SEQUENCED TREATMENT EFFECTIVENESS FOR POSTTRAUMATIC STRESS (STEPS)

STATISTICAL ANALYSIS PLAN (SAP)

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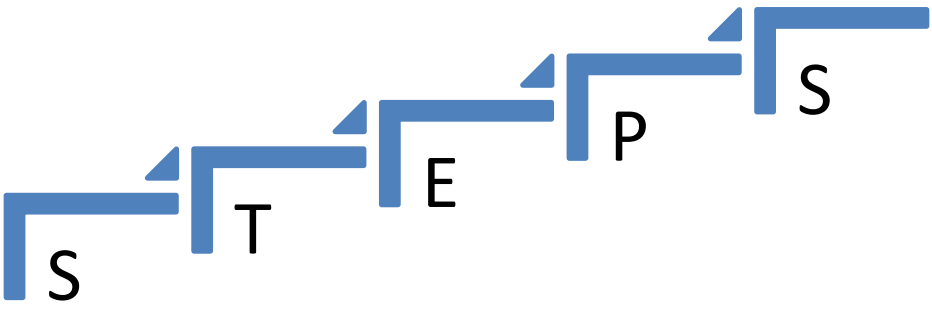


Modifications to the STEPS Statistical Analysis Plan

Change	Reason	Date
Dropped “prefers pharmacotherapy” from the list of moderators examined.	Only 5.8% of respondents preferred pharmacotherapy over psychotherapy, which is too few to have sufficient power to test this hypothesis.	6/21/24

Table of Contents

1. Introduction

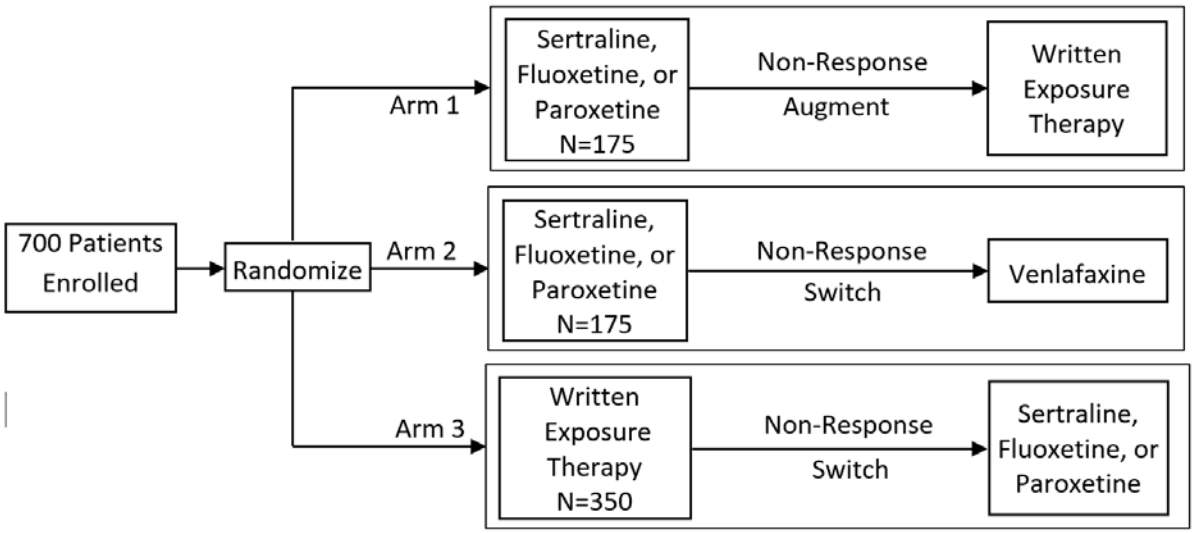
Based on the state of the scientific evidence, the Sequenced Treatment Effectiveness for Posttraumatic Stress (STEPS) Trial was designed to address three specific aims. The first aim is to quantitatively compare engagement, self-reported PTSD symptom severity (primary outcome), quality of life, and recovery outcomes of primary care patients randomized to initially receive brief psychotherapy (Written Exposure Therapy - WET) or their choice of the three selective serotonin reuptake inhibitors (SSRIs). The second aim is, among patients not responding to initial treatment, to quantitatively compare outcomes of primary care patients randomized to: 1) augment the SSRI with WET, 2) switch from the SSRI to another class of antidepressants (serotonin-norepinephrine reuptake inhibitors - SNRI), or 3) switch from WET to the choice of the three SSRIs. The third specific aim is to quantitatively examine treatment heterogeneity among subgroups of primary care patients receiving pharmacotherapy and psychotherapy, including veterans, women, and those using cannabis.

