

Systematized Review of Psychotherapeutic Components of Psilocybin-Assisted Psychotherapy

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Objective: This systematized review sought to fill a gap in psilocybin research by investigating the structure and format of psilocybin-assisted psychotherapy (PAP), with a focus on the counseling components of the treatment.

Methods: A systematized review of PAP was conducted by using the PubMed and PsycInfo databases to search for peer-reviewed studies of human clinical trials, published within the past 25 years, in which psilocybin was administered with psychological support in a clinical setting.

Results: Eleven articles matched the criteria necessary for inclusion in this review. PAP was found to consist of three stages: pretreatment sessions to prepare participants for psilocybin, treatment sessions in which psilocybin was administered, and posttreatment sessions to integrate the

experience with daily life. Conventional psychotherapy was primarily seen in the pre- and posttreatment sessions. Psychotherapies included in PAP differed among studies, but most often included music therapy and a nondirective supportive approach to treatment.

Conclusions: This systematized review found important commonalities among clinical trials of PAP published within the past 25 years and revealed key differences among studies in psychotherapy's incorporation into PAP. Additional research is needed to identify the unique effect of psychotherapy in PAP.

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Research into treatments for mental illness has evolved substantially, encompassing wide-ranging approaches to treatment intervention that span across psychotherapy and pharmacotherapy. A new wave of research has recently emerged with the resurgence of psychedelic drugs in the context of treating mental illness (1). Research into the clinical utility of psychedelics has typically emphasized the pharmacological mechanisms of the psychedelic drug and the psychotherapeutic processes surrounding its administration as the primary mechanisms for change (1, 2). In this way, psychedelic therapy creates a unique and innovative way of bridging the fields of psychotherapy and pharmacotherapy (1, 2).

Psilocybin is one of the most thoroughly studied psychedelic substances in modern clinical research (2). Psilocybin-assisted psychotherapy (PAP) is a term used to define the established research protocol for safely administering psilocybin with psychological support as a clinical intervention (1, 2). PAP has shown clinically significant results in several studies for various psychiatric conditions (3, 4). Most, if not all, published research (1, 2) on psilocybin in the past 25 years has discussed the importance of adequately preparing the participant for psilocybin treatment and of providing psilocybin in an environment that feels safe and welcoming. The importance of these two factors, colloquially known as the “set and

setting,” is held as paramount to safe and efficacious PAP administration (1, 2). In light of this information, one can infer that the context in which psilocybin is administered, including the psychotherapy involved in PAP, has considerable influence on PAP outcomes. Despite this inference, the present PAP literature contains limited research investigating the structure and content of PAP and viable psychotherapeutic treatments to administer in conjunction with psilocybin (2).

The present systematized review was intended to bridge the research gap between psilocybin and psychotherapy by summarizing findings from a review of clinical trials of PAP

HIGHLIGHTS

- Psilocybin-assisted psychotherapy consists of three stages of treatment, spanning pretreatment, treatment, and posttreatment sessions.
- The purpose of each stage was consistent across studies, but the content of these stages differed.
- The role of therapists during treatment sessions was nondirective and supportive, and therapists had a more direct role during the pretreatment and posttreatment sessions.

over the past 25 years. This article answers the following questions: What is the role of therapists in PAP? What is the general structure in which PAP is currently conducted? and What psychotherapeutic modalities and techniques have been integrated into PAP? Treatment outcomes will also be briefly summarized for the studies included. This review is intended to assist future research in refining the PAP process and determining viable psychotherapeutic adjuncts to complement psilocybin in treating mental illness.

METHODS

The authors conducted a systematized review of recent psilocybin literature to provide a structured and detailed representation of current practices in PAP trials. A systematized review includes many aspects of a systematic review; it is conducted in a systematic manner to determine what is known about a particular topic and to establish a rationale for future research (5). This review differed from a systematic review in that it did not evaluate the risk of bias in collected studies and lacked a second independent reviewer (5). A protocol for systematically searching databases for studies including PAP was formulated by the first author (D.M.H.) by using PRISMA guidelines (6) and was then evaluated and refined for appraisal of methodological quality by an additional author (B.M.).

Eligibility Criteria

Human clinical trials of psilocybin published between December 31, 1994, and January 23, 2021, were eligible for inclusion in the study. Studies included in this review were also searched on clinicaltrials.gov to confirm they were clinical trials. To address the variegated nature of psilocybin research, eligible studies must have included administration of psilocybin in a clinical setting with psychological support to investigate the efficacy of PAP for psychological treatment of a particular mental illness or to investigate the structure and/or content of PAP to determine the best practices as a psychological treatment. In this way, the present review sought to narrow the selection criteria to publications pertaining to PAP and not merely psilocybin publications with clinically relevant outcomes. Relevant literature excluded from the systematized protocol was considered for its potential to elaborate on the included studies. Any clinical trial meeting all of the eligibility criteria was incorporated into the review, including phase 1 clinical trials.

Search Strategy

We searched for relevant literature in two databases: PsycInfo and PubMed. These databases were chosen for their relevance and to follow prior systematic reviews of psilocybin research, which have included these databases in their data acquisition (7, 8). Only the term “psilocybin” was searched in each database to ensure all relevant studies were captured in the literature search process. When necessary, attempts to contact study authors were initiated for additional information or

clarification. The authors also searched the reference lists of studies that the authors determined might reveal additional relevant studies.

Study Selection

The PubMed and PsycInfo databases were searched for studies relevant to the present review through two levels of screening. Level 1 screening included reading the title and abstract of every article that appeared as a search result when entering “psilocybin” into the search bar of each database. If the title and abstract did not disqualify an article from inclusion, that article was included in level 2 screening. Level 2 screening assessed full-text articles for study inclusion by using the same eligibility criteria described above.

Recorded Variables, Data Extraction, and Analysis

Recorded variables included the following: study authors, year of publication, presence or absence of blinding (if applicable), sample size, population worked with, therapeutic constructs measured, primary outcomes, credentials of the therapists or sitters involved in the PAP process, quantity and content of meetings between participants and study therapists, and quantity of dosing. Data were extracted from studies and organized into data tables and figures created by using Microsoft Excel.

