

Trauma-Informed Care in Psychedelic Therapy Research: A Qualitative Literature Review of Evidence-Based Psychotherapy Interventions in PTSD and Psychedelic Therapy Across Conditions

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Introduction: Post-traumatic stress disorder (PTSD) is associated with significant patient burden. While pharmacotherapies and evidence-based psychotherapy interventions (EBPI) are effective, studies consistently highlight inadequate outcomes and high treatment dropout. Psychedelic therapy (PT) has shown preliminary promise across difficult-to-treat conditions, including MDMA-assisted therapy for PTSD, however trials of classical psychedelics in PTSD are lacking. Understanding patients' experiences of EBPI could help promote safety in PT.

Aim: To systematically review qualitative research on patients' subjective experience of EBPI for PTSD, and of PT, and examine areas of overlap and divergence between them.

Methods: Systematic literature searches for studies published between 2010 and 2023 were conducted on OVID, PubMed, Web of Science, and PsycInfo. Included were original studies in English that presented qualitative data of patient experiences of EBPI in PTSD, or PT for any indication. Extracted data from included studies were analysed using thematic synthesis. Syntheses were completed separately for EBPI and PT, before similarities and differences between the therapies were identified.

Results: 40 research articles were included for review: 26 studies on EBPI for PTSD, and 14 studies on PT. EBPI studied were CBT, EMDR, CPT and PE. Psychedelic compounds studied were psilocybin, ibogaine, LSD, MDMA and ketamine, for treatment of substance use disorders, anxiety relating to physical illness, depression, and PTSD. Core themes from patient experiences of EBPI: 1) patient burden in PTSD treatment; 2) readiness; 3) key mechanisms of change; 4) psychological safety and trust. Themes identified in the review of PT: 1) indirect trauma processing; 2) reorganisation of self-narratives via processes of relatedness and identification; 3) key treatment characteristics.

Conclusion: This study suggests overlap between patients' experience of EBPI and PT in terms of key mechanisms of change, the importance of psychological safety and readiness to engage in treatment. Trauma-informed care paradigms and practices may improve safety and acceptability of PT research.

Keywords: trauma, PTSD, psychotherapy, psychedelic therapy, qualitative, review

Introduction

Trauma exposure is associated with an increased risk for psychopathology¹⁻³ including post-traumatic stress disorder (PTSD), major depressive disorder (MDD) and dissociative disorders. PTSD, characterised by debilitating comorbid symptomatology and psychosocial dysfunction, is associated with significant individual and societal burden.^{4,5} Pharmacotherapies (eg, paroxetine and sertraline) and evidence-based psychotherapy interventions (EBPI) for PTSD, such as prolonged exposure (PE) or trauma-focused cognitive behavioural therapy (TF-CBT), are considered effective.⁶⁻⁸ Despite EBPIs effectiveness, studies consistently highlight difficulties, including inadequate treatment outcomes^{9,10} and poor patient retention.¹¹ Psychological treatment of PTSD

may be challenging and complex,¹² potentially due to the significant symptomatic and psychosocial burden patients endure (eg, perceived negative experiences related to the treatment across different domains, including emotional, relational, physical, systemic, and practical aspects).¹³ Further, patients who find treatment ineffective and seek additional care are also at increased risk of re-traumatisation due to the need to repeatedly recount their traumatic experiences to providers.¹⁴

In response to the unmet clinical need in PTSD¹⁵ and difficult-to-treat mental-health conditions¹⁶, studies investigating psychedelic forms of therapy have shown promise in so-called “treatment-resistant” patients.^{17–21} Psychedelic therapy (PT) is an umbrella term for interventions administering serotonergic hallucinogens such as 4-phosphoryloxy-N,N-dimethyltryptamine (psilocybin) and lysergic acid diethylamide (LSD) or entactogens such as 3,4-Methyl enedioxy methamphetamine (MDMA) alongside manualised psychological interventions.^{22–25} Despite PT’s favourable safety profile in research settings and advances in understanding of its neurobiological, psychological, and behavioural effects,^{26–29} significant gaps of knowledge remain. Clinically, it is not well understood how PT supports positive outcomes across conditions and compounds.³⁰ Positive results are often associated with patient reports of increased insightfulness,³¹ emotional breakthrough³² and mystical-type experiences,³³ however, experimental studies are needed to establish causality. Importantly, qualitative research has highlighted the significance of the intervention’s non-pharmacological factors,^{34,35} including interpersonal rapport and music listening to positive outcomes.^{36,37}

In PTSD, MDMA-assisted therapy appears highly efficacious in clinical trials, reducing symptoms and improving quality-of-life in patients with chronic PTSD.^{20,38} However, completed trials of classical psychedelics in PTSD are lacking, with several early phase studies recruiting as of October 2023. Correspondingly, there is an absence of trauma-focused clinical practice guidelines in PT. Despite considerable advances in treatments for PTSD in recent years,⁹ there remain significant challenges associated with standard PTSD treatment, including disruptions to the patient’s linguistic capacities and biological stress dysregulation.³⁹ Therefore, considering patients’ experience of EBPI may help personalise care and promote safety outcomes for traumatised participants in PT trials. Further, as the number of psychedelic trials grow⁴⁰ and with Australia approving the therapeutic use of MDMA and psilocybin in mental-health,^{41,42} it is vital that regulators, healthcare systems and clinicians have access to a repository of in-depth knowledge of patient experiences to inform operational, clinical, and training protocols that support patient safety. As most PT trial participants must be unsuccessfully treated by first-line interventions, understanding the positive and negative experiences of EBPI patients could help optimise PT protocols.

Qualitative research is well-placed to provide an in-depth understanding of patients’ subjective experience of trauma and treatment.^{43–45} Therefore, this research aims to review qualitative studies in EBPI for PTSD and PT, examining areas of intersectionality and divergence to promote a multidisciplinary dialogue. A synthesis of the themes in the selected studies will be conducted to provide a broad understanding of patients’ experience of the treatments. Based on the data, areas of clinical interest will be discussed to promote patient outcomes and safety in PT.

Methods

Search Strategy

A systematic literature search was conducted to identify papers studying patients’ qualitative experiences of either EBPI in PTSD, or PT. Given the paucity of existing qualitative literature on PT for PTSD, an expanded second search was conducted to include studies on PT for any clinical indication, including but not limited to depression, substance use disorders, and anxiety associated with life-threatening illness. The search was conducted between January and March 2023. Search terms related to PTSD, psychotherapy, psychedelics, qualitative methods, and patient experience were defined ([Table S1](#)) and entered in major research databases (OVID, PubMed, Web of Science, and PsycInfo). Reference lists of included studies on PT and specific relevant journals specialising in psychedelic science and traumatology were manually searched to ensure suitable articles were not missed. Transparent Reporting of Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed.⁴⁶ The systematic review was registered on the International Prospective Register of Systematic Reviews (PROSPERO).

Eligibility Criteria

Papers deemed eligible for inclusion were original, peer-reviewed studies presenting qualitative data with an identifiable qualitative research methodology (eg, grounded theory, interpretative phenomenological analysis, etc.), focused on patient experiences of either EBPI in PTSD, or PT for any indication. Papers must have been published between

January 2010 and March 2023. This date range was chosen as modern psychedelic research began to emerge after 2010, and such a date range would allow comparison with contemporaneous EBPI literature.

Papers were excluded if they did not present new research (eg, systematic reviews), were not peer-reviewed, not published in English, studied others' experiences (eg, clinicians, family members) or indications other than PTSD (unless studying psychedelics, where any clinical indication was included as previously outlined). Studies were also excluded if they were not specifically studying the experience of EBPI, or if they were studying internet- or phone-based therapy only. Mixed-methods studies were included if qualitative data of patient experiences was clearly presented. PRISMA diagrams for both literature searches are presented in Figures 1 and 2.

