Within-Treatment Markers of Dropout Risk in Integrated Treatment for PTSD+AUD

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Treatment for PTSD+SUD

- **PTSD and substance use disorders (SUD) frequently co-occur[1]**
  - Especially among veterans[2]
  - Greater severity, impairment, negative health correlates relative to either disorder alone[3]
- **Integrated therapies effective in treatment of PTSD+SUD[4]**
  - Exposure-based PTSD treatment: 1st line intervention for comorbid PTSD+SUD[5]

1 Pietrzak et al., 2011
2 Smith et al., 2016
3 Norman et al., 2018
4 Roberts et al., 2015
5 Hamblen et al., 2019

Dropout and impact

- **Retention in PTSD+SUD treatment a significant concern[1]**
  - Dropout typically higher in PTSD+SUD relative to other disorders[2] or PTSD alone[3]
- **Limits effectiveness**
  - Dropout generally a bad clinical outcome
  - Sufficient dose is typically necessary for optimal outcomes[4]
  - "Dropping out of care is clearly the most important predictor of treatment failure…"[5]
- **Drives up service utilization costs[6]**
- **Many patients (~40%) do not return to treatment within 3 years[7]**

1 Roberts et al., 2015 3 Lewis et al., 2020 5 Hoge et al., 2014 7 Bucholz et al., 2017
2 Swift et al., 2014 4 Holmes et al., 2019 6 Tuerk et al., 2013

PTSD+SUD dropout research

- **PTSD+SUD research has often examined baseline patient characteristics as predictors of dropout[1,2,3]**
  - Informative, but: often non-modifiable, inconsistent findings, and prediction remains difficult
  - May not capture fluid nature of dropout risk
  - Minimal information regarding how and why a variable may be linked to dropout
- **Less research targeting dropout-related signals *within* treatment[4,5]**
  - Two recent studies:
    - "Intent to attend" question after each session predictive of attendance in a recent PTSD trial[6]
    - Increases in craving and distress following imaginal exposure associated with dropout in PTSD+SUD treatment[7]

1 Belleau et al., 2017
2 Szafranski et al., 2017
3 Zandberg et al., 2016
4 Cooper et al., 2018
5 Swift et al., 2012
6 Shulman et al., 2019
7 Jarnecke et al., 2019

Why examine within-treatment indicators?

- **Emphasis on fluid, session by session variables rather than static variables**
  - Potential complement to baseline predictors research
- **Assessing variables more proximal to actual dropout**
  - Behavior most likely determined by more recent antecedents[1]
- **Clinical utility**
  - Better understand how and why dropout occurs
  - Inform more immediate, in-session course correction and collaborative problem-solving with patients

1 Sutton., 2001

Study questions

- Data drawn from a recently completed RCT examining integrated coping skills therapy vs. integrated exposure therapy for veterans with comorbid PTSD+AUD[1]

- **1)** Were within-treatment changes in routinely collected clinical markers during therapy associated with dropout risk?

- **2)** Did treatment type moderate the effect of within-treatment markers on dropout risk?

1 Norman et al., 2019

Participants and Procedures

- 119 adult veterans with comorbid PTSD and AUD
- Blind assessors administered CAPS-5[1] and Timeline Followback[2]
  - AUD defined as 20 heavy drinking days in past 90 days
- All service eras
- All index trauma types
- Full study procedures and exclusion/inclusion criteria in Norman et al., 2019

Characteristic	Total (*N*=110) *M* (SD) or *n* (%)
Age	41.8 (12.8)
Female	12 (10.9)
Married	28 (25.5)
College graduate	33 (32.0)
Hispanic	34 (30.9)
Race	
Caucasian	71 (65.1)
African American	15 (13.8)
Asian	6 (5.5)
Other/unknown	17 (15.6)
PTSD severity (CAPS-5)	42.7 (9.5)
% heavy drinking days (TLFB)	51.5 (26.1)

