HTA250

Health-Related Quality of Life Outcomes in Psychedelic-Assisted Therapy Trials for PTSD: A Rapid Review

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Background

- Post-Traumatic Stress Disorder (PTSD) is a debilitating psychiatric condition that develops following a traumatic event.[1] It is characterized by re-experiencing of the traumatic experience, avoidance of reminders of the event, negative emotions and cognitions, and hyperarousal. The World Health Organization estimates that 70% of people globally will experience a traumatic event in their lifetime, and of those 5.6% will develop PTSD (a global lifetime prevalence of 4%).[1]
- PTSD is associated with significant individual and societal burden.[1] The condition is associated with higher risk of suicide attempt and completion, elevated rates of comorbid mental disorders, and reduced health-related quality of life (HRQoL) across all domains. The estimated total excess economic burden of PTSD in the United States (US) in 2018 was estimated to total 232.2 billion USD.[2]
- First-line treatment for PTSD is typically psychotherapy, primarily cognitive behavioral and prolonged exposure-based therapies.[1] However, psychotherapy can be augmented using pharmaceutical treatment. In the US, the approved medications for PTSD are the selective serotonin reuptake inhibitors (SSRIs) sertraline and paroxetine.
- Data suggest that 20-40% of people with PTSD reach remission within one year, however median and mean durations can be much longer, especially in traumas involving combat experience and sexual violence.[1] As many of 50% of patients do not see clinically meaningful improvement, and US-approved drugs show low remission (20–30%). Consequently, there is still a significant unmet need for effective treatment options for PTSD.
- Psychedelic-assisted therapy (PAT) and related psychoactive interventions combining psychotherapy with agents such as MDMA[3] and ketamine[4] and have shown promising clinical results in PTSD and may represent alternatives to SSRIs for augmenting treatment. However, even if such therapies are demonstrated to be clinically effective, they must also be shown to be cost effective to be reimbursed by health technology assessment (HTA) bodies. This will require evidence of improvement in HRQoL.
- Although generic (i.e., disease-agnostic) preference-based measures of HRQoL are preferred by HTAs,[5] disease-specific and non-preference-based measures are frequently employed in research because they may be more sensitive to disease-specific health impacts and changes in health status over time.[6]
- As a consequence, as these therapies move through the clinical trial phase toward the approval and reimbursement process, it will be helpful to understand what HRQoL evidence exists with these therapies and what gaps still need to be filled to meet HTA requirements. A comprehensive understanding of PTSD helps stakes understand the patient's journey and utility of PAT.

Objective

- To assess the extent to which HRQoL outcomes are reported in clinical trials of MDMA- and psilocybin-assisted therapy for PTSD, and to identify the instruments or measures used.

Methods

- A rapid review was conducted using PubMed to identify clinical trials from database inception to May 19th, 2026, in adults with PTSD receiving PAT.
- A broad search strategy using psychedelic-related terms was applied to maximize sensitivity; however, eligibility for synthesis was prespecified and restricted to MDMA- or psilocybin-assisted therapy studies to capture the PATs with the most evidence
- Data were extracted on study characteristics and reported HRQoL, QoL, functional, and related patient-reported outcomes (PROs).

Results

- Ninety-seven articles were identified, and seventeen MDMA-assisted therapy studies (10 unique trials) in PTSD populations met study eligibility criteria. No psilocybin-assisted therapy trials in PTSD populations met eligibility criteria.
- None of the included studies reported preference-based or generic HRQoL measures (e.g., EQ-5D, SF-36). Instead, studies reported a range of symptom-based and related outcomes.
- PTSD symptom severity was most commonly used measure (reported by all 17 studies, **Table 1**). PTSD symptom severity measures included the Clinician-Administered PTSD Scale (16 studies), the Severity of Symptoms Scale for PTSD (a Spanish adaptation of the PTSD Symptom Scale; 1 study), the Impact of Events Scale-Revised (2 studies), the Dissociative Experiences Scale II (2 studies), and the Posttraumatic Diagnostic Scale (1 study).
- Functional impairment was also assessed in five studies. Of these, four studies used the Sheehan Disability Scale, and one study reported the Global Assessment of Functioning scale.

Results (continued)

- PROs pertaining to a range of other domains were also reported:
  - **Depression**: Beck Depression Inventory (6 studies) and the Hamilton Rating Scale (1 study).
  - **Eating Attitudes**: Eating Attitudes Test 26 (1 study).
  - **General psychological functioning**: Inventory of Altered Self Capacities (1 study) and the Symptom Checklist 90-Revised (1 study).
  - **Positive outcomes of traumatic event**: Posttraumatic Growth Inventory (1 study).
  - **Capacity to identify and verbalize emotions**: Toronto Alexithymia Scale (1 study).
  - **Self-compassion**: Self-Compassion Scale (2 studies).
  - **Sleep quality**: Pittsburgh Sleep Quality Index (3 studies).
  - **Substance use**: Alcohol Use Identification Test (3 studies) and the Drug Use Identification Test (3 studies).
  - **Suicidality**: Columbia-Suicide Severity Rating Scale (5 studies).

