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After studying this article, you should be able to:

 Use evidence-based psychotherapies for PTSD whether or not patients have comorbid bipolar disorder or schizophrenia

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Release, Expiration, and Review Dates

This educational activity was published in May 2021 and is eligible for AMA PRA Category 1 Credit[™] through June 30, 2023. The latest review of this material was May 2021.

Financial Disclosure

All individuals in a position to influence the content of this activity were asked to complete a statement regarding all relevant personal financial relationships between themselves or their spouse/partner and any commercial interest. The CME Institute has resolved any conflicts of interest that were identified. In the past year, Marlene P. Freeman, MD, Editor in Chief, has received research funding from JayMac and Sage; has been a member of the advisory boards for Otsuka, Alkermes, and Sunovion; and has been a member of the Independent Data Safety and Monitoring Committee for Janssen. No member of the CME Institute staff reported any relevant personal financial relationships. Faculty financial disclosure appears at the end of the article.

Posttraumatic Stress Disorder in Adults With Comorbid Severe Mental Illness

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ABSTRACT

Objective: To evaluate the efficacy of psychosocial treatments for posttraumatic stress disorder (PTSD) among individuals with a comorbid severe mental illness (SMI; ie, schizophrenia, bipolar disorder, major depressive disorder).

Data Sources: PubMed, PsycINFO, CINAHL, and Cochrane Library were searched from January 1998 to March 2020 using keywords related to PTSD, treatment, and severe mental illness.

Study Selection: All clinical trials for PTSD psychotherapy among individuals with SMI were included. From 38 potentially eligible studies, a total of 14 clinical trials across 684 individuals with comorbid SMI and PTSD were identified and included in the analysis.

Data Extraction: Data on demographic, SMI diagnosis, symptom severity, sample attrition, and treatment protocol received were extracted. Effect size calculations and subsequent meta-analyses were conducted using the Meta-Analysis Package for R (metafor) version 2.1-0 in R (3.6.0).

Results: PTSD treatments had a large effect on PTSD outcomes among individuals with SMI, with patients experiencing a standard deviation reduction in PTSD symptomatology pre- to post-treatment (q = -1.009, P < .001, k = 34). Prolonged exposure (g=-1.464; P<.001; SE=0.276; k=5), eye movement desensitization and reprocessing (q = -1.351; P < .001; SE = 0.276; k = 5), and brief treatment program (q=-1.009; P<.001; SE=0.284; k=5) had the largest effects on PTSD symptoms.

Conclusions: Although underrepresented in the PTSD literature, PTSD psychotherapies are effective for individuals with SMI. Treatments with an exposure-based component may have greater efficacy in this clinical population. J Clin Psychiatry 2021;82(3):20r13584

To cite: Grubaugh AL, Brown WJ, Wojtalik JA, et al. Meta-analysis of the treatment of posttraumatic stress disorder in adults with comorbid severe mental illness. J Clin Psychiatry. 2021;82(3):20r13584.

To share: https://doi.org/10.4088/JCP.20r13584

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he efficacy of evidence-based treatments (EBTs) for posttraumatic stress disorder (PTSD) in the general population is well established in the extant literature. To date, the most robust and well-supported interventions for PTSD include prolonged exposure (PE), eye movement desensitization and reprocessing therapy (EMDR), and cognitive processing therapy (CPT), with pre- to post-treatment PTSD symptom effect sizes (ESs) ranging from 1.43 to 2.74 (Cohen d) and active and control group

It is illegal to post this copyrighted PDF on any website. With SMI have yielded promising results with regard to

Clinical Points

- Despite experiencing high rates of trauma and posttraumatic stress disorder (PTSD), individuals with comorbid severe mental illness (SMI; eq. schizophrenia, bipolar disorder) often do not receive evidence-based psychosocial treatments for PTSD due to concerns that this patient group may be unable to tolerate trauma intensive treatment.
- Clinicians should consider treating PTSD among individuals with SMI, as psychosocial interventions for PTSD are well tolerated by this patient group and result in meaningful PTSD symptom improvement.
- In addition to reducing PTSD symptom severity, evidencebased psychosocial treatments for PTSD can have a positive impact on the primary symptoms of SMI and overall illness

post-treatment ESs ranging from 1.01 to 1.63 (Hedges g). 1-4 Additional meta-analytic findings suggest that EBTs for PTSD are generally comparable to one another with regard to efficacy, treatment nonresponse, and attrition. More specifically, approximately 70% of patients who receive a standard course of PE, CPT, or EMDR experience significant symptom reduction or loss of diagnosis at follow-up. Conversely, approximately 30% of patients who receive a standard course of an EBT for PTSD do not respond, and up to 50% drop out of treatment prematurely without significant symptom improvement. 4-6 Taken together, metaanalytic findings suggest that EBTs for PTSD are effective if a patient receives a sufficient dose of the intervention.

Although the efficacy of EBTs for PTSD in the general population is well documented, far less is known regarding how these same interventions perform with more complicated patient populations, such as those with comorbid forms of severe mental illness (SMI; ie, schizophrenia, bipolar disorder). This is significant because documented rates of PTSD are higher among individuals with SMI relative to the broader population. For example, 2 recent reviews on the prevalence of PTSD in patients with a schizophrenia spectrum disorder^{7,8} found rates of PTSD as high as 55% and 57%, respectively. In one review, a PTSD prevalence of at least 10% was observed in 30 (78.9%) of the 38 studies examined.⁷ In another review on the comorbidity between bipolar affective disorder and anxiety disorders, the authors found a 10.8% lifetime prevalence of PTSD.9 These rates contrast significantly with the 6.8% lifetime prevalence of PTSD found in the general population.¹⁰ Such findings are noteworthy because the presence of both PTSD and SMI is linked with significantly worse outcomes across a range of clinical, functional, and quality of life indices relative to the presence of either disorder alone. ^{7,8,11,12} Frequently reported outcomes include increased substance abuse, depressive severity, suicidality, and neurocognitive impairment. Some studies also report a relationship between the presence of PTSD and exacerbations in the primary symptoms of SMI (ie, positive symptoms of psychosis, severity of delusions).⁸

Published clinical trials for PTSD among individuals

PTSD and other clinical and quality of life measures. However, meta-analytic reviews on the efficacy of EBTs for PTSD in this patient demographic are limited in number and scope relative to those found in the broader (non-SMI) PTSD population. To date, 2 meta-analytic studies on the topic have been published. One is a Cochrane¹³ systematic review that included a total of 300 participants with PTSD and SMI drawn from 4 randomized controlled trials (RCTs) using a trauma-focused intervention. 14-17 Results from 3 of the RCTs using trauma-focused cognitive behavioral therapy were considered limited and inconclusive with regard to PTSD, psychotic symptoms, and other indices of functioning, and the remaining RCT provided "limited preliminary evidence in favor"13(p2) of EMDR to waitlist control. The other meta-analytic review included both RCTs and open trials of trauma-focused treatments for PTSD (n = 12) across 520 participants but was restricted to samples of individuals with a schizophrenia spectrum disorder or psychotic disorder and focused on psychotic symptoms as the primary outcome. 18 Additionally, since PTSD was a secondary outcome of interest, a PTSD diagnosis was not necessary for inclusion in the review. Given these sampling restrictions, and the small number of clinical trials included in Cochrane review, it remains difficult to make conclusions regarding the magnitude of the efficacy of EBTs for PTSD among individuals with SMI.