1 Weathers et al., 2013
2 Sobell et al., 1992

Measures

- Primary clinical markers in analyses:
  - **PTSD severity:** PTSD Checklist for DSM-5 (PCL-5)[1]
  - **Alcohol use:** Substance Use Inventory (SUI)[2]
    - Avg # of drinks consumed per day in prior interval
  - **Patient beliefs/satisfaction:** Client Satisfaction Questionnaire (CSQ-8)[3]
- **Reasons for dropout:** Therapists collected information from patients
  - Categories in line with prior qualitative dropout research[5]
- **Dropout:** Unilateral termination by any patients prior to completion of 12 on-protocol sessions[4]
  - Completer: Attendance of all 12 on-protocol sessions

1 Weathers et al., 2013
2 Weiss et al., 1995
3 Attkisson et al., 1982
4 Schnurr et al., 2007
5 Hundt et al., 2018

Treatments

- Patients randomized to 12 individual 90 min sessions
- **Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure (COPE)**[1]
  - Integrated exposure intervention
  - Prolonged exposure[2] + relapse prevention for SUD[3]
- **Seeking Safety** (**SS**)[4]
  - Integrated coping skills intervention
  - Present focus, with emphasis on skills to manage symptoms of PTSD and SUD

1 Back et al., 2015
2 Foa et al., 2007
3 Carroll, 1998
4 Najavits, 2002

Data analytic plan

- **Survival analyses: Cox proportional hazard models[1]**
  - Dropout status as endpoint
  - Confirmed assumption of proportional hazard to ensure the effect of each predictor/model term constant over time
  - Likelihood ratio and concordance to compare model fit and predictive ability
- **Models**
  - #1: Time invariant predictors (tx type; baseline predictors)
  - #2: Added time-varying predictors (session-level changes in clinical markers)
  - #3: Added interaction terms (tx * time-varying predictors)

1 Gmeinwieser et al., 2020

Results: Descriptives

- **Baseline patient characteristics**
  - Demographics similar between completers and dropouts
  - At first observation (session 1), completers reported higher patient satisfaction (CSQ) relative to dropouts (p = .009, d = 0.57)
- **Attendance**
  - More patients in COPE dropped prior to completion of 12 on-protocol sessions (n=39; 67.2%) compared to SS (n=19; 36.5%), p = .001
  - Greater attendance of on-protocol sessions in SS (M = 11.23, SD = 4.38) relative to COPE (M = 8.07, SD = 3.92), p < .001, d = 0.76.

Results: Reasons for dropout

Theme	*n* (%)	COPE / SS
Practical barriers		
Employment/college	9 (13.4)	5 / 4
Moved	10 (14.9)	7 /3
Other	3 (4.5)	2 / 1
Emotional Barriers		
Treatment too stressful	4 (6.0)	4 / 0
Therapy/therapist Barriers		
Pt referred to higher level care	2 (3.0)	1 / 1
Buy-in to rationale/perceived treatment fit	7 (10.4)	3 / 4
Early response	2 (3.0)	2 / 0
No information/signal	30 (44.8)	22 / 8

Results: Cox proportional hazard models

- **Model 1: Baseline predictors**
  - Significant model fit ($X^2(4) = 14.5$, $p = .006$), c = .69
  - Treatment type significant (HR = 3.33, $p = .028$)
  - Baseline CSQ (patient satisfaction) negatively related to risk (HR = 0.61, $p = .049$)
  - PCL (PTSD sxs) and SUI (substance use) nonsignificant
- **Model 2: Adding time-varying predictors**
  - No increase in model fit ($X^2(3) = 2.9$, $p = .40$)
- **Model 3: Adding treatment interactions**
  - Model fit improvement ($X^2(6) = 19.9$, $p = .003$), c = .75
  - Treatment * Δ SUI interaction significant (HR = 2.33, $p = .009$)

