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RESEARCH ARTICLE

Effects of Psilocybin on Religious and Spiritual Attitudes and Behaviors in Clergy from Various Major World Religions

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Abstract

Background: Although historical writings, anthropological accounts, and experimental studies document associations between psilocybin use and religion, no prospective experimental study has investigated how the effects of psilocybin are experienced and interpreted by religious clergy. This exploratory study evaluated the overall safety and the acute and enduring effects of psilocybin in clergy.

Methods: Participants were psychedelic-naïve clergy from various major world religions. A randomized, parallel group, waitlist control design was used to assess the effects of two supported psilocybin sessions, with participants receiving 20 and then 20 or 30 mg/70 kg about 1 month later. Outcomes were compared between the Immediate Group (n = 13) and the Delayed Group (n = 16) at 6 months after screening using self-report measures. The effects of psilocybin were also assessed on session days and 4 and 16 months after the second psilocybin session in the 24 participants who completed both sessions.

Results: The primary outcome assessment at 6 months after screening showed that, compared with the delayed control group, participants who had received psilocybin reported significantly greater positive changes in their religious practices, attitudes about their religion, and effectiveness as a religious leader, as well as in their non-religious attitudes, moods, and behavior. Follow-up assessments showed that positive changes in religious and non-religious attitudes and behavior were sustained through 16 months after the second psilocybin session. At that time, participants rated at least one of their psilocybin experiences to be among the top five most spiritually significant (96%), profoundly sacred (92%), psychologically insightful (83%), and psychologically meaningful (79%) of their lives. Furthermore, 42% rated one of their experiences to be the single most profound of their lifetime. At 16-months follow-up, most (79%) strongly endorsed that the experiences had positive effects on their religious practices (e.g., prayer or meditation) and their daily sense of the sacred, and most (71%) reported positive changes in

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**In the view of the co-senior authors, Robert Jesse and William A. Richards have contributed equally to this work.

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their appreciation of religious traditions other than their own. Although no serious adverse events were reported, 46% rated a psilocybin experience as among the top five most psychologically challenging of their lives.

Conclusions: In this population of clergy, psilocybin administration was safe and increased multiple domains of overall psychological well-being including positive changes in religious attitudes and behavior as well as their vocation as a religious leader. The study was limited by a waitlist control design, homogenous sample, and the use of some unvalidated outcome measures. Further research with more rigorous control conditions and diverse samples is needed.

Keywords: psilocybin, spirituality, religion, clergy, mystical experience, clinical trial

Introduction

In a growing body of scientific research, psychedelic compounds have been shown to generate experiences that can share some apparent similarities to non-pharmacologically triggered experiences with labels such as "religious," "spiritual," or "mystical," which have been reported across a number of cultures.[1,2] Mystical experiences are characterized by a range of subjective features including a sense of unity, "noetic" quality (e.g., an authoritative sense of truth), transcendence of time and space, a sense of awe or sacredness, intense positive mood, transiency that nevertheless feels timeless, presence in awareness of mutually exclusive states or concepts, and ineffability.[1–8] These qualities are also observed in states of consciousness associated with near-death experiences, meditation, prayer, fasting, breathwork, and music.[9–11] Psilocybin, the principal psychoactive compound in some genera of mushrooms, is similar to other serotonergic psychedelics, including D-lysergic acid diethylamide, dimethyltryptamine, and mescaline, with acute and subjective effects primarily mediated neuropharmacologically by 5HT2A receptor agonism[12,13] and characterized by a unique profile of changes in thoughts, perceptions, and emotions,[14–16] including often profound alterations in senses of reality, world-view, and meaning.[17]

Survey studies have suggested that psychedelics, including psilocybin, can occasion mystical experiences that are associated with enduring increases in well-being and spirituality,[11,18–21] with some evidence suggesting that such experiences induced by psychedelics may be experienced more intensely compared with non-pharmacologically triggered mystical states.[11] In prospective experimental studies with well screened, healthy volunteers, psilocybin-occasioned mystical experiences have been associated with substantial and sustained improvements in personal well-being, meaning, and spiritual significance.[22–26] Further, in clinical trials with psilocybin, the intensity of mystical experiences tends to correlate with or mediate persisting therapeutic effects of psilocybin-assisted psychotherapy across study populations, such as those with advanced cancer-related psychiatric and existential distress,[27–29] alcohol and nicotine use disorders,[30,31] and major depressive disorder.[32,33]

Psilocybin and other psychedelic plants and fungi have been used as sacraments, likely for millennia, and throughout the world by some Indigenous cultures for divinatory, spiritual, and religious purposes.[34–38] Contemporary use of psychedelics in spiritual and religious settings is well-documented including, in the United States, the federally permitted use of peyote by Native Americans and of ayahuasca by the União do Vegetal and by one church in the Santo Daime tradition.[38–41] The ritualized and structured contexts of the use of a psychedelic in these organized practices are believed to minimize the likelihood of adverse effects with safeguards that include restricted access to the sacramental medicine, regimented preparation, guidance and supervision by more experienced practitioners, and a societal appreciation for what these religions believe to be the sacred, powerful, and medicinal properties of the substances.[17,42–44]

While psychedelics continue to be used in some Indigenous religious contexts, they are generally not used within major world religions (e.g., Hinduism, Judaism, Buddhism, Christianity, Islam). Furthermore, there has been little if any investigation on how psychedelic experiences are interpreted by clergy who have been educated in the theology and practices of a major, non-Indigenous religion. Some scholars of religion have argued that psychedelic experiences are not genuine religious experiences but instead represent distorted interpretations, often by those without religious or theological training or knowledge.[45,46] This line of reasoning gives rise to the question of how individuals with religious and theological training would describe and interpret psychedelic experiences. The current study directly addresses this question. Given the association between psilocybin use and spirituality or religion, this study investigated how psychedelic-naïve professional religious leaders would experience and interpret the effects of psilocybin, what if any enduring effects might be observed, and what if any

impact would it have on their professional work as clergy.

The only previous experimental study to assess the impact of psilocybin use among religiously oriented individuals was conducted at Boston University's Marsh Chapel on Good Friday, April 20, 1962. Known colloquially as the "Good Friday Experiment," the study was led by Walter Pahnke (a psychiatrist and graduate student in theology at Harvard Divinity School), who hypothesized that psilocybin could facilitate mystical experiences, resulting in persisting positive changes in attitudes and behavior, in religiously inclined volunteers.[5,47] Pahnke enrolled psychedelic-naïve Protestant seminary students in a group setting during a religious service held at the Marsh chapel. The study used a double-blind randomized control design in which participants received either psilocybin (30 mg; $n = 10$) or an active placebo (200 mg nicotinic acid; $n = 10$). The blinding integrity for this trial was poor with all participants correctly identifying whether they were in the experimental or control condition. Consistent with the main hypotheses, this trial reported that single-dose psilocybin administration to divinity students in a group setting, as compared with single-dose active placebo, produced mystical experiences and was associated with increased positive changes in attitudes and behavior at 6-month follow-up.[5] Twenty-five years later, a follow-up study located and interviewed 7 of the 10 psilocybin participants and all 10 of the controls yielding similar findings. Relative to the participants in the control condition, the participants who had received psilocybin reported more substantial, positive, and persisting effects in attitudes and behavior and that their participation made a uniquely valuable contribution to their spiritual lives.[48] In an open-ended interview, the participants who had received psilocybin 25 years earlier reported that they felt that the experience had significantly affected their lives in positive ways. This included feeling an enhanced appreciation of life and nature, a deepened sense of joy, greater equanimity in the face of difficult life crises, increased tolerance of other religions, and a deepened commitment to their ministry or vocation.[48]

The current study sought to extend this previous research by more rigorously investigating the acute and enduring effects of psilocybin in professionally trained and engaged clergy from a sample of major world religions. Psilocybin was administered to participants individually using a randomized waitlist control design along with additional procedures providing interpersonal support before and after psilocybin sessions. The current study also included a comprehensive set of measures after screening (e.g., baseline), during and immediately after psilocybin sessions, and at 4 and 16 months after psilocybin. A primary objective of the current exploratory study was to characterize persisting changes in psychological functioning, spirituality, well-being, and attitudes and behaviors in professional religious leaders following supported psilocybin sessions. A pre-registered questionnaire (the Interim Questionnaire) was administered 6 months after study enrollment to assess the effects of psilocybin by directly comparing the Immediate Group (which had received psilocybin) with the Delayed Group (which had not yet received psilocybin).

Based on the previously mentioned historical, anthropological, and experimental findings documenting associations of psilocybin use with spirituality and religion, we hypothesized that, after the psilocybin intervention, clergy of various major world religions would show increases in well-being, life satisfaction, and other positive changes, including changes in spiritual practices and changes in attitudes, social interactions, and other behaviors related to their religious vocation.

Materials and Methods

Participants

Participants were required to hold a recognized leadership position in a well-established religious organization with professional activities that included significant time interacting with those seeking religious/spiritual guidance or support. Applicants were required to have formal training and ordination or equivalent in their tradition. Moreover, in the judgment of the study team, a suitable applicant would have to be regarded as an unambiguous representative of their religion by other members of that religion. In this report, the religious leader participants are referred to as "clergy."

Potential participants were recruited through internet announcements and ads, newsletters, and print notices. Typical recruitment advertising sought clergy "to take part in a research study of psilocybin and sacred experiences." After telephone screening of approximately 100 potential participants, 37 provided informed consent and were further screened in-person (see Supplementary Data S1 about screening and inclusion/exclusion criteria). Of these, 33 were accepted and randomized to either the Immediate Group or Delayed Group condition. The Consolidated Standards of Reporting Trials (CONSORT) flow diagram (Fig. 1) provides the sequence of study procedures and reasons for dropouts after randomization. Most of the participants were recruited locally (e.g., Baltimore or New York regions) but some traveled from out of state or country.