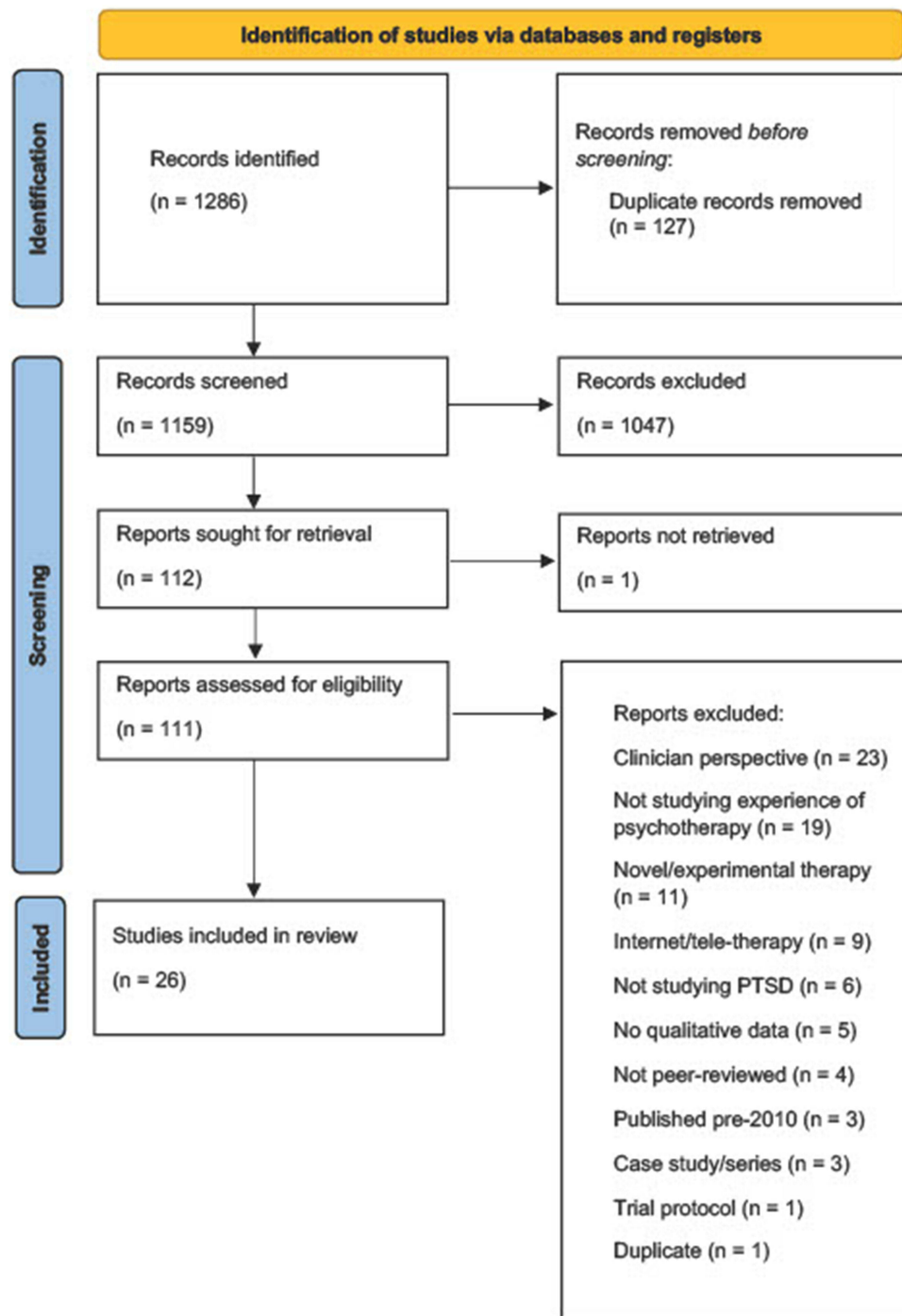


Figure 1 PRISMA flow diagram of evidence-based psychotherapy interventions (EBPI) literature search.

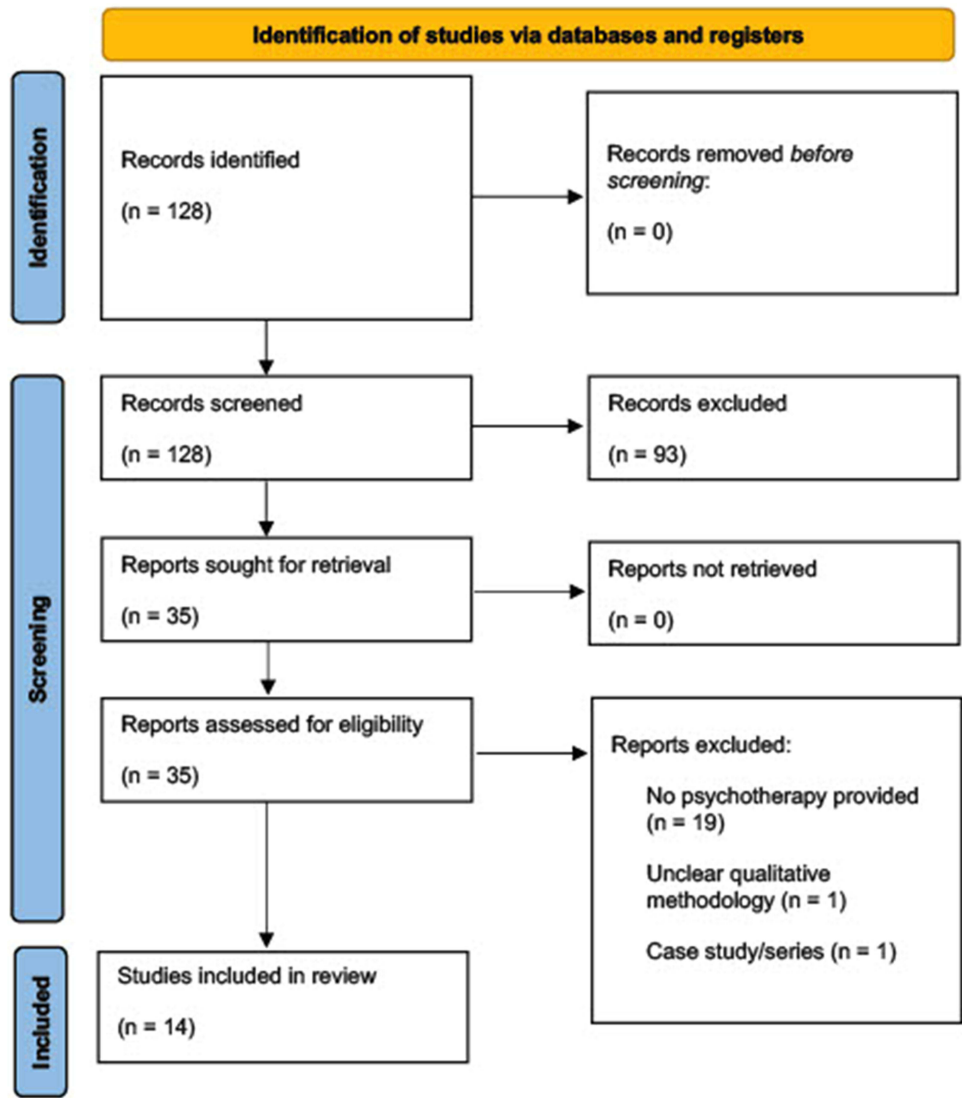


Figure 2 PRISMA flow diagram for psychedelic therapy (PT) literature search.

Selected papers were assessed for quality using the Critical Appraisal Skills Programme (CASP) criteria.⁴⁷ This involves assessing the paper across ten domains, and assigning a score of 0–10, 10 representing a paper of high quality. The overall quality of the included studies was high, with an average rating of 8.2 (range: 5–10) (see Tables 1 and 2).

Table 1 Overview of EBPI Study Methodologies, Settings, Sample Characteristics and CASP Quality Ratings

Author/Year	Study Design	Qualitative Methodology	Type of Intervention (no. of Sessions Where Specified)	Setting	Population	Sample Size/age	CASP Rating
Andersen et al, 2021 ⁹⁴	Non-randomised intervention study	Phenomenology Thematic analysis	CBT with Basic Body Awareness Therapy (BBAT) 12 sessions	Veterans clinic, Denmark	Male veterans	4 Age range: 30–50	10
Booyesen and Kagee, 2023 ⁸⁹	Qualitative study	Semi-structured interviews Thematic analysis	Prolonged exposure (PE) 6 sessions	Outpatient services, South Africa	Female PTSD patients	7 Age range: 20–27	8

(Continued)

Table 1 (Continued).

