., symptoms), alcohol use severity and drug use severity, provided for 2 of the 35 studies where the IRB of the studies forbade the PPI from sharing individual observations but allowed the PPI to share summary data. This summary data was used as the basis for simulating multiple synthetic datasets. Synthetic data generation is a statistical technique drawn from the survey literature(38,39) that allows for the preservation of multivariate relationships between variables in a dataset (e.g., treatment effect sizes) without the use of raw data in cases where data

disclosure risk is high; as Reiter notes, the approach draws on very similar principles to multiple imputation for missing data.

### 4. <u>Predictor/Covariate Standardization and Harmonization</u>

A systematic process was employed for standardization of item/symptom-level measures in order to place each variable on the same metric and/or renaming the item/measure to a common variable name in the dataset. For covariates that were used to estimate propensity scores and inverse probability of treatment weights (IPTWs), the following describes the process of item-level harmonization/standardization across studies:

**Age**. Age was retained in its natural metric from all original studies.

**Gender.** Gender was recoded to a common indicator (Female = 0, Male = 1)

**Race/Ethnicity**. Race/ethnicity categories were harmonized to dummy variable indicators for White, Black, Hispanic, Asian, and Other (some studies allowed the reporting of more than 1 category e.g., Black/Hispanic)

**Education Level**. Most often measured as either ordered categories or years of education, education level was harmonized to a three-category dummy variable: High School or Less, Some College, or College Degree or More.

**Marital Status**. Marital status was harmonized to reflect a common indicator of Married (1) versus all other categories (0).

**Population Type**. Population type was coded into three categories: Civilian, Veteran or Incarcerated.

**Proportion of Intended Treatment Dosage**. Treatment dosage was harmonized across studies to reflect a proportion of intended dosage as the dosage received (number of behavioral treatment sessions attended and/or number of medication doses taken) divided by the maximum possible intervention dosage.

**Depression**. Pre-treatment depression was harmonized into a binary variable indicating either a formal diagnosis of major depression or a clinical cutoff for severe depression for the particular continuous measure of depression that was available.

**Concomitant Medications.** Pre-treatment concomitant psychiatric medication was harmonized into a binary variable indicating the use of any non-study psychiatric medication prior to entry into the RCT.

**Structuring of Chronological Time.** Two time variables were created to reflect two piecewise linear trajectories: an in-treatment outcome trajectory capturing the model-estimated change in the outcome variable from baseline through the end-of-treatment ($Time_1$) and b) a post-treatment outcome trajectory capturing the model-estimated change in the outcome variable from the end-of-treatment through 12-month follow-up ($Time_2$).

| Primary Assessment Periods | $Time_1$ | $Time_2$ |
|---|---|---|
| Baseline | 0 | 0 |
| Mid-Treatment | .5 | 0 |
| End-of-Treatment | 1 | 0 |
| 3-Month Follow-Up | 1 | 1 |
| 6-Month Follow-Up | 1 | 2 |
| 9-Month Follow-Up | 1 | 3 |
| 12-Month Follow-Up | 1 | 4 |

## 5. Harmonization of PTSD/AOD Indicators

Prior to MNLFA scale score estimation of underlying PTSD, alcohol use and drug use severity, items/symptoms for each construct were placed on the same metric (i.e., item harmonization(35)). As noted by Bauer and Hussong(35), harmonizing items across studies, particularly when they were never intended to be combined, is a necessary but not sufficient step to ensure measurement comparability of the construct; this is what is done under the IDA/MNLFA framework described below and also in Saavedra et al.(40)

**PTSD Items/Symptoms**. A total number of 42 PTSD indicators (21 symptoms from a clinical interview, 21 self-report symptoms) were harmonized across the studies that had PTSD item-level data and would formulate the indicators of a 42-item latent PTSD construct estimated under MNLFA; 16 of the 28 "raw" data/item-level studies had both a clinical interview measure and a self-report measure. The primary clinical interview measures available across studies were a) the Clinician Administered PTSD Scale/DSM-IV (CAPS-IV(41)), b) the Clinician Administered PTSD Scale/DSM-5 (CAPS-5(42)) and c) the Post-traumatic Stress Scale-Interview (43); each assessment system has a primary method for converting frequency and intensity items (e.g., CAPS-IV "F1/I2 rule") into binary indicators of symptom presence/absence. These item-to-symptom conversion rules were used to harmonize, across the three clinical interview assessment systems, the 16 PTSD symptoms that are common to both DSM-IV and DSM-5, the 1 symptom that is unique to DSM-IV that was dropped from DSM-5 (Sense of Foreshortened Future) and the 4 symptoms that were added to DSM-5.

A similar process was undertaken for self-report measures. The self-report measures available across studies were a) the PTSD Checklist/DSM-IV (PCL-IV)(44), b) the PTSD Checklist/DSM-5 (PCL-5)(45), c) the Post-traumatic Stress Scale-Self Report/DSM-IV (43), d) the Impact of Events Scale/DSM-IV (IES)(46) and e) the Post-traumatic Diagnostic Scale/DSM-IV (PDS).(47) Each self-report assessment system also has a primary method for converting frequency and/or intensity items into binary indicators of symptom presence/absence. In a manner similar to the clinical interview symptoms, these conversion rules were used to harmonize, the 16 PTSD symptoms that are common to both DSM-IV and DSM-5, the 1 symptom that is unique to DSM-IV that was dropped from DSM-5 (Sense of Foreshortened Future) and the 4 symptoms that were added to DSM-5.

This process resulted in a set of 42 harmonized interview/self-reported PTSD symptoms in the IDA dataset. For patients in the DSM-IV studies, only a maximum of 34 symptoms was possible (17 symptoms from an interview and self-report each) while only a maximum of 40 was possible for patients assessed under DSM-V. Scale scoring under MNLFA, whether there are differences in the measurement parameters for each symptom across assessment system and/or other factors (i.e., measurement non-invariance/differential item functioning (DIF)) is addressed in the Appendix section on latent variable scale score estimation under moderated non-linear factor analysis modeling (MNLFA; .

**Drug Use Items**. Binary indicators of any use in the past 30 days of the following substances were harmonized across three assessment systems: Timeline Followback (TLFB)(48), the Addiction Severity Index (ASI)(49) and the Substance Use Inventory (SUI).(50) The following indicators were then used to support a six-indicator latent substance use variable: cocaine, heroin, opioids (excluding heroin), sedatives, other psychostimulants, and hallucinogens.

**Latent Alcohol Use.** A latent alcohol use variable consisted of two indicators; number of days of alcohol use in the past 30 days and any alcohol use to intoxication in the past 30 days.

Two-indicator latent variables can be supported in factor analysis scoring, so long as the two indicators are highly correlated (51), as are 30-day use and use to intoxication. The TLFB and ASI are naturally structured as 30-day use outcomes but the SUI's natural item-level metric is past 7 days. In order to harmonize the 7-day use item to 30 days, the 7-day use measures for the SUI were multiplied by 4.285 (so that a report of 7 days use per week translated to 30 days of use in the past 30). Assessment of whether this harmonization decision has an impact on cross-assessment measurement and, if it did, incorporation of different item parameters in estimating alcohol severity scale score estimates for the studies with the SUI is part and parcel to the differential item functioning (DIF) analysis under MNLFA (see Table S4 below).

6. **Scale Score Estimation as "Model-Based Standardization"**

**Scale Score Estimation: Individual-Level Observations from Item-Level Data**.

Prior to MNLFA estimation, basic tests for unidimensionality were conducted separately for the three constructs (PTSD severity, alcohol severity, drug severity) using means-and-variance-adjusted weighted least squares (WLSMV) estimation in Mplus (Version 8(52)). For PTSD, the results indicated a good fit for a single-factor model for harmonized PTSD symptoms, e.g., comparative fit index (CFI) = .94, root mean square error of approximation (RMSEA) = .057, 95% CI [.056, .058], meeting the standard for essential unidimensionality.(53) Per the recommendations of McNeish and Wolf (54), a 1-parameter logistic model, where all factor loadings were constrained to equality, was also fit to the data to assess the viability of a sum score "analog" as a psychometric model. This model fit the data significantly worse, $\Delta\chi^2(31) = 4009.616$, p<.0001, suggesting that using sum scores for measuring PTSD would be biased.

For drug use severity, the sum score analog model fit equally well to the model where all factor loadings varied across substance; thus factor loadings were constrained to equality across substances. For alcohol use severity, item parameters cannot be constrained to equality given the differences in the item scales for past month alcohol use (continuous, 0-30) versus any past month intoxication (binary). Thus, a) for PTSD and alcohol severity, scale score estimates needed to account for differences in the relative weight of each item in relation to the latent constructs and b) these models served as the base models for estimating measurement non-invariance (MNI) or differential item functioning (DIF) under the MNLFA framework.

The sequence of MNI/DIF testing followed the general recommendations of Bauer (55). Because of the large number of predictors, indicators, and the complexity of including DIF on both the mean and variance of the factor, models with all items regressed on all predictors of MNI/DIF in a single model for PTSD, alcohol use and drug use (respectively) were prohibitive. We adopted a "sequential analysis" in which Step 1 was a sequence of models where MNI/DIF of one item regressed on one predictor, with mean and variance on the factor. From these models, the MNI/DIF on item thresholds and/or factor loadings identified from Step 1, where the parameter estimate was statistically significant at p<.001, were included simultaneously in a full Step 2 model. The MNI/DIF parameters that remained significant at p<.001 were retained for a final MNLFA scoring model, with MNLFA scores output from Mplus using the SAVEDATA command, for each outcome (PTSD, alcohol, drug); the scale of the scores for PTSD severity, alcohol severity and drug use severity was set to N(0,1) at baseline and allowed to vary across all other timepoints. This allowed for any change over time to be interpreted in standardized mean difference (i.e., Cohen's d) units. All MNLFA analyses in the current study were conducted in M*plus*, following the example codes from the supplemental material of Bauer (2017). We used R

package MplusAutomation (56) to facilitate macro processing of the large number of MNLFA analyses in M*plus*.

**Scale Score Estimation: Individual-Level Observations from Total Scores**. For the 5 studies that did not have item-level data available for estimation of latent variable scale scores, the *total* scores that they did have available for PTSD, alcohol and drug use were "baseline standardized". That is, within each study for each outcome, all observations across all timepoints were standardized based on the baseline mean and standard deviation. This would have the effect of placing the baseline observations as standard normal (i.e., mean = 0, SD = 1) and changes over time for observations for subsequent timepoints reflecting change in a standardized mean difference/Cohen's d metric; the scale score estimation models under MNLFA have a similar structure (i.e., constrained to N(0,1) at baseline), though the MNLFA scores themselves are "weighted" by the factor loadings and the total scores are "unweighted".