Study design and overview

The study was conducted separately at two sites: Johns Hopkins University (JHU) School of Medicine and New York University (NYU) Grossman School of Medicine. The Johns Hopkins Medicine Institutional Review Board (IRB) monitored the JHU site, and the NYU Grossman

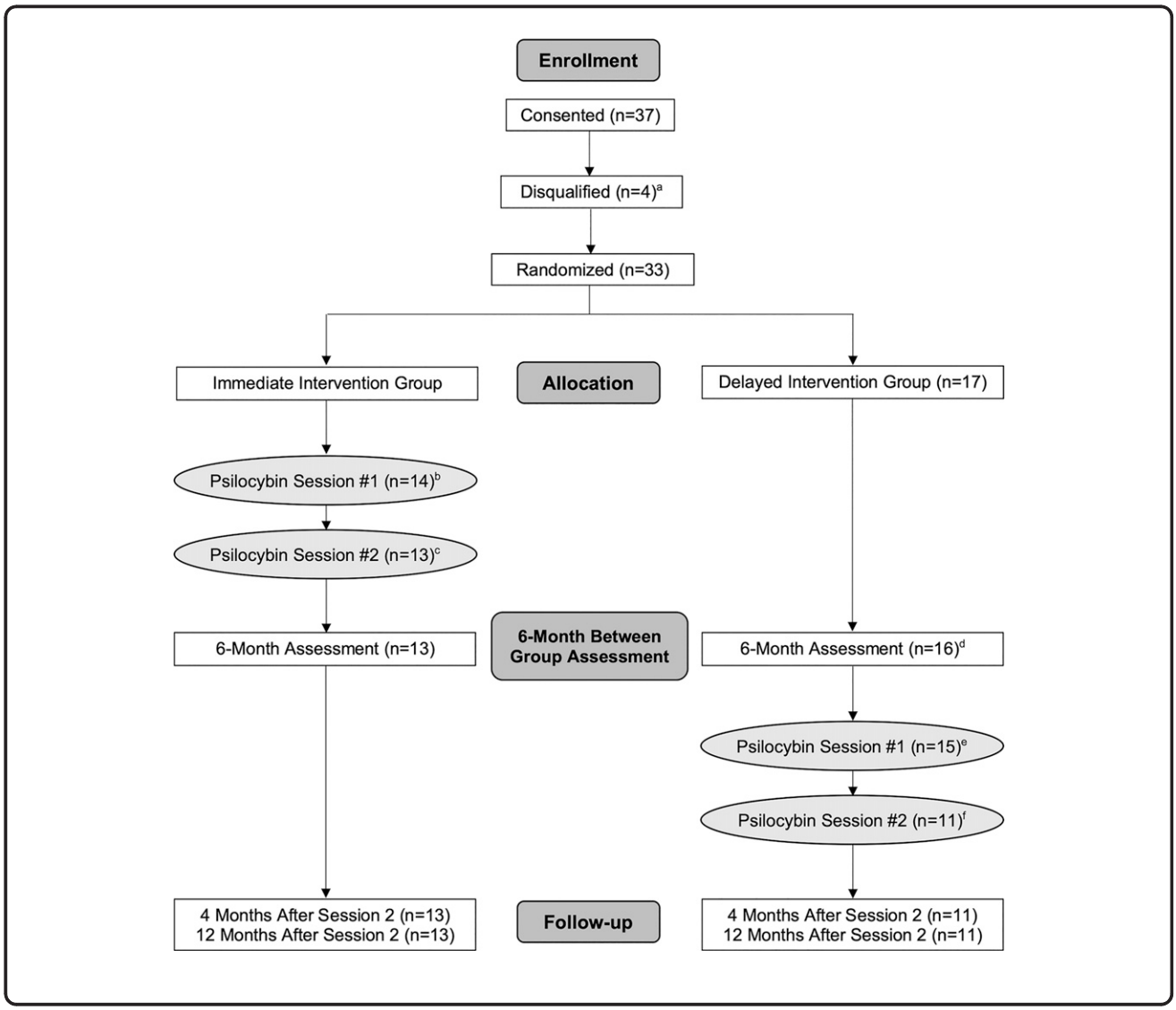
School of Medicine IRB monitored the NYU site. Written informed consent was obtained from participants. At JHU and NYU, respectively, 22 and 11 participants were randomized and 17 and 7 completed all follow-up assessments after having both psilocybin sessions. As shown in Figure 1, after screening, baseline assessments, and consent, 33 participants were randomized to an Immediate Group or a Delayed Group. An urn randomization procedure[49] was used to balance the two groups as closely as possible on two dichotomous variables at screening (gender: female or male; age: <55 years or ≥55 years). Table 1 shows that these and other demographic characteristics did not differ across the two experimental groups.

Figure 2 shows the timeline of study procedures. The study used a randomized parallel group design to assess the effects of psilocybin by comparing outcomes assessed at 6 months after randomization between the Immediate Group and the Delayed Group, which had not yet received psilocybin. The use of a delayed control permitted differentiation of the psilocybin intervention from changes in attitudes, beliefs, and behaviors that might occur spontaneously and/or in response to the extensive screening and decision to participate in the study. After the 6-month assessment, participants in the Delayed Group received the psilocybin intervention. In both groups, follow-up assessments were conducted at 4 and 16 months after the second psilocybin session.

Psilocybin intervention

The same psilocybin intervention was used in both groups using a protocol (e.g., preparation, support during dosing sessions, and integration) consistent with prior studies.[22,24,25,28] Before the first psilocybin session, participants had four preparatory meetings (8 h total) with

Fig. 1. CONSORT flow diagram. [a]Four individuals were disqualified following in-person screening for the following reasons: one had an uncertain career path as a religious professional; one was taking an antidepressant medication; one had elevated blood pressure; one met inclusion/exclusion criteria but opted not to participate prior to randomization. [b]One participant was discontinued before session #1 because of elevated blood pressure. A second participant was dropped from final data analysis because they received an incorrect and substantially lower dose of psilocybin than required in the first session. This participant reported only very mild effects in session #1 and subsequently participated in session #2 reporting generally positive effects at 4 and 12 months. [c]One participant choose not to participate in session #2 because they reported not to be ready for another session; however, this participant reported generally positive effects at 4 and 12 month follow-up including on measures of personal meaning, spiritual significance and effects related to religious vocation. [d]One participant was discontinued soon after randomization because religious ordination in a mainstream religion was uncertain. [e]One participant was discontinued after the interim assessment and before session #1 because of a newly diagnosed cardiac problem. [f]Four participants did not participate in session #2. The first participant chose not to participate in session #2 because they reported not to be ready for another session; this participant reported very positive but psychologically challenging effects in session #1 and reported generally positive effects at 4 and 12 months follow-up including on measures of personal meaning, spiritual significance and effects related to religious vocation. The second participant was discontinued because of elevated blood pressure in session #1; similar to the first participant, this participant reported very positive but psychologically challenging effects in session #1 and reported generally positive effects at 4 and 12 months follow-up including on measures of personal meaning, spiritual significance and effects related to religious vocation. The third participant discontinued after reporting a range of somatic (e.g., incoordination) and visual (e.g., blurry vision) symptoms starting on session #1; these symptoms resolved and neurological workup was negative; this participant reported very positive but psychologically challenging effects in session #1 and reported generally positive effects at 4 and 12 months follow-up including on measures of personal meaning, spiritual significance and effects related to religious vocation. The fourth participant was discontinued after session #1 because of medical concerns about an aneurysm. On screening, the participant did not disclose a history of an aortic aneurysm during the medical review of systems, which would have excluded the participant. Approximately 2 weeks after receiving the first psilocybin dose, the participant disclosed the history of an aortic aneurysm and said that he forgot to mention this at screening. Immediately upon finding out about this new information, the participant was not allowed to proceed to the second psilocybin session although follow-up data continued to be collected until end of study. This participant experienced one adverse event related to the psilocybin session—moderate headache for 4 days subsequent to the dosing session that resolved without treatment or sequelae. This participant reported mild effects in session #1 and at the 4 and 12 months follow-up.



two session facilitators for the purpose of establishing rapport, reviewing safety guidelines, and providing psychoeducational preparation for the psilocybin sessions.[50] After each of the two psilocybin sessions, there were three participant-facilitator "integration" meetings (about 3 h total) to discuss session experiences. The conduct of the preparatory and integration sessions was not manualized, and a client-centered, non-specific, non-directive approach was used. Session facilitators were study staff with varying educational levels (MD/PhD/MSW/BA). There were several facilitators at both JHU and NYU including study authors W.A.R., A.P.B., and S.R. W.A.R. and A.P.B. were the lead facilitators at JHU and NYU, respectively. Following the preparation meetings, two psilocybin sessions were held about a month apart.

