Meta-Analysis of the Treatment of Posttraumatic Stress Disorder in Adults With Comorbid Severe Mental Illness

Anouk L. Grubaugh, PhD a,*; Wilson J. Brown, PhD b; Jessica A. Wojtalik, PhD c; Ursula S. Myers, PhD a; and Shaun M. Eack, PhD d

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 (g = −1.009, P < .001, k = 34). Prolonged exposure (g = −1.464; P < .001; SE = 0.276; k = 5), eye movement desensitization and reprocessing (g = −1.351; P < .001; SE = 0.276; k = 5), and brief treatment program (g = −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.

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The 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
Clinical Points

- Despite experiencing high rates of trauma and posttraumatic stress disorder (PTSD), individuals with comorbid severe mental illness (SMI; eg, 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, evidence-based psychosocial treatments for PTSD can have a positive impact on the primary symptoms of SMI and overall illness burden.

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, meta-analytic 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 disorder7,8 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 with SMI have yielded promising results with regard to 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
adult samples, manuscripts published in English, and peer-reviewed studies published between January 1998 and March 2020. 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. 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

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Figure 1. Systematic Review Flow Diagram of Included Studies

Records identified through database search n = 2,208
Duplicates excluded n = 198
Titles screened n = 2,010
Records excluded by title n = 1,942
Abstracts screened n = 68
Records excluded by abstract n = 30
Not a PTSD-focused treatment (n = 5)
Not a clinical trial (n = 8)
Study methods protocol (n = 2)
Case study/single series design (n = 5)
Theoretical paper (n = 4)
First-episode psychosis (n = 3)
Review paper/meta-analysis (n = 3)
Full text articles assessed for eligibility n = 38
Records excluded by article review n = 24
Secondary analyses (n = 6)
Non-SMI sample (n = 12)
Subsyndromal bipolar disorder sample (n = 1)
PTSD/substance abuse sample (n = 4)
PTSD/substance abuse/traumatic brain injury sample (n = 1)
Articles included in meta-analysis n = 14

Abbreviations: BPD = borderline personality disorder, PTSD = posttraumatic stress disorder, SMI = severe mental illness.

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*January 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.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Design</th>
<th>Analysis</th>
<th>Treatment(s)</th>
<th>N</th>
<th>Dropout, n (%)</th>
<th>Mean (SD), age, y</th>
<th>Male, %</th>
<th>Caucasian, %</th>
<th>SMI diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>de Bont et al (2013)26</td>
<td>WGC</td>
<td>ITT</td>
<td>PE, EMDR</td>
<td>53</td>
<td>13 (24)</td>
<td>42.6 (10.3)</td>
<td>73.3</td>
<td>4.0</td>
<td>(40%) schizophrenia (10%) schizoaffective (4%) psychotic NOS (10%) bipolar disorder</td>
</tr>
<tr>
<td></td>
<td>RCT</td>
<td>ITT</td>
<td>PE, EMDR, Waitlist</td>
<td>47</td>
<td></td>
<td>39.7 (3.0)</td>
<td>69.8</td>
<td>3.4</td>
<td>95% schizophrenia (29%) schizoaffective (1%) brief psychotic (3%) psychotic NOS (4%) bipolar disorder</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2% MDD</td>
</tr>
<tr>
<td>Wolff et al (2008)14</td>
<td>Open trial</td>
<td>Completer</td>
<td>CBT</td>
<td>14</td>
<td>5 (26)</td>
<td>43.9 (8.9)</td>
<td>57.0</td>
<td>4.3</td>
<td>(2%) schizophrenia (2%) schizoaffective (79%) bipolar disorder/MDD</td>
</tr>
<tr>
<td></td>
<td>RCT</td>
<td>ITT</td>
<td>CBT</td>
<td>54</td>
<td>8 (15)</td>
<td>45.1 (9.8)</td>
<td>24.1</td>
<td>4.3</td>
<td>(7%) schizophrenia (9%) schizoaffective (25%) bipolar disorder (66%) MDD</td>
</tr>
<tr>
<td></td>
<td>Open trial</td>
<td>Completor</td>
<td>BTP</td>
<td>18</td>
<td>3 (17)</td>
<td>45.8 (9.7)</td>
<td>11.1</td>
<td>11.1</td>
<td>(3%) schizoaffective (5%) bipolar disorder (22%)</td>
</tr>
<tr>
<td></td>
<td>RCT</td>
<td>ITT</td>
<td>CBT (CR)</td>
<td>104</td>
<td>22 (24)</td>
<td>43.0 (10.5)</td>
<td>29.8</td>
<td>3.4</td>
<td>(28%) psychotic spectrum disorder (49%) mood disorder (41%) mood disorder and BPD (14%) psychotic spectrum disorder and BPD</td>
</tr>
<tr>
<td></td>
<td>Open trial</td>
<td>Completor</td>
<td>BTP</td>
<td>12</td>
<td>9 (41)</td>
<td>43.0 (7.5)</td>
<td>50.0</td>
<td>0.0</td>
<td>(3%) schizoaffective (3%) psychotic NOS (21%) bipolar disorder (52%) MDD</td>
</tr>
<tr>
<td></td>
<td>RCT</td>
<td>ITT</td>
<td>CBT (SS)</td>
<td>61</td>
<td>NR</td>
<td>36.0 (10.0)</td>
<td>0.0</td>
<td>36.5</td>
<td>(74%) schizophrenia (16%) schizoaffective (26%)</td>
</tr>
<tr>
<td></td>
<td>Open trial</td>
<td>Completor</td>
<td>TAU</td>
<td>31</td>
<td></td>
<td>40.7 (10.2)</td>
<td>64.5</td>
<td>0.0</td>
<td>(22%) schizophrenia (52%) psychotic NOS (1%) delusional disorder</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6% MDD</td>
</tr>
</tbody>
</table>