This statistical analysis plan (SAP) will comprehensively enumerate the primary and secondary outcomes, moderating variables, and corresponding analyses.

2. Study design

As described in Figure 1, STEPS is a three-arm sequenced-treatment pragmatic trial.

Figure 1: Three Arm Sequenced Treatment Study Design



Randomization – As depicted in Figure 1. Patients will initially be randomized to an SSRI (either sertraline, fluoxetine or paroxetine based on patient preference and treatment history) or Written Exposure Therapy (WET) in a 1:1 ratio. Randomization used randomly determined blocks sizes of 4, 6, or 8, and was stratified by healthcare system. Patients failing to respond to the initial treatment will receive the second treatment in the sequence.[1] Participants not responding to the SSRI in Arm 1 will have the SSRI augmented by WET. Participants not responding to the SSRI in Arm 2 will be switched from the SSRI to an SNRI (venlafaxine). Participants not responding to WET in Arm 3 will be switched from WET to an SSRI. The randomization scheme allocates patients not responding to treatment to these three sequenced treatments in a 1:1:2 ratio.

3. Outcomes

Primary outcome. The single primary outcome is PTSD symptom severity as measured by the PCL-5 (see Table 1).

Secondary outcomes. This study includes 6 secondary outcomes (Table 1). Secondary outcomes include health-related quality of life, recovery (not dominated by symptoms subscale), depression, anxiety, side-Effects, antidepressant discontinuation symptoms. Note that antidepressant discontinuation symptoms are only assessed for patients discontinuing an antidepressant and therefore we cannot compare this outcome across Arm 3 (WET) and Arms 1 and 2 (SSRI-SNRI and SSRI-WET). Therefore, this secondary outcome will only be reported descriptively for Arms 1 and 2.

Exploratory outcomes. This study includes 5 exploratory outcomes (Table 1). Secondary outcomes include treatment experiences, treatment engagement, clinical outcomes, recovery-oriented outcomes, and other outcomes.

Table 1. Outcome Survey Constructs, Instruments and Timeframes

Construct/Instrument	Instruments	Eligibility Assessment	Baseline	4-Month Follow-Up	8-Month Follow-Up
Primary Outcome					
PTSD Symptom Severity	PCL-5	X		X	X
Secondary Outcomes					
Health-related Quality of Life	VR-12		X	X	X
Recovery, Not Dominated by Symptoms	RAS, subscale		X	X	X
Depression	PHQ-9		X	X	X
Anxiety	GAD-7		X	X	X
Side-Effects	WFS		X	X	X
Antidepressant discontinuation symptoms	WFS		X	X	X
Exploratory Outcomes					
Alcohol Use	AUDIT-C		X	X	X

Drug-Related Consequences	DAST-10		X	X	X
Sleep	PSQI-A		X	X	X
Service Utilization	WFS		X	X	X
Satisfaction with Mental Health Care	ECHO		X	X	X
Medication Adherence	WFS		X	X	X

Note. AUDIT-C – Alcohol Use Disorder Identification Test – Concise; DAST-10 – Drug Abuse Screening Test; ECHO - Experience of Care & Health Outcomes; GAD-7 – Generalized Anxiety Disorder; PHQ-9 – Patient Health Questionnaire; PSQI-A - Pittsburgh Sleep Quality Index Addendum for PTSD; RAS – Recovery Assessment Scale VA – United States Department of Veterans Affairs; VR-12 – Veterans RAND 12-item Health Survey; WFS – Written for Study.