All participants received a moderately high psilocybin dose of 20 mg/70 kg on the first session. Depending on the response to the first session dose, and upon discussion with the study staff and the participant, the psilocybin dose for the second session could be held constant or increased to a high dose 30 mg/70 kg. Although there is not yet an established consensus for these labels (e.g., "moderately high" and "high"), there is a precedent for their use in previous studies.[24,28] Psilocybin was administered orally in an opaque gelatin capsule with approximately 100 mL water. Both facilitators were present in the room and available to respond to participants' physical or emotional needs during the day-long session (approximately 8 h), except for short breaks taken by one facilitator at a time. The living-room-like settings where sessions were conducted, one at each study site, were furnished with comfortable seating for the two facilitators, a couch, end tables, and area rugs. The rooms had paintings and a variety of other decorative items, including a few small religious items such as a Buddha statue. Participants were encouraged to bring

Table 1. Participant Demographics at Enrollment for All Participants at the Interim Analysis (n = 29) and at Follow-up (n = 24) and for the Delayed Intervention Group and the Immediate Intervention Groups Separately

Measure	*All participants at interim analysis* (n = *29*)	*All participants at follow-up* (n = *24*)	*Delayed intervention at interim* (n = *16*)	*Immediate intervention at interim* (n = *13*)	χ^2 *or* t[a]
Gender (% female)	31%	33%	31%	31%	NS
Age in years (mean, SD)	48.8 (10.3)	47.7 (10.4)	47.3 (10.4)	50.7 (10.2)	NS
Weight in kg (mean, SD)	82.6 (16.6)	82.7 (17.4)	80.1 (15.0)	85.7 (18.6)	NS
Race/ethnicity (%)					
White	97%	96%	94%	100%	NS
Black/African American	3%	4%	6%	0%	NS
Hispanic (%)	7%	8%	6%	8%	NS
Education (%)					
Post-graduate	93%	92%	94%	92%	NS
College	7%	8%	6%	8%	NS
Relationship status (% married)	69%	67%	69%	69%	NS
Any lifetime use of hallucinogens (%)	0%	0%	0%	0%	NS
Current psychotherapy (%)	21%	17%	25%	15%	NS
Had previous profound sacred experiences[b]					
Yes (%)	83%	79%	82%	85%	NS
Number of experiences (median, range)	4.0 (0 to many)	4.0 (0 to many)	4.0 (0 to many)	4.0 (0 to 11)	NS
Duration of religious/spiritual vocational activities in years (mean, SD)	22.3 (10.4)	20.4 (9.9)	22.2 (9.8)	22.5 (11.6)	NS

[a]There were no significant differences (NS) between the Delayed and Immediate Intervention Groups on any demographic variable using *t*-tests for continuous data and chi-square tests for categorical data; NS indicates $p > 0.05$.
[b]See Table 5 for definition of sacred experience.
SD, standard deviation.

small personal or religious items with them on session days. During their sessions, participants were encouraged to lie on the couch, to wear eyeshades and headphones, and to focus their attention inward. The same pre-selected program of music was played throughout each session (see Supplementary Data S2 for playlist).

Outcome measures

Between-group effects. The primary pre-registered outcome questionnaire (clinicaltrials.gov NCT02243813; NCT02421263; outcome measure and timepoint specified without further analysis details) was the *Interim Questionnaire*, which was completed by all participants 6 months after screening. This questionnaire asked about experiences and changes in attitudes, mood, and behavior that occurred during the past 5 months. The questionnaire included questions about spiritual experiences, changes in spiritual practices, changes in attitudes, moods, social interactions, and other behaviors related to participants' religious/spiritual vocation (see Table 2). The measure was designed for this study and should be considered exploratory.

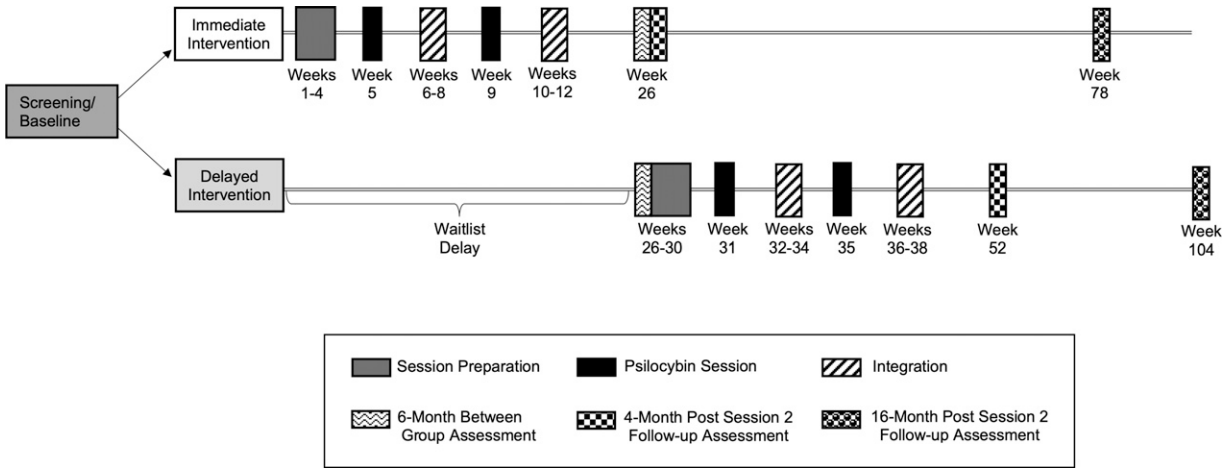


Fig. 2. Timeline of study procedures from screening and baseline assessment through the 16-month post-session 2 follow-up assessment in both the immediate and delayed intervention groups.

Table 2. Comparison of Delayed Intervention Group (*N* = 16) and Immediate Intervention Group (*N* = 13) on Changes in Religious and Non-Religious Attitudes, Moods, and Behaviors Over the Past 5 Months (Interim Questionnaire)[a]

Measure	*Delayed intervention control (N = 16)[b]*	*Immediate intervention psilocybin (N = 13)[b]*	p[c]	d[d]
Rating of spiritually significant experiences during the past 5 months[e]				
Mean (SD), maximum score = 10	4.12 (2.28)	7.46 (2.88)	**0.002**	1.30
Percent of group rating one or more experiences among the five most spiritually significant of their lifetime, including single most	0%	61.54%	**<0.001**[f]	
Past 5 months changes in religious attitudes and behavior (mean [SD], minimum/maximum score from −3 to +3)[g]				
Changes in your social interactions with others related to your spiritual/religious vocation	0.81 (1.42)	1.46 (1.56)	0.258	0.437
Changes in your contemplative, prayer or meditation practices	0.00 (0.97)	1.46 (1.81)	**0.017**	1.04
Changes in other behaviors related to your spiritual/ religious vocation	1.00 (0.97)	1.23 (1.42)	0.623	0.194
Changes in attitudes about your spiritual/religious vocation	0.44 (0.96)	1.85 (1.14)	**0.002**	1.34
Changes in your appreciation or understanding of your own religious tradition	0.25 (0.86)	1.62 (1.26)	**0.003**	1.29
Changes in your appreciation or understanding of religious traditions other than your own	0.88 (0.96)	1.92 (1.32)	**0.026**	0.925
Changes in spiritual awareness in everyday life	0.31 (0.70)	1.85 (1.21)	**<0.001**[h]	1.59
Mean score for the 7 change items	0.53 (0.57)	1.63 (1.08)	**0.004**	1.31
Past 5 months changes in specific religious attitudes (mean [SD], maximum score = 5)[i]				
Feel more effective in role as religious leader	1.88 (1.15)	3.08 (1.32)	**0.016**	0.979
Feel *less* effective in role as religious leader	0.38 (0.62)	0.00 (0.00)	**0.029**	−0.813
Deeper understanding of your religious tradition	1.25 (1.13)	3.15 (1.77)	**0.003**	1.31
Less deep understanding of your religious tradition	0.25 (0.68)	0.00 (0.00)	0.164	−0.491
More passion for sharing your religious understanding/faith	1.38 (1.15)	2.38 (1.56)	0.065	0.751
Less passion for sharing your religious understanding/faith	.56 (0.89)	0.00 (0.00)	**0.023**	−0.846
More eager to engage in world as a religious professional	1.56 (1.50)	2.62 (1.56)	0.078	0.689
Less eager to engage in world as a religious professional	0.44 (0.89)	0.38 (1.12)	0.891	−0.053
More certain about a positive role of religion in the world	1.69 (1.30)	2.92 (1.50)	**0.028**	0.887
Less certain about a positive role of religion in the world	0.69 (1.14)	0.23 (0.60)	0.179	−0.487
Increased tolerance for religious diversity[j]	1.88 (1.36)	3.23 (1.59)	**0.023**	0.925
Decreased tolerance for religious diversity[j]	0.12 (0.34)	0.00 (0.00)	0.164	−0.491
In your religious thinking, you have an increased tolerance of paradox (i.e., "Both/And" instead of "Either/Or")	1.88 (1.54)	3.31 (1.44)	**0.016**	0.957
In your religious thinking, you have a decreased tolerance of paradox (i.e., "Both/And" instead of "Either/Or")	0.06 (0.25)	0.00 (0.00)	0.332	−0.335
More certain about the veracity of certain metaphysical religious teachings or concepts (e.g., nirvana, heaven, hell, karma, reincarnation)[j]	1.12 (1.31)	2.54 (1.94)	**0.036**	0.872
Less certain about the veracity of certain metaphysical religious teachings or concepts (e.g., nirvana, heaven, hell, karma, reincarnation)[j]	0.44 (0.63)	0.00 (0.00)	**0.014**	−0.933
Spend more time for devotional life[j]	1.00 (1.15)	2.69 (1.44)	**0.002**	1.31
Spend less time for devotional life[j]	0.69 (1.14)	0.31 (1.11)	0.373	−0.337
Mean score for the 9 positive change items	1.51 (0.97)	2.88 (1.28)	**0.004**	1.220
Mean score for the 9 negative change items	0.40 (0.46)	0.10 (0.25)	**0.034**	−0.791
Past 5 months changes in attitudes and mood (mean [SD], % of maximum possible score)[k]				
Positive attitudes about life	32.50 (16.39)	61.67 (24.44)	**0.001**	1.43
Negative attitudes about life	11.35 (10.58)	2.95 (2.90)	**0.007**	−1.04
Positive attitudes about self	31.59 (15.78)	57.20 (21.38)	**0.002**	1.39
Negative attitudes about self	10.91 (11.46)	4.06 (5.20)	**0.044**	−0.743
Positive mood changes	28.61 (17.51)	53.85 (26.49)	**0.008**	1.15
Negative mood changes	11.81 (12.87)	02.22 (05.05)	**0.013**	−0.942