**Synthetic Individual-Level Observations from Item-Level Summary Statistics.** As described in the Saavedra et al., (2021) protocol(40), there were 3 studies that met eligibility criteria and had PPIs willing to share data, but the original consent forms had clauses that forbade the sharing of raw data beyond the original PPIs or the original study aims. One of the PPIs representing 2 studies (32,33) was able to provide treatment arm-specific summary data (means/SDs/correlations) across PTSD, alcohol and drug use items; this allowed for the preservation of the original multivariate relations between covariates and outcome variables that were conditional on treatment arm (i.e., treatment x covariate interaction effects) without the use of the original raw datasets. In other words, this allowed for the generation of synthetic data that had the same statistical properties as the original data from Simpson (2015)(57) and Stappenbeck et al., (2015).(58) This is also similar in principle to the use of summary data as input data in models such as multiple regression and structural equation models (SEMs) during the era when computing power was too limited for modeling raw, individual-level observations. (59)

We used this summary data to serve as parameters for the generation of multiple, "fully synthetic" datasets to represent those studies, a practice borne out of survey methodology. The idea is that the synthetic public use dataset(s) will be generated to have the same properties of the actual dataset so that results from analysis of the synthetic data would be no different than results from the original dataset. Yet no original observations would be contained in fully synthetic data so that sensitive individual-level data with geographic identifiers are protected from disclosure. (39,60)

For each of these two studies, we first converted the means, standard deviations and (Pearson) correlations into means/proportions and tetrachoric/point biserial correlations using the 'phi2tetra' function of the R package 'psych'.(61) We then used the converted summary data for each treatment arm as population parameters for generating 20 datasets of size n (equivalent to the reported n for that treatment arm in the study) under a(n underlying) multivariate normal model using the 'randnormal' function in SAS Proc IML. Thresholds corresponding to the proportion cutpoints for each of the binary variables were then imposed on the simulated underlying multivariate normal data. Each of the 20 simulated datasets were combined across treatment arms and prepared for later MNLFA scale scoring for PTSD, alcohol and drug use. These datasets would then be merged with the 20 multiply-imputed datasets (see section on Multiple Imputation below) from the other 33 studies.

**7. <u>Multivariate Multiple Imputation under Chained Equations.</u>**

Missing data on predictors/covariates and outcome variable scale scores for 33 of the 35 RCTs (excluding the 2 RCTs for which synthetic datasets were generated) was estimated using the R package 'mice'. (62) 'mice', unlike many other multiple imputation procedures (e.g., SAS Proc MI), handles missing data that have a multilevel structure (e.g., repeated measures among patients, patients clustered within studies) and can do so when multivariate normality cannot be assumed when there is a mix of continuous and categorical variables using fully conditional specification (FCS). FCS uses a series of univariate conditional imputation models with a random intercept structure for study-level clustering of missingness (conditional on all other available variables in the dataset), with predictive mean matching (63) for continuous variables (e.g., age, PTSD/AOD scale scores) and logistic regression for binary variables (i.e., covariates), respectively. 20 multiply-imputed datasets were estimated for 33 of the 35 studies and merged with the 20 synthetic datasets each of the two studies that were based on summary information.

## 8. Table S1a: Overall and Treatment Class-Specific Descriptives

| Covariates | Overall Sample MEAN | STD | Treatment-as-Usual MEAN | STD | Placebo Med MEAN | STD | AOD Behavioral MEAN | STD | Trauma-Focused MEAN | STD | Integrated MEAN | STD | AOD Med MEAN | STD |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Age | 39.03 | 11.28 | 36.19 | 9.80 | 40.00 | 12.39 | 40.37 | 11.67 | 42.79 | 11.99 | 38.93 | 11.21 | 45.64 | 9.50 |
| % Male | 52.60% | | 45.2% | | 73.4% | | 44.0% | | 62.7% | | 42.3% | | 69.1% | |
| % Hispanic | 7.30% | | 8.3% | | 3.3% | | 4.2% | | 9.1% | | 9.0% | | 3.6% | |
| % White | 65.00% | | 70.5% | | 66.0% | | 64.6% | | 61.1% | | 68.0% | | 41.8% | |
| % Black | 24.70% | | 18.2% | | 28.9% | | 28.9% | | 29.0% | | 19.7% | | 54.5% | |
| % Asian | 0.70% | | 0.4% | | 0.5% | | 0.7% | | 2.1% | | 1.0% | | 0.0% | |
| % Other | 4.40% | | 4.7% | | 2.3% | | 1.5% | | 8.1% | | 5.3% | | 0.0% | |
| % High School or Less | 50.70% | | 54.9% | | 43.3% | | 56.4% | | 48.6% | | 53.2% | | 40.0% | |
| % Some College | 33.20% | | 30.5% | | 36.8% | | 28.0% | | 38.0% | | 31.9% | | 45.5% | |
| % College Degree or More | 16.10% | | 14.6% | | 19.8% | | 15.6% | | 13.3% | | 14.9% | | 14.5% | |
| % Married | 18.60% | | 17.7% | | 16.0% | | 17.1% | | 21.1% | | 15.9% | | 15.0% | |
| % Veteran | 46.60% | | 38.0% | | 55.9% | | 30.5% | | 67.7% | | 44.6% | | 100.0% | |
| % Incarcerated | 1.70% | | 2.5% | | 0.0% | | 0.0% | | 0.0% | | 4.1% | | 0.0% | |
| % of Treatment Dosage Received | 57.80% | | 57.2% | | 70.1% | | 58.3% | | 48.1% | | 55.7% | | 65.6% | |
| % Major Depression | 54.80% | | 54.7% | | 39.6% | | 52.6% | | 53.5% | | 59.6% | | 48.3% | |
| % Pre-Treatment Non-Study Medication | 60.00% | | 61.0% | | 54.2% | | 64.6% | | 65.0% | | 62.0% | | 29.1% | |

## 9. Table S1b: Overall and Treatment Class-Specific Descriptives

| Covariates | AOD Medication + PTSD Medication MEAN | STD | Integrated + AOD Medication + PTSD Medication MEAN | STD | Integrated + Trauma-Focused MEAN | STD | Trauma-Focused + AOD Medication MEAN | STD | PTSD Medication + Placebo MEAN | STD |
|---|---|---|---|---|---|---|---|---|---|---|
| Age | 40.71 | 11.90 | 42.72 | 9.67 | 40.88 | 11.73 | 40.43 | 10.78 | 39.7625 | 11.30157 |
| % Male | 75.9% | | 40.3% | | 70.4% | | 72.4% | | 0.94 | 0.237784 |
| % Hispanic | 6.6% | | 8.0% | | 7.2% | | 4.1% | | 0.0725 | 0.259639 |
| % White | 75.0% | | 26.1% | | 57.4% | | 22.5% | | | |
| % Black | 16.9% | | 48.9% | | 33.9% | | 60.7% | | 0.1375 | 0.344806 |
| % Asian | 0.5% | | 0.0% | | 0.9% | | 0.1% | | 0.0125 | 0.111242 |
| % Other | 3.8% | | 15.8% | | 4.7% | | 0.6% | | 0.1225 | 0.328273 |
| % High School or Less | 40.1% | | 44.3% | | 40.8% | | 43.1% | | | |
| % Some College | 41.4% | | 25.6% | | 38.2% | | 41.9% | | 0.4575 | 0.498814 |
| % College Degree or More | 18.6% | | 30.1% | | 21.0% | | 15.0% | | 0.19 | 0.392792 |
| % Married | 18.0% | | 26.8% | | 22.4% | | 21.5% | | 0.275 | 0.447073 |
| % Veteran | 59.1% | | 8.5% | | 55.5% | | 100.0% | | 0.91 | 0 |
| % Incarcerated | 0.0% | | 0.0% | | 0.0% | | 0.0% | | 0 | 0 |
| % of Treatment Dosage Received | 64.6% | | 45.3% | | 59.5% | | 58.3% | | 0.5875 | 0.357397 |
| % Major Depression | 53.1% | | 61.0% | | 53.4% | | 59.3% | | 0.455 | 0.498595 |
| % Pre-Treatment Non-Study Medication | 56.0% | | 59.0% | | 58.2% | | 31.9% | | 0.7125 | 0.453163 |

## 10. Table S2: Unweighted and Propensity Score-Weighted Covariate Differences Across Treatment Classes

| | Unweighted Covariate Differences | | | | | Propensity Score-Weighted Differences | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Across Treatment Conditions | | | | | Across Treatment Conditions | | | |
| | $F (13, 3895)$ | p-value | $r^2$ | d | | $F (13, 3895)$ | p-value | $r^2$ | d |
| Age | 0.79 | 0.67 | 0.003 | 0.11 | | 0.35 | 0.98 | 0.001 | 0.06 |
| Gender | 1.08 | 0.37 | 0.004 | 0.13 | | 0.35 | 0.98 | 0.001 | 0.06 |
| Race/Ethnicity | 1.75 | 0.04 | 0.006 | 0.15 | | 0.41 | 0.96 | 0.001 | 0.06 |
| Education Level | 1.31 | 0.19 | 0.004 | 0.13 | | 0.42 | 0.96 | 0.001 | 0.06 |
| Marital Status | 1.54 | 0.09 | 0.005 | 0.14 | | 0.44 | 0.95 | 0.001 | 0.06 |
| Population Type | 0.55 | 0.89 | 0.002 | 0.09 | | 0.09 | 0.99 | 0 | 0 |
| % of Treatment Dosage Received | 8.71 | <.001 | 0.028 | 0.34 | | 0.63 | 0.82 | 0.002 | 0.09 |
| % Major Depression | 1.1 | 0.35 | 0.004 | 0.13 | | 0.34 | 0.98 | 0.001 | 0.06 |
| % Pre-Treatment Non-Study Medication | 2.8 | <.001 | 0.009 | 0.19 | | 0.46 | 0.94 | 0.001 | 0.06 |