Author/Year	Study Design	Qualitative Methodology	Type of Intervention (no. of Sessions Where Specified)	Setting	Population	Sample Size/age	CASP Rating
Borges et al, 2019 ⁸²	Qualitative study	Semi-structured interviews Thematic analysis	Various EBPI	Veterans clinic, USA	Male veterans	14 Mean age: 59.5 (range: 25–74)	8
Boterhoven et al, 2021 ⁸⁷	Qualitative study within RCT	Semi-structured interviews Thematic analysis	IREM (imagery rescripting with EMDR) 12 sessions	Outpatient clinics in Australia, Germany, Netherlands	Adult PTSD patients with childhood trauma	44 Mean age: 40	9
Harned and Schmidt, 2019 ⁹¹	Qualitative study within larger implementation project	Mixed-methods Focus groups Inductive content analysis	Dialectical Behavioural Therapy (DBT) with PE	Outpatient services, USA	Female PTSD patients	19 Mean age: 35	8
Hegarty et al, 2022 ⁹⁹	Qualitative study	Analysis of audio-recorded sessions Thematic analysis	Group-based CBT 18 sessions	Outpatient services, UK	Female cPTSD patients	10 Mean age: 44 (range: 26–60)	9
Hundt et al, 2017 ⁹⁰	Qualitative study of treatment acceptability	Semi-structured interview Grounded theory	PE Cognitive Processing Therapy (CPT) At least 8 sessions	Veterans clinic, USA	Veterans	23 Mean age: 53.7	8
Hundt et al, 2020 ⁸⁸	Qualitative study of treatment dropout	Grounded theory Semi-structured interview	PE CPT Fewer than 8 sessions	Veterans clinic, USA	Veterans	28 Mean age: 45.3	8
Jackson et al, 2020 ¹⁰⁰	Mixed-methods feasibility study	Semi-structured interview Inductive content analysis	Trauma and violence-informed CBT	Perinatal mental health service, USA	Expectant mothers, victims of intimate partner violence	3 No age data	8
Kehle-Forbes et al, 2022 ⁹²	Qualitative study comparing treatment completers vs non-completers	Semi-structured interview Thematic analysis	PE CPT Completers: at least 10 sessions Non-completers: 1–6 sessions	Veterans clinic, USA	Veterans	126 No age data	9
Lowe and Murray, 2014 ⁵⁰	Qualitative	Semi-structured interviews IPA	TFCBT 6–15 sessions (avg.: 12)	Outpatient services, UK	PTSD patients	9 Mean age: 53 (range: 30–63)	8
Matheson and Weightman, 2019 ⁸³	Participatory research	Semi-structured interview Thematic analysis	Various EBPI 12–60 sessions	Secondary mental health, UK	Complex PTSD (cPTSD) patients	24 Mean age: 45.5 (range: 27–71)	9
Meis et al, 2023 ⁸⁰	Qualitative study of treatment dropout from trial	Dyadic qualitative approach Semi-structured interview	CPT	Veterans clinic, USA	Veterans	29 Mean age: 50.9	8
Mott et al, 2013 ⁵¹	Qualitative study of treatment acceptability	Mixed-methods Open-ended written responses Thematic analysis	Group-based PE 12 sessions	Veterans clinic, USA	Male veterans	20 Mean age: 55 (range: 27–69)	5

(Continued)

Table I (Continued).

Author/Year	Study Design	Qualitative Methodology	Type of Intervention (no. of Sessions Where Specified)	Setting	Population	Sample Size/age	CASP Rating
Murray et al, 2016 ⁵²	Mixed-methods study	Grounded theory Written questionnaire	TFCBT	Outpatient services, UK	PTSD patients	25 Mean age: 41 (range: 28–65)	7
Price et al, 2016 ¹⁰¹	Add-on qualitative study to RCT	Written impact statements Thematic analysis	CPT 12 sessions	Veterans clinic, USA	Veterans	15 Mean age: 52.8	6
Sandberg et al, 2017 ⁸⁴	Qualitative study	Semi-structured interviews Thematic analysis	Trauma focused psychotherapy (integrating CBT, EMDR and psychodynamic psychotherapy)	Outpatient services, Sweden	PTSD patients	5 Age range: 26–50	9
Shearing et al, 2011 ⁴⁸	Qualitative study	Semi-structured interviews IPA	TFCBT	Outpatient services, UK	PTSD patients with single event trauma	7 Age range: 20–50	9
Sherrill et al, 2022 ⁸¹	Mixed-methods non-randomised study	Written questionnaire Theoretical thematic analysis	Group-based PE 18 sessions	Intensive veterans outpatient program, USA	Veterans	25 Mean age: 42.2	7
Sripada and Walters, 2022 ⁵⁴	Qualitative study informed by previous quantitative work	Semi-structured interviews Hypothesized thematic analysis	Individual and group EBPIs (various)	Veterans residential treatment programmes, USA	Veterans	24 No age data	8
Thoresen et al, 2022 ⁸⁶	Qualitative study	Semi-structured interviews Thematic analysis	PE with EMDR (plus physical activity and psychoeducation) 16 sessions (8 PE, 8 EMDR)	Intensive outpatient treatment service, Norway	PTSD patients	8 Mean age: 39.5 (range: 25–57)	10
Unwin et al, 2019 ¹⁷²	Open-label pilot study	Semi-structured interviews Thematic analysis	EMDR	Outpatient intellectual disabilities service, UK	PTSD patients with intellectual disabilities	2 Age range: 23–50	8
van Gelderen et al, 2020 ⁹⁵	Qualitative study within RCT	Grounded theory Open-ended question interviews Thematic analysis	3MDR (multimodal motion-assisted memory desensitization and reconsolidation) 16 sessions (6 3MDR, 10 treatment as usual)	Outpatient tertiary care, Netherlands	Veterans	10 Mean age: 43 (range: 25–59)	10
Vincent et al, 2013 ⁸⁵	Qualitative study	Semi-structured interview Interpretative phenomenological analysis (IPA)	TFCBT within stage-based treatment 7–20 total sessions (2–10 of TF-CBT)	Primary and secondary care, UK	Asylum-seekers	7 Age range: 19–42	7
Wells et al, 2022 ⁷⁰	Add-on qualitative study to RCT (studying treatment dropout)	Semi-structured interview Thematic analysis	PE 4–14 sessions	Veterans clinic, USA	Veterans	22 Mean age: 43 (range: 25–67)	9
Zielinski et al, 2021 ⁹³	Mixed-methods acceptability study	Written feedback form Thematic analysis	Group-based PE 8 sessions	Prison, USA	Incarcerated women	61 Mean age: 33 (range: 19–57)	9

Table 2 Overview of PT Study Methodologies, Settings, Sample Sizes and CASP Quality Ratings

Author/Year	Study Design	Qualitative Methodology	Substance Studied	Psychological Support Model (No. of Sessions Where Specified)	Treatment Indication	Setting	Sample Size/ Age	CASP Scoring
Agin-Liebes et al, 2021 ¹⁰⁷	Open label pilot study	Microphenomenological interviews IPA	Psilocybin	Group PSI (preparation, support, integration) 8–10 group sessions (4 prep, 4–6 integration) 2 individual sessions (1 psychedelic treatment session, 1 post-dosing integration)	AIDS survivors	Inpatient medical facility, USA	9 Mean age: 57.9 (range 50–66)	7
Agin-Liebes et al, 2023 ¹⁰⁸	Retrospective follow-up to double-blind RCT	Semi-structured interviews IPA	Psilocybin	Motivational interviewing + CBT + PSI	Alcohol use disorder	USA	13 Mean age: 48.1 (28–63)	8
Barone et al, 2019 ³⁸	Retrospective follow-up to crossover, double-blind RCT	Semi-structured interviews IPA	MDMA	Weekly psychotherapy	Treatment-resistant PTSD Veterans, police, firefighters	Clinical research facility, USA	19 Mean age: 35.9 (24–56)	10
Belser et al, 2017 ¹⁰⁹	Retrospective follow-up to crossover, double-blind RCT	Semi-structured interviews IPA	Psilocybin	Psychotherapy derived from diverse modalities 9 sessions	Anxiety associated with life-threatening illness	Clinical research facility, USA	13 Mean age: 50 (22–69)	9
Camlin et al, 2018 ¹¹⁰	Qualitative study	Semi-structured interviews Constant comparative thematic analysis	Ibogaine	Unspecified psychological support	Opioid use disorder	Inpatient medical facility, Mexico	10 Mean age: 28.8 (21–48)	8
Gasser et al, 2015 ¹¹¹	Follow-up qualitative study to RCT	Semi-structured interviews Qualitative Content Analysis	LSD	Unspecified psychotherapy 6–8 sessions	Anxiety associated with life-threatening illness	Inpatient medical facility, Switzerland	10 Mean age: 51.1 (39–64)	7
Malone et al, 2018 ¹¹²	Add on qualitative study to RCT Case series	Semi-structured interviews Analysis of study therapist notes	Psilocybin	PSI 11 sessions (3 prep, 2 psychedelic treatment sessions, 6 integration)	Anxiety associated with life-threatening illness	Cancer centre, USA	4 Age range: 20–70	7
Mollaahmetoglu et al, 2021 ¹¹³	Parent study: double-blind RCT	Semi-structured interviews Reflexive thematic analysis	Ketamine	Manualised relapse-prevention psychotherapy 7 sessions	Alcohol use disorder	Clinical research facility, UK	12 Mean age: 46.5 (22–59)	9
Nielson et al, 2018 ¹²³	Qualitative follow-up to open-label proof-of-concept study	Directive content analysis of debriefing sessions	Psilocybin	Integrated therapy model (motivational interviewing + CBT + PSI)	Alcohol use disorder	Clinical research facility, USA	10 Mean age: 40.1 (25–56)	9

(Continued)

Table 2 (Continued).