(*continued*)

Table 2. (Continued)

Measure	*Delayed intervention control (N = 16)*[b]	*Immediate intervention psilocybin (N = 13)*[b]	p[c]	d[d]
Altruistic/positive social effects	33.50 (17.60)	53.08 (25.50)	**0.029**	0.912
Antisocial/negative social effects	06.88 (05.61)	01.08 (02.25)	**0.001**	−1.31
Positive behavior changes	36.25 (24.46)	53.85 (34.04)	0.133	0.604
Negative behavior changes	5.00 (11.55)	04.62 (16.64)	0.944	−0.027
Increased spirituality	30.30 (20.58)	61.59 (27.16)	**0.002**	1.32
Decreased spirituality	6.88 (8.51)	0.71 (1.62)	**0.012**	−0.958
Past 5 months change in personal well-being or life satisfaction (mean [SD], minimum/maximum score from −3 to +3)[g]	0.44 (1.41)	1.77 (1.64)	**0.030**	0.877

Assessment occurred 6 months after randomization.

[a]Data in table are from the Interim Questionnaire.

[b]Continuous data in these columns are means (SD); percentage data indicate the percentage of participants in the group.

[c]*p* values are from *t*-tests for continuous data and from chi-square tests for categorical data; bold font designates $p < 0.05$.

[d]*d* indicates Cohen's *d* effect size.

[e]For this question, participants were asked if they had had one or more spiritually significant experiences during the past 5 months and to provide the highest rating that applied: 0 = No [No significant spiritual experience]; 1 = Yes, of a level of significance similar to spiritually significant experiences that occur on average once a day; 3 = . . .once a week; 4 = . . .once a month; 5 = . . .once a year; 6 = . . .once every 5 years; 7 = . . .once every 10 years; 8 = . . .among the 10 most spiritually significant experiences of my life; 9 = among the 5 most spiritually significant experiences of my life; 10 =. . .single most spiritually significant experience of my life.

[f]Exact *p* value: 0.0002265389.

[g]These items were scored on a 7-point scale from −3 = Strong negative change that I consider detrimental; 0 = No change; +1 = Slight positive change that I consider desirable; +2 = Moderate positive change that I consider desirable; +3 = Strong positive change that I consider desirable.

[h]Exact *p* value: 0.0007491.

[i]These items were scored from 0 = none, not at all; 1 = so slight I cannot decide; 2 = slight; 3 = moderate; 4 = strong; 5 = extreme (more than ever before in your life).

[j]This item was reproduced from the spirituality subscale of the Persisting Effects Questionnaire because it was relevant to changes in religious attitudes.

[k]Twelve subscales of the Persisting Effects Questionnaire were completed based on changes over the past 5 months from about 1 month after randomization to the 6-month assessment.

Acute effects. Participants completed these measures about 7 h after capsule administration when the effects of psilocybin had subsided:

End of session retrospective questionnaire. This questionnaire consisted of several questions for retrospectively rating the relative spiritual significance, personal meaning, psychological insight, and psychological challenge of the session experience. Qualitative features of the psilocybin experience (e.g., overall peak intensity; joy or happiness; anxiety or fearfulness) were also rated. Supplementary Table S3 provides additional details. Variations of this questionnaire have been used in previous psilocybin studies.[22,25]

Mystical Experience Questionnaire. Thirty items on the States of Consciousness Questionnaire[22] comprise the Mystical Experience Questionnaire (MEQ30), which assesses mystical experiences and yields 4 factor scores (Mystical, Positive mood, Transcendence of time and space, Ineffability) and a Total score. The MEQ30 has been shown to be sensitive to mystical subjective effects of psilocybin in laboratory studies as well as in survey studies of psilocybin mushroom use.[8,19] Participants were instructed to rate the degree to which they experienced the given phenomenon at any time during the session. A participant was designated as having had a "complete" mystical experience if scores on each of the four factors was ≥60% of the maximum possible factor score.[8]

Mysticism Scale. This is a modified version of the Mysticism Scale that assesses primary mystical experience across an individual's lifetime.[7,51] This 32-item questionnaire generates a total score and three empirically derived factors of the mystical experience: *Interpretation* corresponding to the noetic quality, deeply felt positive mood, and sacredness; *Introvertive* measuring internal unity, transcendence of time and space, and ineffability; and *Extrovertive* corresponding to the dimension of unity of all things.[51,52] In the modified version, participants were instructed to answer the questions in reference to their experiences since taking the capsule that morning. This version assessing acute effects was shown to be sensitive to the effects of psilocybin in previous studies.[22,25]

Challenging Experience Questionnaire. The Challenging Experience Questionnaire is a 26-item measure that assesses psychologically difficult psilocybin experiences.[53] Participants were instructed to provide ratings based on their session experience. In this version of the questionnaire, the ratings were based on data from three larger questionnaires (see Barrett et al., 2016 for details): Hallucinogen Rating Scale,[54] 5-Dimension Altered States of Consciousness,[55] and the States of Consciousness Questionnaire.[22]

Persisting effects. The secondary measure of most relevance to the purpose of this study was the *Retrospective*

Psilocybin Session and Persisting Effects Questionnaire, which was completed at 4 and 16 months after the second psilocybin session in participants who completed *both* sessions ($N = 24$). The questionnaire asked specifically about experiences that occurred during psilocybin sessions, as well as changes that the participant later attributed to their session experiences. It assessed changes in attitudes, moods, social interactions, and behavior including changes directly relevant to participants' religious/spiritual vocation (see Tables 3–6). A final question asked participants if they would want to take psilocybin again.

Several additional questions asked about participants' professional role, or vocation, in their religious traditions. At screening, participants were asked if, during their spiritual/religious career, and except for normal consideration of age-appropriate retirement, they had seriously considered leaving to pursue alternative activities. At screening, at 6 months after randomization (as part of the Interim Questionnaire), and at 4 and 16 months after psilocybin session 2, participants were asked a similar question about their thoughts *at the present time* about leaving their spiritual/religious vocation. At these same timepoints, participants were also asked to rate if they were suffering from "burnout" in their current spiritual/religious vocation (0 = not at all, 1 = to a small extent, 2 = to some extent, and 3 = to a great extent). Also, at these same timepoints, participants were administered the Mysticism Scale.[51]

The study assessed the occurrence, phenomenology, and attributions associated with *sacred experiences* (e.g., profound spiritual experiences). At screening, participants

Table 3. Assessments of Changes in Religious Attitudes and Behaviors Attributed to Psilocybin Experiences[a]

Measure	*4-month follow-up[b]*	*16-month follow-up[b]*	p[c]
Do you believe that the experiences during the two sessions and your contemplation of the experiences resulted in changes. . .[d]			
. . .changes in your social interactions with others related to your spiritual/religious vocation? For example, for a minister, rabbi, imam, or roshi, this could refer to supportive interactions with members of your spiritual community or interactions with other clergy or leaders in your community.[d]			
Percent rating moderate or strong positive change considered desirable	62.5%	70.8%	0.617
Percent rating moderate or strong negative change considered detrimental	0%	0%	1.000
. . .changes in your contemplative, prayer, or meditation practices?[d]			
Percent rating moderate or strong positive change considered desirable	50.00%	66.7%	0.289
Percent rating moderate or strong negative change considered detrimental	4.2%	0%	1.000
. . .changes in other behaviors related to your spiritual/religious vocation? This rating refers to changes in behavior other than the possible changes in social interactions or in your contemplative, prayer, or meditation practices rated above. For example, this could refer to changes in how you allocate your professional time; how you prepare for and give public talks; how you prepare for or participate in group or individual meetings; how you teach contemplative, prayer or meditation practices; the amount or quality of your pastoral care; etc.[d]			
Percent rating moderate or strong positive change considered desirable	58.3%	66.7%	0.617
Percent rating moderate or strong negative change considered detrimental	4.2%	4.2%	1.000
. . .changes in your attitudes about your spiritual/religious vocation?[d]			
Percent rating moderate or strong positive change considered desirable	50.00%	62.5%	0.248
Percent rating moderate or strong negative change considered detrimental	0.00%	4.2%	1.000
. . .changes in your appreciation or understanding of your own religious tradition?[d]			
Percent rating moderate or strong positive change considered desirable	50.00%	54.2%	1.000
Percent rating moderate or strong negative change considered detrimental	0.00%	4.2%	1.000
. . .changes in your appreciation or understanding religious traditions other than your own?[d]			
Percent rating moderate or strong positive change considered desirable	58.3%	70.8%	0.248
Percent rating moderate or strong negative change considered detrimental	0%	0%	1.000
. . .changes in your overall spiritual awareness in everyday life (e.g., mindfulness or sense of the divine in daily activities including vocational activities)?[d]			
Percent rating moderate or strong positive change considered desirable	70.8%	70.8%	1.000
Percent rating moderate or strong negative change considered detrimental	0%	0%	1.000

Assessments occurred 4 and 16 months after the second psilocybin session ($N = 24$).