Results: Cox proportional hazard final model

Predictors	Coefficient (SE)	Hazard Ratio [95% CI]	*p*
Baseline Predictors			
Treatment Type (COPE)	1.09 (0.59)	3.00 [0.95, 9.49]	.06
Baseline SUI	0.01 (0.39)	1.01 [0.46, 2.19]	.98
Baseline CSQ	-0.27 (0.24)	0.76 [0.48, 1.21]	.25
Baseline PCL	0.66 (0.89)	1.93 [0.33, 11.10]	.46
Time-Varying Predictors			
Δ SUI	-0.29 (0.25)	0.75 [0.46, 1.21]	.24
Δ CSQ	0.06 (0.23)	1.06 [0.68, 1.64]	.80
Δ PCL	0.11 (0.32)	1.12 [0.59, 2.09]	.72
Interactions with Treatment			
Treatment * Baseline SUI	0.04 (0.63)	1.04 [0.31, 3.56]	.95
Treatment * Baseline CSQ	-0.49 (0.40)	0.61 [0.28, 1.34]	.22
Treatment * Baseline PCL	-0.94 (0.96)	0.39 [0.06, 2.57]	.33
Treatment * Δ SUI	0.85 (0.32)	2.33 [1.24, 4.39]	.01
Treatment * Δ CSQ	-0.17 (0.34)	0.84 [0.43, 1.65]	.62
Treatment * Δ PCL	0.09 (0.37)	1.10 [0.53, 2.28]	.79

Results: Cox proportional hazard models

- Increases in SUI (substance use) associated with significant increase in dropout hazard rate in COPE (HR = 1.87, $p < .001$), but not SS (HR = 0.78, $p = .31$)
- Among COPE patients, recent increase in 1 SD of SUI (*SD* = 0.49; i.e., about a half drink daily) increased by 87% (almost doubled) the risk of dropout
  - Translated: An increase in one drink consumed per day in the interval since last assessment (typically 1-2 weeks) was associated with 3.6-fold increase in dropout hazard rate

Discussion

- **Preliminary evidence of detectable markers *within* treatment that signal dropout risk**
  - Increases in alcohol use in integrated exposure therapy
  - Patient satisfaction early in treatment also associated with attendance in both treatments
- **No links between PTSD symptoms and dropout likelihood**
  - Complement literature suggestive that PTSD symptom change alone–often exacerbations–not predictive of dropout[1,2,3,4]
- **Self-reported reasons why patients dropped most commonly defined by practical barriers and psychosocial stressors, similar to prior research[5,6,7]**
  - Challenges notion that dropout typically occurs because patients cannot tolerate exposure

1 Foa et al., 2002
2 Jayawickreme et al., 2014
3 Larsen et al., 2020
4 Larsen et al., 2016
5 Hundt et al., 2018
6 Galovski et al., 2012
7 Doran et al., 2021

Clinical implications

- **Reinforce rationale for clinicians to consistently gather information during therapy**
  - Alcohol use: Increases between sessions may reflect warning signal
    - Prompt in-session intervention strategies by provider
  - Patient satisfaction: Utility of early discussions with patients regarding buy-in and treatment beliefs
    - Troubleshooting early sources of dissatisfaction
  - Barriers/stressors: Importance of monitoring and problem-solving these during therapy
    - Life stress/chaos often observed among PTSD+AUD patients

Limitations

- **Generalizability**
  - Sample mostly male combat veterans with PTSD+AUD
- **Measures administered every other session**
  - Possible impact on specificity of findings
  - Timing of measures in line with PE manual[1]
- **Sample size (N=119) / power**
  - Possible that complex interaction of factors affects dropout
  - Within-patient changes possibly moderated by stable patient characteristics
- **Seeking Safety implementation**
  - Often administered in 60 min sessions, but modified to 90 min to match dose with COPE

1 Foa et al., 2007

Conclusions

- **Integrated therapies effective for PTSD+SUD, but high dropout limits their efficacy and reach**
  - Alcohol use as potential risk factor for dropout *during* tx
  - Frequent assessment of alcohol use and cravings in identifying patients at high risk for dropout
  - Barriers/stressors throughout treatment and patient satisfaction early in treatment
- **Proof of concept for more complex, larger studies examining risk factors proximal to dropout**
- **Reliability and accuracy in detecting within-treatment signals of dropout risk holds promise in boosting retention**

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