Author/Year	Study Design	Qualitative Methodology	Substance Studied	Psychological Support Model (No. of Sessions Where Specified)	Treatment Indication	Setting	Sample Size/ Age	CASP Scoring
Noorani et al, 2018 ¹¹⁴	Retrospective follow-up to open-label pilot study	Semi-structured interviews Thematic analysis	Psilocybin	Smoking cessation CBT + mindfulness PSI 14 sessions (4 prep, 10 integration)	Smoking cessation	Clinical research facility, USA	12 Mean age: 54 (31–67)	8
Schenberg et al, 2017 ¹¹⁵	Qualitative study	Semi-structured interviews Directive content analysis	Ibogaine	CBT with relapse prevention	Substance use disorder (various)	Private residential clinic and hospital, Brazil	22 Mean age: 33 (22–53)	8
Schenberg et al, 2017 ¹¹⁶	Qualitative study	Semi-structured interviews Interpretative phenomenological analysis (IPA)	Ibogaine	CBT with relapse prevention	Substance use disorder (various)	Private residential clinic and hospital, Brazil	22 Mean age: 33 (22–53)	8
Swift et al, 2017 ¹¹⁷	Retrospective follow-up to crossover, double-blind RCT	Semi structured interviews IPA	Psilocybin	Psychotherapy derived from diverse modalities 9 sessions	Anxiety associated with life-threatening illness	Clinical research facility, USA	13 Mean age: 50 (18–69)	8
Watts et al, 2017 ⁵⁵	Open label feasibility study	Semi-structured interviews Constant comparative thematic analysis	Psilocybin	PSI 5 sessions (1 prep, 2 psychedelic treatment sessions, 2 integration)	Treatment-resistant depression	Clinical research facility, UK	20 Mean age: 44 (30–64)	8

Data Extraction

Data from the included studies were extracted and included: author/year; study design; qualitative methodology; psychological intervention; setting; sample size; demographics; key themes identified; and data relating to patients' reported experiences. Authors NLM and MC systematically reviewed papers and extracted the data, cross-checking data for concordance.

Data Analysis

Extracted data from the studies was analysed using thematic synthesis.⁷⁹ Author NLM read and re-read the data before assigning open-coded descriptive themes to the results. Once all themes were assigned, these were then distilled into core themes, with sub-themes to supplement and expand on the core themes. These themes were then reviewed by VW and MC and agreed upon by all authors.

A thematic synthesis was completed separately for the studies of EBPI and studies of PT. After completing these thematic syntheses, similarities and differences between the therapies were identified. Our findings from the EBPI synthesis are presented first, followed by the key themes found across PT studies. Excerpts from included studies are presented to illustrate key findings with additional excerpts in [Table S2](#).

Results

EBPI in PTSD

The initial search returned 1286 papers. After screening and assessing papers for eligibility, the final number included was 26 (see [Figure 1](#) for screening details).

Of the included studies, the majority were conducted in the USA (n=12) and the UK (n=6), with one study each in Denmark, the Netherlands, South Africa, Norway, and Sweden. Psychotherapies studied were TF-CBT (n=6), PE (n=5), eye-movement desensitisation and reprocessing (EMDR, n=3), cognitive processing therapy (CPT, n=2), with a number of studies (n=9) on various or combined therapies. Study designs varied between standalone qualitative studies (n=11), qualitative analyses within clinical trials (n=7), treatment acceptability studies (n=4), and mixed methods (n=3). See [Table 1](#) for further details.

Psychedelic Therapy

128 papers were initially found on PT. After screening and eligibility assessment, 14 papers were included in the review (see [Figure 2](#) for screening details).

Studies were primarily conducted in the USA (n=8), with others in the UK (n=2), Brazil (n=2), Mexico (n=1) and Switzerland (n=1). Psilocybin (n=8) was the substance most studied, with other studies investigating ibogaine (n=3), LSD, MDMA and ketamine (all n=1). Indications for treatment included substance use disorders (n=7), anxiety relating to physical illness (n=5), depression and PTSD (both n=1). See [Table 2](#) for further details.

EBPI in PTSD

Patient Burden in PTSD Treatment

All EBPI studies (n=26) highlighted patient-reported burdens associated with PTSD treatment. For some patients, tolerating these challenges appeared to increase feelings of agency. However, in many cases, this experience caused distress and destabilisation, at times, impacting patient retention.

This synthesis found 4 prominent sub-themes associated with patient-reported burden:

1. Real-World Barriers
2. Tolerating Treatment Emergent Adverse Events
3. Misaligned Treatment Rationale and Expectancy
4. Interpersonal difficulties with staff and peers

Real-World Barriers

Related to engaging in treatment, patients across studies reported practical concerns regarding scheduling and travel difficulties and competing practical, financial and/or relational demands.^{88,91} This was compounded by the psychological burden associated with the treatment (eg, symptom exacerbation) and pre-existing psychosocial stressors. Patients expressed concerns about the potential adverse impact of the treatment on their psychosocial functioning during and after treatment.^{52,80,81,92} Patients discussed feeling conflicted about complying with the treatment as this often competed with their on-going “real-world” responsibilities.

I felt very overwhelmed, and I felt very lost and very frantic in what I had to do [for therapy]. Especially having the homework to do, but then knowing I could not do it. Because I knew my reaction was going to upset my daughters. So, then trying to find time later at night, but then writing about all of that would disturb my sleep - what little I get. And the disturbed sleep would mean I was up all night. so it just kind of snowballed.⁸⁰

Some patients reported concerns about the insufficient time allocated for treatment.^{81–83} These patients expressed their perception that the structure of weekly psychotherapy did not support the full achievement of therapeutic gains.

With weekly sessions, you never truly get over the trauma.⁸¹

For some patients, concerns regarding premature endings were also reported.⁸³ This may be due to the short-term nature of the outpatient treatment, the treatment failing to address integral aspects of patients’ difficulties, and/or attachment-related anxieties known to contribute to PTSD psychopathology.⁴⁹

The therapy has really helped, but I need more because I am just open, you know when you get that blast and you see that mushroom cloud, I am like the mushroom cloud it has not dissipated yet.⁸³

This was contrasted with findings from residential or intensive treatment programs which seemed to mitigate patients’ avoidance of challenging feelings/symptoms, with some patients reporting that this type of care allowed them to get more out of the treatment.

Tolerating Treatment Emergent Adverse Events

All studies reported patients’ experience of intense and difficult to tolerate responses to treatment. Frequently reported internal states associated with exposure to traumatic material included fears about the pain associated with reliving due to the need to openly talk about and/or vividly imagine certain aspects of patients’ index-trauma. Correspondingly, trauma-related “maladaptive defenses”,⁸⁴ such as experiential avoidance, were reported across most studies.

When you come, you have to really like talk about it and how you’re feeling and that brings it like to the surface and it’s really raw and that’s really hard and sometimes, you know, you don’t feel like doing that ‘cause it’s painful.⁸⁵

Misaligned Treatment Rationale and Expectancy

Several studies^{50,80,86,87} highlighted the importance of providing psychoeducation regarding PTSD symptoms, the treatment’s rationale, and its expected effects to positive outcomes.

I really do not understand CPT. Like what it’s supposed to do? I would not really know.⁸⁰

Studies also reported the significance of managing patient’s pre-treatment expectations and considering the degree of alignment between the treatment’s rationale, procedures, and patient’s needs.^{80,82,88–90}

They [the clinicians] just want to go into the past, but we need or what I need is how to cope with what I have right now, and then everyday civilian life, instead of just regressing and getting to the roots.⁸⁸

Interpersonal Difficulties with Staff and Peers

Studies highlighted patients’ interpersonal difficulties with clinical staff and, in group-based interventions with their

peers, as factors influencing engagement in treatment and outcomes.^{70,82,91–93} At times these gave rise to patient feelings of disconnection and invalidation.⁸⁰

I was pissed off that people were trying to desensitize me to something horrible that happened because it almost seems like, ‘Oh you’re overreacting just think about, just be around it enough and you won’t feel that way anymore.’⁹¹

In group settings, studies reported the impact of negative perceptions of other group members on patient retention and outcomes.

I was overwhelmed with knowing that I would soon have to tell my story. The fear of exposure was almost too much.⁹³

Demonstrating the clinical relevance of strong social support systems outside of the clinic on recovery, patients appeared to use relationships to adhere to the treatment protocol.