[a]Data in table are from the Retrospective Psilocybin Session Questionnaire.

[b]Percentage data indicate the percentage of the 24 participants; continuous data in these columns are means (1SD).

[c]p values are from paired t-tests for continuous data and from McNemar's tests for categorical data; bold font designates $p < 0.05$.

[d]Positive items were scored on a 4-point scale: 0 = No change; 1 = Slight positive change that I consider desirable; 2 = Moderate positive change that I consider desirable; 3 = Strong positive change that I consider desirable. Negative items were scored a 4-point scale: 0 = No change; 1 = Slight negative change that I consider detrimental; 2 = Moderate positive change that I consider detrimental; 3 = Strong positive change that I consider detrimental.

Table 4. Assessments of Psilocybin Experiences and Changes in Non-Religious Attitudes and Behaviors Attributed to Psilocybin Experiences[a]

Measure	*4-month Follow-up[b]*	*16-month Follow-up[b]*	p[c]	d[d]
Rating of psilocybin experiences during either or both of your two sessions and your contemplation of those experiences[e]				
Overall spiritual significance of psilocybin experience[e]				
Mean (SD), maximum score = 8	7.04 (0.81)	7.13 (0.61)	0.426	0.109
Percent rating among the five most of lifetime including single most	87.5%	95.8%	0.480	
Percent rating single most of lifetime	25%	20.8%	1.000	
Overall personal meaning of psilocybin experience[e]				
Mean (SD), maximum score = 8	6.88 (0.85)	6.96 (0.75)	0.328	0.101
Percent rating among the five most of lifetime including single most	83.3%	79.2%	1.000	
Percent rating single most	16.7%	20.8%	1.000	
Overall psychological insight of psilocybin experiences[e]				
Mean (SD), maximum score = 8	6.67 (1.05)	6.92 (0.93)	0.207	0.251
Percent rating among the five most of lifetime including single most	75.0%	83.3%	0.617	
Percent rating single most	12.5%	20.8%	0.683	
Psychological challenge at the most psychologically challenging portion of the experience?[e]				
Mean (SD), maximum score = 8	5.21 (2.26)	5.00 (2.43)	0.559	–0.088
Percent rating among the five most of lifetime including single most	37.5%	41.7%	1.000	
Percent rating single most	12.5%	12.5%	1.000	
Do you believe that the psilocybin experiences during the two sessions and your contemplation of those experiences resulted in [changes. . .] (rating among 4 options [no change; slight; moderate; and strong] were made independently for positive changes and for negative changes[f]				
Changes in your current sense of personal well-being or life satisfaction?[f]				
Percent rating moderate or strong positive change considered desirable	66.7%	87.5%	0.074	
Percent rating moderate or strong negative change considered detrimental	4.2%	4.2%	1.000	
Changes in your attitudes about yourself and your life not related to your spiritual/religious vocation?[f]				
Percent rating moderate or strong positive change considered desirable	70.8%	83.3%	1.000	
Percent rating moderate or strong negative change considered detrimental	0%	4.2%	1.000	
*Changes in behaviors not related to your spiritual/religious vocation (*e.g., *recreational activities, exercise, dietary, social, alcohol use, etc.)?*[g]				
Percent rating moderate or strong positive change considered desirable	41.7%	54.2%	0.371	
Percent rating moderate or strong negative change considered detrimental	0%	0%	1.000	
Changes in attitudes and mood that you consider due to the experiences during either or both of your two psilocybin sessions and your contemplation of those experiences. Rate your present state compared with your state before your first session. *(mean [SD], % of maximum possible score*[g]				
Positive attitudes about life	61.54 (22.37)	66.41 (23.75)	0.106	0.210
Negative attitudes about life	3.40 (4.37)	4.74 (11.21)	0.516	0.140
Positive attitudes about self	56.44 (23.09)	61.36 (23.71)	**0.044**	0.210
Negative attitudes about self	5.23 (8.98)	5.98 (10.36)	0.609	0.077
Positive mood changes	54.17 (26.18)	58.43 (27.33)	0.093	0.158
Negative mood changes	4.07 (7.32)	6.20 (14.12)	0.379	0.170
Altruistic/positive social effects	52.17 (26.84)	60.08 (25.89)	**0.001**	0.299
Antisocial/negative social effects	1.25 (2.75)	1.58 (3.44)	0.656	0.106
Positive behavior changes	59.17 (30.35)	66.67 (28.08)	0.154	0.256
Negative behavior changes	5.00 (16.94)	3.33 (12.74)	0.679	–0.111
Increased spirituality	63.42 (24.61)	67.36 (25.65)	**0.043**	0.156
Decreased spirituality	1.73 (3.50)	2.17 (4.66)	0.583	0.106

[a]Data in table are from the Retrospective Psilocybin Session Questionnaire.

[b]Continuous data in these columns are means (1SD); percentage data indicate the percentage of the 24 participants.

[c]*p* values are from paired *t*-tests for continuous data and from McNemar's tests for categorical data; bold font designates $p < 0.05$.

[d]*d* indicates Cohen's *d* effect size.

[e]These items were scored on an 8-point scale from 1 = No more than routine, everyday experience; 5 = Similar to [meaningful; spiritually significant; psychologically insightful; psychologically challenging] experiences that occur on average once every 5 years; 6 = Among the 10 most [. . .] experiences of my life; 7 = Among the 5 most [. . .] experiences of my life; 8 = The single most [ ] experience of my life.

[f]Positive items were scored on a 4-point scale: 0 = No change; 1 = Slight positive change that I consider desirable; 2 = Moderate positive change that I consider desirable; 3 = Strong positive change that I consider desirable. Negative items were scored a 4-point scale: 0 = No change; 1 = Slight negative change that I consider detrimental; 2 = Moderate positive change that I consider detrimental; 3 = Strong positive change that I consider detrimental.

[g]Twelve subscales of the Persisting Effects Questionnaire, which was presented within the Retrospective Psilocybin Session Questionnaire.

were asked if they had had a sacred experience and, if so, approximately how many such experiences they have had. Most (83%) reported some history of sacred experiences prior to the study with a median of 4 (range of zero to "many"). At 4 and 16 months after the second psilocybin session, participants were given identical descriptive information about sacred experience. For these questions, participants were asked if, during one or both psilocybin

Table 5. Assessments of Sacred Experiences During Psilocybin Sessions[a]

Measure	*4-month Follow-up[b]*	*16-month Follow-up[b]*	p[c]	d[d]
Sacred experiences during psilocybin sessions. To orient participants to questions about sacred experiences in this table, participants were asked if, at some point during the two psilocybin sessions, they had one or more particularly profound spiritual experiences that they would consider to be a sacred experience. They were told that such experiences may go by many names, e. g., an encounter with God or with the God of your understanding; Mystical Experience; Unity Consciousness; Non-Dual Awareness; Buddha Mind; Kensho; Transcendental Consciousness; Brahman; Enlightenment; Cosmic Consciousness. They were told that if they had more than one such experience, they should rate the most profound experience.				
Rate the profound nature of the sacred experience compared with previous such experiences[e]				
Mean (SD), maximum score = 10	8.75 (1.45)	9.17 (1.13)	0.086	0.312
Percent rating no profound sacred experience	0%	0%	1.000	
Percent rating among five most including single most profound sacred experience	83.3%	91.7%	0.480	
Percent rating single most profound sacred experience	25.0%	41.7%	0.221	
Rating of duration of sacred experience				
Percent rating the duration as longer than any previous sacred experience	87.5%	79.2%	0.617	
Rate the degree to which you believe that your sacred experience showed you something absolutely true, and was not just an illusion[f]				
Mean (SD), maximum score = 5	4.50 (0.51)	4.46 (0.66)	0.714	–0.069
Percent rating strong or absolutely true	100%	91.7%	0.480	
Percent rating absolutely true	50.0%	54.2%	1.000	
Some sacred experiences include an authoritative (i.e., *utterly convincing) experience of Unity. Rate the intensity of Unity*[g]				
Mean (SD), maximum score = 5	4.33 (0.96)	4.46 (0.72)	0.503	0.144
Percent rating strong or extreme	83.3%	87.5%	1.000	
Percent rating extreme (5)	58.3%	58.3%	1.00	
Was the intensity of the experience of Unity as great or greater than any other sacred experience in your life?				
Percent rating the experience of Unity was greater than ever before	79.2%	79.2%	1.000	
Rate the degree to which you believe that your sacred experience has. . .[h]				
. . .enriched your contemplative, prayer or meditation practices				
Mean (SD), maximum score = 5	3.71 (1.37)	4.00 (1.18)	0.129	0.225
Percent rating strong or extreme	66.7%	79.2%	0.371	
Percent rating extreme	33.3%	37.5%	1.000	
. . .led to an increase in your effectiveness in your spiritual/religious vocation				
Mean (SD), maximum score = 5	3.46 (1.22)	3.92 (0.83)	0.053	0.428
Percent rating strong or extreme	54.2%	79.2%	**0.041**	
Percent rating extreme	20.8%	20.8%	1.000	
. . .increased your sense of the sacred in daily life				
Mean (SD), maximum score = 5	3.79 (0.98)	4.04 (1.04)	0.162	0.247
Percent rating strong or extreme	66.7%	79.2%	0.371	
Percent rating extreme	25.0%	37.5%	0.371	

Assessments occurred 4 and 16 months after the second psilocybin session ($N = 24$).

[a]Data in table are from the Retrospective Psilocybin Session Questionnaire.