4. Analyses

4.1. Primary, Secondary and Exploratory Outcomes (Hypotheses 1 and 2)

- Aim 1: To quantitatively compare engagement, self-reported PTSD symptom severity (primary outcome), quality of life, and recovery outcomes of primary care patients randomized to initially receive brief psychotherapy (WET) or their choice of the three SSRIs.
-
    - *Primary Hypothesis 1a – Patients randomized to receive WET (Arm 3) will have better outcomes at 4 months than those randomized to an SSRI (Arms 1 and 2).*

Data from the baseline and 4-month follow-up surveys will be used in the analysis. To account for potential intraclass correlation at the healthcare system level and the randomization stratified by healthcare system, healthcare system will be included as a fixed effect. Generalized linear models will be specified with the appropriate distribution and link functions, normal (linear), binary (logit), ordinal (logit), and count (Poisson/negative binomial depending on dispersion). The equation for a linear model is as follows:

$$Y_i = \beta_0 + \beta_1(WET\ Arm3) + C_i + e_i \quad \text{(Eq. 1)}$$

Y_i denotes the outcome (measured at 4 months) for individual *i* . β_0 denotes the intercept. *C* denotes a vector of covariates (measured at baseline) that serve two functions: (1) dummy variables for healthcare systems to account for variation across systems as a fixed effect[2] and (2) additional baseline covariates and/or clinical outcomes theoretically related to both the outcome and the probability of missing follow-up surveys at 4-months. The effect of interest will be $\beta 1$, which represents the mean difference between SSRI (Arms 1 and 2) and WET (Arm 3) outcomes at 4 months. Table S2 presents a shell table for the primary outcome. Table S3 presents a shell table for the secondary and exploratory outcomes.

- Aim 2: For patients <u>not responding to initial treatment by 4 months</u>, to quantitatively compare engagement, self-reported PTSD symptom severity (primary outcome), quality of life, and recovery outcomes at 8 months of primary care patients randomized to: 1) switch

from brief psychotherapy (WET) to their choice of the three SSRIs, 2) augment the SSRI with brief psychotherapy (WET), or 3) switch from one class of antidepressants (SSRI) to another class of antidepressants (SNRI - venlafaxine).

- *Primary Hypotheses 2a – Patients not responding to initial SSRI treatment, randomized to an SSRI augmented by WET (Arm 1) will have better outcomes at 8-months than those randomized to switching from an SSRI to an SNRI (Arm 2).*
- *Exploratory Hypotheses 2b – Patient not responding to initial treatment randomized to an SSRI augmented by WET (Arm 1) will have better outcomes at 8-months than those randomized to switching from WET to their choice of the three SSRIs (Arm 3).*

Data from the baseline and 8-month follow-up surveys will be used in the analysis, with the subset of patients not responding to the initial treatment. Otherwise, the analytical models will be specified the same as for Aim 1. There will be two models estimated represented by equation 2. The first model represents the comparison between Arm 1 (SSRI Augmented with WET) and Arm 2 (switched to SNRI). The second model represents the comparison between Arm 1 (SSRI augmented with WET) and Arm 3 (WET switched to SSRI). Table S4 presents a shell table for the primary outcome. Table S5 presents a shell table for the secondary and exploratory outcomes. The equation for a linear model is as follows:

$$Y_i = \beta_0 + \beta_1(SSRI\ Augment\ WET\ Arm\ 1) + C_i + e_i \quad \text{(Eq. 2)}$$

Effect sizes. Effect sizes will be reported for all outcomes. Cohen's *d* effect sizes will be calculated and presented with 95% confidence intervals. Between group effect sizes will be calculated as the model-estimated treatment effect divided by the pooled, raw baseline standard deviation.

Statistical tests. Statistical tests will be only be conducted for the primary outcome (PCL-5). There will be a single hypothesis test for hypothesis 1a involving 4-month outcomes for the entire sample, and a single separate hypothesis for hypothesis 2a involving 8-month outcomes among those not responding to the initiation SSRI treatment.

4.2 Risk Factor and Treatment Moderator Analyses (Hypothesis 3)

Risk Factors. The following risk factors for poor outcomes will be examined (see Table 2): veteran status, combat exposure (reported as the most bothersome trauma), benzodiazepines use, current antidepressant use at baseline, and drug problems.