Studies^{70,88,91,92} also discussed how psychosocial stressors such as isolation adversely impacted participants’ experience of the treatment.

I did not really have anyone in-person to talk to. I did not really have a lot of support in terms of like family or friends, or relationships around me that were good.⁷⁰

Readiness

Studies highlighted the contribution of intrapersonal factors (eg, patient traits, beliefs, and internal resources) to the overall experience of treatment.^{50–52,81,82,84,85,89–95} Most studies referred to the significant psychological burden PTSD treatment entails (eg, fear of re-traumatisation, worsening of symptoms and functional destabilization). Correspondingly, in this synthesis, we found that intrapersonal factors reportedly influenced patients’ perception of their experience of treatment, and conversely, their willingness to engage in often-challenging therapeutic processes. The umbrella term “readiness” was chosen by authors to reflect various sub-themes identified.⁹⁶

Patients described processes of coming to terms with the severity of their PTSD symptoms and psychosocial difficulties. This form of tentative acceptance seemed important in overcoming ambivalence about seeking treatment and then, tolerating challenging aspects of the therapeutic process.

Some patients referred to deeply held personal desires and values that encouraged engagement in treatment.

I’m really scared to go into [dialectical behavioral therapy (DBT) prolonged exposure (PE)]. But, you get your DBT skills first [and] I think that’s what’s going to help me the most. I don’t want to live like this anymore. I deserve to be happy.⁹¹

Once in treatment, some patients reported intentional behaviors aimed at making the most out of their treatment, cultivating a willingness to face fears associated with reliving their index-trauma.^{50–52,81,82,84,85,89–95} In contrast, in the context of possessing a willingness to confront pain, some participants reported feeling incapable of engaging fully in imaginal exposure to traumatic events. This may be due to use of defenses, such as avoidance, and hesitancy about engaging in treatment due to psychosocial instability.^{53,97}

Because I avoided talking about things, I probably didn’t get the full help I could have gotten.⁸²

Key Mechanisms of Change

Reviewed studies suggested a variety of key mechanisms of change associated with positive outcomes. EBPI in PTSD usually entails revisiting traumatic memories to gradually reduce hyper- and hypo-arousal states, characterised by nervous system dysregulation, depersonalisation or dissociation.⁹⁸ Aspects related to the previous theme (eg, “readiness”) appeared to support patients make use of the treatment process. Mechanisms of change identified in this synthesis include attainment of insight, behavioral activation, corrective emotional experiences, and changes in trauma narratives during and after treatment.

Patients who responded to treatment described attaining insight into their persistent responses to internal states associated with their index-trauma.^{50–52,81,87–90,95,99–101} Conversely, this may have also supported patients to feel

validated and achieve a sense of mastery over their symptoms. Studies discussed the importance of cultivating self-awareness and possessing the capacity to notice “signals”⁹⁴ surrounding the need for self-regulation.

If I was being triggered, usually it would come out in anger or fear. Before I did not really know why I was doing that and then throughout my therapy I realized it was the fear of their vulnerability.¹⁰⁰

In addition to consolidating learning pertaining to individual responses to traumatic stimuli, some treatment responders discussed achieving greater recall of the event, which appeared to play a significant part in the therapeutic process.⁹⁵

That went a little deeper with every session. And with every trauma, actually. At some point, I could recall things that I had never. That I had never thought about again, that never crossed my mind.⁹⁵

Beyond attaining insight into emotional and behavioral responses to trauma, some patients described how greater insight facilitated corrective emotional experiences and shifts in their trauma narratives, accompanied by greater compassion towards self.^{51,87,93,101} Further, referring to the support and encouragement of the therapist, patients detailed how behavioral activation was facilitated by empowering therapists who promoted patients’ sense of agency and autonomy.

[The clinician] left a lot of decisions up to me. I felt like he was taking my experience into consideration and not just his diagnosis [of me]. I felt like he allowed me to take part in what I felt was going to work for me.⁹²

In group-based interventions, fears of exposure and difficult relational dynamics could make it hard to engage in group-based interventions. However, for patients who responded well to the group setting, insights and corrective emotional experiences were facilitated by processes of identification with others, leading to feelings of validation and belonging.^{51,54}

Psychological Safety and Trust

All studies highlighted the importance of psychological safety and trust in patient experience and PTSD treatment outcomes. This core theme distinguishes between psychological safety (PS) and trust. PS in healthcare settings refers to a myriad of systemic and interpersonal attributes leading to a shared belief that the treatment setting is safe to engage in interpersonal risk-taking.¹⁰² In the context of mental-health care, PS enhances patient security and feelings of empowerment through promoting an organisational culture imbued with openness and mutual respect.¹⁰³ Conversely, trust refers to the interpersonal dynamic established between the provider and patient.¹⁰⁴ Trust is considered a fundamental component in trauma-informed models of care due to high rates of betrayal and harmful relational power dynamics reported in trauma survivors.^{105,106}

This synthesis identified 3 sub-themes, which taken together, were found to contribute towards and determine the quality of PS and trust perceived by the patient.

These include:

- 4a. Experience of Therapist
- 4b. Experience of Group and Wider Psychosocial Setting
- 4c. Experience of Self

Experience of Therapist

Across all studies, patients reported positive and negative reactions to their therapists which impacted their engagement in treatment. Possessing trust in the therapists’ attunement and competency was associated with patient feelings of safety and validation. This appeared to enhance patients’ ability to engage in the often-challenging treatment processes by supporting openness and affective regulation. On the other hand, some studies^{70,80,82,92} reported patients felt misunderstood or interpersonally hurt following interactions with their therapists. These occurrences appeared to hinder treatment engagement, highlighting the centrality of interpersonal trust in trauma-focused psychotherapy.

The trust in her [the clinician] and the fact that she understands me and can keep up with me and actually get to know me. This is very, very important.⁹⁴

Experience of Group and Wider Psychosocial Setting

Patients reported both positive and negative reactions to the impact and clinical utility of group-based interventions. Positive perceptions of the group were characterised by increased feelings of belonging, confidence, and openness. Some patients reported increased anxiety about exposure in a group setting. Hearing the traumatic narratives and experiences of their peers appeared to be challenging in itself.^{93,99} Others discussed the presence and impact of difficult interpersonal dynamics that emerged in the group.^{93,99}

I found some parts a bit triggering when people recounted their personal experiences. I felt quite frozen and couldn't speak. I found it harder to concentrate and felt myself go into a darker place when discussing suicide.⁹⁹

Experience of Self

Patients described a range of positive and negative responses to PTSD treatment that affected their sense of trust and confidence in self.^{70,85,89,90,95,101} In turn, this seemed, at times, to impact their belief in their ability to endure and benefit from the treatment. Patients described a gradual process characterised by noticing moderate positive changes or differences in their self-narratives, beliefs, and emotional responses.

I noticed changes, I noticed differences. I thought, it is helping. So, let me just come back.⁸⁹

Correspondingly, patients also described how adverse responses to treatment negatively impacted their perception of self and capacity to utilise the treatment.

I became depressed, withdrawn, I started to have some nightmares again, and I tried it for about a week, and it kept getting worse and worse and I said this is not worth it. I did not feel physically and mentally able to continue because of those reasons.⁷⁰

Psychedelic Therapy

Although the studies varied in their methodology, patient populations, and psychedelic compounds, there were themes relating to the patient experience of PT in clinical trials that were consistently reported. We present a snapshot of our findings relating to trauma-informed PT below.

Themes identified in this review:

1. Indirect Trauma Processing
2. Reorganisation of self-narratives via processes of relatedness and identification
3. Key Treatment Characteristics

Indirect Trauma Processing

Studies referred to traumatic stress as being a main contributing factor to psychopathology.^{55,107–117} In most studies, processing traumatic incidents appeared to be an integral part of the narrative surrounding patients' experience of the therapeutic process. Researchers reported patients confronting adverse childhood events and present-day stressors such as life-threatening diagnoses. Although not the explicit focus of the PT intervention, trauma-related material appeared in the form of visualisations, disturbing conscious and previously repressed memories, somatic trauma responses, and emotional states such as grief and fear. Some patients reported how the treatment supported integrating traumatic incidents into their lives or unburdening themselves from its weight as part of the change process.

Mostly from my childhood, related to my parents quarrelling. I saw a lot of bad things. I saw my father bribing my mother with jewelry, flattering her with leisure activities, with superfluous things. I saw him drinking, falling down where he stored his drinks.¹¹⁵

Reorganisation of Self-Narratives via Processes of Relatedness and Identification

All studies reported themes concerning patients' perceived changes in self-narratives after PT. Reported changes in self-narratives may be catalysed or accompanied by the previously highlighted mechanisms of change in PT.^{56,71,118,119} Further, increases in caring emotional responses towards self,⁵⁷ connectedness towards others,⁵⁵ experience of positive affect¹²⁰ and health behavior change¹²¹ have been reported.