[b]Continuous data in these columns are means (1SD); percentage data indicate the percentage of the 24 participants.

[c]*p* values are from paired *t*-tests for continuous data and from McNemar's tests for categorical data; bold font designates $p < 0.05$.

[d]*d* indicates Cohen's *d* effect size.

[e]The profound nature of the sacred experience was rated on 10-point scale from 1 = No, I did not have a profound sacred experience; 2 = Yes, of a profound nature similar in degree to sacred experiences that occur on average once a day; 8 = Yes, of a profound nature similar in degree to sacred experiences that were among the 10 most sacred experiences of my life; 9 = Yes, of a profound nature similar in degree to sacred experiences that were among the 5 most sacred experiences of my life; 10 = Yes, I had an experience that was the single most profound sacred experience of my life.

[f]This item was scored from 0 = Not at all (was just an illusion); 1 = So slight cannot decide; 2 = Slight; 3 = Moderate; 4 = Strong; 5 = Extreme (was absolutely true).

[g]The intensity of the experience of Unity within the psilocybin-occasioned sacred experience was rated on a 5-point scale from 1 = very low intensity; 5 = extreme intensity. To orient participants to the questions about the Unity within sacred experiences, participants were given the following information, which includes various descriptors of Unity of both the internal type (e.g., "pure awareness") and the external type (*e.g.,* "living presence in all things"). *Participants were told some sacred experiences include an authoritative (i.e., utterly convincing) experience of Unity, which may include one or more of the following: Experience of pure being and pure awareness (beyond the world of sense impressions); experience of oneness in relation to an "inner world" within; experience of the fusion of your personal self into a larger whole; experience of unity with ultimate reality; experience of eternity or infinity; experience of oneness or unity with objects and/or persons perceived in your surroundings; experience of the insight that "all is one"; awareness of the life or living presence in all things.*

[h]These items were scored from 0 = Not at all; 1 = So slight cannot decide; 2 = Slight; 3 = Moderate; 4 = Strong; 5 = Extreme.

Table 6. Assessments of Experiences of Unconditional Love During Psilocybin Sessions[a]

Measure	*4-month Follow-up[b]*	*16-month Follow-up[b]*	p[c]	d[d]
Unconditional love experiences during psilocybin sessions. At some point during the two sessions did you have one or more experiences of unconditional love (also sometimes called divine love, grace, metta)? If you had more than one such experience during the two sessions, please make the following ratings with respect to the most salient of the experiences.[e]				
Mean (SD), maximum score = 10	8.58 (2.30)	8.46 (2.62)	0.714	–0.050
Percent rating no experiment of unconditional love	4.2%	8.3%	1.000	
Percent rating among 5 most including single most	79.2%	79.2%	1.000	
Percent rating single most	41.7%	45.8%	1.000	
Rating of duration of experience of unconditional love				
Percent rating the duration of experience as longer than any previous experience	62.5%	66.7%	1.000	
Rating of intensity of experience of unconditional love				
Percent rating the intensity of experience as greater than any previous experience	70.8%	66.7%	1.000	
Rate the degree to which you believe that your experience of unconditional love has. . .[f]				
. . .enriched your contemplative, prayer or meditation practices				
Mean (SD), maximum score = 5	3.42 (1.56)	3.50 (1.50)	0.732	0.054
Percent rating strong or extreme	50.0%	66.7%	0.343	
Percent rating extreme	33.3%	25.0%	0.617	
. . .led to an increase in your effectiveness in your spiritual/religious vocation				
Mean (SD), maximum score = 5	3.33 (1.40)	3.62 (1.47)	0.307	0.203
Percent rating strong or extreme	50.0%	75.0%	0.077	
Percent rating extreme	25.0%	25.0%	1.000	
. . .increased your sense of the sacred in daily life				
Mean (SD), maximum score = 5	3.71 (1.33)	3.67 (1.37)	0.862	–0.031
Percent rating strong or extreme	70.8%	62.5%	0.724	
Percent rating extreme	29.2%	33.3%	1.000	

Assessments occurred 4 and 16 months after the second psilocybin session ($N = 24$).
[a]Data in table are from the Retrospective Psilocybin Session Questionnaire.
[b]Continuous data in these columns are means (1SD); percentage data indicate the percentage of the 24 participants.
[c]*p* values are from paired *t*-tests for continuous data and from McNemar's tests for categorical data; bold font designates $p < 0.05$.
[d]*d* indicates Cohen's *d* effect size.
[e]This item was scored on an 10-point scale from 1 = No, I did not have an experience of unconditional love; 8 = Yes, of a degree that was similar to experiences of unconditional love that were among the 10 most salient experiences of unconditional love of my life; 9 = Yes, of a degree that was similar to experiences of unconditional love that were among the five most salient experiences of unconditional love of my life; 10 = Yes, I had an experience that was the single most salient experiences of unconditional love of my life.
[f]These items were scored from 0 = Not at all; 1 = So slight cannot decide; 2 = Slight; 3 = Moderate; 4 = Strong; 5 = Extreme.

sessions, they had had one or more particularly profound spiritual experiences that they would consider to be a sacred experience. For several subsequent questions, participants were instructed that if they had more than one such experience during psilocybin sessions, that their ratings should be made with respect to the most profound of the experiences. Also, two additional questions relating to the noetic dimension of mystical experience asked participants to rate the degree to which they believed that their sacred experience showed them something that was "absolutely true" and was not just an illusion.

Other secondary measures (see Supplementary Data S2) described in this report were: demographic data at the time of screening (see Table 1), cardiovascular measures and session facilitator ratings assessed 10 min before and 30, 60, 90, 120, 180, 240, 300, and 360 min after capsule administration (see Supplementary Table S1), various questionnaires assessed 7 h after psilocybin administration (see Supplementary Table S3), and assessment of adverse effects (see Supplementary Tables S4 and S5). The study also included a wide variety of other secondary, exploratory measures assessed at screening and follow-up assessments (see Protocol in Supplementary Data S3).

Data analysis

All analyses were performed using R Statistical Software (v4.1.3).[56] Pearson's chi-square test was used to compare participants between groups on categorical variables. McNemar's test was used to compare paired categorical data within persons across timepoints (proportion endorsing specific responses). For comparisons of continuous data between groups, Welch's *t*-test was used, as it is a slightly more conservative test and less prone to type I error and more appropriate in variables with different variance across groups.[57] Paired *t*-tests were used for

within-person comparison at different timepoints. Effect sizes were calculated with Cohen's *d* for unpaired and paired comparisons as appropriate. Correlations were calculated using Pearson's *r*.

Statistical threshold was set at $p < 0.05$. Given the exploratory nature of this study, a large number of comparisons are reported across many items of interest. These results are not corrected for multiple comparisons because doing so would inflate the risk of type II errors and limit the value of these exploratory analyses. However, because the results are at increased risk of type I errors, they should be considered preliminary.

Results

Demographics

Participant demographics are shown in Table 1. The 29 participants who completed the interim analysis had a mean (SD) age of 49.8 (10.3) years. The group was 31% female, 97% White, 69% married, with most having post-graduate degrees (93%). The group had a mean (SD) of 22.3 (10.4) years of professional religious/spiritual engagement.

Representation of major world religions

The participant sample included representation of four major world religions with several denominations: **Christianity: 22** (four Episcopalian, four Presbyterian, three United Methodist, two Lutheran, two United Church of Christ, one Congregational, one Baptist, one Eastern Orthodox, one Pentecostal, one Reformed Church in America, one Roman Catholic, and one Unitarian Universalist); **Judaism: 5** (three Orthodox, one Reconstructionist, one Renewal); **Islam: 1** (Sunni); **Buddhism: 1** (Zen). Other major world religions, such as Indigenous traditions, Hinduism, Confucianism, and Taoism, were not represented.

The representation of four of the major religious traditions, as a percentage of total participants, is approximately as follows: Christianity 76%, Judaism 17%, Islam 3%, and Buddhism 3%. The representation of these major world religions in this trial is similar to their prevalence in the United States based on data from the Religious Landscape survey study, conducted in English and Spanish, among a nationally representative sample of adults estimated to cover 97% of the non-institutionalized U.S. adult population: Christianity 71%, Judaism 2%, Islam 1%, and Buddhism 1%.[58]

Between-group effects

Comparison of delayed group ($N = 16$) and immediate group ($N = 13$) on changes in attitudes, moods, and behaviors 6 months after randomization. At 6 months after randomization, the Immediate Group (which had received psilocybin) differed significantly from the Delayed Group across a range of measures assessing experiences, attitudes, behavior, and well-being over the past 5 months (Table 2). Sixty-two percent of the Immediate Group versus. 0% of the Delayed Group reported having had a spiritual experience they rated as among the five most spiritually significant experiences of their lifetime. The Immediate Group had significantly higher ratings than the Delayed Group on five of seven questions that assessed positive changes in several categories of religious attitudes and behavior (e.g., changes in attitudes about their vocation). Likewise, the Immediate Group had significantly higher ratings of changes in seven of nine positive religious attitudes (e.g., feel more effective as a religious leader). The Immediate Group also had significantly higher ratings on measures assessing positive changes in mood, altruistic effects, spirituality, and attitudes about life and self. On several items assessing negative changes on those same dimensions, the Delayed Group showed higher scores (more negative) than the Immediate Group, although generally showing smaller effect sizes. Finally, the Immediate Group had significantly higher ratings of personal well-being and life satisfaction than the Delayed Group.