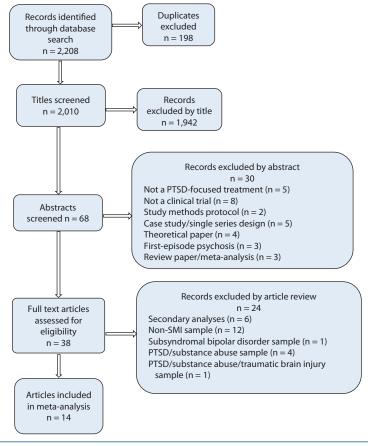
Based on these identified gaps in the PTSD treatment outcome literature, we conducted a meta-analytic review of clinical trials for PTSD among individuals with SMI inclusive of both open trials and RCTs. In addition to PTSD outcomes, we examined treatment effect sizes across measures of general psychopathology and psychosis severity. We also compared treatment effects by intervention type (eg, PE, EMDR) and examined potential moderators of intervention effects (ie, demographics [age, sex, race], treatment characteristics [duration, group vs individual mode of delivery, inclusion of exposure], and study design). It is anticipated that these data will provide a better understanding of the relative impact of EBTs for PTSD among individuals with SMI relative to the general population as well as help determine if and how these interventions may need to be modified for equivalent or increased efficacy.

METHODS

Information Sources and Search Terms

Literature searches were conducted independently by the research team using PubMed/Ovid MEDLINE, PsycINFO, CINAHL, and The Cochrane Library. Search terms included Posttraumatic Stress Disorder/PTSD and treatment/intervention/therapy combined with severe mental illness/serious mental illness or Schizophrenia/ Psychotic Disorder/psychosis/psychoses/Schizophrenic Disorder/Schizoaffective Disorder or Bipolar Disorder/ manic depression or Major Depression/Major Depressive Disorder/MDD. Our literature search was restricted to

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 $Abbreviations: BPD = , PTSD = posttraumatic stress \ disorder, SMI = severe \ mental \ illness.$

adult samples, manuscripts published in English, and peerreviewed studies published between January 1998 and March 2020.^a Although a published review protocol does not exist, the authors screened identified articles using the approaches suggested by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.¹⁹ See Figure 1 for selection of studies for inclusion. This search and the subsequent meta-analysis did not require IRB review as they did not involve human subjects.

Inclusion Criteria

Inclusion criteria for the review were restricted to studies consisting of patients with diagnosed PTSD and a severe and persistent comorbid mental illness inclusive of schizophrenia or a psychotic spectrum disorder (ie, schizophrenia, schizoaffective disorder, psychotic disorder) or mood disorder (ie, unipolar depression, bipolar disorder). Patients typically presented with a history of impaired psychosocial functioning, ongoing outpatient psychiatric care, and/or a

history of psychiatric hospitalization. Studies focused on first episode illness onset were excluded due to the inability to determine the chronicity of the disorder. Additionally, we excluded samples focusing specifically on substance abuse disorders or Axis II populations. Both open trials and RCTs were considered for inclusion. Selected clinical trials had to meet the following criteria: (1) use of a psychosocial intervention for PTSD using a standardized protocol; (2) use of a validated self-report or clinician administered measure of PTSD symptomatology; and (3) sample(s) composed of individuals with a diagnosis of PTSD and concurrent SMI. Single subject design and case studies were excluded from the review.

Study Coding and Analysis

Following identification of studies meeting inclusion criteria, relevant study characteristics and statistics were extracted. The study characteristics included study design, statistical analysis approach (eg, intent-to-treat or completer), treatment protocol (eg, CBT, PE, EMDR, treatment as usual), sample size, sample attrition, sample demographics (age, sex, race, and SMI diagnosis), and the PTSD and SMI symptom measures used in each study. For analysis, SMI measures were further organized into general psychopathology and psychotic symptom outcomes. After

^aJanuary 1998 was chosen as the cutoff date for the earliest publications included in the literature search as this date is consistent with the emergence of evidence-based treatments for PTSD in the general population, as well as the availability of manualized protocols for prolonged exposure for PTSD, eye movement desensitization and reprocessing therapy, and cognitive processing therapy.