This synthesis found patients reported changes in self-narratives after describing meaningful PT experiences characterised by processes of relatedness and identification across the following domains:

- 1a. With psychedelic compound
- 1b. With condition
- 1c. With the known biographical self, including body
- 1d. With significant others
- 1e. With spiritual or transcendental states
- 1f. With clinical team

Psychedelic Compound

Patients reported perceiving the compound itself as possessing intentions and wisdom, attributing personifying meaning to the elicited subjective effects, and experiencing a helpful intrapersonal form of communication between self and the compound. Patients discussed how the compound seemingly “gave” or “showed” them something of importance, highlighting areas that required their attention and encouraging engagement with previously avoided challenging experiences.^{38,55,110,111} Infused with this knowledge or newfound sense of direction, patients reportedly felt reassured and had a perceived sense of empowerment. It is possible that these occurrences may have in turn supported better treatment engagement.

During the session the thoughts were ... “Do I travel the right path”? That was my question. Not dealing with death during the session but if I am on the right path. LSD gave me the feeling intensively that I am on the right path. That was nice.¹¹¹

Condition

Patients reported the presence of a helping relationship between the compound and their condition. Potentially promoting cognitive flexibility,¹²² patients appeared to have gained a sense of internal space or distance between self and the condition via the interaction between the compound and the condition.^{55,110,112,116,117,123} Correspondingly, these processes were often accompanied by positive cognitive reconstructions related to the nature of the condition, increased positive affect and reduction in adverse psychological symptoms.

I would say [I have] less anxiety about my body and my sickness coming back, my cancer coming back...I saw this body for what it's worth, I picked it, it's mine... I think that acceptance has been liberating.¹¹²

Known Biographical Self, Including Body

Patients described how PT appeared to facilitate a reexamination of past as well as present and at times, imagined future oriented, life experiences.^{38,55,107,112–116} Patients reported perceiving important life experiences during their treatment via imagery, cognitions, emotions, physical sensations, and memories. These biographical remembrances, directly linked with patients' self-narratives, were reportedly imbued with meaning and affect, which in turn promoted a more open and reflective stance towards their challenging experience and self-representation.

I don't know if I really learned – it was more like letting back in stuff that I had blocked out?... I don't think I changed my values, just remembered more of them. Or just remembered to honor them more, or...allow them more.¹¹⁴

Significant Others

Patients described exploring past and present relationships with loved ones and friends.^{55,107,109,111,113,117,123} Patients

described perceiving with more clarity and appropriate affect relational ruptures and experiencing resolution. Some patients reported feeling supported by their loved ones during the psychedelic treatment session, enhancing feelings of connectedness and the significance of others in their own self-narratives.^{117,123} Notably, some patients reported perceiving the presence of an internal “guide” or a “being” which appeared to have their best interests at heart; at times appearing as a loved one.^{109,112}

I was thinking about relationships I had with other people and thinking I could see them clearly almost as if for the first time. I had fresh insight into things. It was almost as if suddenly the scales dropped from my eyes, I could see things as they really are.⁵⁵

Transcendental / Spiritual States

Across the included studies, patients reported various transcendental or spiritual states.^{55,107–117} Patients reported feelings of unity, ego dissolution, profound connection to others, the natural world and the universe. These states, potentially leading to perspective change and feelings of greater contentedness, were often accompanied by a range of intense affects and a visceral sense of knowing. Within these states, some patients reported grappling with existential themes concerning birth and dying. Overall, patients reported dramatically changed perspectives concerning everyday reality, at times accompanied by a greater appreciation towards self, others, and life itself. These experiences were also characterised by an overarching sense of persuasiveness and purposefulness.

I see myself as part of something bigger. I felt myself connected into what had to be the collective mind yesterday, realizing it's like “Oh, this exists, and we're all just facets of this. It's me connected to a wider sense of life or consciousness. And it's, like, I know that rationally, but it was a time to feel it in a very real sense and experience it as real”.¹⁰⁷

Clinical Team

Patients described the significance of therapists' presence across most studies to positive outcomes. The degree of rapport and interpersonal safety with therapists was associated with feelings of trust towards the often challenging and unfamiliar treatment process. Some, but not all, patients discussed their therapists as an integral component of the treatment, supporting engagement by conveying a sense of confidence in the patient's capacity to leverage their experience towards improvement.^{38,55,107–109,113,114} Notably, only one study⁵⁵ highlighted instances of negative perceptions of therapists and its potential adverse influence on outcomes. These incidents included a brief discussion of a “problematic transference”, in which the patient linked their negative responses towards a therapist with previous experiences of care.

It's not just the psilocybin sessions [but] it's that human connection, and the support that comes with that human connection, that ultimately leads to success at the end of the day.¹¹⁴

Key Treatment Characteristics

Ineffability and Awe

Some patients found it difficult to describe or find the “right words” to convey their experience of the psychedelic session.^{55,107,109–111,113,114,117,123} The richness of the reported experiences and its corresponding therapeutic impact can be inferred by observing treatment responders' language, often laden with metaphors, symbols, affect and a sense of meaningfulness. When describing their experience, patients appeared to be struck by the multifaceted nature and novelty of PT. Acknowledging the limits of intellectual understanding, most patients in the reviewed studies appeared to be curious about their experience, or positively affected by this sense of awe¹⁷³ as opposed to being disturbed by it. Of note, the MDMA-AT study¹¹² did not report similar themes. This may be due to the mechanism of action and subjective effects of MDMA, an entactogen, as opposed to classical psychedelics.

It was a feeling beyond an intellectual feeling—it was a feeling to the bottom of my core. that's one reason that it's hard to talk about. it's beyond words.¹¹⁷

Immersive Experiential Immediacy and Intensity

Patients across most studies reported vivid descriptions of intense experiential processes characterised by immersive and dramatic physiological and psychological responses to the compound's subjective effects and treatment process.^{38,55,109–116,123} The immediacy effect of the treatment was reported in the context of having direct and unavoidable encounters with the unfolding phenomena observed during their psychedelic treatment session. Of note, the immersive and intense nature of the treatment appeared to empower patients to confront rather than avoid both negative and positive cognitions, emotions, and somatic reactions to the treatment.

I feel like what happened was that in a very short period of intense time I dealt with some really powerful things and put it behind me.¹⁰⁹

Arc of Struggle and Distress Towards Resolution

Patients reported being compelled to engage with challenging experiences in the service of promoting healing and change.^{38,55,107–111,114–117,123} Patients reported a sense of working through burdensome aspects of their experience catalysed by the compound (eg, intense emotional states, somatic reactions, ego-dissolution, and complex imagery) to eventually perceive a sense of resolution. These experiences were characterised by a sense of movement between previously avoided internal states, and a sense of momentum, which appeared to support patients to engage with the unfolding experience. Terms such as “rollercoaster”¹¹¹ or “turbulence”¹¹⁴ were identified. Acceptance of the struggle and possessing a willingness to engage in experiential excursions into challenging states, appeared supportive in achieving a meaningful perception of resolution.

It was an intense, intense struggle, and that's where it became medicinal because it allowed that struggle to happen. It didn't coat it, it wasn't an antidepressant. it brought it all out.¹¹⁷

Change Beyond Symptom Reduction

Across all studies patients reported responses to treatment that appeared beyond the scope of symptomatic reduction. Patients' post-treatment made references to possessing a changed perspective regarding self, others, and the world. These shifts were accompanied by a sense of clarity about what matters most (eg, values) and a determination to make meaningful changes aligned with these values. At times philosophical, these changes appeared to be a consequence of and catalyst for increased positive affect post-treatment. Frequently reported values pertained to the importance of meaningful relationships, possessing a more curious stance towards self and others, and a sense of connection to spiritual aspects in everyday life, including the natural world. Of note, patients often reported changes in behavior that appeared to support these shifts, including initiating meditation practices, engaging in new hobbies, and repairing relationships.

I've been involved with the local literacy council all the time now ... And then the other thing is I've become very involved with this environmental group as well ... instead of sitting around and just watching television and smoking and doing nothing.¹¹⁴

Difference from Other Treatments

Some studies described patients' reports of how PT differed from standard treatment.^{55,110,111,115,117} These accounts were in support of PT over first-line treatments. This is unsurprising given that PT trials are for patients who have not been helped by standard treatments. PT appeared to accelerate therapeutic processes (eg, promoting insights, enhancing access to a wider range of affects, and facilitating a more immediate connection to self during and after treatment). Patients reported confronting, as opposed to avoiding, challenging and yet necessary therapeutic processes. In the context of addressing psychophysical ailments including addiction and cancer-related distress, patients referred to the need for a holistic and integrated approach to care.