Table 1: Patient-reported, functional, and related outcomes reported in MDMA-assisted therapy studies for PTSD.

PMID	First Author (Year)	NCT #	Measure(s) Reported		
			PTSD Symptom Severity	Functional Impairment	Other PROs / Related Constructs
40331914	Agin-Liebes (2025)	NCT03537014	CAPS-5	None	AUDIT; BDI-II; DUDIT; SCS
19004414	Bouso (2008)	N/A	SSSPTSD	None	BDI-I; HAM-D
35272210	Brewerton (2022)	NCT04454684	CAPS-5	SDS	EAT-26
26998697	Corey (2016)	NCT00090064	CAPS-3	None	None
32073177	Gorman (2020)	NCT01958593 NCT01211405 NCT01793610	CAPS-4	None	PTGI
33972795	Mitchell (2021)	NCT03537014	CAPS-5	SDS	AUDIT; BDI-II; C-SSRS; DUDIT
37709999	Mitchell (2023)	NCT04077437	CAPS-5	SDS	C-SSRS
20643699	Mithoefer (2011)	NCT00090064	CAPS-4; IES-R	None	SCL-90-R
23172889	Mithoefer (2013)	NCT00090064	CAPS-4; IES-R	None	None
29728331	Mithoefer (2018)	NCT01211405	CAPS-4; DES-II	GAF	BDI-II; C-SSRS; PSQI; PTGI
35286849	Nicholas (2022)	NCT03537014	CAPS-5	SDS	AUDIT; BDI-II; C-SSRS; DUDIT
23118021	Oehen (2013)	NCT00353938	CAPS-4; PDS	None	None
30371148	Ot'alora (2018)	NCT01793610	CAPS-4; DES-II	None	BDI-II; C-SSRS; PSQI
34114250	Ponte (2021)	NCT01958593 NCT01211405 NCT01689740 NCT01793610	CAPS-4	None	PSQI
38198456	van der Kolk (2024)	NCT03537014	CAPS-4	None	None
28635375	Wagner (2017)	NCT00090064	CAPS-4	None	None
38174611	Zeifman (2024)	NCT00090064	CAPS-5	None	IASC; SCS; TAS-20

Abbreviations = AUDIT: Alcohol Use Identification Test, BDI-I: Beck Depression Inventory-I, BDI-II: Beck Depression Inventory-II, BDI: C-SSRS: Columbia-Suicide Severity Rating Scale, CAPS-3: Clinician-Administered PTSD Scale for DSM-3, CAPS-4: Clinician-Administered PTSD Scale for DSM-4, CAPS-5: Clinician-Administered PTSD Scale for DSM-5, DES-II: Dissociative Experiences Scale II, DSM: Diagnostic and Statistical Manual of Mental Disorders, DUDIT: Drug Use Identification Test, EAT-26: Eating Attitudes Test 26, GAF: Global Assessment of Functioning, HAM-D: Hamilton Rating Scale, IASC: Inventory of Altered Self Capacities, IES-R: Impact of Events Scale-Revised, N/A: Not Applicable, NCT: National Clinical Trial identifier, PCL-5: PTSD Checklist for DSM-5, PDS: Posttraumatic Diagnostic Scale, PMID: PubMed Identifier, PSQI: Pittsburgh Sleep Quality Index, PTGI: Posttraumatic Growth Inventory, PTSD: Post-Traumatic Stress Disorder, SCL-90-R: Symptom Checklist 90-Revised, SCS: Self-Compassion Scale, SDS: Sheehan Disability Scale, SSSPTSD: Severity of Symptoms Scale for Post-traumatic Stress Disorder, TAS-20: Toronto Alexithymia Scale.

Conclusions

- Clinical studies of MDMA-assisted therapy for PTSD report a range of symptom-based and related patient-reported measures but do not include preference-based HRQoL measures, limiting their usefulness for determining cost-utility within HTA.
- Although a recently published psilocybin-assisted therapy study in PTSD (NCT05554094)[7] became available after completion of the review, the current evidence base remains sparse and continues to lack preference-based HRQoL assessment.
- Future PAT trials should incorporate standardized generic and preference-based HRQoL instruments such as SF-36 and EQ-5D, to support comparative and value-based decision-making.
- Limitations: As a rapid review limited to PubMed, relevant studies indexed exclusively in other databases (e.g., Embase) or reported in grey literature may not have been captured.

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