# 11. Table S3a: Final Moderated Non-Linear Factor Analysis (MNLFA) Scale Scoring Item Parameters for Latent PTSD Severity (Threshold DIF for Clinical Interview Symptoms)

| Symptoms - Interview | Item Thresholds | Factor Loadings | Threshold Difference | | | | | | | | | | | | | CAPS-5 | PSS-I |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Age | Black | College | Dep | Jail | Male | Veteran | Mid-Tx | EOT | 3-mo FU | 6-mo FU | 9-mo FU | 12-mo FU | | |
| Intrusive Recollections | -0.951 | 1.567 | | | | | | | | | | | -0.381 | | | 1.237 | |
| Nightmares | -0.139 | 1.149 | | | | | | | | | | | | | | | -0.863 |
| Flashbacks | 1.147 | 1.238 | | | | | | | -0.35 | | | | | | | -1.19 | -0.431 |
| Psychological Cues | -1.126 | 1.563 | | | | | | -0.627 | | | | | | | | | -0.871 |
| Physiological Cues | -0.533 | 1.523 | | | | | | | | | | | | | | | -1.05 |
| Thought Avoidance | -1.695 | 1.389 | | | | | | | | | -0.621 | -0.64 | -0.663 | -1.062 | | | -0.595 |
| Activity Avoidance | -0.276 | 1.248 | | 0.607 | | | | | | | | | | | | | |
| Inability to Recall | 0.705 | 0.595 | | -0.807 | | | | -0.452 | | | | | | | | | |
| Diminished interest | -0.299 | 1.148 | 0.01 | | | 0.293 | | 0.439 | | | | -0.459 | -0.447 | | | | |
| Detachment | -1.101 | 1.349 | | | | | | 0.57 | | | | | | | | | -0.685 |
| Restricted Affect | -0.832 | 1.735 | | | | | | 0.27 | | | | | | | | | -0.589 |
| Foreshortened Future | 0.789 | 1.065 | | | | | | | | | | | | | | | 1.401 |
| Sleep | -1.27 | 0.988 | | | | | -0.869 | | 0.465 | | | | | | | | |
| Irritability | -0.689 | 0.963 | -0.02 | | | | | | 0.478 | | | | | | | | -0.975 |

| Symptoms - Interview | Item Thresholds | Factor Loadings | Threshold Difference | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Age | Black | College | Dep | Jail | Male | Veteran | Mid-Tx | EOT | 3-mo FU | 6-mo FU | 9-mo FU | 12-mo FU | CAPS-5 | PSS-I |
| Concentration Probs | -0.676 | 1.171 | | | | | | | 0.306 | | | | | | | | |
| Hypervigilance | -0.964 | 1.069 | | 0.51 | | | -0.783 | 0.715 | | | | | | | -0.717 | | |
| Startle | -0.122 | 1.056 | | | | | | | 0.305 | | | | | | | | |
| Negative Beliefs | -0.926 | 1.677 | | | | | | | | | | | | | | | |
| Blame | 0.831 | 0.87 | | | | | | | | | | | | | | | |
| Guilt | -2.154 | 2.156 | | | | | | | | | | | | | | | |
| Reckless Behavior | 1.116 | 0.725 | | | | | | | | | | | | | | | |

**Table S3b: Final Moderated Non-Linear Factor Analysis (MNLFA) Scale Scoring Item Parameters for Latent PTSD Severity (Threshold DIF for Self-Report Symptoms)**

| Symptoms - Self Report | Item Thresholds | Factor Loadings | Age | Black | College | Dep | Jail | Male | Veteran | IES | PCL-5 | PDS | PSS-SR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Intrusive Recollections | -1.574 | 2.136 | | | | | | | -0.797 | | | | |
| Nightmares | -0.518 | 1.769 | | | | | | | | | | | |
| Flashbacks | -0.036 | 1.873 | | 0.481 | | | | | | | -0.553 | | |
| Psychological Cues | -2.519 | 2.159 | | | | | | -0.778 | -0.77 | | | | |
| Physiological Cues | -0.956 | 2.101 | | | | | | | | | | | |
| Thought Avoidance | -1.601 | 1.961 | | | | | | | | | 0.608 | | |
| Activity Avoidance | -0.943 | 1.75 | | 0.707 | | | | | | | | | |
| Inability to Recall | 0.296 | 1.13 | | | | | | | | | | | |
| Diminished interest | -0.58 | 1.844 | | | | | -12.63 | 0.526 | | | | | |
| Detachment | -1.221 | 1.751 | | | | | | | | | -0.1987 | | |
| Restricted Affect | -0.962 | 1.491 | | | | | | | | | | | |
| Foreshortened Future | -0.536 | 1.44 | | | | | | | | | | 0.927 | |
| Sleep | -1.86 | 1.353 | | | | | | | | | | | |
| Irritability | -1 | 1.479 | -0.014 | | | | | | | | 0.13 | | |
| Concentration Probs | -1.619 | 1.759 | | | | | | -0.418 | | | | | |
| Hypervigilance | -1.452 | 1.687 | | | | | | | | | | | |
| Startle | -1.22 | 1.738 | | | | | | | | | | 0.561 | |

| Symptoms - Self Report | Item Thresholds | Factor Loadings | Age | Black | College | Dep | Jail | Male | Veteran | IES | PCL-5 | PDS | PSS-SR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Negative Beliefs | -0.603 | 1.447 | | | | | | | | | | | |
| Blame | 0.061 | 1.657 | | | | | | | | | | | |
| Guilt | -0.688 | 2.109 | | | | | | | | | | | |
| Reckless Behavior | 0.383 | 1.185 | | | | | | | | | | | |

## 13. Table S3c: Final Moderated Non-Linear Factor Analysis (MNLFA) Scale Scoring Item Parameters for Latent PTSD Severity (Factor Loading DIF for Clinical Interview Symptoms)

| Symptoms – Interview | Item Thresholds | Factor Loadings | Factor Loading Diff | | PSS-I | IES |
|---|---|---|---|---|---|---|
| | | | Black | Veteran | | |
| Intrusive Recollections | -0.951 | 1.567 | | | 0.475 | |
| Nightmares | -0.139 | 1.149 | | | | |
| Flashbacks | 1.147 | 1.238 | | | | |
| Psychological Cues | -1.126 | 1.563 | | | | |
| Physiological Cues | -0.533 | 1.523 | | | | |
| Thought Avoidance | -1.695 | 1.389 | -0.369 | | | |
| Activity Avoidance | -0.276 | 1.248 | | | | |
| Inability to Recall | 0.705 | 0.595 | | | | |
| Diminished Interest | -0.299 | 1.148 | | | | |
| Detachment | -1.101 | 1.349 | | | -0.358 | |
| Restricted Affect | -0.832 | 1.735 | | | -0.493 | |
| Foreshortened Future | 0.789 | 1.065 | | | | |
| Sleep | -1.27 | 0.988 | | | | |
| Irritability | -0.689 | 0.963 | | | -0.288 | |
| Concentration Probs | -0.676 | 1.171 | | | | |
| Hypervigilance | -0.964 | 1.069 | | | | |
| Startle | -0.122 | 1.056 | | -0.284 | | |
| Negative Beliefs | -0.926 | 1.677 | | | | |
| Blame | 0.831 | 0.87 | | | | |
| Guilt | -2.154 | 2.156 | | | | |
| Reckless Behavior | 1.116 | 0.725 | | | | |

## 14. Table S3d: Final Moderated Non-Linear Factor Analysis (MNLFA) Scale Scoring Item Parameters for Latent PTSD Severity (Factor Loading DIF for Self-Report Symptoms)

| Symptoms – Self Report | Item Thresholds | Factor Loadings | Black | Veteran | PSS-I | IES |
|---|---|---|---|---|---|---|
| Intrusive Recollections | -1.574 | 2.136 | | | | |
| Nightmares | -0.518 | 1.769 | | | | |
| Flashbacks | -0.036 | 1.873 | | | | |
| Psychological Cues | -2.519 | 2.159 | | | | |
| Physiological Cues | -0.956 | 2.101 | | | | |
| Thought Avoidance | -1.601 | 1.961 | | | | |
| Activity Avoidance | -0.943 | 1.75 | | | | |
| Inability to Recall | 0.296 | 1.13 | | | | |
| Diminished Interest | -0.58 | 1.844 | | | | -0.688 |
| Detachment | -1.221 | 1.751 | | | | |
| Restricted Affect | -0.962 | 1.491 | | | | |
| Foreshortened Future | -0.536 | 1.44 | | | | |
| Sleep | -1.86 | 1.353 | | | | |
| Irritability | -1 | 1.479 | | | | |
| Concentration Probs | -1.619 | 1.759 | | | | |
| Hypervigilance | -1.452 | 1.687 | | | | |
| Startle | -1.22 | 1.738 | | | | |
| Negative Beliefs | -0.603 | 1.447 | | | | |
| Blame | 0.061 | 1.657 | | | | |
| Guilt | -0.688 | 2.109 | | | | |
| Reckless Behavior | 0.383 | 1.185 | | | | |

### 15. Table S4: Final Moderated Non-Linear Factor Analysis (MNLFA) Scale Scoring Item Parameters for Latent Alcohol Severity

| Alcohol Symptoms | Item Intercepts/Thresholds | Factor Loadings |
|---|---|---|
| **Days Used Past Month** | 8.081 | 6.37 |
| **Any Intoxication Past Month** | 2.868 | 18.292 |

### 16. Table S5: Final Moderated Non-Linear Factor Analysis (MNLFA) Scale Scoring Item Parameters for Latent Drug Severity

| | | Threshold Difference | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Symptoms - Interview** | **Item Thresholds** | **Factor Loadings** | **Black** | **Dose** | **High School** | **Jail** | **Married** | **Veteran** | **Mid Treatment** | **3 Month** | **12 Month** | **TLFB** | **SUI** | **Other AOD Measure** |
| **Any Heroin Past Month** | 3.536 | 1.446 | | | | | | | | 0.381 | | | | 1.774 |
| **Any Opiate Past Month** | 2.853 | 1.446 | -1.501 | | | -3.739 | | | | | | | -2.01 | |
| **Any Sedative Past Month** | 2.85 | 1.446 | -2.122 | | | -3.512 | | | | | | | | |
| **Any Cocaine Past Month** | 1.677 | 1.446 | | | | | | | -0.682 | | | | | -1.523 |
| **Any Stimulant Past Month** | 5.775 | 1.446 | -1.271 | | | | -1.289 | | 2.558 | | | -1.579 | -3.785 | |
| **Any Hallucinogen Past Month** | 7.381 | 1.446 | | | | | | | | | | | | |