RESULTS

Details regarding the phases of the systematized review process for both databases are illustrated in a flow diagram (see online supplement). In total, 1,058 articles were reviewed for level 1 title and abstract screening. After a review of the titles and abstracts, 912 articles failed to meet the eligibility criteria and were excluded from the analysis, leaving 146 full-text articles for level 2 screening. After accounting for duplicates, 11 clinical trials (3, 4, 9–17) were included in the present review. Table 1 summarizes the 11 trials and their target populations. Several of these trials (3, 4, 10, 15) provided data relevant to this review in separate publications (18–23).

Role of Therapists in PAP

All 11 trials included the presence of session therapists, whose core responsibilities included preparing participants for psilocybin treatment, providing psychological support during treatment, and facilitating integration of the psilocybin experience into the area of desired change (1, 2). Therapists were also referred to as sitters, guides, or monitors (1, 2, 23); for consistency, they will be referred to as therapists for the remainder of this review. All 11 studies had at least two therapists present during psilocybin administration. Research with psilocybin has historically used a dyadic structure of two session therapists, as outlined by the guidelines for human hallucinogen research (1). According to these guidelines (1), at least one therapist is present at each study stage, and both therapists must be present when the psilocybin is administered.

TABLE 1. Characteristics and outcomes of psilocybin clinical trials^a

Study	Target population	N	Therapeutically relevant constructs	Measure	Effect size	p
Anderson et al., 2020 (9)	Male OLTAS with moderate-to-severe demoralization	18	Demoralization	DS-II	$d_{rm}=.78^b$	
Bogenschutz et al., 2015 (10)	AUD	10	Days drinking	TLFB	$d=1.19^c$	.007**
Carhart-Harris et al., 2016 (3)	TRD	20 ^d	Depression and anxiety	BDI, STAI-T	$d=1.40^d$ $d=1.50^d$	<.0001,*** <.0001***
Davis et al., 2021 (11)	MDD	24	Depression and anxiety	BDI, STAI-T	$\eta^2=.79^e$ $\eta^2=.55^e$	<.001,*** <.001***
Griffiths et al., 2016 (12)	Palliative care	51	Depression and anxiety	BDI, STAI-T	$d=1.63^f$ $d=1.20^f$	<.001,*** <.001***
Griffiths et al., 2018 (13)	Healthy participants	75	Ratings of attitude, mood, and behavior	PEQ ^g	$d=1.56$, 2.02^h	<.05*
Grob et al., 2011 (14)	Palliative care	12	Depression and anxiety	BDI, STAI-T	$t_{11}=2.17^i$ $t_{11}=4.36^j$	.05, .001***
Johnson et al., 2014 (15)	TUD	15	Tobacco use	TLFB	$t_{14}=11.10^j$	<.001***
Moreno et al., 2006 (16)	OCD	9	OCD	YBOCS	$F=9.37^k$	.028*
Nicholas et al., 2018 (17)	Healthy participants	12	Ratings of attitude, mood, and behavior	PEQ ^g	$t=7.87^l$	<.001***
Ross et al., 2016 (4)	Palliative care	29	Depression and anxiety	BDI, STAI-T	$d=1.03$, .93; ^m $d=1.72$, 1.03^m	

^a AUD, alcohol use disorder; BDI, Beck Depression Inventory; DS-II, Demoralization Scale-II; MDD, major depressive disorder; OCD, obsessive-compulsive disorder; OLTAS, older long-term AIDS survivor; PEQ, Persisting Effects Questionnaire; STAI-T, State-Trait Anxiety Inventory, Trait Version; TLFB, timeline follow-back; TRD, treatment-resistant depression; TUD, tobacco use disorder; YBOCS, Yale-Brown Obsessive-Compulsive Scale.

^b Cohen's d repeated measures presented for change in mean demoralization from baseline to 3-month follow-up (95% CI=.33–1.28); assessed with repeated measures two-way analysis of variance (ANOVA).

^c Cohen's d presented for change in mean percentage of days drinking from baseline to 6-month follow-up. Assessed with paired t tests.

^d Sample size includes additional participants enrolled in the study after the original publication. Information for these participants was provided in the 6-month follow-up study. Cohen's d presented for change in BDI and STAI-T scores from baseline to 6-month follow-up; assessed with two-tailed t tests.

^e Eta-squared presented for differences in mean BDI and STAI-T scores; assessed with repeated-measures ANOVA with time (baseline and follow-up) and condition (immediate vs. delayed treatment groups).

^f Cohen's d presented for differences in mean BDI and STAI-T scores between baseline and 6-month follow-up; assessed with repeated-measures regressions.

^g The PEQ included items covering a number of different domains, but with no composite score. The effect size presented relates to items addressing participants' attitudes toward life.

^h Cohen's d presented for differences in ratings of positive attitude between groups 1 and 2 ($d=1.56$) and groups 1 and 3 ($d=2.02$); assessed with ANOVA with planned comparisons between groups.

ⁱ The t scores are presented for differences in BDI and STAI-T scores between baseline and 1-month follow-up; assessed with t tests. The 1-month follow-up was selected because of decline in participants completing latter follow-ups.

^j The t score is presented for changes in smoking between baseline and 6-month follow-up; assessed with two-tailed paired t tests.

^k The t score is presented for changes in mean YBOCS scores between baseline and 24 hours postdose; assessed with multivariate ANOVA.

^l The t score is presented for changes in mean ratings of positive attitude between baseline and 1-month follow-up; assessed with repeated-measures ANOVA.

^m Cohen's d presented for changes in mean BDI and STAI-T scores between baseline and 6.5 months posttreatment for the psilocybin-first group and the niacin-first group; assessed with planned between-group comparisons.

* $p<.05$, ** $p<.01$, *** $p<.001$

All but one study indicated that at least two therapists were present during the treatment sessions; the exception was Johnson et al. (15). Three of the studies (16–18) indicated intentional inclusion of both a male and female therapist during the treatment sessions. The reasons for this arrangement stem from early psychedelic research, which suggested that a male-female dyad provides a sense of security to the participant during the treatment sessions (1). The guidelines for human hallucinogen research (1) suggest that having two therapists of the same gender as the participant is an acceptable alternative.