In usual psychotherapy it is mainly about talking, about words. In LSD-assisted psychotherapy it is mainly about inner processes, inner change, inner experience, it gets enriched by it.¹¹¹

Importance of Non-Pharmacological Factors

Studies highlighted patients' accounts concerning the central importance of the treatment's non-pharmacological factors.^{38,55,107,109,111,112,114,116,121,123} Factors often referred to include the impact of therapist presence and interventions, the significance of music and the focus of the non-psychedelic sessions (eg, preparation / integration). Patients made references to the therapeutic utility of the actual physical environment of the psychedelic session, including the lights and sonic ambience inside the treatment room. In a group-based intervention, patients made references to other patients undergoing the treatment. Positive reactions to these factors appeared to enhance feelings of safety and in turn encourage greater immersion in the psychedelic state.

I started not just hearing, but playing the music. My entire body was the musical instrument for every sound which was coming through my head.¹¹²

Discussion

This synthesis explores salient themes in patient experience of EBPI in PTSD and PT for mental-health indications in authorised, medically supervised, clinical trials. This study identified a total of 7 key themes from the thematic analysis of the included papers. In EBPI: Patient Burden, Psychological Safety and Trust, Readiness and Key Mechanisms of Change. In PT: Reorganisation of Self-Narratives via Processes of Relatedness and Identification, Indirect Trauma Processing and Key Treatment Characteristics (Figure 3).

Overall, the included studies demonstrated that EBPI in PTSD and PT across indications compel the patient to contend with a range of arduous processes in the service of recovery. In both treatment paradigms, patients highlighted the intense biopsychosocial nature and heavy demands of treatment. Applying insights from this review, below we expand on 5 areas relevant to positive safety outcomes in future PT research and practice.

Traumatic Stress in PT

An integral finding of this study pertains to the overarching presence of trauma-related psychopathology across indications in PT research. This may be due to higher prevalence of trauma exposure in treatment-resistant patient populations.^{124,125} Correspondingly, researchers have discussed the potential utility of PT to treat PTSD,⁷² citing psychedelics' mechanisms of action^{58,126} and its hypothesised transdiagnostic utility.^{59,127}

Given the prevalence of trauma-related psychopathology across mental-health conditions, the results of this study indicate it is crucial that PT research protocols consider the impact of trauma exposure on patients and the potential value

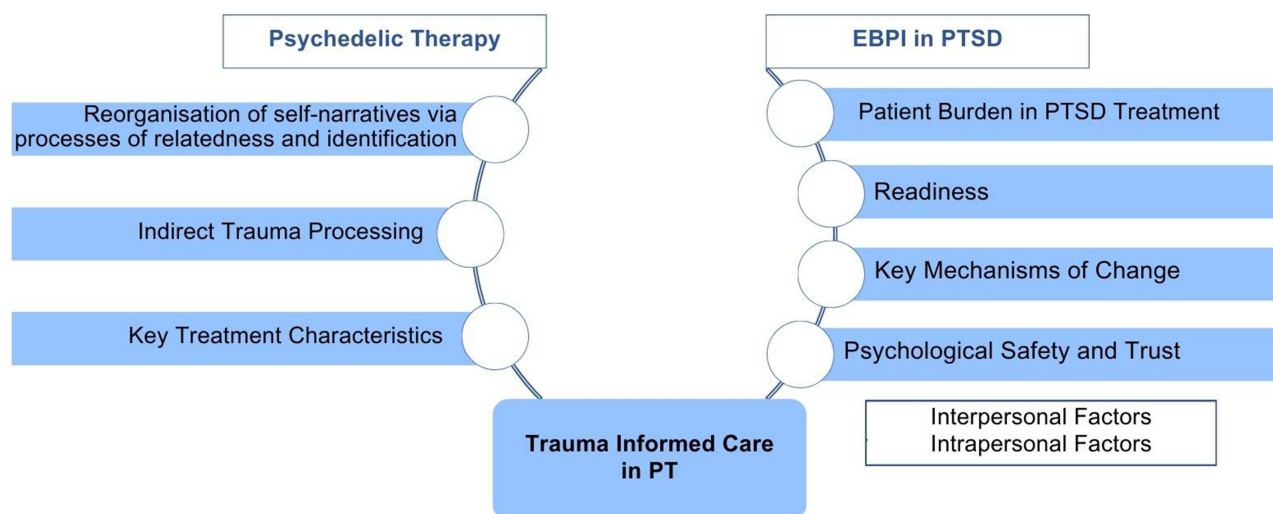


Figure 3 Core Themes diagram demonstrating the 7 key themes from Psychedelic Therapy (PT) and Evidence-based Psychotherapy Interventions (EBPI) in PTSD which may contribute to Trauma Informed Care (TIC) in PT.

of trauma-informed care (TIC)^{14,128,129} in mitigating adverse events. Adding to DSM-based conceptualisations of mental ill health,¹³⁰ TIC considers the unique predispositions patients who have been exposed to traumatic events present with;⁷³ treating the person, rather than the condition, within the context of their psychosocial and cultural lived-experience. Further, comparative research studies investigating the safety and effectiveness of adjunct psychotherapeutic interventions in PT are absent. In this context, some have advocated for CBT to be considered the “default” model in PT,¹³¹ while others have highlighted the utility of the common factors theory of psychotherapy,⁷⁴ psychoanalytic psychology¹³² and non-specific psychological support.²² It is important that data is gathered to support or refute these hypotheses. However, until an evidence base is developed, implementing trauma-informed approaches, that carefully consider the biopsychosocial effects of psychedelics, may promote positive safety outcomes in PT research by personalising care.

As traumatic experiences may have elements of interpersonal or institutional betrayal, secrecy, or persecution,^{133,134} TIC highlights interpersonal and intrapersonal dimensions that require careful clinical consideration.^{135,136} Here we discuss factors relating to psychological safety and trust, which may help inform clinical practice in PT research.

Interpersonal Factors

Adverse interpersonal dynamics, also influenced by patients’ and therapists’ attachment styles contribute to the quality of the therapeutic alliance (TA).^{137–139} Higher TA scores are associated with greater symptom reduction in PTSD psychotherapy.⁶⁰ In PT, one study found a correlation between TA and positive outcomes¹⁴⁰ while another, larger and multi-centre study, did not find TA to moderate outcomes.¹⁴¹ Nevertheless, given the importance of non-pharmacological factors in PT and healthcare,¹⁴² the quality of interpersonal care is considered important to positive outcomes.¹⁴³

This synthesis suggests that traumatised patients may be acutely sensitive to adverse relational and attachment dynamics that may emerge during and in response to treatment. These may include instances of empathic failures and therapist mis-attunement and power imbalances and ruptures.^{61,144,145} For example, in this synthesis EBPI patients highlighted the adverse impact of therapists prioritising rigid adherence to the treatment protocol over meaningful interpersonal contact.^{80,92}

Further, excessive shame, past experiences of betrayal, and moral injury might make it difficult for traumatised patients to request support during intense PT sessions, potentially leading to feelings of isolation and withdrawal.^{75,133} Slipping into traumatic awareness,⁷⁶ some patients may experience these occurrences as traumatic reenactments, reminiscent of past experiences of neglect and abandonment.¹⁴⁶ Taken together, clinicians should be mindful of patients’ experiences of interpersonal trauma, associated impact on personality¹⁴⁷ and subsequent capacity to engage in PT, an intervention that may elicit profound regressive states.¹⁴⁸

Intrapersonal Factors

Traumatised patients may be burdened by demoralising self-narratives often accompanied by persistent negative affect and negatively biased cognitions.^{9,149} Failing to achieve progress in treatment may reinforce these self-narratives, potentially leading to increased psychiatric destabilisation and psychosocial dysfunction. Correspondingly, PT trial participants may be more susceptible to these intrapersonal dispositions, perceiving themselves as having failed standard treatments as opposed to have been failed by treatments. Coupled with the high expectations some patients hold towards PT,¹⁵⁰ failing to achieve progress may further corroborate these harmful self-narratives, increasing feelings of hopelessness and potentially leading to increased risk. Therefore, viewing these self-narratives as maladaptive but necessary psychological defenses in response to traumatic events may help mitigate patients’ pathologising styles of relating to self, increase curiosity and enhance safety outcomes. Taken together, to promote psychological safety and trust, this theme demonstrates the need to establish clinical and organisational cultures that promote consent, collaboration, agency, transparency, trustworthiness, and cultural humility in EBPI and PT.