## 17. Table S6: IPD Meta-Analysis Results on PTSD Severity at End-of-Treatment

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 1 | Back (2017) | Placebo Med | N-Acetylcysteine | -0.16 | -1.02 | -0.86 | -1.62 | -0.08 |
| 2 | Back (2018) | RP | COPE | -1.34 | -2.13 | -0.80 | -1.56 | -0.02 |
| 3 | Boden (2012) | TAU | SS | -0.36 | -0.35 | 0.01 | -0.66 | 0.69 |
| 4 | Hien (2004) | Community Care | SS | -1.59 | -1.50 | 0.09 | -1.02 | 1.19 |
| 4 | Hien (2004) | Community Care | RP | -1.59 | -1.85 | -0.27 | -1.39 | 0.87 |
| 5 | Hien (2015) | SS | SS + Sertraline | -0.82 | -1.01 | -0.20 | -0.97 | 0.59 |
| 6 | Hien (2009) | Womens Health | SS | -1.05 | -1.05 | 0.00 | -0.33 | 0.31 |
| 7 | Ruglass (2017) | AMCG | COPE | -1.03 | -0.99 | 0.04 | -1.03 | 1.19 |
| 7 | Ruglass (2017) | AMCG | RP | -1.03 | -1.40 | -0.37 | -1.48 | 0.70 |
| 8 | McDevitt-Murphy (2015) | Feedback-Only | MI | -0.24 | -0.65 | -0.41 | -0.79 | 0.01 |
| 9 | McGovern (2011) | Individual Addiction Counseling | Integrated CBT | -0.40 | -1.77 | -1.36 | -3.50 | 0.82 |
| 10 | McGovern (2015) | TAU | Integrated CBT | -0.74 | -0.69 | 0.05 | -0.97 | 1.06 |
| 10 | McGovern (2015) | TAU | Individual Addiction Counseling | -0.74 | -0.38 | 0.36 | -0.68 | 1.33 |
| 11 | Mills (2012) | TAU | COPE | -1.01 | -1.18 | -0.17 | -1.09 | 0.72 |
| 12 | Myers (2015) | 12-Step | SS | -1.24 | -0.88 | 0.37 | -0.47 | 1.26 |
| 13 | Norman (2018) | SS | COPE | -1.30 | -1.83 | -0.52 | -1.18 | 0.13 |
| 14 | Haller (2016) | Integrated CBT | Modified CPT | -0.55 | -0.61 | -0.06 | -0.46 | 0.32 |
| 15 | Petrakis (2016) | Placebo | Prazosin | -1.37 | -1.55 | -0.18 | -0.68 | 0.35 |

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 16 | Petrakis (2020) | CPT | CPT + Zonisamide | -1.08 | -1.00 | 0.08 | -0.99 | 1.19 |
| 17 | Saladin (unpublished) | Placebo Med | Propranolol | -0.90 | -1.12 | -0.22 | -1.30 | 0.83 |
| 18 | Sannibale (2012) | CBT for Alcohol Support | Integrated CBT | -0.69 | -0.65 | 0.04 | -0.81 | 0.88 |
| 19 | Schacht (2017) | PE | PE + Contingency Management | -0.98 | -1.58 | -0.61 | -1.30 | 0.08 |
| 20 | Schafer (2019) | RP | SS | -0.38 | -0.58 | -0.19 | -0.59 | 0.18 |
| 20 | Schafer (2019) | RP | TAU | -0.38 | -0.52 | -0.14 | -0.58 | 0.27 |
| 21 | Sonne (unpublished) | Placebo | Paroxetine | -2.40 | -2.47 | -0.07 | -1.98 | 1.88 |
| 22 | Zlotnick (2003) | Residential TAU | SS | -1.47 | -1.45 | 0.02 | -1.58 | 1.64 |
| 23 | Zlotnick (2009) | Residential TAU | SS | -0.98 | -0.72 | 0.26 | -0.49 | 1.02 |
| 24 | Vujanovic (2018) | CBT for SUD | TIPSS (integrated CBT) | -2.15 | -1.61 | 0.54 | -0.37 | 1.43 |
| 25 | Foa (2013) | TAU | PE + Naltrexone | -0.94 | -1.84 | -0.90 | -1.38 | -0.41 |
| 25 | Foa (2013) | TAU | Naltrexone | -0.94 | -1.24 | -0.30 | -0.78 | 0.20 |
| 25 | Foa (2013) | TAU | PE | -0.94 | -1.24 | -0.30 | -0.77 | 0.20 |
| 26 | Brief (2013) | Waitlist | Vet Change | -0.50 | -0.31 | 0.19 | -0.01 | 0.39 |
| 28 | Van Dam (2013) | CBT for SUD | Structured Writing | -0.46 | -1.18 | -0.72 | -1.68 | 0.21 |
| 29 | Rosenthal (2013) | PE | PE + Virtual Reality | -2.54 | -2.56 | -0.02 | -1.92 | 1.81 |
| 30 | Batki (2014) | Placebo | Topiramate | -0.58 | -1.16 | -0.58 | -1.26 | 0.14 |
| 32 | Brady (2005) | Placebo | Sertraline | -0.87 | -1.03 | -0.16 | -0.66 | 0.34 |

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 33 | Frisman (2008) | Trauma-sensitive TAU | TARGET | -0.19 | -0.25 | -0.05 | -0.70 | 0.61 |
| 34 | Petrakis (2012) | Desipramine + Placebo | Desipramine + Naltrexone | -1.53 | -1.89 | -0.36 | -1.06 | 0.35 |
| 34 | Petrakis (2012) | Desipramine + Placebo | Paroxetine + Placebo | -1.53 | -1.18 | 0.34 | -0.37 | 1.06 |
| 34 | Petrakis (2012) | Desipramine + Placebo | Paroxetine + Naltrexone | -1.53 | -1.32 | 0.20 | -0.81 | 1.28 |
| 35 | Perez-Dandieu (2014) | TAU | EMDR | 0.01 | -3.17 | -3.17 | -4.49 | -1.83 |
| 36 | Stappenbeck (2015) | TAU | Cognitive Restructuring | -0.69 | -0.87 | -0.17 | -0.82 | 0.48 |
| 36 | Stappenbeck (2015) | TAU | Experiential Acceptance | -0.69 | -0.72 | -0.03 | -0.78 | 0.68 |
| 37 | Simpson (2015) | Placebo | Prazosin | -1.20 | -1.12 | 0.08 | -0.94 | 1.08 |
| 38 | Kehle-Forbes (2016) | Phased MET/PE | Integrated MET/PE | -1.48 | -1.25 | 0.24 | -0.28 | 0.68 |

## 18. Table S7: IPD Meta-Analysis Results on PTSD Severity at 12-Month Follow-Up

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 1 | Back (2017) | Placebo Med | N-Acetylcysteine | | | | | |
| 2 | Back (2018) | RP | COPE | -1.74 | -0.97 | 0.77 | -1.66 | 3.43 |
| 3 | Boden (2012) | TAU | SS | -1.43 | -1.22 | 0.20 | -0.96 | 1.47 |
| 4 | Hien (2004) | Community Care | SS | -3.15 | -2.36 | 0.79 | -1.54 | 3.07 |
| 4 | Hien (2004) | Community Care | RP | -3.15 | -2.84 | 0.32 | -2.04 | 2.61 |
| 5 | Hien (2015) | SS | SS + Sertraline | -1.64 | -2.31 | -0.67 | -2.30 | 0.98 |
| 6 | Hien (2009) | Womens Health | SS | -1.98 | -2.22 | -0.24 | -0.82 | 0.36 |
| 7 | Ruglass (2017) | AMCG | COPE | -1.50 | -4.29 | -2.78 | -8.79 | 3.21 |
| 7 | Ruglass (2017) | AMCG | RP | -1.50 | -1.47 | 0.03 | -6.14 | 5.92 |
| 8 | McDevitt-Murphy (2015) | Feedback-Only | MI | -0.95 | -1.02 | -0.07 | -1.23 | 1.04 |
| 9 | McGovern (2011) | Individual Addiction Counseling | Integrated CBT | -2.04 | -0.61 | 1.43 | -4.52 | 7.19 |
| 10 | McGovern (2015) | TAU | Integrated CBT | -1.65 | -1.99 | -0.34 | -3.08 | 2.35 |
| 10 | McGovern (2015) | TAU | Individual Addiction Counseling | -1.65 | -2.32 | -0.67 | -3.29 | 2.04 |
| 11 | Mills (2012) | TAU | COPE | -1.61 | -2.56 | -0.94 | -2.68 | 0.89 |
| 12 | Myers (2015) | 12-Step | SS | -1.88 | -1.40 | 0.48 | -2.31 | 3.23 |
| 13 | Norman (2018) | SS | COPE | -1.93 | -2.69 | -0.76 | -2.68 | 1.07 |
| 14 | Haller (2016) | Integrated CBT | Modified CPT | -1.27 | -1.13 | 0.14 | -0.52 | 0.78 |

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 15 | Petrakis (2016) | Placebo | Prazosin | | | | | |
| 16 | Petrakis (2020) | CPT | CPT + Zonisamide | | | | | |
| 17 | Saladin (unpublished) | Placebo Med | Propranolol | | | | | |
| 18 | Sannibale (2012) | CBT for Alcohol Support | Integrated CBT | -1.52 | -1.26 | 0.26 | -1.49 | 2.10 |
| 19 | Schacht (2017) | PE | PE + Contingency Management | -1.45 | -1.96 | -0.51 | -3.68 | 2.63 |
| 20 | Schafer (2019) | RP | SS | -0.84 | -0.88 | -0.05 | -1.11 | 1.03 |
| 20 | Schafer (2019) | RP | TAU | -0.84 | -1.11 | -0.27 | -1.53 | 1.02 |
| 21 | Sonne (unpublished) | Placebo | Paroxetine | -4.01 | -1.73 | 2.28 | -11.42 | 16.04 |
| 22 | Zlotnick (2003) | Residential TAU | SS | -2.70 | -4.01 | -1.31 | -10.56 | 8.10 |
| 23 | Zlotnick (2009) | Residential TAU | SS | -2.00 | -2.48 | -0.48 | -2.56 | 1.64 |
| 24 | Vujanovic (2018) | CBT for SUD | TIPSS (integrated CBT) | | | | | |
| 25 | Foa (2013) | TAU | PE + Naltrexone | -2.38 | -3.73 | -1.35 | -2.41 | -0.13 |
| 25 | Foa (2013) | TAU | Naltrexone | -2.38 | -2.93 | -0.55 | -1.86 | 0.67 |
| 25 | Foa (2013) | TAU | PE | -2.38 | -2.82 | -0.43 | -1.66 | 0.74 |
| 26 | Brief (2013) | Waitlist | Vet Change | -0.88 | -1.57 | -0.69 | -1.73 | 0.39 |
| 28 | Van Dam (2013) | CBT for SUD | Structured Writing | -1.41 | 0.01 | 1.43 | -3.60 | 6.24 |
| 29 | Rosenthal (2013) | PE | PE + Virtual Reality | -3.56 | -2.60 | 0.96 | -3.43 | 5.35 |
| 30 | Batki (2014) | Placebo | Topiramate | | | | | |
| 32 | Brady (2005) | Placebo | Sertraline | | | | | |