Treatment Moderators. The following moderators will be examined in the treatment heterogeneity analysis (see Table 2): Male gender, poor access, and cannabis use.

Table 2. Risk Factors and Treatment Moderator Survey Constructs, Instruments and Timeframes

Construct/Instrument	Instruments	Eligibility Assessment	Baseline	4-Month Follow-Up	8-Month Follow-Up
Risk Factors					
Veteran status (for FQHC patients)	WFS		X		
Combat Trauma Exposure	STQ[3]	X			
Benzodiazepines Use	BAM-R[4,5]		X		
Current Antidepressant Use	WFS		X		
Drug Problems	DAST-10[6]		X		
Treatment Moderators					
Gender	WFS		X		
Perceived Access to Mental Health Care	APAC[7]		X		
Cannabis Use	WFS†		X		

† Only asked in states were cannabis use is legal

Note. APAC – BAM-R - Brief Addiction Monitor Revised; DAST-10 – Drug Abuse Screening Test; STQ – Short Trauma Questionnaire (first part of Posttraumatic Diagnostic Scale for DSM-5).

- Aim 3: To quantitatively examine treatment heterogeneity among subgroups of primary care patients receiving pharmacotherapy and psychotherapy.
  - *Primary Hypothesis 3a: Improvements in PTSD symptom severity at 4-months will be less for: 1) veterans compared with non-veterans (adjusting for gender), 2) those with combat exposure (adjusting for gender) compared with other types of traumas, 3) those currently prescribed benzodiazepines, 4) those taking SSRIs/SNRIs at study entry, and 5) those with self-reported alcohol use and drug-related consequences.*
  - *Primary Hypothesis 3b: Male gender, poor access, and cannabis use will be treatment moderators of 4-month outcomes that reduce the differential effectiveness of psychotherapy compared to pharmacotherapy.*

Risk factor main effects (Hypothesis 3a) will be evaluated jointly using the same model as described for the primary outcome (Equation 1). The equation for a linear model is as follows:

$$Y_i = \beta_0 + \beta_1(Arm3 - WET) + \beta_2 R_i + C_i + e_i \quad \text{(Eq. 3)}$$

R_i denotes a vector of risk factors (measured at baseline) for individual *i*. The effect of interest for hypothesis 3a will be β_2. Table S7 presents a shell table for the primary outcome.

Treatment moderator main effects (Hypothesis 3a) and interaction effects (Hypothesis 3b) will be tested jointly using the same model as described for the primary outcome (Equation 1). All moderators will be grand mean centered. The equation for the analytical model is as follows:

$$Y_i = \beta_0 + \beta_1(Arm3 - WET) + \beta_2 M_i + \beta_3(M_i \; x \; (Arm3 - WET)) + C_i + e_i \quad \text{(Eq. 4)}$$

M_i denotes a vector of moderators (measured at baseline) for individual *i*. β_1, represents the main effect of the moderator. The effect of interest for hypothesis 3b will be β_3, which represents the interaction effect of the moderators as a group with the initial treatment group assignment. Table S7 presents a shell table for the primary outcome.

5. Missing data

Estimates from the models are unbiased under conditions of *Missing at Random* (MAR), which means that the mechanism of missingness is observed in the data. Most relevant to the current analysis, estimates will be unbiased when missingness is caused by previously observed values of the dependent variable, but not if missingness is caused by the unobserved value at the missing wave. For missing data, we will use multiple imputation with auxiliary variables. We will also attempt to make the MAR assumption more plausible by incorporating correlates with the reasons for missingness into the model.[8]