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(2017) ¹⁶ TAU 31 40.7 (10.2) 64.5 70.0 16 (26%) schizoaffective PTCI scale ^b	Table 1. St	udy Ch	aracterist	ics of the P	TSD T	reatmer	nt Studies	That N	let Inclusi	ion for Meta-Analysis		
Depart Carlo Car	Authors	Docier	Analysis	Troatmont/-\	N							CMI outcom
CO19 CO20 C												
A		WGC	111		10	2 (20)	43.0 (10.6)	20.0	100	1 (10%) schizoaffective 4 (40%) psychotic NOS		
EMDR 55 11 201 40.4 11.3 45.4 69.1 45 2910 51.0	de Bont et al	RCT	ITT	PE	53	13 (24)	42.6 (10.3)	43.4	77.3	· · · ·	NA	GPTS ^b
Waltilist												
Composition Composition Composition Caps				Waitlist					59.6	4 (3%) psychotic NOS 7 (4%) bipolar disorder		
Luct al			ITT	CBT	20	7 (35)	42.3 (8.4)	25.0	60.0			NA
Mueser et al (2007) ²⁵ Vial Completer CBT 12 9 (41) 43.0 (7.5) 5.0 5.0 4.2 (9.9) 11.1 38.9 7.1399 5.1299 5.			ITT	PE	34	14 (41)	47.8 (13.4)	88.2	35.3	disorder 10 (29%) bipolar disorder 14 (41%) mood disorder with		NA
Composition			Completer	CBT	14	5 (26)	43.9 (8.9)	57.0	36.0	schizoaffective		BPRS ^c
TAU 54 43.3 (11.4) 18.5 83.3 9 (8%) schizoaffective PTC KPTSD			ITT	Group CBT	80	28 (41)	42.9 (7.9)	21.2	98.7	16 (20%) MDD 10 (12%) psychotic spectrum disorder 7 (9%) bipolar disorder	PTCI	NA
Mueser et al (2015) RCT RCT RCT CBT (CR) 104 22 (24) 43.0 (10.5) 29.8 39.4 53 (28%) psychotic spectrum CAPS PTCI RCT (2015) STORES RCT (2015) RCT RCT (2015) RCT (Mueser et al	RCT	ITT	CBT	54	8 (15)	45.1 (9.8)	24.1	85.2	8 (7%) schizophrenia	CAPS	BPRS ^c
Rosenberg et al (2004) ²⁷ Variable RCT ITT CBT 30 6 (20) 43.8 (10.1) 60.0 74.2 45 (74%) schizoaffective FTCl Scorec RCPS RCS	(2008) ¹⁴			TAU	54		43.3 (11.4)	18.5	83.3	25 (23%) bipolar disorder		
Nishith et al (2015) ²⁶ Union trial Completer BTP 18 ^d 3 (17) 45.8 (9.7) 11.1 38.9 7 (39%) schizoaffective CAPS BPRS' (2015) ²⁶ Union trial		RCT	ITT	CBT (CR)	104	22 (24)	43.0 (10.5)	29.8	39.4			
Steel et al (2004) ²⁷ Van den Berg and van der Gaag (2012) ²⁸ Van den Berg et al (2015) ¹⁷ RCT ITT PE S3 13 (24) 42.6 (10.3) 43.4 77.3 77.3 48.9 59.6 Waitlist 47 Waitlist Waitlist 47 Waitlist 47 Waitlist Wa	(2015)13			BTP	97	4 (4)	44.5 (11.6)	33.0	28.9	93 (49%) mood disorder 41 (21%) mood disorder and BPD 14 (7%) psychotic spectrum		score ^c
Rosenberg et al (2004) ²⁷ Virial CBT CBT 12 9 (41) 43.0 (7.5) 50.0 NR 1 (8%) schizophrenia 3 (25%) schizoaffective 1 (8%) psychotic NOS 2 (17%) bipolar disorder 5 (42%) MDD CAPS PANSS positive Scale ^b PSYRATS DRS ^b			Completer	ВТР	18 ^d	3 (17)	45.8 (9.7)	11.1	38.9	5 (28%) MDD		BPRS ^c
TAU 31 40.7 (10.2) 64.5 70.0 16 (26%) schizoaffective PTCI scale PSYRATS AHRS PSYRATS DRS PS			Completer	CBT	12	9 (41)	43.0 (7.5)	50.0	NR	1 (8%) schizophrenia 3 (25%) schizoaffective 1 (8%) psychotic NOS 2 (17%) bipolar disorder	CAPS	BPRS ^c
PSYRATS AHRS PSYRATS DRSb PSS-SR P	Steel et al	RCT	ITT	CBT	30	6 (20)	43.8 (10.1)	60.0	74.2	45 (74%) schizophrenia	CAPS	PANSS positive
and van der Gaag (2012) ²⁸ van der Berg et al (2015) ¹⁷ Waitlist Wolff et al Open Completer CBT (SS) 61e NR 36.0 (10.0) 0 36.5 d (22%) schizoaffective 14 (52%) psychotic NOS 1 (4%) delusional disorder PSS-SR 14 (52%) psychotic NOS 1 (4%) delusional disorder 43.4 (52%) psychotic NOS 1 (4%) delusional disorder 14 (52%) psychotic NOS 1 (4%) delusional disorder 45 (22%) schizoaffective PSS-SR PSS-	(2017) ¹⁶			TAU	31		40.7 (10.2)	64.5	70.0	16 (26%) schizoaffective	PTCI	PSYRATS AHRS
et al (2015) ¹⁷ EMDR 55 11 (20) 40.4 (11.3) 45.4 69.1 45 (29%) schizoaffective 1 (1%) brief psychotic 4 (3%) psychotic NOS 7 (4%) bipolar disorder 3 (2%) MDD Wolff et al Open Completer CBT (SS) 61e NR 36.0 (10.0) 0 36.5 46 (75%) MDD PCL NA	and van der Gaag		ІТТ	EMDR	27	5 (18)	45.0 (9.4)	55.5	63.0	6 (22%) schizoaffective 14 (52%) psychotic NOS		GPTS ^b
Waitlist 47 40.3 (9.7) 48.9 59.6 1 (1%) brief psychotic 4 (3%) psychotic NOS 7 (4%) bipolar disorder 3 (2%) MDD Wolff et al Open Completer CBT (SS) 61e NR 36.0 (10.0) 0 36.5 46 (75%) MDD PCL NA	van den Berg	RCT	ITT		53	13 (24)	42.6 (10.3)		77.3			NA
Waltist 47 40.5 (5.7) 46.9 35.0 4 (3%) psychotic NOS 7 (4%) bipolar disorder 3 (2%) MDD Wolff et al Open Completer CBT (SS) 61e NR 36.0 (10.0) 0 36.5 46 (75%) MDD PCL NA	et al (2015) ¹⁷				55	11 (20)		45.4	69.1			
				Waitlist	47		40.3 (9.7)	48.9	59.6	4 (3%) psychotic NOS 7 (4%) bipolar disorder	PICI	
·			Completer	CBT (SS)	61 ^e	NR	36.0 (10.0)	0	36.5		PCL	NA

^aEffect of treatment was averaged across both PE (n=5) and EMDR (n=5).

^bPsychotic symptom outcome.

^cGeneral psychopathology outcome.

^dDemographic characteristics in Nishith et al²⁶ were presented for the total intent-to-treat sample (N = 18) and not the completer sample (N = 15).

^eDemographic characteristics in Wolff et al²⁹ were presented for the total sample (N = 74) of treatment completers, not for the SMI subsample. Demographic characteristics were not presented for the total number of individuals assigned to SS (N = 111), and 37 participants were designated as noncompleters. Abbreviations: BPRS = Brief Psychiatric Rating Scale, ³⁰ BTP = brief treatment program, CAPS = Clinician-Administered PTSD Scale³¹, CBT = cognitive behavioral therapy, EMDR = eye movement desensitization and reprocessing, GPTS = Green Paranoid Thoughts Scale, ³² ITT = intention-to-treat, KPTSD = Knowledge of PTSD Test, ³³ MDD = major depressive disorder, NA = not available, NOS = not otherwise specified, NR = not reported, PANSS = Positive and Negative Syndrome Scale, ³⁴ PCL = PTSD Checklist, ³⁵ PDS = Posttraumatic Diagnostic Scale, ³⁶ PE = prolonged exposure, PSS-SR = PTSD Symptom Scale-Self, ³⁷ PSYRATS AHRS = Psychotic Symptom Rating Scales — Delusions Rating Scales — Delusions Rating Scales — Destraumatic Cognitions Inventory, ³⁸ PTSD = posttraumatic stress disorder, RCT = randomized controlled trial, SS = seeking safety,