All 11 studies included therapist training in facilitating psychedelic psychotherapy and in understanding the treatment. This training often included didactic instruction on psychedelic experiences and possible adverse effects as well as role-playing or discussion of vignettes to train therapists in the accompanying therapy. This training was prioritized over academic credentials in terms of qualifications for therapists (1, 24). The guidelines for human hallucinogenic research (1) indicate that therapists should be knowledgeable and skilled in human relations and provide an empathic abiding presence. Table 2 summarizes the

credentials of the therapists in psilocybin clinical trials. Credentials varied widely throughout the studies, but the most common titles were psychologist (N=19) and psychiatrist (N=19). Therapists also held master's-level degrees (N=15), often in social work (N=8). Eight therapists held a bachelor's degree. Other therapist titles (N=8) included chaplain, nurse, shiatsu therapist, and life coach.

Five of the 11 studies (7–10, 12) indicated that therapists served different roles in the study, typically a primary role or an assistant or cofacilitator role (8, 10). This separation of roles may explain the varied range of therapist credentials. The responsibilities of the therapists hinged on the stage of treatment and the varying components of therapy embedded in PAP across studies; a close examination of the structure and contents of PAP will illuminate the role and responsibilities of therapists at each stage of PAP.

Structure of PAP

Each of the 11 studies consisted of three stages: pretreatment, treatment, and posttreatment. The three stages of PAP are discussed in detail below, and their structure and psychotherapy content are presented in Table 3.

Pretreatment sessions. The first stage of PAP included at least one pretreatment session (N=11, 100%). During pretreatment, therapists met with participants to discuss psilocybin's effects and to build the therapeutic alliance prior to treatment (N=11). The primary intention of these sessions across all 11 trials was to prepare participants to receive psilocybin safely and to help them feel supported while under psilocybin's effects. This aspect of pretreatment has led some researchers to describe this stage of treatment as the preparatory stage (17). Pretreatment sessions varied among studies in total hours (mean $\pm$ SD=6.06 $\pm$ 1.70) and number of sessions (3.31 $\pm$ 1.44). Preparation for psilocybin occurred before the first psilocybin treatment session in all 11 studies, and two studies indicated inclusion of additional preparatory sessions for subsequent treatment sessions (10, 17). With one exception (16), all of the studies involved a discussion of the participant's life experiences, experiences with the presenting problem, and/or setting intentions or goals for the treatment.

Treatment sessions. Treatment sessions were the next stage of PAP, during which psilocybin was administered to participants; this was the only stage of psilocybin treatment in which psilocybin was administered (N=11, 100%). Details regarding the dosage of psilocybin or control in each clinical trial are provided in Table 4. Treatment sessions varied both in

TABLE 2. Credentials of therapists in psilocybin clinical trials

Study	Psychiatrist	Psychologist	Master's-level social worker or counselor	Other licensed professional	Bachelor's-level staff
Anderson et al., 2020 (9)	5	5	2	2	1
Bogenschutz et al., 2015 (10)	2	1			
Carhart-Harris et al., 2016 (3)	2				
Davis et al., 2021 (11)	2	3	1		4
Griffiths et al., 2016 (12)		1	2	1	1
Griffiths et al., 2018 (13)		2	2	1	
Grob et al., 2011 (14)	2			1	
Johnson et al., 2014 (15)		2	2		2
Moreno et al., 2006 (16)					
Nicholas et al., 2018 (17)		2		4	
Ross et al., 2016 (4)	6	2	6	1	

frequency (mean=2.08 $\pm$ 0.76) and length (7.46 $\pm$ 0.78 hours), but all 11 studies asked the participant to lie down, wear eye-shades, and listen to a standardized playlist of music for the majority of the session or sessions. Ten studies (91%) administered psilocybin to participants in a decorated room intended to make the participant comfortable; decorations were often designed to resemble a living room (N=8, 73%). The remaining study (15) did not specify the room design. In each study, direct interaction between participants and therapists increased toward the end of the session, typically during the last hour.

Treatment sessions were conducted in a nondirective and supportive setting (N=11). Research suggests that psilocybin administered in a nondirective and supportive setting facilitates spiritually or meaningfully significant experiences (2, 25) and the relaxing of beliefs underlying psychological distress (26). This nondirective supportive model of therapy with psilocybin is analogous to the psychedelic model used as early as the 1950s; the key difference between the mid-20th century model and today's updated psychedelic model is the implementation of carefully constructed control conditions (1, 2). Therapists are present throughout the session to provide this support. This laissez-faire approach to treatment sessions shares many similarities with MDMA-assisted psychotherapy, which identifies an individual's inner healing intelligence as the primary mechanism of change in treatment (27). The nondirective approach to therapy takes this model one step further, suggesting that the individual, not the psychedelic nor the therapists, is the source of the healing; PAP only facilitates this process of inner healing (27). Therapy involved in treatment sessions has been referred to as a modified form of Rogerian, existential, and logotherapy modalities (17).