6. Power and Sample Size Calculation

With 350 patients randomized to pharmacotherapy (Arms 1 & 2) and 350 randomized to psychotherapy (Arm 3) and assuming a 20% attrition rate and α significance level of 0.05, we will have 80% power for Hypothesis 1 to detect mean differences of 0.24 standard deviations (effect size), or 4.08 points on the PCL-5 our primary outcome. With 175 patients in each arm, and conservatively assuming a 40% treatment non-response rate, and 20% attrition rate, we will have 80% power for Hypothesis 2a to detect means differences of 0.47 standard deviations, or 7.99 points for the PCL-5 score. For the heterogeneity analyses of current versus no SSRI/SNRI use at baseline we will have 80% power to detect differences in treatment effects comparing those subjects with and without SSRIs at baseline of 0.52, 0.48and 0.47 standard deviations depending on the proportion of patients not taking SSRIs at study entry (30%, 40% or 50%). Assuming that 30% of patients are not taking SSRIs/SNRIs at study entry, we will have 80% power to detect difference in treatment effects of 8.84 on the PCL-5. Because we would have more power to detect treatment heterogeneity if 50% of patients were taking SSRIs/SNRIs at baseline, we now propose to prioritize enrollment of patients not taking SSRIs/SNRIs. If 50% of patients were taking SSRIs/SNRIs at baseline, we will have 80% power to detect differences in treatment effects of 7.99 on the PCL-5.

7. References

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8. Shell Tables and Figures

Table S1. Baseline characteristics of patients enrolled in SPIRIT

	Overall (N = 700)	*Arm 1 (n = 179)*	*Arm2 (n = 169)*	*Arm3 (n = 352)*
	N(%) or μ(SD)	*n(%) or μ(SD)*	*n(%) or μ(SD)*	*n(%) or μ(SD)*
Socio-Demographic Characteristics				
Age				
Ethnicity				
Hispanic or Latina/o/e				
Not Hispanic or Latina/o/e				
Missing				
Race and Ethnicity				
American Indian, Alaskan Native, or other Indigenous group				
Arab or Middle Eastern				
Asian				
Black or African American				
Multi-race				
Native Hawaiian or Pacific Islander				
White				
Another identity				
Missing				
Gender				
Man				
Woman				
Transgender Man				
Transgender Woman				
Non-binary or gender fluid				
Another identity				
Missing				

	Overall (N = 700)	*Arm 1 (n = 179)*	*Arm2 (n = 169)*	*Arm3 (n = 352)*
	N(%) or μ(SD)	*n(%) or μ(SD)*	*n(%) or μ(SD)*	*n(%) or μ(SD)*
Sexual Orientation				
Bisexual				
Lesbian or gay				
Straight or heterosexual				
Another identity				
Missing				
Marital Status				
Divorced				
Married/Living with partner				
Separated				
Single, never married				
Widowed				
Missing				
Education				
<= 8th grade				
Some high school				
High school graduate				
Some college				
College graduate				
Any postgraduate work				
Missing				
Veteran Status				
No				
Yes				
Missing				
Employment				
Full-time				
Part-time				
Temporarily laid off/on-strike				
Unemployed				

	Overall (N = 700)	*Arm 1 (n = 179)*	*Arm2 (n = 169)*	*Arm3 (n = 352)*
	N(%) or μ(SD)	*n(%) or μ(SD)*	*n(%) or μ(SD)*	*n(%) or μ(SD)*
Retired				
Disabled				
Student				
Missing				
Household Poverty				
Above				
Below				
Missing				
Health Insurance[1]				
Uninsured				
Medicaid				
Medicare				
Government Insurance				
Private Insurance				
Missing				
Endorsed and Anticipated Stigma Inventory (EASI)				
Beliefs About Mental Health Treatment (range: 8-40)				
Perceived Access to Mental Health Care (APAC) (range: 1-5)				
Social Support (ESSI)				
Low Social Support (ESSI <= 18)				
High Social Support (ESSI > 18)				
Missing				
Number of people that can give you support				
Health Literacy Screener (range: 3-15)				
Home Internet Access on Computer				
Yes				
No				
Missing				

	Overall (N = 700)	*Arm 1 (n = 179)*	*Arm2 (n = 169)*	*Arm3 (n = 352)*
	N(%) or μ(SD)	*n(%) or μ(SD)*	*n(%) or μ(SD)*	*n(%) or μ(SD)*
Clinical Characteristics				
Perceived need for treatment (NCS-R)				
Yes				
No				
Missing				
Treatment history (NCS-R)				
Past use of psychotropic medication				
Yes				
No				
Missing				
Age first used psychotropic medication				
Past use of psychotherapy				
Yes				
No				
Missing				
Age at first psychotherapy session				
Currently taking antidepressant[1]				
No				
Yes, Sertraline				
Yes, fluoxetine				
Yes, paroxetine				
Yes, venlafaxine				
Yes, citalopram				
Yes, escitalopram				
Yes, duloxetine				
Yes, bupropion				
Missing				
Most Bothersome Trauma (Short Trauma Questionnaire)				
Serious Life Threatening Illness				
Physical Assault				