It is illegal to post this copyrighted PDF on any website coding study characteristics, raw group mean scores and standard deviations (SDs) for the PTSD and SMI outcome measures were extracted from the included studies for both are and immediate post treatment (in treatment).

standard deviations (SDs) for the PTSD and SMI outcome measures were extracted from the included studies for both pre- and immediate post-treatment (ie, treatment completion) time points. All the PTSD and SMI measures are validated, well-known, and commonly used measures in the PTSD and SMI literatures (see Table 1). Except for the Knowledge of PTSD Test (KPTSD),³³ which assesses for an individual's understanding of trauma and PTSD, lower scores on all the PTSD/SMI measures are representative of better PTSD/SMI outcomes (ie, reduction in symptomatology). Therefore, prior to meta-analyses, the KPTSD ESs were reverse coded (multiplied by –1) to match the directionality of the other measures (ie, lower score, better outcome). Outcome data (eg, raw group means and SDs) were available for all included studies, and none of the samples were overlapping across studies.

All effect size calculations and subsequent meta-analyses were conducted using the Meta-Analysis Package for R (metafor) version 2.1-0 in R (3.6.0). Within-group biascorrected ESs (g) and associated sampling variances for the PTSD/SMI outcome measures were calculated using the escalc function with the standardized mean change using raw score standardization (SMCR) option, which is most appropriate for studies using a pretest-posttest design.⁴¹ Specifically, ESs were estimated by subtracting immediate post-treatment mean scores from pre-treatment (baseline) mean scores and standardizing this mean change based on the average pre-treatment (baseline) SD within each group. 41 A negative ES is indicative of improved PTSD/ SMI outcomes (ie, reduction in symptoms). Because the reliability of the PTSD and SMI measures was not reported in the included studies, a test-retest reliability estimate of 0.70, based on the psychometric properties of the CAPS and PCL in individuals with SMI,42 was used to calculate the variances of the within-group ESs. Sensitivity analyses demonstrated similar variance estimates with test-retest reliabilities of 0.60, 0.70, and 0.80. After calculating the within-group ESs and variances for all measures, a funnel plot was generated to observe risk of bias in individual studies. Due to observation of asymmetry in the funnel plot, which was expected because of "small study effects" (ie, small sample sizes in some trials, substantial heterogeneity across trials, and difficulty in recruitment of patients with PTSD and comorbid SMI; see Sterne et al⁴³), random-effects multilevel meta-analytic models (rma. mv function) were performed to summarize the effects of PTSD treatments on PTSD and SMI psychotic symptom outcomes. Multilevel models were used because studies could contribute multiple effect sizes. Random nesting factors for study and result per study were used to account for correlated ESs. Multilevel modeling was not required for pooling SMI general psychopathology ESs due to no overlapping outcome measures (rma function). Given the low number of RCTs (n=4/5) that included a traditional control group (ie, treatment as usual, waitlist control), it was not feasible to calculate between-group ESs. Thus, the

RESULTS

Included Studies

Altogether, 14 intervention studies with 684 subjects were analyzed. Two of these studies^{17,21} reported results for the same subjects in different outcome domains (ie, PTSD outcomes¹⁷ and SMI outcomes²¹), and these subjects were not counted twice in the current analysis. Study characteristics are presented in Tables 1 and 2. A total of 48 findings of PTSD (34/48), psychotic symptoms (8/48), and general psychopathology (6/48) outcomes were reported across these studies. With respect to study design, 5 (36%) studies were RCTs, 8 (57%) were open trials, and 1 (7%) was a within-group controlled trial.²⁰ A multitude of treatment approaches were examined across studies, including CBT (n=7, 50%), PE (n=2, 14%), EMDR (n=2, 14%), a brief treatment program (BTP; n = 2, 14%), and a within-group evaluation of PE and EMDR²⁰ (n = 1, 7%). One RCT study used BTP as a control condition.¹⁵ For the purposes of this study and the use of within-group ESs, BTP was coded as a treatment condition, rather than a control condition, because it is an active, although brief, intervention directly targeting PTSD symptomatology. Treatment dropout was highly variable across studies, ranging between 4% and 41% and exceeding at least 20% within the experimental conditions of 10 studies (77%). Only 1 study²⁹ did not report treatment dropout within its SMI designated sample. Despite the small sample size, publication bias was low, as a file drawer analysis indicated that a total of 12,644 unpublished null studies would be needed to reduce the observed significant effects of PTSD treatments on PTSD outcomes to nonsignificant thresholds.

With respect to study sample characteristics (Table 1), mean ages of participants ranged between 36.0 years and 48.0 years. Study samples were predominantly female, as 11 studies (78%) reported majority female samples. The included studies were diverse with respect to racial/ethnic composition of their samples, as only 8 studies (61%) included a majority White/Caucasian population. One study did not include data on racial/ethnic identification of their participants.²⁷ Examined outcomes were identified as empirically validated measures of PTSD, psychotic symptoms, and general psychopathology utilized within each study to assess baseline and post-treatment symptoms of patients enrolled in PTSD treatment. All studies, save for 1,21 included a metric of PTSD symptom outcome. PTSD symptom outcomes for participants in this study²¹ were previously reported in van den Berg et al.¹⁷ That is, both studies^{17,21} were derived from the same sample of participants, but PTSD symptoms were reported on in van den Berg et al¹⁷ and SMI symptoms were reported on in de Bont et al.²¹ Contrary to the almost unanimous inclusion of PTSD symptom measures, 5 studies (36%) did not include a metric of SMI symptom outcome.