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 33 | Frisman (2008) | Trauma-sensitive TAU | TARGET | -0.28 | -0.53 | -0.24 | -1.23 | 0.84 |
| 34 | Petrakis (2012) | Desipramine + Placebo | Desipramine + Naltrexone | | | | | |
| 34 | Petrakis (2012) | Desipramine + Placebo | Paroxetine + Placebo | | | | | |
| 34 | Petrakis (2012) | Desipramine + Placebo | Paroxetine + Naltrexone | | | | | |
| 35 | Perez-Dandieu (2014) | TAU | EMDR | | | | | |
| 36 | Stappenbeck (2015) | TAU | Cognitive Restructuring | | | | | |
| 36 | Stappenbeck (2015) | TAU | Experiential Acceptance | | | | | |
| 37 | Simpson (2015) | Placebo | Prazosin | | | | | |
| 38 | Kehle-Forbes (2016) | Phased MET/PE | Integrated MET/PE | -1.51 | -1.00 | 0.51 | -0.70 | 1.70 |

## 19. Table S8: IPD Meta-Analysis Results: Alcohol Severity at End-of-Treatment

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 1 | Back (2017) | Placebo Med | N-Acetylcysteine | -0.06 | -0.12 | -0.06 | -0.93 | 0.82 |
| 2 | Back (2018) | RP | COPE | -0.66 | -0.69 | -0.03 | -0.51 | 0.45 |
| 3 | Boden (2012) | TAU | SS | -0.45 | -0.28 | 0.17 | -0.26 | 0.60 |
| 4 | Hien (2004) | Community Care | SS | -0.46 | -0.77 | -0.31 | -0.80 | 0.18 |
| 4 | Hien (2004) | Community Care | RP | -0.46 | -0.87 | -0.41 | -0.92 | 0.11 |
| 5 | Hien (2015) | SS | SS + Sertraline | -0.14 | -0.26 | -0.12 | -0.63 | 0.38 |
| 6 | Hien (2009) | Womens Health | SS | -0.23 | -0.22 | 0.02 | -0.17 | 0.19 |
| 7 | Ruglass (2017) | AMCG | COPE | -1.56 | -0.97 | 0.58 | 0.00 | 1.21 |
| 7 | Ruglass (2017) | AMCG | RP | -1.56 | -1.20 | 0.36 | -0.26 | 0.95 |
| 8 | McDevitt-Murphy (2015) | Feedback-Only | MI | 0.13 | 0.11 | -0.02 | -0.43 | 0.43 |
| 9 | McGovern (2011) | Individual Addiction Counseling | Integrated CBT | -0.46 | -0.55 | -0.09 | -1.27 | 1.12 |
| 10 | McGovern (2015) | TAU | Integrated CBT | 0.07 | 0.23 | 0.16 | -0.67 | 0.98 |
| 10 | McGovern (2015) | TAU | Individual Addiction Counseling | 0.07 | 0.30 | 0.22 | -0.88 | 1.25 |
| 11 | Mills (2012) | TAU | COPE | -0.43 | -0.34 | 0.09 | -0.36 | 0.53 |
| 12 | Myers (2015) | 12-Step | SS | 0.04 | -0.30 | -0.35 | -1.17 | 0.53 |
| 13 | Norman (2018) | SS | COPE | -1.46 | -1.60 | -0.14 | -0.67 | 0.38 |

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 14 | Haller (2016) | Integrated CBT | Modified CPT | -0.70 | -0.81 | -0.11 | -0.40 | 0.17 |
| 15 | Petrakis (2016) | Placebo | Prazosin | -1.17 | -1.25 | -0.08 | -0.50 | 0.35 |
| 16 | Petrakis (2020) | CPT | CPT + Zonisamide | -1.31 | -1.67 | -0.36 | -1.30 | 0.63 |
| 17 | Saladin (unpublished) | Placebo Med | Propranolol | -0.13 | -0.01 | 0.13 | -0.53 | 0.76 |
| 18 | Sannibale (2012) | CBT for Alcohol Support | Integrated CBT | -2.59 | -2.00 | 0.60 | -0.28 | 1.47 |
| 19 | Schacht (2017) | PE | PE + Contingency Management | 0.12 | -0.48 | -0.61 | -1.07 | -0.14 |
| 20 | Schafer (2019) | RP | SS | -0.14 | -0.29 | -0.14 | -0.42 | 0.11 |
| 20 | Schafer (2019) | RP | TAU | -0.14 | -0.22 | -0.07 | -0.32 | 0.15 |
| 21 | Sonne (unpublished) | Placebo | Paroxetine | -0.33 | -0.38 | -0.04 | -0.70 | 0.63 |
| 22 | Zlotnick (2003) | Residential TAU | SS | -0.35 | -0.44 | -0.08 | -1.02 | 0.87 |
| 23 | Zlotnick (2009) | Residential TAU | SS | -0.57 | -0.41 | 0.16 | -0.39 | 0.71 |
| 24 | Vujanovic (2018) | CBT for SUD | TIPSS (integrated CBT) | -0.69 | -0.26 | 0.43 | -0.08 | 0.93 |
| 25 | Foa (2013) | TAU | PE + Naltrexone | -2.18 | -2.45 | -0.26 | -0.59 | 0.07 |
| 25 | Foa (2013) | TAU | Naltrexone | -2.18 | -2.47 | -0.28 | -0.62 | 0.07 |
| 25 | Foa (2013) | TAU | PE | -2.18 | -2.14 | 0.04 | -0.29 | 0.40 |
| 26 | Brief (2013) | Waitlist | Vet Change | -0.90 | -0.60 | 0.30 | 0.02 | 0.58 |
| 28 | Van Dam (2013) | CBT for SUD | Structured Writing | -0.72 | -0.92 | -0.19 | -0.82 | 0.42 |
| 29 | Rosenthal (2013) | PE | PE + Virtual Reality | -0.52 | -0.35 | 0.17 | -0.57 | 0.88 |
| 30 | Batki (2014) | Placebo | Topiramate | -0.96 | -1.54 | -0.58 | -1.24 | 0.12 |

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 32 | Brady (2005) | Placebo | Sertraline | -1.69 | -1.67 | 0.02 | -0.44 | 0.47 |
| 33 | Frisman (2008) | Trauma-sensitive TAU | TARGET | -0.20 | -0.17 | 0.03 | -0.58 | 0.65 |
| 34 | Petrakis (2012) | Desipramine + Placebo | Desipramine + Naltrexone | -1.41 | -1.53 | -0.11 | -0.65 | 0.44 |
| 34 | Petrakis (2012) | Desipramine + Placebo | Paroxetine + Placebo | -1.41 | -1.16 | 0.26 | -0.29 | 0.80 |
| 34 | Petrakis (2012) | Desipramine + Placebo | Paroxetine + Naltrexone | -1.41 | -1.60 | -0.19 | -0.96 | 0.63 |
| 35 | Perez-Dandieu (2014) | TAU | EMDR | 0.16 | -0.26 | -0.41 | -1.66 | 0.86 |
| 36 | Stappenbeck (2015) | TAU | Cognitive Restructuring | -0.74 | -0.39 | 0.35 | -0.37 | 1.08 |
| 36 | Stappenbeck (2015) | TAU | Experiential Acceptance | -0.74 | -0.86 | -0.12 | -0.71 | 0.43 |
| 37 | Simpson (2015) | Placebo | Prazosin | -1.22 | -1.49 | -0.26 | -1.40 | 0.88 |
| 38 | Kehle-Forbes (2016) | Phased MET/PE | Integrated MET/PE | -4.05 | -3.63 | 0.42 | -0.27 | 1.01 |

## 20. Table S9: IPD Meta-Analysis Results: Alcohol Severity at 12-Month Follow-Up

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 1 | Back (2017) | Placebo Med | N-Acetylcysteine | | | | | |
| 2 | Back (2018) | RP | COPE | -0.16 | -0.03 | 0.13 | -1.35 | 1.71 |
| 3 | Boden (2012) | TAU | SS | -0.36 | -0.25 | 0.12 | -0.62 | 0.92 |
| 4 | Hien (2004) | Community Care | SS | -1.30 | -1.09 | 0.21 | -0.79 | 1.15 |
| 4 | Hien (2004) | Community Care | RP | -1.30 | -1.03 | 0.27 | -0.77 | 1.28 |
| 5 | Hien (2015) | SS | SS + Sertraline | -0.13 | -0.21 | -0.08 | -1.11 | 0.95 |
| 6 | Hien (2009) | Womens Health | SS | -0.06 | -0.07 | -0.01 | -0.30 | 0.32 |
| 7 | Ruglass (2017) | AMCG | COPE | 1.05 | -0.34 | -1.38 | -4.94 | 2.24 |
| 7 | Ruglass (2017) | AMCG | RP | 1.05 | -0.44 | -1.49 | -5.13 | 1.95 |
| 8 | McDevitt-Murphy (2015) | Feedback-Only | MI | -0.27 | -0.26 | 0.01 | -1.26 | 1.23 |
| 9 | McGovern (2011) | Individual Addiction Counseling | Integrated CBT | -0.05 | 0.04 | 0.09 | -3.14 | 3.22 |
| 10 | McGovern (2015) | TAU | Integrated CBT | -0.46 | -0.77 | -0.31 | -2.59 | 1.95 |
| 10 | McGovern (2015) | TAU | Individual Addiction Counseling | -0.46 | -1.14 | -0.67 | -3.52 | 2.33 |
| 11 | Mills (2012) | TAU | COPE | -0.23 | -0.37 | -0.14 | -1.05 | 0.76 |
| 12 | Myers (2015) | 12-Step | SS | -0.40 | 0.17 | 0.57 | -2.37 | 3.41 |
| 13 | Norman (2018) | SS | COPE | -1.74 | -1.87 | -0.13 | -1.88 | 1.46 |
| 14 | Haller (2016) | Integrated CBT | Modified CPT | -0.46 | -0.41 | 0.05 | -0.44 | 0.52 |