All 11 studies explicitly directed participants to focus their intention on their internal experience or journey. Each of the 11 studies followed the nondirective supportive therapeutic model, which attempts to facilitate a transformative, mystical-type experience (2, 10, 25). The therapists provided psychological support in several forms during the session, such as through physical reassurance and supportive touch (3, 4),

TABLE 3. Structure and psychotherapy content of psilocybin sessions^a

Study	Pretreatment			Treatment			Posttreatment		
	Sessions ^b	Hours ^c	Therapy content	Sessions ^d	Hours ^e	Therapy content	Sessions ^f	Hours ^g	Therapy content
Anderson et al., 2020 (9), group 1	5	7.5	Modified SEGT	1	8	Nondirective supportive	5	8	Modified SEGT
Anderson et al., 2020 (9), group 2	5	7.5	Modified SEGT	1	8	Nondirective supportive	7	11	Modified SEGT
Bogenschutz et al., 2015 (10)	4		MET	2	8	Nondirective supportive	6		MET
Carhart-Harris et al., 2016 (3)	1	4		2	6	Nondirective supportive	6		Integrative
Davis et al., 2021 (11)	2	6	Supportive therapy	2	7	Nondirective supportive	5	11	Integrative
Griffiths et al., 2016 (12)	2	8	Therapeutic relationship	2	8	Nondirective supportive	4	4	Support available as needed
Griffiths et al., 2018 (13), group 1	4	5	Therapeutic relationship, group sessions	2	7	Nondirective supportive	1	1	Journaling, group sessions
Griffiths et al., 2018 (13), groups 2 and 3	5	10	Therapeutic relationship, group sessions	2	7	Nondirective supportive	18	22	Journaling, group sessions
Grob et al., 2011 (14)	3		Supportive, existential	2	6	Nondirective supportive	3		Integrative, existential
Johnson et al., 2014 (15)	4	6	CBT	2	8	Nondirective supportive	12	9.5	CBT
Moreno et al., 2006 (16)	1		Therapeutic relationship	4	8	Nondirective supportive			
Nicholas et al., 2018 (17)	4	6	Supportive	3	8	Nondirective supportive	4	6	Integrative
Ross et al., 2016 (4)	3	6	Eclectic	2	8	Nondirective supportive	3	6	Eclectic

^a Missing data were unable to be obtained, even after reaching out to at least two of the study authors. Missing data were excluded from calculations of means and standard deviations. SEGT, supportive-expressive group therapy; MET, motivational enhancement therapy; CBT, cognitive-behavioral therapy.

^b Mean $\pm$ SD = 3.31 $\pm$ 1.44.

^c Mean $\pm$ SD = 6.60 $\pm$ 1.70.

^d Mean $\pm$ SD = 2.08 $\pm$ 0.76.

^e Mean $\pm$ SD = 7.46 $\pm$ 0.78.

^f Mean $\pm$ SD = 6.17 $\pm$ 4.61.

^g Mean $\pm$ SD = 8.72 $\pm$ 5.96.

reality orientation (4, 17), and interpersonal support with non-judgmental, empathic listening (3, 4, 17).

Posttreatment sessions. At least 10 of the studies, with the possible exception of Moreno et al. (16), included posttreatment sessions pertaining to the experience and resulting effects of the previous psilocybin treatment session. Nine studies reported the number of posttreatment sessions, and seven of the studies also provided the total number of hours devoted to posttreatment sessions. Attempts to contact study authors for missing data relevant to posttreatment sessions were unsuccessful.

The number of posttreatment sessions (mean = 6.17 $\pm$ 4.61, N = 10), as well as the length of these sessions (8.72 $\pm$ 5.96, N = 7), differed among studies. Ten studies (91%) indicated discussion of the participant's experiences in at least one post-treatment session; Moreno et al. (16) included this discussion at the end of the treatment session but did not suggest the presence of posttreatment sessions. Discussion of the treatment session was often referred to as the "integration

process" of the treatment, leading some studies to label post-treatment sessions as "integration sessions" (4, 16). Posttreatment or integration sessions often occurred between doses (N = 8), and four studies (36%) included at least three sessions between administrations of psilocybin.

Psychotherapy Modalities Integrated in PAP Studies

All 11 of the collected studies indicated use of psychotherapy modalities or mechanisms of change in varying degrees over the course of the treatment. Four of the studies (4, 9, 10, 15) cited specific psychotherapy modalities; the remaining seven studies included psychotherapeutic components, although no particular modality was described. The role of therapists in the treatment process depended on the psychotherapeutic components or modalities incorporated into the PAP.

Music therapy. Music was used during the treatment sessions of all 11 clinical trials. A study (28) on the role of music in psychedelic therapy has stated that the purpose of including music is to support and foster meaningful experiences

during the session. This purpose is in accord with early psychedelic research, in which music's role in psychedelic therapy was to facilitate emotional release and provide direction and structure to the experience (29). The use of music with psilocybin corresponds to the purpose of music therapy, namely, to induce or magnify an emotional state to achieve therapeutic progress (30). Specifically, psilocybin research has relied on the passive or receptive components of music therapy rather than on active or creative components (30).

All 11 studies included a standardized playlist of music during treatment sessions, although two studies allowed some flexibility in the music selection either toward the end of the session (16) or when it seemed appropriate (9). Grob et al. (14) standardized the playlist shortly after the trial began. The content of the playlists varied among studies, but generally included a mix of neoclassical, classical, or ambient music with minimal lyrics (3, 11). Traditionally, music in psychedelic therapy has been tailored to the individual; however, some authors (14) indicated that they decided to standardize the playlist to allow for more accurate comparisons of outcomes between participants.

Motivational enhancement therapy. Bogenschutz et al. (10) incorporated seven sessions of motivational enhancement therapy (MET) into the pretreatment and posttreatment sessions. MET uses motivational interviewing and cognitive-behavioral therapy (CBT) to support individuals' efforts to reduce or quit drinking, which was the behavior targeted by that particular study (10). The study authors indicated that 12 sessions of psychosocial interventions were included in the study, consisting of seven sessions of MET, three preparation sessions, and two debriefing sessions. The authors further elaborated that these 12 sessions were split into four sessions prior to the first treatment session, four between treatment sessions, and four after the second treatment session. Although the authors did not indicate the placement of psychosocial interventions into these groups of four sessions, the information provided suggests that MET was incorporated before and after treatment sessions.