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Table 2. Study Recruitment and Treatment Characteristics								
Design	Target sample	N	Inclusion/exclusion criteria ^a	Intervention characteristics				
WGC	Mental health outpatients	10	(1) Severe psychotic episode in last 3 years with current positive or negative symptoms remaining; (2) PTSD diagnosis on SCID-I and CAPS; (3) enrolled in program of care for psychotic disorder; (4) no acute suicidality; (5) IQ above 70; (6) sufficient language skills	PE and EMDR; ≥ 12 individual sessions, 90 minutes				
RCT	SMI outpatients	155	(1) Lifetime diagnosis of a psychotic disorder or mood disorder with psychotic features on the MINI; (2) current PTSD on the CAPS; (3) not acutely suicidal or at high risk for suicide; (4) no recent (2 months within enrollment) changes in psychiatric medications; (5) IQ above 70; (6) competent in Dutch language; (7) current admission in a closed ward	PE, EMDR, and waitlist; 8 individual sessions, 90 minutes				
Open trial	CMHC outpatients	20	(1) Enrolled in program of care at CMHC; (2) PTSD diagnosis on the CAPS; (3) diagnosis of schizophrenia or schizoaffective disorder; (4) no active substance dependence; (5) no psychiatric hospitalization or suicide attempts within 2 months of study enrollment	TMT+PE; 14 group followed by 8 individual sessions of PE, 60–90 minutes				
Open trial	VAMC outpatients	34	(1) Enrolled in program of care at VAMC; (2) PTSD diagnosis on the CAPS; (3) diagnosis of SMI (ie, psychotic disorder, major depression, bipolar)	PE; 10–15 individual sessions, 60–90 minutes				
Open trial	CMHC outpatients	19	(1) Primary diagnosis of major depression, bipolar disorder, or psychotic disorder; (2) state criteria for SMI; (3) enrolled in CMHC; (4) PTSD diagnosis on the PDS; (5) no psychiatric hospitalization within 3 months of study enrollment; (6) sufficient English fluency	CBT; 12–16 individual sessions (minimum of 12 sessions)				
Open trial	CMHC outpatients	80	(1) State-defined diagnosis of SMI; (2) enrolled in CMHC; (3) PTSD diagnosis on the THQ and PCL; (4) no psychiatric hospitalization within 1 month of study enrollment; (5) not floridly psychotic or disorganized; (6) not a significant threat to self/others	CBT; 21 group sessions				
RCT	CMHC outpatients	108	(1) State-defined diagnosis of SMI; (2) <i>DSM-IV</i> diagnosis of major depression, bipolar disorder, schizophrenia, or schizoaffective disorder; (3) PTSD diagnosis on the CAPS; (4) no psychiatric hospitalization or suicide attempt within 3 months of enrollment; (5) no current substance dependence	CBT and TAU; (CBT) 12–16 individual sessions; (TAU) supportive counseling				
RCT	Rutgers University Healthcare System partial/outpatients	201	(1) State-defined diagnosis of SMI; (2) diagnosis of major depression, bipolar disorder, schizophrenia, or schizoaffective disorder on the SCID-I; (3) PTSD diagnosis on the CAPS, minimum score of 65; (4) interested in receiving treatment	CBT and BTP; (CBT) 12–16 individual sessions; (BTP) 3 individual sessions				
Open trial	CMHC outpatients	18	(1) State-defined diagnosis of SMI; (2) current PTSD on the CAPS; (3) interested in receiving treatment; (4) no current suicidal/homicidal ideation; (5) no suicide attempt in past 3 months; (6) no organic brain condition; (7) no current participation in trauma-focused treatment	BTP; 3 individual sessions				
Open trial	CMHC and VAMC outpatients	22	(1) State-defined diagnosis of SMI or 100% service connected VA disability status; (2) diagnosis of major depression, bipolar disorder, schizophrenia, or schizoaffective disorder on the SCID-I; (3) PTSD diagnosis on the CAPS; (4) not a significant threat to self or others; (5) no psychiatric hospitalization or suicide attempt within 2 months of enrollment	CBT; 12–16 individual sessions				
RCT	National Health Service Trusts outpatients	61	(1) DSM-IV diagnosis of schizophrenia, schizoaffective disorder, or schizophreniform disorder; (2) DSM-IV diagnosis of PTSD; (3) stable living arrangements; (4) sufficient English proficiency; (5) no organic impairment	CBT and TAU; (CBT) 12–16 individual sessions				
Open trial	Mental health outpatients	27	(1) Chart diagnosis of schizophreniform disorder; (2) current PTSD on the CAPS; (3) IQ above 70; (4) competent in Dutch language	EMDR; 6 individual sessions				
Open trial	Incarcerated female patients	61	(1) Self-referred for trauma treatment; (2) diagnosis of an Axis I disorder, PTSD (full or subthreshold), and SUD; (3) residing in maximum, medium, or minimum security compounds of a prison for women; (4) diagnosis of serious mental disorder	Seeking safety (CBT); 28 group sessions, 90 minutes				
	Design WGC RCT Open trial Open trial Open trial RCT Open trial Open trial Open trial Open trial	DesignTarget sampleWGCMental health outpatientsRCTSMI outpatientsOpen trialCMHC outpatientsOpen trialCMHC outpatientsOpen trialCMHC outpatientsRCTCMHC outpatientsRCTCMHC outpatientsRCTRutgers University Healthcare System partial/outpatientsOpen trialCMHC outpatientsCMHC outpatientsCMHC outpatientsOpen trialCMHC outpatientsOpen trialCMHC and VAMC outpatientsOpen trialCMHC and VAMC outpatientsOpen trialMental health outpatientsOpen IncarceratedIncarcerated	DesignTarget sampleNWGCMental health outpatients10RCTSMI outpatients155Open trialCMHC outpatients20Open trialCMHC outpatients19Open trialCMHC outpatients80RCTCMHC outpatients108RCTRutgers University Healthcare System partial/outpatients201Open trialCMHC outpatients18Open trialCMHC and VAMC outpatients22Open trialCMHC and VAMC outpatients22Open trialMental health outpatients61Open trialMental health outpatients27Open trialIncarcerated61	Design Target sample N Inclusion/exclusion criteria³ WGC Mental health outpatients 10 (1) Severe psychotic episode in last 3 years with current positive or negative symptoms remaining; (2) PTSD diagnosis on SCID-1 and CAPS; (3) enrolled in program of care for psychotic disorder; (4) no acute suicidality; (5) IQ above 70; (6) sufficient language skills RCT SMI outpatients 155 (1) Lifetime diagnosis of a psychotic disorder or mood disorder with psychotic features on the MINI; (2) current PTSD on the CAPS; (3) not acutely suicidal or at high risk for suicide; (4) no recent (2 months within enrollment) changes in psychiatric medications; (5) IQ above 70; (6) competent in Dutch language; (7) current admission in a closed ward of care at CMHC; (2) PTSD diagnosis on the CAPS; (3) diagnosis of schizophrenia or schizoaffective disorder; (4) no active substance dependence; (5) no psychiatric hospitalization or suicide attempts within 2 months of study enrollment Open trial CMHC outpatients 34 (1) Enrolled in program of care at VAMC; (2) PTSD diagnosis on the CAPS; (3) diagnosis of SMI ((e, psychotic disorder, substance dependence; (5) no psychiatric hospitalization within 3 months of study enrollment; (6) sufficient English fluency Open trial CMHC outpatients 19 (1) Enrolled in program of care at VAMC; (2) PTSD diagnosis on the CAPS; (3) diagnosis of SMI; (2) enrolled in CMHC; (4) PTSD diagnosis on the PDS; (5) no psychiatric hospitalization within 3 months of study enrollment; (6) sufficient English fluency Open trial CMHC outpatients 80				

^aAll participants were 18 years of age or older, were able to provide informed consent, and were enrolled in a program of care for SMI.