**Table 1. Study Characteristics of the PTSD Treatment Studies That Met Inclusion for Meta-Analysis**

- Effect of treatment was averaged across both PE (n = 5) and EMDR (n = 5).
- General psychopathology outcome.
- Demographic characteristics were not presented for the total number of individuals assigned to SS (N = 111), and 37 participants were designated as noncompleters. Demographic characteristics were not 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 = 15), and 15 participants were designated as noncompleters.
- Abbreviations: BPRS = Brief Psychiatric Rating Scale, BTP = brief treatment program, CAPS = Clinician-Administered PTSD Scale, CBT = cognitive behavioral therapy, EMDR = eye movement desensitization and reprocessing, GPTS = Green Paranoid Thoughts Scale, ITT = intention-to-treatment, KPTSD = Knowledge of PTSD Test, MDD = major depressive disorder, NA = not available, NOS = not otherwise specified, NR = not reported, PANSS = Positive and Negative Syndrome Scale, PCL = PTSD Checklist, PDS = Posttraumatic Diagnostic Scale, PE = prolonged exposure, PSS-SR = PTSD Symptom Scale Self-Report, PTSD = posttraumatic stress disorder, RCT = randomized controlled trial, SS = seeking safety, TAU = treatment as usual, WGC = within-group controlled.
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 outcomes\(^{17}\) and SMI outcomes\(^{21}\)), 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 EMDR\(^{20}\) (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 study\(^{29}\) 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 study\(^{21}\) 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 al\(^{17}\) 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.
### Table 2. Study Recruitment and Treatment Characteristics