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 15 | Petrakis (2016) | Placebo | Prazosin | | | | | |
| 16 | Petrakis (2020) | CPT | CPT + Zonisamide | | | | | |
| 17 | Saladin (unpublished) | Placebo Med | Propranolol | | | | | |
| 18 | Sannibale (2012) | CBT for Alcohol Support | Integrated CBT | -2.65 | -2.19 | 0.46 | -1.31 | 2.28 |
| 19 | Schacht (2017) | PE | PE + Contingency Management | -0.26 | 1.25 | 1.51 | -0.77 | 3.76 |
| 20 | Schafer (2019) | RP | SS | -0.28 | -0.08 | 0.20 | -0.62 | 1.04 |
| 20 | Schafer (2019) | RP | TAU | -0.28 | -0.70 | -0.42 | -1.09 | 0.27 |
| 21 | Sonne (unpublished) | Placebo | Paroxetine | 0.14 | -0.58 | -0.72 | -5.92 | 4.62 |
| 22 | Zlotnick (2003) | Residential TAU | SS | 0.60 | 0.60 | 0.00 | -5.41 | 5.50 |
| 23 | Zlotnick (2009) | Residential TAU | SS | -0.50 | -1.18 | -0.68 | -2.27 | 0.92 |
| 24 | Vujanovic (2018) | CBT for SUD | TIPSS (integrated CBT) | | | | | |
| 25 | Foa (2013) | TAU | PE + Naltrexone | -1.90 | -2.64 | -0.74 | -1.47 | 0.09 |
| 25 | Foa (2013) | TAU | Naltrexone | -1.90 | -2.31 | -0.41 | -1.27 | 0.42 |
| 25 | Foa (2013) | TAU | PE | -1.90 | -2.26 | -0.35 | -1.21 | 0.45 |
| 26 | Brief (2013) | Waitlist | Vet Change | -2.08 | -2.19 | -0.11 | -1.46 | 1.25 |
| 28 | Van Dam (2013) | CBT for SUD | Structured Writing | -0.48 | -0.02 | 0.46 | -2.84 | 3.71 |
| 29 | Rosenthal (2013) | PE | PE + Virtual Reality | -0.93 | -0.42 | 0.50 | -1.64 | 2.76 |
| 30 | Batki (2014) | Placebo | Topiramate | | | | | |
| 32 | Brady (2005) | Placebo | Sertraline | | | | | |

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 33 | Frisman (2008) | Trauma-sensitive TAU | TARGET | -0.47 | -0.35 | 0.13 | -0.83 | 1.13 |
| 34 | Petrakis (2012) | Desipramine + Placebo | Desipramine + Naltrexone | | | | | |
| 34 | Petrakis (2012) | Desipramine + Placebo | Paroxetine + Placebo | | | | | |
| 34 | Petrakis (2012) | Desipramine + Placebo | Paroxetine + Naltrexone | | | | | |
| 35 | Perez-Dandieu (2014) | TAU | EMDR | | | | | |
| 36 | Stappenbeck (2015) | TAU | Cognitive Restructuring | | | | | |
| 36 | Stappenbeck (2015) | TAU | Experiential Acceptance | | | | | |
| 37 | Simpson (2015) | Placebo | Prazosin | | | | | |
| 38 | Kehle-Forbes (2016) | Phased MET/PE | Integrated MET/PE | -1.47 | -1.37 | 0.10 | -1.34 | 1.53 |

## 21. Table S10: IPD Meta-Analysis Results: Drug Severity at End-of-Treatment

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 1 | Back (2017) | Placebo Med | N-Acetylcysteine | -0.38 | -0.56 | -0.18 | -1.15 | 0.80 |
| 2 | Back (2018) | RP | COPE | -0.42 | -0.74 | -0.31 | -0.76 | 0.15 |
| 3 | Boden (2012) | TAU | SS | -0.64 | -0.83 | -0.18 | -0.62 | 0.25 |
| 4 | Hien (2004) | Community Care | SS | -0.62 | -0.63 | -0.02 | -0.50 | 0.46 |
| 4 | Hien (2004) | Community Care | RP | -0.62 | -0.71 | -0.10 | -0.58 | 0.39 |
| 5 | Hien (2015) | SS | SS + Sertraline | -0.78 | -0.68 | 0.10 | -0.43 | 0.64 |
| 6 | Hien (2009) | Womens Health | SS | -0.62 | -0.67 | -0.05 | -0.22 | 0.11 |
| 7 | Ruglass (2017) | AMCG | COPE | -0.71 | -0.59 | 0.12 | -0.54 | 0.84 |
| 7 | Ruglass (2017) | AMCG | RP | -0.71 | -0.31 | 0.40 | -0.28 | 1.06 |
| 8 | McDevitt-Murphy (2015) | Feedback-Only | MI | -0.80 | -0.77 | 0.03 | -0.56 | 0.66 |
| 9 | McGovern (2011) | Individual Addiction Counseling | Integrated CBT | -0.81 | -0.78 | 0.03 | -1.16 | 1.24 |
| 10 | McGovern (2015) | TAU | Integrated CBT | -0.65 | -0.50 | 0.15 | -0.61 | 0.90 |
| 10 | McGovern (2015) | TAU | Individual Addiction Counseling | -0.65 | -0.50 | 0.15 | -0.80 | 1.04 |
| 11 | Mills (2012) | TAU | COPE | -1.26 | -1.78 | -0.52 | -1.11 | 0.05 |
| 12 | Myers (2015) | 12-Step | SS | -0.84 | -0.86 | -0.02 | -0.94 | 0.95 |
| 13 | Norman (2018) | SS | COPE | -0.79 | -0.67 | 0.12 | -0.25 | 0.49 |

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 14 | Haller (2016) | Integrated CBT | Modified CPT | -0.95 | -1.01 | -0.06 | -0.36 | 0.22 |
| 15 | Petrakis (2016) | Placebo | Prazosin | -0.84 | -0.67 | 0.17 | -0.25 | 0.61 |
| 16 | Petrakis (2020) | CPT | CPT + Zonisamide | -0.91 | -0.81 | 0.10 | -1.30 | 1.56 |
| 17 | Saladin (unpublished) | Placebo Med | Propranolol | -0.61 | -0.61 | 0.00 | -0.70 | 0.68 |
| 18 | Sannibale (2012) | CBT for Alcohol Support | Integrated CBT | -0.84 | -0.72 | 0.12 | -0.54 | 0.77 |
| 19 | Schacht (2017) | PE | PE + Contingency Management | -0.34 | -0.71 | -0.37 | -0.80 | 0.05 |
| 20 | Schafer (2019) | RP | SS | -0.84 | -0.85 | -0.01 | -0.28 | 0.24 |
| 20 | Schafer (2019) | RP | TAU | -0.84 | -0.81 | 0.03 | -0.23 | 0.27 |
| 21 | Sonne (unpublished) | Placebo | Paroxetine | -0.65 | -0.64 | 0.01 | -0.61 | 0.65 |
| 22 | Zlotnick (2003) | Residential TAU | SS | -0.31 | -0.44 | -0.13 | -1.15 | 0.91 |
| 23 | Zlotnick (2009) | Residential TAU | SS | -1.14 | -1.16 | -0.01 | -0.63 | 0.61 |
| 24 | Vujanovic (2018) | CBT for SUD | TIPSS (integrated CBT) | -1.14 | -0.67 | 0.47 | -0.03 | 0.96 |
| 25 | Foa (2013) | TAU | PE + Naltrexone | -0.51 | -0.39 | 0.12 | -0.34 | 0.59 |
| 25 | Foa (2013) | TAU | Naltrexone | -0.51 | -0.77 | -0.26 | -0.63 | 0.13 |
| 25 | Foa (2013) | TAU | PE | -0.51 | -0.41 | 0.10 | -0.26 | 0.49 |
| 26 | Brief (2013) | Waitlist | Vet Change | -0.96 | -0.92 | 0.04 | -0.20 | 0.27 |
| 28 | Van Dam (2013) | CBT for SUD | Structured Writing | -0.79 | -1.07 | -0.27 | -0.95 | 0.38 |
| 29 | Rosenthal (2013) | PE | PE + Virtual Reality | -0.75 | -0.86 | -0.11 | -0.78 | 0.53 |
| 30 | Batki (2014) | Placebo | Topiramate | -0.20 | -0.59 | -0.39 | -1.14 | 0.42 |

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 32 | Brady (2005) | Placebo | Sertraline | -0.44 | -0.09 | 0.34 | -0.20 | 0.87 |
| 33 | Frisman (2008) | Trauma-sensitive TAU | TARGET | -0.43 | -0.32 | 0.11 | -0.49 | 0.73 |
| 34 | Petrakis (2012) | Desipramine + Placebo | Desipramine + Naltrexone | -0.55 | -0.45 | 0.10 | -0.62 | 0.83 |
| 34 | Petrakis (2012) | Desipramine + Placebo | Paroxetine + Placebo | -0.55 | -0.56 | -0.01 | -0.70 | 0.68 |
| 34 | Petrakis (2012) | Desipramine + Placebo | Paroxetine + Naltrexone | -0.55 | -0.49 | 0.06 | -0.92 | 1.11 |
| 35 | Perez-Dandieu (2014) | TAU | EMDR | 0.14 | -0.75 | -0.89 | -2.02 | 0.26 |
| 36 | Stappenbeck (2015) | TAU | Cognitive Restructuring | | | | | |
| 36 | Stappenbeck (2015) | TAU | Experiential Acceptance | | | | | |
| 37 | Simpson (2015) | Placebo | Prazosin | | | | | |
| 38 | Kehle-Forbes (2016) | Phased MET/PE | Integrated MET/PE | -1.26 | -1.42 | -0.16 | -0.48 | 0.16 |