Abbreviations: BTP = brief treatment program, CAPS = Clinician-Administered PTSD Scale, CBT = cognitive behavioral therapy, CMHC = community mental health center, EMDR = eye movement desensitization and reprocessing, IQ = intelligence quotient, MDD = major depressive disorder, MINI = Mini-International Neuropsychiatric Interview, AND = not otherwise specified, PCL = PTSD Checklist, BDS = Posttraumatic Diagnostic Scale, E = prolonged exposure, PTSD = posttraumatic stress disorder, RCT = randomized controlled trial, SCID-I = Structured Clinical Interview for DSM-IV Axis I Disorders, SMI = severe mental illness, SUD = substance use disorder, TAU = treatment as usual, THQ = Trauma History Questionnaire, AG TMT = trauma management therapy, VAMC = Veterans Administration Medical Center, WGC = within-group controlled.

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Study; treatment; outcome measure		Effect size [95% CI]
de Bont et al, 2013 ²⁰ ; PE/EMDR; CAPS	<u> </u>	-0.935 [-1.566 to -0.304]
de Bont et al. 2013 ²⁰ ; PE/EMDR; PSS-SR	——	-0.886 [-1.504 to -0.269]
Frueh et al, 2009 ²² ; CBT; CAPS	 ■	-1.127 [-1.614 to -0.640]
Frueh et al, 2009 ²² ; CBT; PCL	 ■	-1.149 [-1.641 to -0.657]
Grubaugh et al, 2016 ²³ ; PE; CAPS	⊢ ■─	-1.525 [-1.971 to -1.079]
Grubaugh et al, 2016 ²³ ; PE; PCL	├─ ■	-1.236 [-1.628 to -0.843]
Lu et al, 2009 ²⁴ ; CBT; PCL	——	■ -0.852 [-1.366 to -0.338]
Lu et al, 2009 ²⁴ ; CBT; PDS		-1.224 [-1.832 to -0.615]
Mueser et al, 2007 ²⁵ ; CBT; PCL	⊢■→	-1.388 [-1.662 to -1.114]
Mueser et al, 2007 ²⁵ ; CBT; PTCI	⊢=	
Mueser et al, 2007 ²⁵ ; CBT; KPTSD		-0.329 [-0.506 to -0.151]
Mueser et al, 2008 ¹⁴ ; CBT; CAPS	⊢-	→ -1.063 [-1.351 to -0.775]
Mueser et al, 2008 ¹⁴ ; CBT; PTCI		-0.617 [-0.854 to -0.380]
Mueser et al, 2008 ¹⁴ ; CBT; KPTSD		-0.302 [-0.516 to -0.088]
Mueser et al, 2015 ¹⁵ ; CBT; CAPS	⊢■→	-1.660 [-1.930 to -1.390]
Mueser et al, 2015 ¹⁵ ; BTP; CAPS	⊢=-	−1.164 [−1.389 to −0.939]
Mueser et al, 2015 ¹⁵ ; CBT; PTCI		- 0.174 [−0.325 to −0.024]
Mueser et al, 2015 ¹⁵ ; BTP; PTCI		-0.062 [-0.216 to 0.092]
Mueser et al, 2015 ¹⁵ ; CBT; KPTSD		- 0.259 [−0.412 to −0.106]
Mueser et al, 2015 ¹⁵ ; BTP; KPTSD		+ ■ †
Nishith et al, 2015 ²⁶ ; BTP; CAPS	-	−2.785 [−3.856 to −1.714]
Nishith et al, 2015 ²⁶ ; BTP; PCL	──	−1.964 [−2.769 to −1.160]
Rosenberg et al, 2004 ²⁷ ; CBT; CAPS	⊢	-0.845 [-1.398 to -0.291]
Steel et al, 2017 ¹⁶ ; CBT; CAPS		— ■ — 0.358 [−0.650 to −0.066]
Steel et al, 2017 ¹⁶ ; CBT; PTCI		-0.425 [-0.722 to -0.127]
van den Berg and van der Gaag, 2012 ²⁸ ; EMDR; CAPS	⊢	-1.547 [-2.053 to -1.041]
van den Berg and van der Gaag, 2012 ²⁸ ; EMDR; PSS-SR	⊢ •	── -0.958 [-1.346 to -0.570]
van den Berg et al, 2015 ¹⁷ ; PE; CAPS	├──■	−2.103 [−2.555 to −1.652]
van den Berg et al, 2015 ¹⁷ ; EMDR; CAPS	⊢ ■	−1.782 [−2.172 to −1.391]
van den Berg et al, 2015 ¹⁷ ; PE; PSS-SR	⊢-≣- I	−1.528 [−1.885 to −1.170]
van den Berg et al, 2015 ¹⁷ ; EMDR; PSS-SR	⊢ ■	−1.795 [−2.188 to −1.402]
van den Berg et al, 2015 ¹⁷ ; PE; PTCI		-1.0/9[-1.3/2(0-0./60]
van den Berg et al, 2015 ¹⁷ ; EMDR; PTCI	F	■ -0.823 [-1.079 to -0.567]
Wolff et al, 2012 ²⁹ ; CBT; PCL		-0.554 [-0.772 to -0.336]
RE Model		−1.009 [−1.269 to −0.750]*
PTSD Outcomes ($k = 34$, $Q = 534.324$, $P = .000$; $I^2 = 94.21\%$)	_	
		
	-4.000 -3.000 -2.000 -1.0	000 0.000 1.000
	Effect size [95%	CII
	266.5126 [257.6	

P<.001

Abbreviations: BTP = brief treatment program, CAPS = Clinician-Administered PTSD Scale, ³¹ CBT = cognitive behavioral therapy, EMDR = eye movement desensitization and reprocessing, KPTSD = Knowledge of PTSD Test, ³³ PCL = PTSD Checklist, ³⁵ PDS = Posttraumatic Diagnostic Scale, ³⁶ PE = prolonged exposure, PSS-SR = PTSD Symptom Scale-Self Report, ³⁷ PTCI = Posttraumatic Cognitions Inventory, ³⁸ PTSD = posttraumatic stress disorder, RE = random effects.