<table>
<thead>
<tr>
<th>Authors</th>
<th>Design</th>
<th>Target sample</th>
<th>N</th>
<th>Inclusion/exclusion criteria</th>
<th>Intervention characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>de Bont et al (2013)</td>
<td>WGC</td>
<td>Mental health outpatients</td>
<td>10</td>
<td>(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</td>
<td>PE and EMDR; ≥ 12 individual sessions, 90 minutes</td>
</tr>
<tr>
<td>van den Berg et al (2015)</td>
<td>RCT</td>
<td>SMI outpatients</td>
<td>155</td>
<td>(1) Lifetime diagnosis of a psychotic disorder or mood disorder with psychiatric 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</td>
<td>PE, EMDR, and waitlist; 8 individual sessions, 90 minutes</td>
</tr>
<tr>
<td>Friehe et al (2009)</td>
<td>Open trial</td>
<td>CMHC outpatients</td>
<td>20</td>
<td>(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</td>
<td>TMT + PE; 14 group followed by 8 individual sessions of PE, 60–90 minutes</td>
</tr>
<tr>
<td>Grubaugh et al (2016)</td>
<td>Open trial</td>
<td>VAMC outpatients</td>
<td>34</td>
<td>(1) Enrolled in program of care at VAMC; (2) PTSD diagnosis on the CAPS; (3) diagnosis of SMI (ie, psychotic disorder, major depression, bipolar)</td>
<td>PE; 10–15 individual sessions, 60–90 minutes</td>
</tr>
<tr>
<td>Lu et al (2009)</td>
<td>Open trial</td>
<td>CMHC outpatients</td>
<td>19</td>
<td>(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</td>
<td>CBT; 12–16 individual sessions (minimum of 12 sessions)</td>
</tr>
<tr>
<td>Mueser et al (2007)</td>
<td>Open trial</td>
<td>CMHC outpatients</td>
<td>80</td>
<td>(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</td>
<td>CBT; 21 group sessions</td>
</tr>
<tr>
<td>Mueser et al (2008)</td>
<td>RCT</td>
<td>CMHC outpatients</td>
<td>108</td>
<td>(1) State-defined diagnosis of SMI; (2) DSM-IV 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</td>
<td>CBT and TAU; (CBT) 12–16 individual sessions; (TAU) supportive counseling</td>
</tr>
<tr>
<td>Mueser et al (2015)</td>
<td>RCT</td>
<td>Rutgers University Healthcare System partial/outpatients</td>
<td>201</td>
<td>(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</td>
<td>CBT and BTP; (CBT) 12–16 individual sessions; (BTP) 3 individual sessions</td>
</tr>
<tr>
<td>Nishith et al (2015)</td>
<td>Open trial</td>
<td>CMHC outpatients</td>
<td>18</td>
<td>(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</td>
<td>BTP; 3 individual sessions</td>
</tr>
<tr>
<td>Rosenberg et al (2004)</td>
<td>Open trial</td>
<td>CMHC and VAMC outpatients</td>
<td>22</td>
<td>(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</td>
<td>CBT; 12–16 individual sessions</td>
</tr>
<tr>
<td>Steel et al (2017)</td>
<td>RCT</td>
<td>National Health Service Trusts outpatients</td>
<td>61</td>
<td>(1) DSM-IV diagnosis of schizophrenia, schizoaffective disorder, or schizoaffective disorder; (2) DSM-IV diagnosis of PTSD; (3) stable living arrangements; (4) sufficient English proficiency; (5) no organic impairment</td>
<td>CBT and TAU; (CBT) 12–16 individual sessions</td>
</tr>
<tr>
<td>van den Berg and van der Gaag (2012)</td>
<td>Open trial</td>
<td>Mental health outpatients</td>
<td>27</td>
<td>(1) Chart diagnosis of schizoaffective disorder; (2) current PTSD on the CAPS; (3) IQ above 70; (4) competent in Dutch language</td>
<td>EMDR; 6 individual sessions</td>
</tr>
<tr>
<td>Wolff et al (2012)</td>
<td>Open trial</td>
<td>Incarcerated female patients</td>
<td>61</td>
<td>(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</td>
<td>Seeking safety (CBT); 28 group sessions, 90 minutes</td>
</tr>
</tbody>
</table>

*All 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, NOS = not otherwise specified, PCL = PTSD Checklist, PDS = Posttraumatic Diagnostic Scale, PE = 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, TMT = trauma management therapy, VAMC = Veterans Administration Medical Center, WGC = within-group controlled.
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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 ($Q_A = 4.316$, $df = 1$, $P = .038$), 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, $P = .038$).
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 ($g = -0.496; P < .001; SE = 0.078; k = 6$) and a significant, small-to-medium-sized effect on psychotic symptoms ($g = -0.290; P < .001; SE = 0.106; k = 8$). 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, 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 within-group ESs found in the broader PTSD treatment outcome literature. 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. 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. 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.

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. Third, similar to most meta-analytic studies, treatment characteristics, including type, modality (ie, individual versus group), length, clinician expertise, and sample composition, were variable. The
Within the context of public practice settings, the treatment of PTSD among individuals with SMI aligns well with recovery models of care. 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. The findings of this meta-analytic 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 PTSD-related 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. 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. 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.
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REFERENCES

Treatment of PTSD in Patients With Severe Mental Illness

1. 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 evidence-based 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
   c. 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

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