Key Mechanisms of Change

This review highlighted a potential thematic overlap between EBPI and PT in the context of psychological mechanisms of change. Broadly, patients discussed how the treatments encouraged behavioral activation, and catalysed novel insights and corrective emotional experiences related to their symptoms and beliefs about self and others. While EBPI patients’

narratives were often focused on the impact of treatment on PTSD symptoms, PT patients reported therapeutic processes that were also linked to obtaining a greater sense of connection to their values, increased meaningfulness, and appreciation of the importance of spirituality. When delivering care in PT trials, it is important that clinicians working primarily in evidence-based approaches possess an appreciation of the clinical utility of value-based,¹⁵¹ meaning reconstructing,¹⁵² and psychospiritual processes^{153,154} on positive outcomes. Further, it has been suggested that PT may modulate psychological defenses,^{77,155} potentially leading to the immersive, experiential immediacy and intensity of the treatment. Correspondingly, this theme suggests that clinicians should be prepared to support patients through intense therapeutic processes, initiated and completed in a relatively short period of time. Modelling confidence and purposefulness without negating patient safety, clinicians should approach instances of struggle during PT as a potentially valuable component of the treatment process; sensitively conveying trust in the patients' resources to utilise challenging occurrences during PT. Importantly, clinicians should be prepared to support patients who did not perceive an immediate sense of resolution and treatment non-responders, who may perceive challenging PT experiences as destabilising, potentially reinforcing harmful core beliefs and intensifying negative affect associated with unresolved conflicts.

Re-Organisation of Self-Narratives via Processes of Relatedness and Identification

Along with symptoms such as avoidance and hyperarousal, negative self-narratives may be a consequence of, and a maintaining factor, in trauma-related psychopathology.^{156,157} Broadly, self-narratives construct identities by organising life experiences into seemingly coherent stories that define the person's subjective experience of self.¹⁵⁸ Correspondingly, harmful self-narratives may include

Negative convictions about the self, low expectations about one's efficacy and value, and an exaggerated preoccupation with the projected negative judgment of others.⁶⁵

This study highlighted the potential transformative interaction between patient's self-narratives and experiences elicited by the psychedelic compound and therapeutic context. Patients reported processes of relatedness and identification with the compound, significant others, and transcendental states. These intrapersonal processes, supported by the treatment's non-pharmacological factors and potentially facilitated by the patients enhanced neural and cognitive plasticity,⁶⁶ appeared to help participants re-organise damaging self-narratives. Shifting from "what is wrong with you?", a self-narrative indicative of cognitive rigidity and blame, to "what happened to you?"; an exploratory and accepting stance towards self.¹⁵⁹ This in turn appeared to support therapeutic gains by promoting curiosity towards entrenched negative autobiographies and increase openness to change. However, PT sessions are inherently unpredictable,⁶⁷ potentially catalysing anxious ego-dissolution and intense negative affect^{160,161} that may reinforce patient's harmful self-narratives. Further, positive and negative experiences in PT may increase patients' suggestibility and vulnerability,⁶⁸ potentially enhancing patients need and capacity for relatedness and identification. Correspondingly, this may enhance the potential for adverse idealising transferences¹⁶² and perceived instances of neglect, requiring thoughtful clinical management. Taken together, on-going therapist training, supervision, and ethical oversight is crucial to mitigate potential risks associated with PT.

Readiness

This research suggested that factors pertaining to patients' perceived sense of readiness to engage in treatment contribute to positive outcomes. Readiness in this study refers to the patients' capacity to tolerate intense negative affect, overcome defenses, possess an intentional desire to change and admit that one needs support.^{78,163} Despite the lack of empirical data, patients' lack of readiness for treatment may be associated with poorer outcomes, including adverse reactions such as symptomatic deterioration and suicidality.¹⁶⁴ Correspondingly, there is a lack of standardised best practices across PT studies, including screening measures evaluating patient's suitability, rather than medical eligibility, for PT.^{69,165} Considering the novelty and multifaceted nature of PT, there is an urgent need to provide healthcare systems with validated assessment tools, personalising PT protocols to the patient's presentation to promote positive and durable outcomes.

Further, this research demonstrated the significance of careful treatment staging and expectancy in outcomes. Treatment staging seeks to optimise outcomes by personalising the type and timing of the intervention to the patients' current needs, resources, and risk of illness progression.¹⁶⁶ As patients may perceive a discrepancy between their needs and abilities or lack a clear understanding concerning the treatment's rationale, this review highlights the importance of accessible psychoeducation regarding PTs rationale and procedures prior, during and after treatment.

Real-World Barriers

This review demonstrates how patient burden can conflate both logistical factors and the often-demanding treatment procedures. PTSD treatment-specific challenges (eg, exacerbation of existing symptoms) may enhance patients' sensitivity to so-called "real world" barriers (eg, travel, employment, relationships).¹⁶⁷ Correspondingly, real-world difficulties may make it more challenging for patients to utilise interventions that in and of themselves may produce significant distress. Therefore, it is important clinicians pay attention to the patient's everyday psychosocial circumstances during treatment; failing to situate the patient in the "real-world" or considering the impact of treatment emergent adverse events on psychosocial functioning may lead to poor outcomes. Of note, this finding was prominent in the EBPI group. This is likely due to EBPI being well-established and delivered across healthcare settings and the longer-term structure of treatment, mostly delivered on a weekly basis over the course of weeks/months. Given the immediate and intense effects of PT, if approved and delivered within public healthcare systems, significant consideration to the patient's real-world responsibilities and realities will be required to promote durable safety and efficacy outcomes.

Implications

Reviewing the results presented in this paper, it is important to consider the implications of these findings. Firstly, our sample contains multiple and different interventions, indications, and cultures. However, we identified several thematic consistencies across the studies. Few of the studies presented conflicting ideas, thus it would be fair to conclude that the identified themes provide a fitting representation of patients' experiences of EBPI and PT. Correspondingly, the results may support the design of future, trauma-informed, PT research studies exploring the potential safety and effectiveness of first-line psychological therapies as an adjunct to PT. Further, should psychedelic forms of therapy receive regulatory approval, providers will require specialist training to ensure patient safety. The findings of this study may support the development of patient-centred training and supervision programmes by demonstrating a clinical overlap between EBPI and PT and highlighting the similarities and differences of patients' experience of the treatments.

Limitations

This study has several limitations. Firstly, we were unable to include papers not written in English. As a result, 37 EBPI in PTSD and 2 PT papers were excluded, which may have provided insight into patients' experiences. An additional limitation is that PT studies generally appeared positively biased, often reporting the experience of treatment responders, and rarely discussing adverse events/responses. As psilocybin and MDMA edge nearer towards regulatory approval and rapid-onset, short-acting psychedelics with limited safety data are developed,^{168–170} it is vital that future qualitative studies target treatment emergent adverse events in PT to ensure patient safety and inform ethical practice guidelines.

Conclusions

Overall, this synthesis provides important insights into patients' experience of EBPI in PTSD and PT across conditions. The synthesis provides clinicians unfamiliar with PT with an introductory understanding of the treatment's opportunities, challenges, and procedures via the analysis of patients' experiences. Correspondingly, this work provides PT research teams with a broader understanding of PTSD patients' experience of first-line interventions, including barriers to treatment and the critical impact of traumatic-stress psychopathology on outcomes. Given the potential prevalence of trauma exposure in PT trial participants,¹⁷¹ incorporating transdiagnostic, trauma-informed paradigms of care in PT research protocols may improve safety and acceptability outcomes. Further, this study highlights the need for additional qualitative research in PT, with a particular focus on treatment non-responders. Critical qualitative methods and long-term follow up studies may provide valuable insights into potential interpersonal, intrapersonal, and psychosocial factors

impacting outcomes. Lastly, as the field of PT matures, studies investigating the significance of the intervention's non-pharmacological factors, therapist effects and the suitability of adjunct psychotherapeutic modalities on outcomes are needed. Focusing on patients' experience, these studies may support a broader, multidisciplinary understanding of PT, identify potential psychological predictors of response, optimise clinical care, and improve treatment outcomes.

Ethical Approval

Ethical approval was not required for this study.

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Author Contributions

NLM, MC, VW and JR designed the study, in consultation with CM and MS. The first draft of the manuscript was written by NLM. All authors contributed to the execution of the study including search strategy, data extraction, data analysis, writing and critically reviewing the manuscript. NLM, MC and MS contributed to the preparation of the supplementary material. All authors have approved the final manuscript.

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All authors declare:

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- No shareholdings in companies developing psychedelics
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