Acute effects

Effects of psilocybin on session days in participants who completed both sessions ($N = 24$). Of the 24 participants who completed both sessions, 75% had their second dose increased to 30 mg/70 kg and the other 25% remained at 20 mg/70 kg.

For session facilitator ratings of cardiovascular measures and overall drug effect, inspection of group mean data over time from immediately before to 360 min after psilocybin administration showed the expected psilocybin time course with onset of effects occurring by 30 min and time to peak effects occurring between 113 and 159 min (Supplementary Table S2). Peak effects between the sessions 1 and 2 were generally not significantly different, except that in session 2, heart rate was higher and rating of joy/intense happiness was lower (Supplementary Table S1).

At 20 and 30 mg/70 kg dosing sessions, Total MEQ30 scores were 82 and 80, respectively, and the percentage of participants fulfilling *a priori* criteria for having had a "complete" mystical experience were 75% and 71%, respectively (see Supplementary Table S3). Eighty-eight percent of participants met *a priori* criteria for having had a "complete" mystical experience on one or both sessions (see Supplementary Table S3).

Participant ratings of various features of the psilocybin experiences 7 h after capsule administration showed no significant difference between sessions 1 and 2 (Supplementary Table S3). Based on the highest rating across the two sessions, participants rated the experience as

among the top five most spiritually significant (83%), personally meaningful (79%), psychologically insightful (71%), and psychologically challenging (46%) experiences of their lifetime. Mean participant ratings of overall drug effect intensity, peak joy or happiness, peak peace or harmony, and overall drug liking were intermediate between "Strong" and "Extreme." Participants also provided high ratings, 87% and 91% of mean maximum possible scores, on two measures assessing the mystical experience, MEQ30 Total and Mysticism Scale Total, respectively (Supplementary Table S3).

Persisting effects

Follow-up at 4 and 16 months after the second psilocybin session in participants who completed both sessions ($N = 24$). As shown in Tables 3–6, across the 40 questions or scales assessed at 4 and 16 months after the second psilocybin session, only four measures differed significantly between those two timepoints. These four measures were higher at 16 than 4 months and all related to beneficial persisting effects of psilocybin. Because of the similarity of the 4- and 16-month follow-ups, the results below focus on the final time-point (16 months).

Retrospective ratings of qualitative features of the psilocybin experiences at 16 months. Similar to ratings at the end of session days (Supplementary Table S3), at 16 months participants rated the psilocybin session experiences to be among the top five most spiritually significant (96%), personally meaningful (79%), psychologically insightful (83%), and psychologically challenging (42%) experiences of their lifetime (Table 4). For this study with clergy, several questions focused on ratings of the most profound sacred experience the participant may have had during the psilocybin sessions (Table 5), 92% of participants rated their experience to be among the five most profound sacred experiences of their lifetime, with 42% rating as the single most profound. Most (54%) rated the sacred experience as showing something "absolutely true" (e.g., not an illusion), and an additional 38% rated its truth as "strong." Most (79%) rated the sacred experience as including an experience of unity (e.g., "all is one" or "pure awareness") greater than ever before in their lifetime. Most also endorsed as "strong or extreme" that their sacred experience enriched their contemplative, prayer, or meditation practices (79%), increased their effectiveness in their spiritual/religious vocation (79%), and increased their sense of the sacred in daily life (79%). Table 6 shows that, when asked about the most salient experience of unconditional love during psilocybin sessions, 79% rated that experience as among the top five such experiences of their lifetime.

Changes in religious attitudes and behaviors attributed to psilocybin experiences at 16 months. Table 3 shows the percentage of participants who endorsed moderately or strongly positive (e.g., desirable) and negative (e.g., detrimental) changes in seven domains of spiritual/religious attitudes and behavior that they attributed to their psilocybin experiences. Most participants endorsed positive changes moderately or strongly (mean across domains was 65%, range 54–71%), whereas very few endorsed negative changes moderately or strongly (mean across domains was 2%, range 0–4%). Tables 5 and 6 show that most participants provided strong or extreme ratings that these experiences, which they largely regarded as sacred and encompassing of unconditional love: (1) enriched their contemplative, prayer, or meditation practices; (2) led to an increase in their effectiveness in their spiritual/religious vocation; and (3) increased their sense of the sacred in daily life.

Changes in non-religious attitudes and behaviors attributed to psilocybin experiences at 16 months. Attributions to psilocybin of positive and negative changes in non-religious attitudes and behaviors at 16 months are shown in Table 4. Most participants endorsed moderately or strongly positive changes in their current sense of personal well-being or life satisfaction (88%), their attitudes about themselves and life not related to their spiritual/religious vocation (83%), and behaviors not related to their spiritual/religious vocation (54%). A few (0–4%) endorsed negative changes in these three domains. Table 4 also shows that ratings of changes in attitudes about life and self, mood, altruistic and social effects, behavior, and spirituality were much higher for positive changes than negative changes (mean of 63% vs. mean of 4% of maximum possible score, respectively).

A final question at the 4- and 16-month follow-ups asked: "Would you want to take psilocybin again, assuming that you could do so under lawful circumstances?" There were three mutually exclusive response options. The percentage of the 24 participants that endorsed each of the response options at 4 and 16 months, respectively, were: "no, never," 0%, 0%; "possibly—perhaps sometime in the future," 8%, 13%; and "yes," 92%, 88%.

Lifetime mystical experience. At screening, the total mean (SD) scores on the lifetime version of the Mysticism Scale were 211.9 (45.7). As shown in Figure 3, total scores on the lifetime version of the Mysticism Scale at both 4 and 16 months after the second psilocybin session were significantly higher than at screening ($p < 0.001$). Means and SDs were 211.88 (45.66), 252.38 (25.87), and 265.83 (21.40) at screening, 4 months, and 16 months, respectively. Scores at 16 months were also higher than at 4 months ($p = 0.005$).

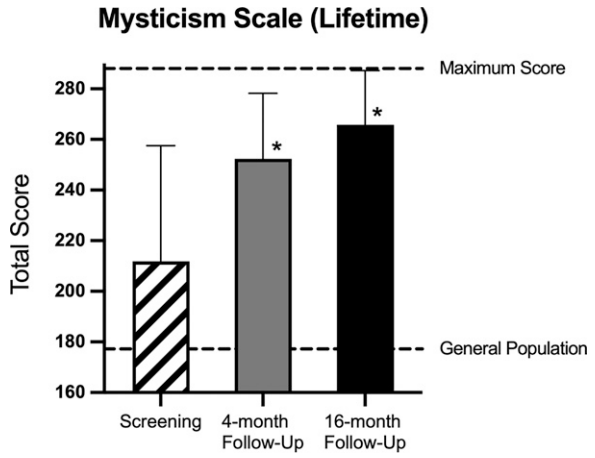


Fig. 3. Mysticism Scale (Lifetime). Total score on lifetime version of the Mysticism Scale at screening and at 4 and 16 months after the second psilocybin session. Bars are mean scores with brackets showing 1 SD ($N = 24$). Asterisks show significant differences from the screening assessment ($p < 0.001$). Scores at 16 months were also significantly higher than at 4 months ($p = 0.005$). For comparison, lower dashed line shows mean score at screening from a psilocybin study with participants ($N = 75$) from the general population. (25) Upper dashed line shows maximum possible score.

Consideration of leaving their spiritual/religious vocation. At screening, 71% of the 24 participants who later completed both psilocybin sessions endorsed that, sometime before the study, they had seriously considered leaving their spiritual/religious vocation to pursue alternative activities, with 8% endorsing that they were currently considering leaving their vocation. At 6 months after randomization (Interim Questionnaire), the Delayed Group and Immediate Group did not significantly differ in their endorsement of currently considering leaving their vocation (0% and 15%, respectively, $p = 0.104$). At 4 and 16 months after the second psilocybin session, 25% and 17%, respectively, of the 24 completers endorsed currently considering leaving their vocation. These rates of endorsement were not significantly different from the 8% endorsement at screening ($p = 0.289$ and 0.683, respectively).

Rating of suffering from vocational burnout. At screening, participant ratings of suffering from burnout in their current spiritual/religious vocation were low (1.00 [0.66], mean [SD]) in the 24 participants who completed both psilocybin sessions. This numerical value corresponds to suffering burnout to a small extent. At 6 months after randomization (Interim Questionnaire), ratings of the Delayed Group and the Immediate Group were not significantly different (mean [SD], respectively, 0.94 [0.77] and 1.08 [0.64], $p = 0.599$). At 4 and 16 months after the second psilocybin session, mean [SD] ratings were 0.96 [1.00] and 0.79 [0.93], respectively, for the 24 participant completers. These ratings were not significantly different from each other ($p = 0.328$), nor were they significantly different from screening ($p = 0.833$ and 0.307, respectively).

Adverse events

There were no serious adverse events in this study. Supplementary Tables S4 and S5 show adverse effects recorded during and after both the 20 and 30 mg/70 kg dose of psilocybin.

Discussion

The present study found that a group of clergy from four major world religions reported a variety of benefits from their psilocybin experiences relevant to their religious as well as to their non-religious lives. Of particular interest in this study were the effects of psilocybin administration on religious attitudes and behavior. The primary outcome assessment was a questionnaire that measured positive and negative changes in religious and non-religious attitudes, moods, and behaviors over the past 5 months (6 months after screening). Compared with participants in the Delayed Group (who had not yet received psilocybin), participants in the Immediate Group who received psilocybin shortly after screening reported significantly greater changes that they considered positive in their religious practices (e.g., contemplation or prayer), attitudes about their religious vocation, appreciation of both their own and other religious traditions, spiritual awareness in everyday life, feeling more effective as a spiritual leader, having a deeper understanding of their religious tradition, being more certain about the positive role of religion in the world, increased appreciation for religious traditions other than their own, being more certain about the truth of certain metaphysical religious teachings, and taking more time for devotional life.