## 22. Table S11: IPD Meta-Analysis Results: Drug Severity at 12-Month Follow-Up

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 1 | Back (2017) | Placebo Med | N-Acetylcysteine | | | | | |
| 2 | Back (2018) | RP | COPE | -0.73 | -0.75 | -0.01 | -1.26 | 1.30 |
| 3 | Boden (2012) | TAU | SS | -1.12 | -1.05 | 0.07 | -0.64 | 0.88 |
| 4 | Hien (2004) | Community Care | SS | -0.95 | -0.90 | 0.05 | -0.92 | 0.97 |
| 4 | Hien (2004) | Community Care | RP | -0.95 | -0.76 | 0.19 | -0.78 | 1.12 |
| 5 | Hien (2015) | SS | SS + Sertraline | -0.89 | -0.79 | 0.10 | -1.12 | 1.33 |
| 6 | Hien (2009) | Womens Health | SS | -0.79 | -0.83 | -0.04 | -0.32 | 0.27 |
| 7 | Ruglass (2017) | AMCG | COPE | -0.15 | -0.19 | -0.05 | -3.64 | 3.49 |
| 7 | Ruglass (2017) | AMCG | RP | -0.15 | -0.89 | -0.74 | -4.61 | 2.94 |
| 8 | McDevitt-Murphy (2015) | Feedback-Only | MI | -0.88 | -0.82 | 0.06 | -1.59 | 1.67 |
| 9 | McGovern (2011) | Individual Addiction Counseling | Integrated CBT | -0.98 | -0.54 | 0.44 | -2.88 | 3.68 |
| 10 | McGovern (2015) | TAU | Integrated CBT | -1.43 | -1.35 | 0.09 | -1.85 | 1.98 |
| 10 | McGovern (2015) | TAU | Individual Addiction Counseling | -1.43 | -1.50 | -0.07 | -2.49 | 2.43 |
| 11 | Mills (2012) | TAU | COPE | -1.60 | -1.64 | -0.04 | -1.22 | 1.13 |
| 12 | Myers (2015) | 12-Step | SS | -0.62 | -1.03 | -0.40 | -3.30 | 2.48 |
| 13 | Norman (2018) | SS | COPE | -1.05 | -0.99 | 0.06 | -1.02 | 1.09 |

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 14 | Haller (2016) | Integrated CBT | Modified CPT | -1.22 | -1.13 | 0.08 | -0.37 | 0.54 |
| 15 | Petrakis (2016) | Placebo | Prazosin | | | | | |
| 16 | Petrakis (2020) | CPT | CPT + Zonisamide | | | | | |
| 17 | Saladin (unpublished) | Placebo Med | Propranolol | | | | | |
| 18 | Sannibale (2012) | CBT for Alcohol Support | Integrated CBT | -0.71 | -0.63 | 0.08 | -1.24 | 1.44 |
| 19 | Schacht (2017) | PE | PE + Contingency Management | -0.28 | 0.18 | 0.45 | -1.68 | 2.56 |
| 20 | Schafer (2019) | RP | SS | -1.01 | -1.24 | -0.23 | -0.95 | 0.49 |
| 20 | Schafer (2019) | RP | TAU | -1.01 | -1.15 | -0.14 | -0.84 | 0.57 |
| 21 | Sonne (unpublished) | Placebo | Paroxetine | -0.69 | 0.63 | 1.32 | -2.78 | 5.64 |
| 22 | Zlotnick (2003) | Residential TAU | SS | -1.00 | -1.54 | -0.54 | -5.90 | 5.21 |
| 23 | Zlotnick (2009) | Residential TAU | SS | -1.42 | -1.20 | 0.21 | -1.55 | 2.00 |
| 24 | Vujanovic (2018) | CBT for SUD | TIPSS (integrated CBT) | | | | | |
| 25 | Foa (2013) | TAU | PE + Naltrexone | -1.16 | -1.18 | -0.02 | -0.85 | 0.91 |
| 25 | Foa (2013) | TAU | Naltrexone | -1.16 | -1.29 | -0.13 | -0.94 | 0.64 |
| 25 | Foa (2013) | TAU | PE | -1.16 | -1.10 | 0.06 | -0.86 | 0.93 |
| 26 | Brief (2013) | Waitlist | Vet Change | -0.85 | -0.92 | -0.07 | -1.24 | 1.14 |
| 28 | Van Dam (2013) | CBT for SUD | Structured Writing | -1.87 | -0.62 | 1.25 | -2.16 | 4.63 |
| 29 | Rosenthal (2013) | PE | PE + Virtual Reality | -0.99 | -1.28 | -0.29 | -2.13 | 1.65 |
| 30 | Batki (2014) | Placebo | Topiramate | | | | | |

| Study ID Number | Principal Investigator/1st Author | Comparator | Focal Treatment | Comparator Condition Effect Size | Focal Treatment Effect Size | "Comparative Effectiveness" (CE) Effect Size | "CE" ES LCL | "CE" ES UCL |
|---|---|---|---|---|---|---|---|---|
| 32 | Brady (2005) | Placebo | Sertraline | | | | | |
| 33 | Frisman (2008) | Trauma-sensitive TAU | TARGET | -0.43 | -0.35 | 0.09 | -0.82 | 1.04 |
| 34 | Petrakis (2012) | Desipramine + Placebo | Desipramine + Naltrexone | | | | | |
| 34 | Petrakis (2012) | Desipramine + Placebo | Paroxetine + Placebo | | | | | |
| 34 | Petrakis (2012) | Desipramine + Placebo | Paroxetine + Naltrexone | | | | | |
| 35 | Perez-Dandieu (2014) | TAU | EMDR | | | | | |
| 36 | Stappenbeck (2015) | TAU | Cognitive Restructuring | | | | | |
| 36 | Stappenbeck (2015) | TAU | Experiential Acceptance | | | | | |
| 37 | Simpson (2015) | Placebo | Prazosin | | | | | |
| 38 | Kehle-Forbes (2016) | Phased MET/PE | Integrated MET/PE | -1.20 | -0.95 | 0.25 | -0.46 | 0.94 |

## 21. Table S12: Treatment Class-Specific Effect Sizes and Comparative Effect Sizes: PTSD Severity at End-of-Treatment and 12-Month Follow-Up

| EFFECT | ES Estimate | ES SE | ES LCL | ES UCL |
|---|---|---|---|---|
| TAU ES @ EOT | -0.62 | 0.05 | -0.72 | -0.52 |
| Trauma-Focused ES @ EOT | -0.86 | 0.14 | -1.13 | -0.58 |
| Integrated ES @ EOT | -0.59 | 0.09 | -0.77 | -0.39 |
| PTSD Med ES @ EOT | -0.89 | 0.27 | -1.43 | -0.36 |
| AOD Med ES @ EOT | -1.03 | 0.18 | -1.39 | -0.68 |
| AOD Behavioral ES @ EOT | -0.60 | 0.11 | -0.81 | -0.39 |
| Placebo Med ES @ EOT | -0.94 | 0.12 | -1.17 | -0.71 |
| Trauma-Focused/Integrated ES @ EOT | -1.10 | 0.24 | -1.57 | -0.62 |
| Trauma-Focused/AOD Med ES @ EOT | -1.54 | 0.33 | -2.16 | -0.88 |
| TAU ES @ 12 Month | -1.17 | 0.12 | -1.41 | -0.92 |
| Trauma-Focused ES @ 12 Month | -1.63 | 0.26 | -2.11 | -1.10 |
| Integrated ES @ 12 Month | -1.39 | 0.21 | -1.80 | -0.99 |
| PTSD Med ES @ 12 Month | -0.04 | 2.48 | -4.81 | 4.83 |
| AOD Med ES @ 12 Month | -2.54 | 0.41 | -3.33 | -1.72 |
| AOD Behavioral ES @ 12 Month | -1.32 | 0.23 | -1.77 | -0.89 |
| Placebo Med ES @ 12 Month | -1.74 | 0.30 | -2.34 | -1.16 |
| Trauma-Focused/Integrated ES @ 12 Month | -1.50 | 0.48 | -2.43 | -0.57 |
| Trauma-Focused/AOD Med ES @ 12 Month | -3.17 | 0.71 | -4.50 | -1.77 |
| | | | | |
| Comparative Effectiveness ES: TAU versus Trauma-Focused @ EOT | -0.24 | 0.13 | -0.50 | 0.01 |
| Comparative Effectiveness ES: TAU versus Integrated @ EOT | 0.03 | 0.08 | -0.12 | 0.19 |
| Comparative Effectiveness ES: TAU versus PTSD Med @ EOT | -0.28 | 0.27 | -0.79 | 0.25 |
| Comparative Effectiveness ES: TAU versus AOD Med @ EOT | -0.41 | 0.18 | -0.77 | -0.08 |
| Comparative Effectiveness ES: TAU versus AOD Behavioral @ EOT | 0.02 | 0.09 | -0.16 | 0.20 |
| Comparative Effectiveness ES: TAU versus Placebo Med @ EOT | -0.32 | 0.10 | -0.53 | -0.12 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused/Integrated @ EOT | -0.48 | 0.24 | -0.94 | -0.01 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused/AOD Med @ EOT | -0.92 | 0.33 | -1.57 | -0.30 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused @ 12 Month | -0.46 | 0.23 | -0.93 | -0.04 |
| Comparative Effectiveness ES: TAU versus Integrated @ 12 Month | -0.22 | 0.16 | -0.54 | 0.09 |
| Comparative Effectiveness ES: TAU versus PTSD Med @ 12 Month | 1.13 | 2.48 | -3.67 | 6.01 |
| Comparative Effectiveness ES: TAU versus AOD Med @ 12 Month | -1.37 | 0.39 | -2.16 | -0.63 |
| Comparative Effectiveness ES: TAU versus AOD Behavioral @ 12 Month | -0.15 | 0.19 | -0.53 | 0.22 |
| Comparative Effectiveness ES: TAU versus Placebo Med @ 12 Month | -0.57 | 0.27 | -1.08 | -0.01 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused/Integrated @ 12 Month | -0.33 | 0.47 | -1.20 | 0.61 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused/AOD Med @ 12 Month | -2.00 | 0.69 | -3.39 | -0.68 |

| | | | | |
|---|---|---|---|---|
| Comparative Effectiveness ES: Placebo Med versus AOD Med @ EOT | -0.09 | 0.20 | -0.47 | 0.32 |
| Comparative Effectiveness ES: Placebo Med versus PTSD Med @ EOT | 0.05 | 0.29 | -0.49 | 0.63 |
| Comparative Effectiveness ES: Placebo Med versus TF/AOD Med @ EOT | -0.59 | 0.34 | -1.26 | 0.06 |
| Comparative Effectiveness ES: Placebo Med versus AOD Med @ 12 Month | -0.80 | 0.48 | -1.71 | 0.16 |
| Comparative Effectiveness ES: Placebo Med versus PTSD Med @ 12 Month | 1.70 | 2.50 | -2.93 | 6.82 |
| Comparative Effectiveness ES: Placebo Med versus TF/AOD Med @ 12 Month | -1.43 | 0.75 | -2.90 | 0.01 |