CBT. Johnson et al. (15) used CBT in pretreatment sessions for tobacco cessation with a sample of 15 individuals who smoked

TABLE 4. Characteristics of dosing in psilocybin clinical trials

Study	Study type ^a	Placebo	Randomization	Low-dose session(s) mg/kg	High-dose session(s) mg/kg
Anderson et al., 2020 (9)	Open label	None	None	N/A	.30 for cohort 1, .36 for cohorts 2 and 3
Bogenschutz et al., 2015 (10)	Open label	None	No	.3	.4
Carhart-Harris et al., 2016 (3)	Open label	None	No	10 mg ^b	25 mg ^b
Davis et al., 2021 (11)	RCT	None	Yes	.2	.3
Griffiths et al., 2016 (12)	RCT	None	Yes	.04 or .01 ^c	.43 or .31 ^c
Griffiths et al., 2018 (13)	RCT	.01 mg/kg psilocybin	Yes	.01 or .29	.43
Grob et al., 2011 (14)	RCT	250 mg niacin	Yes	.2	N/A
Johnson et al., 2014 (15)	Open label	None	No	.3	.4
Moreno et al., 2006 (16)	Modified double blind	.025 mg/kg psilocybin	No	.10, .20 ^d	.3 ^d
Nicholas et al., 2018 (17)	Open label	None	No	.30, .45	.6
Ross et al., 2016 (4)	RCT	250 mg niacin	Yes	N/A	.3

^a RCT, randomized controlled trial.

^b Administered 10 mg and 25 mg to each participant, irrespective of participant weight.

^c Dosing was reduced from 0.43 to 0.31 mg/kg in the high dose session, because 0.43 resulted in heightened reporting of psychologically challenging experiences. Likewise, the low-dose session (functionally a placebo) was lowered from 0.04 mg/kg to 0.01 mg/kg to ensure it was an inactive placebo.

^d Participants participated in up to four treatment sessions, beginning with the lowest dose and increasing the dose in subsequent sessions.

an average of 19 cigarettes per day. The study implemented four pretreatment sessions of CBT for tobacco cessation. Components of CBT used in the study included a signed contract to quit, program cards to be read each time a participant smoked a cigarette or had an urge to smoke, a smoking diary, a brief motivational statement, psychoeducation regarding the financial and health consequences of smoking, cognitive reframing, assignment of a target quit date, and support for dealing with urges after the target date. In addition to these CBT components, pretreatment sessions included preparation of individuals for psilocybin treatment and discussion of the participant's developmental years, interpersonal relationships, work, hobbies, and other relevant information. Material covered in the pretreatment CBT sessions was reviewed during the posttreatment sessions, along with staff provision of support for smoking abstinence and discussion of the session experience.

Supportive-expressive group therapy. Anderson et al. (9) modified an existing adaptation of supportive-expressive group therapy (SEGT), a palliative care-focused existential modality of therapy. The authors cited SEGT's focus on facilitating present-moment processing, emotional expression, and reducing death anxiety (9), which has been described in qualitative reports of psilocybin sessions (20, 21). Modifications to SEGT for this study included the substitution of

breathing exercises and guided meditations instead of auto-hypnosis. These modifications were intended to aid in facilitating group sessions and to provide tools for mindfulness and self-regulation for use in psilocybin sessions.

Eclectic psychotherapeutic intervention. Ross et al. (4) used CBT in posttreatment sessions for individuals experiencing anxiety and depression in the context of life-threatening cancer. This study used other modalities in addition to CBT, including supportive psychotherapy, existentially oriented psychotherapies, and psychodynamic and/or psychoanalytic therapy. The authors justified incorporating CBT, supportive therapy, and existential therapy by emphasizing the relevance of these therapies for treating anxiety and depression of individuals with advanced-stage cancer (4). Psychodynamic and psychoanalytic therapy, on the other hand, were selected to assist participants in interpreting the experiences of treatment sessions (4). Psychoanalysis was used in psycholytic therapy, a modified form of psychoanalytic therapy incorporating low-to-moderate doses of psychedelics, which was used in early studies of psychedelics (2, 4).

Ross et al. (4) began the integration process of PAP toward the end of the treatment sessions in a format the study authors likened to that of psycholytic therapy. The study authors (4) provided three 2-hour sessions of psychotherapy in the pretreatment stage and after each treatment session, for a total of 12 sessions of psychotherapy. Although the authors did not indicate the specific modalities used in the pretreatment sessions, the stated goals of these preparatory meetings included intention setting, discussion of psychological and existential distress related to the cancer, and the status of the individual's present relationships. After being contacted for additional information, some study authors revealed that in all stages of psilocybin therapy, they took an eclectic approach to preparing, facilitating, and integrating the psilocybin experiences, borrowing primarily from supportive and existential therapy (11, 14, 17).

Psychotherapeutic Techniques Integrated in PAP

Throughout all stages of treatment, psilocybin studies have incorporated psychotherapeutic components not tied to one specific modality. Notably, eight of the 11 studies (73%) designated development of the therapeutic relationship, described in some studies (10) as building rapport and trust, as one of the primary goals of the pretreatment sessions. Emphasis on the therapeutic relationship aligns with the conceptual framework of a person-centered therapy orientation, which also emphasizes the therapeutic relationship (31). Moreover, mandates for therapists have underscored the importance of empathy and adopting a client-centered approach over any academic or professional credentials (1, 24). The nondirective supportive approach in treatment sessions also aligns with a person-centered orientation, which views the individual as an expert in his or her own life and places the responsibility of guiding the therapeutic goals, process, and outcomes on the individual rather than the therapist (31). Several

psychotherapeutic tools were used within a person-centered orientation.

Body scanning and writing. Body scanning is a mindfulness technique for developing attentive flexibility by shifting focus through different regions of the body (32). One study (15) had participants engage in a 10-minute body scan at the beginning of each pretreatment session and in open-ended narrative writing at the end of treatment sessions to describe their psilocybin experiences. This narrative writing was discussed with therapists the next day during a 1-hour integration meeting (15). Similarly, another study (13) asked participants to journal about their experiences and struggles with incorporating aspects of the psilocybin treatment into their daily lives.

Guided imagery. Guided imagery is a therapeutic technique often associated with psychodynamic therapy, in which individuals lie on a couch with minimal external stimuli as the clinician depicts visual scenery (such as a meadow) to the individual (33). Guided imagery was used in two of the studies (3, 15). Johnson et al. (15) included guided imagery during pretreatment and posttreatment sessions and in the last hour of the first treatment session; the authors of this study did not indicate the intended effects of guided imagery, although Carhart-Harris et al. (3) indicated use of guided imagery to enhance relaxation. Nicholas et al. (17) also offered guided meditation to aid participants in relaxing prior to psilocybin administration.