	Overall (N = 700)	*Arm 1 (n = 179)*	*Arm2 (n = 169)*	*Arm3 (n = 352)*
	N(%) or μ(SD)	*n(%) or μ(SD)*	*n(%) or μ(SD)*	*n(%) or μ(SD)*
Sexual Assault				
Military combat or lived in a war zone				
Child Abuse				
Accident				
Natural Disaster				
Other				
Missing				
Treatment Acceptability				
Medication Acceptability				
Definitely Not Acceptable				
Probably Not Acceptable				
Probably Acceptable				
Definitely Acceptable				
Missing				
Psychotherapy Acceptability				
Definitely Not Acceptable				
Probably Not Acceptable				
Probably Acceptable				
Definitely Acceptable				
Missing				
Short Form (VR12)				
Physical Health Component Summary (range: 0-100)				
Outcomes				
PTSD Checklist (PCL-5) (range: 0-80)				
Short Form (VR12)				
Mental Health Component Summary (range: 0-100)				
Recovery Assessment Scale (RAS)				
Not dominated by symptoms (range: 1-5)				

	Overall (N = 700)	*Arm 1 (n = 179)*	*Arm2 (n = 169)*	*Arm3 (n = 352)*
	N(%) or μ(SD)	*n(%) or μ(SD)*	*n(%) or μ(SD)*	*n(%) or μ(SD)*
Patient Health Questionnaire (PHQ-9) (range: 0-27)				
Generalized Anxiety (GAD-7) (range: 0-21)				
Sleep (PSQI-A) (range: 0-21)				
Alcohol Use (AUDIT) (range: 0-12)				
Number of days using cannabis in the past 30 days				
Not Applicable[2]				
On days using cannabis, how many times using per day				
Not Applicable[2]				
Drug Use (DAST-10)				
No drug use				
Low level (1-2)				
Moderate level (3-5)				
Substantial level (6-8)				
Severe level (6-8)				
Missing				
Side Effects				
Average number of 'Often' or 'Always' responses to being bothered by side effects in the past 30 days				
Not Applicable (not currently taking psychotropic medication)				

1. Not mutually exclusive

Table S2. Primary Outcomes: PTSD Symptom Severity Across Initial Treatment Arms

		Arms 1 and 2 (SSRI)		Arm 3 (WET)		Difference in Treatment Arms		
PCL-5	No.	Mean (SD)	95% CI	Mean (SD)	95% CI	Adjusted Group Difference, β	95% CI	Cohen's d
Baseline						-	-	-
4-Months								

Table S3. Secondary and Exploratory Outcomes Across Initial Treatment Arms

		Arms 1 and 2 (SSRI)		Arm 3 (WET)		Difference in Treatment Arms		
Secondary Outcomes	No.	Mean (SD)	95% CI	Mean (SD)	95% CI	Adjusted Group Difference, β	95% CI	Cohen's d
Mental Health-related Quality of Life								
Baseline						-	-	-
4-Months								
Recovery, Not Dominated by Symptoms								
Baseline						-	-	-
4-Months								
Depression								
Baseline						-	-	-
4-Months								
Anxiety								
Baseline						-	-	-
4-Months								
Side-Effects								
Baseline						-	-	-
4-Months								
Antidepressant discontinuation symptoms								
Baseline						-	-	-
4-Months								

Table S3. Secondary and Exploratory Outcomes Across Initial Treatment Arms, Continued

		Arms 1 and 2 (SSRI)		Arm 3 (WET)		Difference in Treatment Arms		
Exploratory Outcomes	No.	Mean (SD)	95% CI	Mean (SD)	95% CI	Adjusted Group Difference, β	95% CI	Cohen's d
Alcohol Use								
Baseline						-	-	-
4-Months								
Drug Problems								
Baseline						-	-	-
4-Months								
Sleep								
Baseline						-	-	-
4-Months								
Service Utilization								
Baseline						-	-	-
4-Months								
Satisfaction with Mental Health Care								
Baseline						-	-	-
4-Months								
Treatment Engagement								
4-Months								