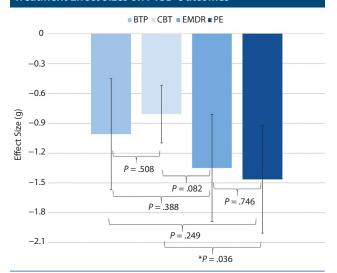
Meta-Analytic Results

As can be seen in Figure 2, PTSD treatments had a large and beneficial effect on PTSD outcomes among individuals with SMI, with patients experiencing an SD reduction in PTSD symptomatology over the course of treatment (g=-1.009, P<.001, k=34). Regarding the individual treatments, a nonsignificant moderating effect of treatment type was observed ($Q_B = 5.522$, df = 3, P = .137), as each treatment demonstrated a significant and large impact on PTSD symptom reduction. PE (g = -1.464; P < .001; SE = 0.276; k = 5), EMDR (g = -1.351; P < .001; SE = 0.276; k=5), and BTP (g=-1.009; P<.001; SE=0.284; k=5) had the largest effects on PTSD outcomes among individuals with SMI. CBT (g = -0.807; P < .001; SE = 0.148; k = 17)exhibited a large treatment effect as well, with greater precision in its estimates (Figure 3). Pairwise comparisons among the ESs of the individual treatments are presented in Figure 3. The effect of PE at reducing PTSD symptoms was

significantly larger relative to CBT among individuals with SMI. EMDR also had a greater effect on reduced PTSD symptoms compared to CBT, although this comparison did not meet conventional significance testing. No other ES comparisons among the treatments were significant (Figure 3).

Due to significant heterogeneity among the PTSD outcome findings (Figure 2), meta-regression models were used to examine the potential moderating effects of study demographics (age, sex, race), treatment characteristics (duration, individual vs group mode of delivery, inclusion of exposure), and study design. Only inclusion of exposure emerged as a significant moderator ($Q_B = 4.316$, df = 1, P = .038), such that treatments with an exposure element (PE, EMDR, g = -1.318, k = 12) were associated with greater reductions in PTSD symptoms compared to nonexposure treatments (CBT, BTP; g = -0.842; k = 22, B = -0.476, SE = 0.229, P = .038).

Figure 3. Pairwise Comparisons of Individual PTSD Treatment Effect Sizes on PTSD Outcomes^a



 a Pairwise comparisons calculated using Tukey method. *Statistically significant (P < .05).

Abbreviations: BTP = brief treatment program, CBT = cognitive behavioral therapy, EMDR = eye movement desensitization and reprocessing, PE = prolonged exposure, PTSD = posttraumatic stress disorder.

Given the greater accuracy of clinician-administered versus self-report measures to assess symptom change, the effect of treatment on both types of assessment strategies for PTSD outcomes was examined. The ESs between the clinician-administered and self-report measures were comparable ($Q_B = 2.234$, df = 1, P = .135). A large overall effect was observed from pre-treatment to post-treatment on the Clinician-Administered PTSD Scale (CAPS; g = -1.275, SE = 0.152, P < .001; k = 12) and the PTSD self-report measures (eg, PCL, PSS-SR, PDS; g = -1.059, SE = 0.144, P < .001; k = 11).

Concerning SMI outcomes, PTSD treatments among individuals with SMI had a significant, medium-sized effect on general psychopathology (g = -0.499; P < .001; SE = 0.078; k=6) and a significant, small-to-medium-sized effect on psychotic symptoms (g = -0.290; P = .006; SE = 0.106; k = 8). Individual treatment ESs on general psychopathology and psychotic symptoms were not compared among the treatment types due to the small number of findings. No significant heterogeneity was observed among the general psychopathology findings (Q = 10.122; P = .072, $I^2 = 46.89\%$), unlike the psychotic symptoms (Q = 14.622; P = .041, $I^2 = 57.28\%$). Therefore, meta-regressions were used to examine the same moderating effects mentioned above on psychotic symptoms, with the exception of individual vs group treatment modality as all were individual based. All moderator analyses for psychotic symptoms were nonsignificant.

DISCUSSION

This meta-analytic review examined the efficacy of PTSD treatments for individuals with PTSD and comorbid SMI,

ghted PDF on any website, a group that is often excluded from PTSD treatments in practice and clinical trials and is underrepresented in the PTSD treatment outcome literature. Our results indicate that EBTs for PTSD meaningfully impact PTSD outcomes with patients experiencing an SD decrease in PTSD symptom severity pre- to post-treatment (g = -1.009, P < .001, k = 34). With regard to the individual treatments evaluated, PE (g=-1.464), EMDR (g=-1.351), and BTP (g=-1.009)demonstrated a slight advantage over CBT (g = -0.807). These ESs are consistent with the lower range of withingroup ESs found in the broader PTSD treatment outcome literature. 1-4 Additional moderator analyses suggest that interventions with an exposure component (PE, EMDR) may be particularly effective for this patient population relative to other EBTs for PTSD. However, this finding warrants confirmation in adequately powered comparative effectiveness studies.

Attrition across treatment conditions ranged from 15%-41%. These rates are comparable if not slightly lower to those found in the broader PTSD treatment outcome literature. 1,5,6 As such, it does not appear that individuals with comorbid PTSD and SMI are at increased risk of dropping out of PTSD treatment relative to those with only PTSD. Finally, it appears that PTSD treatment had a significant positive impact on the primary symptoms of SMI (eg, psychotic symptoms), as well as measures of general psychopathology that include indices of depression and anxiety, which are highly correlated with both PTSD and SMI. The moderate ESs on these indices are similar to those found in meta-analyses of CBT for SMI. 47,48 These findings are promising and run counter to initial concerns by public sector clinicians that addressing trauma and PTSD in this clinical population could result in an exacerbation of the symptoms of SMI or lead to unwanted adverse events. 49

The current meta-analytic review is limited by a few factors. First, the analysis consisted of 14 studies. As such, between-group treatment ESs could not be calculated, but pre-treatment to post-treatment within-group findings were robust. This limitation highlights the need for additional controlled PTSD treatment studies in this population. As noted previously, despite the small sample size, publication bias was low, as a file drawer analysis indicated that a total of 12,644 unpublished null studies would be needed to reduce the observed significant effects of PTSD treatments on PTSD outcomes to nonsignificant thresholds. The publication bias was higher for general psychopathology (fail-safe N = 184) and psychotic symptoms (fail-safe N = 81), but this is not surprising given the small number of SMI findings. Indeed, a number of the studies did not report on SMI outcomes. Despite this limitation, it is promising that ESs of the 9 studies that did include SMI outcome measures were similar to those reported in other meta-analytic studies investigating CBT for the symptoms of SMI. 47,48 Third, similar to most metaanalytic studies, treatment characteristics, including type, modality (ie, individual versus group), length, clinician expertise, and sample composition, were variable. The

It is illegal to post this convirgorous standards used to select studies for the current analysis addressed this issue to a degree, but future PTSD treatment efficacy and effectiveness trials should attempt to adhere to common criteria for sample selection and intervention implementation. Despite some limitations, the current review has several strengths. These include the use of a meta-analytic strategy that allowed for more robust trial inclusion (ie, inclusion of open trials⁴¹), the diversity of the study samples with regard to race/ethnicity, a more uniform assessment of PTSD outcomes across studies, and inclusion of trials with a broad range of comorbid forms of SMI. Additionally, the current findings provide support for the validity of self-report measures of PTSD relative to clinician administered measures for this patient population as well as information on the efficacy of EBTs for PTSD across a broader range of outcomes (general psychopathology, psychosis severity).