Integration. Integration is loosely defined as reflecting on the unusual thoughts and feelings arising from the psilocybin experience and exploring implications of the experience for the targeted areas of change (1, 2, 24). Eight studies indicated incorporation of integration into posttreatment sessions. Grob et al. (14) and Moreno et al. (16) did not indicate inclusion of any posttreatment sessions, and Carhart-Harris et al. (3) did not specify the content of posttreatment sessions. Attempts to contact the authors of these studies failed. Integration sessions were sometimes referred to as "debriefing sessions" (3, 10) or "support meetings" (1, 15).

Meditation. Griffiths et al. (13) explored the use of meditation practices with psilocybin, asking participants to engage in sitting meditation and daily awareness practice before and after treatment sessions. After the psilocybin treatment, this study incorporated individual meetings and dialogue-group sessions into the intervention. In these group sessions, participants discussed their psilocybin treatment experiences, although these sessions primarily focused on implementing and sustaining meditation and journaling practices into daily life. The study relied on Easwaran et al.'s (34) book on meditation as the primary teaching resource for the group. No specific therapeutic modality was specified for the group. Nicholas et al. (17) also offered opportunities for meditation before and during the final hour of treatment sessions.

Outcomes Across PAP Studies

The section below briefly summarizes outcomes of the clinical trials collected in this review. None of the 11 studies reported serious adverse outcomes attributed to psilocybin, and no participant in any of the studies required the rescue medication available for participants during treatment sessions. Adverse events common in the studies included hypertension, headaches, and anxiety; these adverse events were transient and often mild.

Quantitative outcomes. Quantitative outcomes of the clinical trials are displayed in Table 1. Each study used several psychological outcome measures, including the Beck Depression Inventory (35), State-Trait Anxiety Inventory (36), Persisting Effects Questionnaire (25), Timeline Follow-Back (37), and the Yale-Brown Obsessive-Compulsive Scale (38). Table 1 presents results for measures common to each of the studies working with a particular population, regardless of whether these measures were of primary or secondary outcomes. All but one study (14) achieved statistically significant improvements in the targeted outcomes, such as depression and anxiety (3, 4, 11, 12).

Johnson et al. (15) demonstrated 7-day point prevalence of abstinence from smoking among 80% of participants at the 6-month follow-up. A 12-month follow-up of this trial indicated that 53% of participants had maintained abstinence since the target quit date (39). Nicholas et al. (17) demonstrated moderate effect sizes for increased positive attitudes and mood in their study of healthy participants. Seven studies (3, 4, 9–13) reported large effect sizes for the therapeutically relevant constructs (Table 1). Four of the five studies measuring depression and anxiety demonstrated clinically significant reductions in these conditions (3, 4, 11, 12). Grob et al. (14) eventually reached significance at the 6-month follow-up. These outcomes suggest that psilocybin may be an effective treatment for a range of psychological disturbances.

Qualitative outcomes. Qualitative data can capture valuable information missed by quantitative analysis, especially in the field of psychopathology (40). Noorani et al. (19) identified pretreatment sessions and the therapeutic relationship as two essential components of successful treatment. Watts et al. (21) used thematic analysis with participants from Carhart-Harris et al.'s study (3); through conversations with participants, they identified two fundamental change processes underlying PAP. One of these changes was a shift from feeling disconnected to feeling connected with oneself, others, and the world (21). The second change was a process of shifting from avoidance of emotions to acceptance of emotions during and after PAP. Participants from another study (15) stated that they gained insight into themselves and their reasons for smoking. These examples revealed a common thread between these four studies: in PAP, participants seem to gain novel insights into themselves, their presenting problems, or their relationship with those problems. A participant from another study (18) indicated that she began practicing meditation after

PAP in order to return to a state of mind she referred to as a “really wonderful emptiness—that kind of really good feeling of nothingness” (20).

Effects of psychotherapy on outcomes. Griffiths et al. (13) published the only study in this review that measured the effects of psychotherapy in the analysis. This study included psychotherapy as an independent variable to ascertain the effects of psychotherapy on outcomes in PAP. Although the study did not indicate use of a specific psychotherapeutic modality, the authors reported the use of meditation practices, journaling, spiritual practices, and group discussion of the psilocybin experience. The results of this study suggested that individuals with greater psychotherapeutic support throughout treatment exhibited greater short- and long-term effects in domains such as daily life experiences, gratitude, and meaning or purpose in life (13). No other study in this review accounted for the effects of psychotherapy interventions on participant outcomes, except for the effect of music in treatment sessions (21–23). Qualitative studies (20–22) revealed that music was identified by participants as an important component of the experience. A follow-up study (22) of Ross and colleagues' clinical trial revealed that all 13 participants described the music played during the session as having a central role in their experiencing of the treatment. In fact, participants described the music as a conduit to the experience (22) and a guide through challenging emotions (23). Watts et al.'s (21) qualitative study of individuals who received psilocybin for treatment-resistant depression revealed that music enabled participants to experience and accept painful emotions. Together, these data suggest that music therapy may be integral in producing the clinically significant outcomes seen in PAP studies.

DISCUSSION

This article reviewed the psilocybin literature regarding the structure and format of PAP, including the role of therapists and differences among studies in the structure and format of sessions. Treatment with psilocybin demonstrated significant improvements in symptoms of depression and anxiety (3, 4, 11, 12), demoralization (9), substance use (10, 15), and attitude and mood (12, 13, 17).

The results revealed three distinct stages of PAP across all 11 clinical trials: pretreatment, treatment, and posttreatment. Pretreatment sessions involved direct interaction with therapists. The primary goals of these sessions were to build a therapeutic relationship between participants and therapists and to prepare the participant for the psilocybin treatment. The psilocybin treatment sessions were the only sessions in which psilocybin was administered. These sessions involved nondirective supportive therapy as well as a modified form of music therapy. Posttreatment sessions included data collection and integration of treatment session experiences into the participant's life.