Table S4. Primary Outcomes: PTSD Symptom Severity Across Sequenced Treatment Arms

		Arm 1 (Augment SSRI-WET)		Arm 2 (Switch SSRI-SNRI)		Difference in Treatment Arms		
PCL-5	No.	Mean (SD)	95% CI	Mean (SD)	95% CI	Adjusted Group Difference, β	95% CI	Cohen's d
Baseline						-	-	-
4-Months						-	-	-
8-Months								
		Arm 1 (Augment SSRI-WET)		**Arm 3 (Switch WET-SSRI)**		**Difference in Treatment Arms**		
	No.	Mean (SD)	95% CI	Mean (SD)	95% CI	Adjusted Group Difference, β	95% CI	Cohen's d
Baseline						-	-	-
4-Months						-	-	-
8-Months								

Table S6. Secondary and Exploratory Outcomes Across Sequenced Treatment Arms

		Arm 1 (Augment SSRI-WET)		**Arm 2 (Switch SSRI-SNRI)**		**Difference in Treatment Arms**		
Secondary Outcomes	No.	Mean (SD)	95% CI	Mean (SD)	95% CI	Adjusted Group Difference, β	95% CI	Cohen's d
Mental Health-related Quality of Life								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Recovery, Not Dominated by Symptoms								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Depression								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Anxiety								
Baseline						-	-	-
4-Months						-	-	-
8-Months								

Side Effects								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Antidepressant discontinuation symptoms								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
		Arm 1 (Augment SSRI-WET)		**Arm 3 (Switch WET-SSRI)**		**Difference in Treatment Arms**		
	No.	Mean (SD)	95% CI	Mean (SD)	95% CI	Adjusted Group Difference, β	95% CI	Cohen's d
Mental Health-related Quality of Life								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Recovery, Not Dominated by Symptoms								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Depression								
Baseline						-	-	-

4-Months						-	-	-
8-Months								
Anxiety								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Side Effects								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Antidepressant discontinuation symptoms								
Baseline						-	-	-
4-Months						-	-	-
8-Months								

Table S6. Secondary and Exploratory Outcomes Across Sequenced Treatment Arms, continued

		Arm 1 (Augment SSRI-WET)		Arm 2 (Switch SSRI-SNRI)		Difference in Treatment Arms		
Exploratory Outcomes	No.	Mean (SD)	95% CI	Mean (SD)	95% CI	Adjusted Group Difference, β	95% CI	Cohen's d
Alcohol Use								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Drug Problems								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Sleep								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Service Utilization								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Satisfaction with Mental Health Care								

Baseline						-	-	-
4-Months						-	-	-
8-Months								
Treatment Engagement								
4-Months						-	-	-
8-Months								
		Arm 1 (Augment SSRI-WET)		**Arm 3 (Switch WET-SSRI)**		**Difference in Treatment Arms**		
	No.	Mean (SD)	95% CI	Mean (SD)	95% CI	Adjusted Group Difference, β	95% CI	Cohen's d
Alcohol Use								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Drug Problems								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Sleep								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Service Utilization								

Baseline						-	-	-
4-Months						-	-	-
8-Months								
Satisfaction with Mental Health Care								
Baseline						-	-	-
4-Months						-	-	-
8-Months								
Treatment Engagement								
4-Months						-	-	-
8-Months								

Table S7. Main Effects of Risk Factors and Interaction Effects of Moderators on Primary Outcome

	Main Effect		Treatment Arm 3 (WET) Interaction	
	B	p	B	p
Risk Factors				
Veteran status			-	-
Combat Trauma Exposure			-	-
Benzodiazepines Use			-	-
Current Antidepressant Use			-	-
Drug Problems			-	-
Treatment Moderator				
Gender				
Perceived Access to Mental Health Care				
Cannabis Use				
Medication Acceptability > Therapy Acceptability				