## 22. Table S13: Treatment Class-Specific Effect Sizes and Comparative Effect Sizes: Alcohol Severity at End-of-Treatment and 12-Month Follow-Up

| EFFECT | ES Estimate | ES SE | ES LCL | ES UCL |
|---|---|---|---|---|
| TAU ES @ EOT | -0.37 | 0.03 | -0.44 | -0.31 |
| Trauma-Focused ES @ EOT | -0.82 | 0.10 | -1.02 | -0.63 |
| Integrated ES @ EOT | -0.35 | 0.06 | -0.46 | -0.22 |
| PTSD Med ES @ EOT | -0.47 | 0.16 | -0.77 | -0.16 |
| AOD Med ES @ EOT | -1.20 | 0.12 | -1.44 | -0.96 |
| AOD Behavioral ES @ EOT | -0.44 | 0.07 | -0.57 | -0.30 |
| Placebo Med ES @ EOT | -0.85 | 0.09 | -1.02 | -0.67 |
| Trauma-Focused/Integrated ES @ EOT | -0.80 | 0.17 | -1.12 | -0.47 |
| Trauma-Focused/AOD Med ES @ EOT | -1.47 | 0.22 | -1.91 | -1.03 |
| TAU ES @ 12 Month | -0.37 | 0.07 | -0.51 | -0.22 |
| Trauma-Focused ES @ 12 Month | -0.60 | 0.16 | -0.91 | -0.29 |
| Integrated ES @ 12 Month | -0.29 | 0.12 | -0.52 | -0.06 |
| PTSD Med ES @ 12 Month | 0.09 | 1.30 | -2.41 | 2.63 |
| AOD Med ES @ 12 Month | -1.21 | 0.24 | -1.69 | -0.75 |
| AOD Behavioral ES @ 12 Month | -0.48 | 0.15 | -0.76 | -0.20 |
| Placebo Med ES @ 12 Month | -0.66 | 0.20 | -1.07 | -0.27 |
| Trauma-Focused/Integrated ES @ 12 Month | -0.71 | 0.28 | -1.26 | -0.19 |
| Trauma-Focused/AOD Med ES @ 12 Month | -1.61 | 0.43 | -2.44 | -0.77 |
| | | | | |
| Comparative Effectiveness ES: TAU versus Trauma-Focused @ EOT | -0.45 | 0.10 | -0.64 | -0.26 |
| Comparative Effectiveness ES: TAU versus Integrated @ EOT | 0.02 | 0.05 | -0.07 | 0.12 |
| Comparative Effectiveness ES: TAU versus PTSD Med @ EOT | -0.10 | 0.15 | -0.39 | 0.20 |
| Comparative Effectiveness ES: TAU versus AOD Med @ EOT | -0.83 | 0.12 | -1.07 | -0.60 |
| Comparative Effectiveness ES: TAU versus AOD Behavioral @ EOT | -0.07 | 0.06 | -0.18 | 0.05 |
| Comparative Effectiveness ES: TAU versus Placebo Med @ EOT | -0.48 | 0.08 | -0.64 | -0.31 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused/Integrated @ EOT | -0.42 | 0.16 | -0.74 | -0.11 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused/AOD Med @ EOT | -1.10 | 0.22 | -1.54 | -0.68 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused @ 12 Month | -0.24 | 0.14 | -0.52 | 0.04 |
| Comparative Effectiveness ES: TAU versus Integrated @ 12 Month | 0.07 | 0.09 | -0.10 | 0.25 |
| Comparative Effectiveness ES: TAU versus PTSD Med @ 12 Month | 0.45 | 1.30 | -2.05 | 3.02 |
| Comparative Effectiveness ES: TAU versus AOD Med @ 12 Month | -0.85 | 0.23 | -1.30 | -0.41 |
| Comparative Effectiveness ES: TAU versus AOD Behavioral @ 12 Month | -0.12 | 0.13 | -0.37 | 0.13 |
| Comparative Effectiveness ES: TAU versus Placebo Med @ 12 Month | -0.29 | 0.19 | -0.66 | 0.09 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused/Integrated @ 12 Month | -0.35 | 0.27 | -0.84 | 0.19 |

| | | | | |
|---|---|---|---|---|
| **Comparative Effectiveness ES: TAU versus Trauma-Focused/AOD Med @ 12 Month** | -1.24 | 0.42 | -2.04 | -0.40 |
| | | | | |
| **Comparative Effectiveness ES: Placebo Med versus AOD Med @ EOT** | -0.35 | 0.15 | -0.62 | -0.05 |
| **Comparative Effectiveness ES: Placebo Med versus PTSD Med @ EOT** | 0.38 | 0.17 | 0.05 | 0.73 |
| **Comparative Effectiveness ES: Placebo Med versus TF/AOD Med @ EOT** | -0.62 | 0.24 | -1.09 | -0.17 |
| **Comparative Effectiveness ES: Placebo Med versus AOD Med @ 12 Month** | -0.55 | 0.30 | -1.14 | 0.03 |
| **Comparative Effectiveness ES: Placebo Med versus PTSD Med @ 12 Month** | 0.74 | 1.31 | -1.77 | 3.37 |
| **Comparative Effectiveness ES: Placebo Med versus TF/AOD Med @ 12 Month** | -0.95 | 0.47 | -1.87 | -0.05 |

## 23. Table S14: Treatment Class-Specific Effect Sizes and Comparative Effect Sizes: Drug Severity at End-of-Treatment and 12-Month Follow-Up

| EFFECT | ES Estimate | ES SE | ES LCL | ES UCL |
|---|---|---|---|---|
| TAU ES @ EOT | -0.54 | 0.03 | -0.61 | -0.47 |
| Trauma-Focused ES @ EOT | -0.52 | 0.08 | -0.67 | -0.37 |
| Integrated ES @ EOT | -0.55 | 0.05 | -0.66 | -0.44 |
| PTSD Med ES @ EOT | -0.53 | 0.16 | -0.83 | -0.22 |
| AOD Med ES @ EOT | -0.50 | 0.13 | -0.75 | -0.24 |
| AOD Behavioral ES @ EOT | -0.52 | 0.06 | -0.63 | -0.40 |
| Placebo Med ES @ EOT | -0.35 | 0.09 | -0.52 | -0.18 |
| Trauma-Focused/Integrated ES @ EOT | -0.56 | 0.13 | -0.81 | -0.32 |
| Trauma-Focused/AOD Med ES @ EOT | -0.31 | 0.22 | -0.72 | 0.14 |
| TAU ES @ 12 Month | -0.63 | 0.08 | -0.79 | -0.47 |
| Trauma-Focused ES @ 12 Month | -0.76 | 0.16 | -1.06 | -0.43 |
| Integrated ES @ 12 Month | -0.69 | 0.12 | -0.93 | -0.46 |
| PTSD Med ES @ 12 Month | 0.19 | 1.08 | -1.90 | 2.27 |
| AOD Med ES @ 12 Month | -0.95 | 0.24 | -1.43 | -0.48 |
| AOD Behavioral ES @ 12 Month | -0.69 | 0.14 | -0.97 | -0.42 |
| Placebo Med ES @ 12 Month | -0.71 | 0.20 | -1.11 | -0.32 |
| Trauma-Focused/Integrated ES @ 12 Month | -0.73 | 0.25 | -1.23 | -0.26 |
| Trauma-Focused/AOD Med ES @ 12 Month | -0.91 | 0.42 | -1.72 | -0.07 |
|  |  |  |  |  |
| Comparative Effectiveness ES: TAU versus Trauma-Focused @ EOT | 0.02 | 0.07 | -0.11 | 0.16 |
| Comparative Effectiveness ES: TAU versus Integrated @ EOT | -0.01 | 0.04 | -0.09 | 0.07 |
| Comparative Effectiveness ES: TAU versus PTSD Med @ EOT | 0.01 | 0.15 | -0.28 | 0.31 |
| Comparative Effectiveness ES: TAU versus AOD Med @ EOT | 0.04 | 0.13 | -0.22 | 0.28 |
| Comparative Effectiveness ES: TAU versus AOD Behavioral @ EOT | 0.02 | 0.05 | -0.07 | 0.11 |
| Comparative Effectiveness ES: TAU versus Placebo Med @ EOT | 0.19 | 0.08 | 0.03 | 0.34 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused/Integrated @ EOT | -0.02 | 0.12 | -0.27 | 0.20 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused/AOD Med @ EOT | 0.23 | 0.22 | -0.19 | 0.66 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused @ 12 Month | -0.13 | 0.14 | -0.39 | 0.15 |
| Comparative Effectiveness ES: TAU versus Integrated @ 12 Month | -0.06 | 0.09 | -0.23 | 0.11 |
| Comparative Effectiveness ES: TAU versus PTSD Med @ 12 Month | 0.83 | 1.07 | -1.21 | 2.99 |
| Comparative Effectiveness ES: TAU versus AOD Med @ 12 Month | -0.32 | 0.23 | -0.79 | 0.11 |
| Comparative Effectiveness ES: TAU versus AOD Behavioral @ 12 Month | -0.06 | 0.12 | -0.29 | 0.16 |
| Comparative Effectiveness ES: TAU versus Placebo Med @ 12 Month | -0.07 | 0.18 | -0.42 | 0.30 |
| Comparative Effectiveness ES: TAU versus Trauma-Focused/Integrated @ 12 Month | -0.10 | 0.24 | -0.56 | 0.37 |

| | | | | |
|---|---|---|---|---|
| **Comparative Effectiveness ES: TAU versus Trauma-Focused/AOD Med @ 12 Month** | -0.27 | 0.42 | -1.07 | 0.54 |
| | | | | |
| **Comparative Effectiveness ES: Placebo Med versus AOD Med @ EOT** | -0.15 | 0.15 | -0.43 | 0.16 |
| **Comparative Effectiveness ES: Placebo Med versus PTSD Med @ EOT** | -0.18 | 0.17 | -0.50 | 0.16 |
| **Comparative Effectiveness ES: Placebo Med versus TF/AOD Med @ EOT** | 0.05 | 0.23 | -0.40 | 0.50 |
| **Comparative Effectiveness ES: Placebo Med versus AOD Med @ 12 Month** | -0.24 | 0.30 | -0.81 | 0.34 |
| **Comparative Effectiveness ES: Placebo Med versus PTSD Med @ 12 Month** | 0.90 | 1.09 | -1.29 | 2.98 |
| **Comparative Effectiveness ES: Placebo Med versus TF/AOD Med @ 12 Month** | -0.20 | 0.46 | -1.12 | 0.65 |

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