The review also found several conventional psychotherapeutic modalities modified for use in psilocybin clinical trials:

MET (10), CBT (4, 15), existential psychotherapy (4, 14, 17), SEGT (9), and psychodynamic therapy (4). Many of the collected studies used psychotherapeutic techniques during the treatment session, such as guided imagery (3, 15, 17), open-ended narrative writing (15), supportive touch (3, 4), reality orientation (3), empathic support (3, 4, 15, 17), and nonjudgmental listening (3, 4, 15, 17).

Implementation of conventional psychotherapy techniques in these PAP studies occurred almost exclusively outside of or in the last hour of treatment sessions, regardless of the dosage provided to participants. The dosage administered to participants had no effect on the therapeutic model used in the reviewed studies, which contrasts with early psychedelic research models, where the model of psychotherapy used during treatment sessions often depended on the dose administered in each session (2). Two modalities of therapy widely used in the mid-20th century in the context of psychedelic treatment of mental illnesses were labeled psycholytic therapy and psychedelic therapy (2). The psycholytic model was often implemented during sessions with a low-to-moderate dose and included in-session psychoanalytic therapy, which focused on bringing awareness to the unconscious (2). The psychedelic model focused on occasioning a mystical experience and was primarily used during high-dose sessions (2). According to the literature gathered for this review, no psilocybin studies published within the past 25 years have followed this model of using direct, interactive psychotherapy during a low-dose psilocybin session.

Given the differing study designs and mixed results in this review, future psilocybin research would benefit from investigating which psychotherapeutic modalities and techniques are most appropriate for incorporation into PAP. Such research is a prerequisite for determining best practices in this novel clinical treatment of mental illness. Research could explore which psychotherapies work best at low versus high doses of psilocybin as well as modifications to make PAP beneficial for individuals from all cultural, racial-ethnic, and socioeconomic backgrounds and for those with disabilities or chronic illness. For instance, the requirement of some studies to include a male-female dyad may be seen as heteronormative and insensitive to certain minority groups.

The present research acknowledges the impact that session structure, context, and setting have on the psilocybin treatment session; individual experiences during treatment are affected by nonpsilocybin factors to such an extent that participants and researchers have described them as integral to the therapy (1, 22). In light of the importance of nonpsilocybin factors, research must explore how to optimize the structure, setting, and components of PAP to enhance the clinical efficacy of psilocybin sessions. Specifically, the inclusion of psychotherapies that are evidenced to be effective for the relevant mental illness, aligned with the structure and intentions of PAP, and sufficiently controlled to allow for adequate analysis of treatment outcomes could maximize psilocybin's effects and provide optimal outcomes for individuals seeking treatment.

Trials similar to Griffiths et al. (13), in which groups of participants receive psilocybin with minimal (i.e., supportive, largely nondirective) compared with extensive (e.g., an evidenced-based treatment such as CBT) therapeutic support, could be fruitful in determining the impact of psychotherapy in PAP. The effects of therapy could be further isolated by using a placebo dose of psilocybin (i.e., a very low dose) in both treatment groups and hiring assessors blinded to the treatment condition to collect primary measures. Moreover, PAP research might seek to account for therapist allegiance by finding experts in the fields of the adjunctive treatment and the nonspecific supportive structure common across PAP studies and assign each type of expert to their respective group to better determine PAP's efficacy.

The bedrock of PAP rests on providing nonjudgmental listening, empathic support, and a strong therapeutic relationship (1, 2, 24). Although the PAP studies in this review have largely been conducted and published within the domain of psychiatry (4, 10, 14), and may thus seem distant from the world of therapists, the fundamental components of PAP are integral to nearly every model of psychotherapy. Moreover, the therapists in the reviewed clinical trials were often not psychiatrists, but master's level counselors (N=7), social workers (N=8), and clinical psychologists (N=19). This finding suggests that, if PAP becomes a clinical practice, the individuals who will work directly with clients before, during, and after psilocybin administration will likely be practicing therapists. Clinicians may be able to incorporate their preexisting knowledge and skills along with specific training in PAP to help facilitate immediate and enduring positive changes in the lives of their clients.

CONCLUSIONS

The present systematized review outlined the role of therapists in PAP and consolidated the structure of sessions and range of psychotherapeutic modalities and techniques implemented in this therapy. The importance of isolating psilocybin's effects to better understand its mechanistic functions is unquestionable. Additionally, the content of each stage of PAP is essential to the efficacy of psilocybin treatment, and the influence of psychotherapy on outcomes is likely higher than current research suggests (2). Counselors and therapists are poised to contribute immensely to the field of PAP, as they will likely provide the in-session therapeutic services if or when psilocybin becomes an FDA-approved treatment. Therapists can get involved with PAP today by completing PAP training, becoming a therapist on a PAP study, or simply staying informed on PAP's developments as this new form of psychotherapy progresses toward clinical practice.