Altogether, the results of this meta-analysis support the use of EBTs for PTSD among individuals with comorbid SMI, consistent with best practice guidelines for PTSD.⁵⁰ Although these meta-analytic findings are promising, there remains a need to further study the efficacy of the treatments evaluated as well as other EBTs for PTSD, given the small number of RCTs and modest sample sizes available. For example, although the largest ESs in the current metaanalysis were for PE and EMDR, heterogeneity in observed outcomes likely influenced the results for BTP. Along a similar theme, one study comparing CBT to treatment as usual¹⁶ reported statistically nonsignificant differences between groups on the CAPS, with the control group yielding a 16-point difference from baseline to follow-up. Although there is currently no consensus for defining clinically significant change on the CAPS, change scores of 10 or 15 are often used as cutoffs for defining clinical improvement on this measure, with others using more conservative change scores.⁵¹ Spontaneous decreases in PTSD severity from baseline to follow-up in the absence of an active intervention are not uncommon; however, such decreases are generally fairly modest (ie, CAPS change scores less than 10). Thus, this finding is fairly atypical, and it is unknown how elements of TAU in this study contributed to improvements in the absence of a trauma focused intervention. Finally, it is worth noting that most of the studies using CBT or BTP were conducted by 1 or 2 groups in the US, whereas most of the research on PE and EMDR was conducted by 1 or 2 groups in the Netherlands. As such, it is unclear to what degree, if any, the research team and/or the selection of study participants or treatment setting impacted the observed effect sizes. Given our findings with regard to SMI outcomes, there is also a need to more uniformly examine the impact of PTSD treatment on the course of SMI severity as well as other indices of functioning and quality of life. These additional efforts, as well as comparative effectiveness evaluations, would serve to establish a more robust treatment outcome literature for individuals with SMI commensurate to what is available for the broader population of individuals with PTSD.

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Within the context of public practice settings, the treatment of PTSD among individuals with SMI aligns well with recovery models of care.⁵² Broadly, these models emphasize the ability of individuals with severe mental illnesses to lead productive lives and assert that the course of mental illness is a process that is not necessarily static or linear or all defining. These models also typically stress the importance of patient empowerment. Consistent with this, a number of studies have demonstrated that interventions designed to involve people with severe mental illnesses in their own treatment planning yield better outcomes than those that do not. 53-55 The findings of this metaanalytic review suggest a significant benefit to assessing for PTSD among patients with SMI and to allowing them the opportunity to participate in the decision process to engage in treatment given their current circumstances, other treatment priorities, and perceived readiness. With regard to PTSDrelated distress, the benefits are clear. Additionally, however, there is the potential that PTSD treatment engagement will improve some of the primary symptoms of SMI, resulting in reductions in overall illness burden and less reliance on pharmacologic treatment.

In addition to building the treatment outcome literature, however, concentrated effort will need to focus on addressing the wide range of barriers to dissemination that are observed in the broader PTSD literature. Most relevant on this list are beliefs among practitioners regarding who is appropriate for trauma intensive treatment. That is, clinicians continue to endorse concerns that EBTs for PTSD may cause undue distress to their patients or cause them to worsen, particularly those with more severe and complicated clinical profiles.^{56–60} Notably, one study found that having a comorbid diagnosis of psychosis was one of 3 client characteristics most likely to result in exclusion from exposure therapy, and another found that 85% of providers believed exposure therapy for PTSD is contraindicated for patients with a psychotic disorder.^{56,60} Thus, in addition to efficacy and effectiveness data, future efforts should focus on more systematically evaluating the cost/benefit ratio of treating PTSD among individuals with SMI at the patient, provider, and systems levels. Although promoting the adoption of EBTs for PTSD among individuals with SMI presents a challenging task, it is a necessary one given the pronounced rates of PTSD among individuals with SMI relative to the general population and the documented impact of PTSD on their functioning and quality of life.

Submitted: July 26, 2020; accepted February 8, 2021.

Published online: May 25, 2021.

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents or device therapies that is outside US Food and Drug Administrationapproved labeling has been presented in this article.

Author contributions: All authors contributed to the development of the submitted manuscript. Drs Grubaugh and Brown contributed to the conceptualization, research of background/studies for inclusion, methodology, analysis, and write-up. Dr Wojtalik contributed to the research of background/studies for inclusion, methodology, analysis, and write-up. Dr Myers contributed to the research of background/studies for inclusion and write-up. Dr Eack contributed to the methodology, analysis, and write-up.

Financial disclosure: Drs Grubaugh, Brown, Wojtalik, Myers, and Eack have no personal Schizophrenia: a randomized controlled trial. Psychol Med. 2017;47(1):43–51. Scales (GPTS). Psychol Med. 2008;38(1):101–111. 33. Pratt SI, Rosenberg SD, Mueser KT, et al.

Wojtalik, Myers, and Eack have no personal affiliations or financial relationships with any commercial interest to disclose relative to the article.

Funding/support: No direct funding/financial support was received for this work.

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POSTTEST

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- Evidence-based treatments for posttraumatic stress disorder (PTSD) that have been evaluated for individuals with a comorbid severe mental illness include all of the following except:
 - a. Prolonged exposure for PTSD
 - b. Brief treatment program
 - c. Exposure and response prevention
 - d. Eye movement desensitization and reprocessing
- 2. Clinical trials with individuals who have PTSD and a comorbid severe mental illness have documented improvements in which outcome other than PTSD?
 - a. Psychosis severity
 - b. Tardive dyskinesia
 - c. Obsessive-compulsive symptoms
 - d. Migraines
- 3. Janelle is a 56-year-old woman with a history of schizophrenia who is admitted to the inpatient unit. As part of her intake evaluation, she endorses a history of childhood sexual abuse spanning 4 years. Which statement reflects an evidencebased practice that you could implement with Janelle?
 - a. Discuss the importance of staying busy so that Janelle does not spend too much time thinking about what happened and being upset about it
 - b. Inform Janelle that she may have PTSD from that abuse, but currently PTSD is not a treatment priority given her other symptoms
 - Conduct a formal trauma exposure/PTSD evaluation prior to discharge to assess severity
 of symptoms and impact on functioning and to collaboratively discuss treatment options
 - d. Encourage Janelle to get enough sleep, eat well, and exercise regularly after her discharge