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REFERENCES

- Johnson M, Richards W, Griffiths R: Human hallucinogen research: guidelines for safety. *J Psychopharmacol* 2008; 22:603–620
- Bogenschutz MP, Forcehimes AA: Development of a psychotherapeutic model for psilocybin-assisted treatment of alcoholism. *J Humanist Psychol* 2017; 57:389–414
- Carhart-Harris RL, Bolstridge M, Rucker J, et al: Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study. *Lancet Psychiatry* 2016; 3:619–627
- Ross S, Bossis A, Guss J, et al: Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial. *J Psychopharmacol* 2016; 30:1165–1180
- Grant MJ, Booth A: A typology of reviews: an analysis of 14 review types and associated methodologies. *Health Info Libr J* 2009; 26:91–108
- Moher D, Shamseer L, Clarke M, et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015; 4:1
- Rucker JJ, Jelen LA, Flynn S, et al: Psychedelics in the treatment of unipolar mood disorders: a systematic review. *J Psychopharmacol* 2016; 30:1220–1229
- Dos Santos RG, Bouso JC, Alcázar-Córcoles MÁ, et al: Efficacy, tolerability, and safety of serotonergic psychedelics for the management of mood, anxiety, and substance-use disorders: a systematic review of systematic reviews. *Expert Rev Clin Pharmacol* 2018; 11:889–902
- Anderson BT, Danforth A, Daroff PR, et al: Psilocybin-assisted group therapy for demoralized older long-term AIDS survivor men: an open-label safety and feasibility pilot study. *EClinicalMedicine* 2020; 27:100538
- Bogenschutz MP, Forcehimes AA, Pommy JA, et al: Psilocybin-assisted treatment for alcohol dependence: a proof-of-concept study. *J Psychopharmacol* 2015; 29:289–299
- Davis AK, Barrett FS, May DG, et al: Effects of psilocybin-assisted therapy on major depressive disorder: a randomized clinical trial. *JAMA Psychiatry* 2021; 78:481–489
- Griffiths RR, Johnson MW, Carducci MA, et al: Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: a randomized double-blind trial. *J Psychopharmacol* 2016; 30:1181–1197
- Griffiths RR, Johnson MW, Richards WA, et al: Psilocybin-occasioned mystical-type experience in combination with meditation and other spiritual practices produces enduring positive changes in psychological functioning and in trait measures of prosocial attitudes and behaviors. *J Psychopharmacol* 2018; 32:49–69
- Grob CS, Danforth AL, Chopra GS, et al: Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Arch Gen Psychiatry* 2011; 68:71–78
- Johnson MW, Garcia-Romeu A, Cosimano MP, et al: Pilot study of the 5-HT_{2A}R agonist psilocybin in the treatment of tobacco addiction. *J Psychopharmacol* 2014; 28:983–992
- Moreno FA, Wiegand CB, Taitano EK, et al: Safety, tolerability, and efficacy of psilocybin in 9 patients with obsessive-compulsive disorder. *J Clin Psychiatry* 2006; 67:1735–1740
- Nicholas CR, Henriquez KM, Gassman MC, et al: High dose psilocybin is associated with positive subjective effects in healthy volunteers. *J Psychopharmacol* 2018; 32:770–778
- Bogenschutz MP, Podrebarac SK, Duane JH, et al: Clinical interpretations of patient experience in a trial of psilocybin-assisted psychotherapy for alcohol use disorder. *Front Pharmacol* 2018; 9:100
- Noorani T, Garcia-Romeu A, Swift TC, et al: Psychedelic therapy for smoking cessation: qualitative analysis of participant accounts. *J Psychopharmacol* 2018; 32:756–769
- Swift TC, Belser AB, Agin-Liebes G, et al: Cancer at the dinner table: experiences of psilocybin-assisted psychotherapy for the treatment of cancer-related distress. *J Humanist Psychol* 2017; 57:488–519
- Watts R, Day C, Krzanowski J, et al: Patients' accounts of increased "connectedness" and "acceptance" after psilocybin for treatment-resistant depression. *J Humanist Psychol* 2017; 57:520–564
- Belser AB, Agin-Liebes G, Swift TC, et al: Patient experiences of psilocybin-assisted psychotherapy: an interpretative phenomenological analysis. *J Humanist Psychol* 2017; 57:354–388
- Malone TC, Mennenga SE, Guss J, et al: Individual experiences in four cancer patients following psilocybin-assisted psychotherapy. *Front Pharmacol* 2018; 9:256
- Phelps J: Developing guidelines and competencies for the training of psychedelic therapists. *J Humanist Psychol* 2017; 57:450–487
- Griffiths RR, Richards WA, McCann U, et al: Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology* 2006; 187:268–283
- Carhart-Harris RL: How do psychedelics work? *Curr Opin Psychiatry* 2019; 32:16–21
- Mithoefer MC, Grob CS, Brewerton TD: Novel psychopharmacological therapies for psychiatric disorders: psilocybin and MDMA. *Lancet Psychiatry* 2016; 3:481–488
- Kaelen M, Giribaldi B, Raine J, et al: The hidden therapist: evidence for a central role of music in psychedelic therapy. *Psychopharmacology* 2018; 235:505–519
- Bonny HL, Pahnke WN: The use of music in psychedelic (LSD) psychotherapy. *J Music Ther* 1972; 9:64–87
- Theorell T: Psychological Health Effects of Musical Experiences: Theories, Studies and Reflections in Music Health Science. Stockholm, Springer, 2014
- Waters RA, Buchanan A: An exploration of person-centered concepts in human services: a thematic analysis of the literature. *Health Policy* 2017; 121:1031–1039
- Kabat-Zinn J: Full Catastrophe Living: Using the Wisdom of Your Body and Mind to Face Stress, Pain, and Illness. New York, Delacorte, 1990
- Leuner H: Guided affective imagery (GAI). A method of intensive psychotherapy. *Am J Psychother* 1969; 23:4–21
- Easwaran E: Meditation: A Simple 8-Point Program for Translating Spiritual Ideals Into Daily Life. Tomales, CA, Nilgiri Press, 1991
- Beck AT, Ward CH, Mendelson M, et al: An inventory for measuring depression. *Arch Gen Psychiatry* 1961; 4:561–571
- Spielberger CD: Manual for the State-Trait Anxiety Inventory (Form Y). Palo Alto, CA, Mind Garden, 1983
- Sobell LC, Sobell MB: Timeline follow-back: a technique for assessing self-reported alcohol consumption; in *Measuring Alcohol Consumption: Psychosocial and Biochemical Methods*. Edited by Litten RZ, Allen JP. Rockville, MD, Humana Press, 1992
- Goodman WK, Price LH, Rasmussen SA, et al: The Yale-Brown Obsessive Compulsive Scale. I. Development, use, and reliability. *Arch Gen Psychiatry* 1989; 46:1006–1011
- Johnson MW, Garcia-Romeu A, Griffiths RR: Long-term follow-up of psilocybin-facilitated smoking cessation. *Am J Drug Alcohol Abuse* 2017; 43:55–60
- Palinkas LA: Qualitative and mixed methods in mental health services and implementation research. *J Clin Child Adolesc Psychol* 2014; 43:851–861