These reported beneficial effects of psilocybin on religious attitudes and behavior persisted. Consistent with the results above, follow-up assessments at 16 months after the second psilocybin session in participants who completed both sessions ($n = 24$) showed that a majority of participants endorsed having moderate-to-strong positive and desirable changes in religious attitudes and behavior that they attributed to their psilocybin sessions. These included their attitudes (63%), behavior (67%), and social interactions (71%) related to their religious

vocation, their contemplative, prayer, or meditation practices (67%), their appreciation of their own religious tradition (63%), their appreciation of religious traditions other than their own (71%), and their spiritual awareness in everyday life (71%). Also, at the 16-month follow-up, almost all participants (96%) retrospectively rated the overall spiritual significance of the psilocybin experiences to be among the top five such experiences of their lifetime, and (92%) endorsed having had at least one sacred experience during a psilocybin session that they considered to be among the top five such experiences of their lives, with 42% rating it to be the single most profound experience of their lifetime. Additionally, at 16 months, most participants provided strong or extreme endorsement that the experience: enriched their contemplative, prayer, or meditation practices (79%), increased their effectiveness in their religious vocation (79%), and increased the sense of the sacred in daily life (79%).

Although the primary aim of this study was to assess enduring changes in moods, attitudes, and behavior after psilocybin of specific relevance to religious leaders, the study also included a variety of acute (e.g., psilocybin session day) and enduring (e.g., post-session) assessments that can be compared with previous studies that used some identical assessments of the effects of similarly high doses of psilocybin in different participant populations (see Supplementary Data S4).

The current study improves upon and extends the previously described Good Friday Experiment,[5,47,48] which documented that administration of psilocybin to Protestant seminary students in a group religious setting occasioned mystical experiences having enduring positive changes in attitudes and behavior. This study does so specifically by: (1) studying professionally engaged clergy from four major world religions; (2) conducting psilocybin sessions individually to maximize the independence of each participant's data; (3) administering psilocybin as part of a standard approach using a dyad facilitator team with careful screening, preparation, monitoring during psilocybin sessions, and post-session integration; (4) administering psilocybin in a controlled living-room-like setting rather than in a chapel during a religious service; (5) including additional measures of attitudes, social relationships, and other behaviors related to participants' religious/spiritual vocation; and (6) increasing the number of psilocybin sessions from one to two.

Potential follow-ups to the present study could include larger and more rigorously designed trials in samples of professional clergy to evaluate safety and replicability. Investigations, as addressed elsewhere, could further explore the potential role of psychedelic-facilitated spiritual experiences in religious education and training,[5,48] in increasing tolerance of other religious traditions,[48,58] and for chaplains, given their existential and spiritual training, to serve as facilitators in psychedelic sessions, notably in palliative and end-of-life care.[59,60]

We note that this study's findings could lead to inflated expectations of benefits and under-appreciation of risks. Widespread, indiscriminate, and insufficiently supported use of psychedelics likely played a large role in the almost complete functional prohibition of human psychedelic research starting in the mid-1960s, which endured for decades despite early promising research.[61] With the recent renewal of psychedelic research beginning to more rigorously document beneficial effects, some media accounts are once again promoting scientifically un-verified benefits and omitting mention of very real risks.[62,63] Further systematic research can help to improve upon paths taken in decades past. This caution applies to the emerging therapeutic psychedelic research but even more so for the very preliminary research on psychedelics and religion, as anticipated by Walter Pahnke six decades ago.[47] Future research in this domain should include additional and more rigorous assessments of both short- and longer-term risks, including risks of epistemic harm, which is developing false or maladaptive beliefs. Psychedelic experiences that bring about false beliefs could, for example, lead to toxic cults and cult-like behavior.[64–66] There is also concern among some scholars that psychedelic experiences may lead people to unfounded supernatural explanations instead of naturalistic understandings of the world.[67] While participants in this trial rated many of the changes such as increased certainty regarding their religious metaphysical beliefs as beneficial, future research could explore the personal and social consequences of reinforcing such beliefs.

Limitations

Further research is needed to address the many limitations of the current study, including its small sample size and that participants were primarily White, male, married, and had high levels of educational attainment. Expectancy bias of the self-selected participants as well as of study staff and study facilitators may have affected outcomes. There was no representation of Indigenous religious traditions, Hinduism, Taoism, Confucianism, and other world religions. However, although the number of participants from the religions represented differed substantially, the prevalence approximately matched the representation of each of those religions in the United States.[68] Clergy members willing to participate in a psychedelic study may well hold more open or liberal religious attitudes on average compared with the general population of clergy, which may limit generalizability of results to larger clergy populations.

Methodological limitations include the use of a waitlist control, the absence of a pharmacologically active comparison condition, use of some unvalidated outcome

measures, and the complete reliance on self-reported outcome measures. It has been argued based on evidence in therapeutic clinical trials that delayed intervention designs are particularly poor controls in that participants randomized to wait may have worse behavioral outcomes than they would have if they had not joined the study.[69] Future research designs should consider randomized comparison to active placebo rather than waitlist controls. In addition, several of the questions, including those reported in Table 5, included the phrase "your sacred experience" or "sacred experience" in reference to session experiences, which may have biased responses to them. Similarly, advertisements describing this as a study of "sacred experiences" could have biased its results.

Finally, the term "mystical experience" in this study refers to the phenomenologically descriptive use of the term informed by scholars representing a diverse particular set of theoretical, religious, and/or spiritual orientations, including William James (1), Bertrand Russell (3), Aldous Huxley (4), Walter Stace (2), Walter Pahnke (5), Ralph Hood (7), and others (6, 8). Some scholars have noted limitations in these definitions of mystical experience and have called for research to consider a wider range of adjacent states of consciousness.[70] This study did not assess that wider range of experiences nor their potential effects on study participants.

Conclusion

This study found that psychedelic-naïve, professionally trained and engaged clergy from four major world religions experienced and interpreted their experiences with psilocybin to be religiously significant, meaningful, and generally beneficial. The frequency and types of reported adverse effects were similar to those reported in previous studies with psilocybin in healthy participants and in patient populations, and no serious adverse events were reported. The study found that the intervention given to clergy participants showed a similar risk/benefit profile to that reported previously in other participant samples, including persisting benefits and enduring attributions of high degrees of meaning and significance to the psilocybin experience. A primary implication is that further psychedelic research among religious leaders can proceed with reasonable safety given similarly rigorous informed consent, screening, preparation, and support during and after psychedelic administration. Given the widespread understanding that set and setting are important factors in shaping psychedelic effects, future well-controlled trials could examine such effects in larger samples of participants representing different religious traditions and non-religious groups in order to understand the effects of worldviews and cultural expectancies on experiences and their consequences. The historical associations between psychedelic experiences and religious and spiritual attributions have long been noted,[71] and we believe it is compelling to better understand, through ongoing study, the nature of these associations and why they are so persistent.

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Authors' Contributions

R.R.G.: Conceptualization, methodology, investigation, writing—original draft, visualization, supervision, project administration, funding acquisition. R.J: Conceptualization, methodology, writing—review and editing, funding acquisition. W.A.R: Conceptualization, methodology, investigation, writing—review and editing, supervision. M.W.J: Conceptualization, methodology, software, writing—review and editing. N.D.S: Formal analysis, data curation, writing—review and editing. A.P.B: Conceptualization, methodology, investigation, writing—review and editing, supervision. S.R: Conceptualization, methodology, investigation, writing—review and editing, supervision, project administration, funding acquisition.

Author Disclosure Statement

R.R.G. (deceased 16 October 2023) was a member of the Board of Directors of the Heffter Research Institute. W.A.R. was Director of Therapy at Sunstone Therapies and has conducted research supported by Compass Pathways. He is a Senior Advisor to Sunstone Therapies, and he owns stock in Compass Pathways and Sunstone Therapies. R.J. advises the CSP Fund, Usona Institute, and the UC Berkeley Center for the Science of Psychedelics. M.W.J. has served as a consultant to AJNA Labs LLC, AWAKN Life Sciences Inc., Beckley Psychedelic Ltd., Clarion Clinics, Reunion Neurosciences, Mind Medicine Inc., Negev Capital, and Otsuka Pharmaceutical Development & Commercialization Inc, and has received research funding from NIDA, Heffter Research Institute, Fifth Generation, Inc., and Mydecine Innovations Group. N.S. is a consultant to the data safety monitoring board member for the Lundquist Institute. A.P.B. is on the Scientific Advisory Board for the Steven & Alexandra Cohen Foundation, a consultant for the Center for Psychedelic Therapies and Research at the California Institute of Integral Studies. He receives funding support for clinical research from the Steven & Alexandra Cohen Foundation and the Joe and Sandy Samberg Foundation. S.R. currently receives, or has received in the

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The studies were conceived together with the intention to combine data from the JHU and NYU studies as done in this article. The studies used nearly identical protocols. However, the studies were run with separate institutional review boards (IRBs) (Johns Hopkins Medicine IRB monitored the JHU site while the NYU Grossman School of Medicine IRB monitored the NYU site), separate investigator-initiated INDs, and separate participants. R.G. was the principal investigator (PI) at the JHU site and S.R. was the PI at the NYU site.

The Johns Hopkins Medicine Institutional Review Board (JHM IRB) conducted an audit of the JHU site (IRB00036973—"Effects of Psilocybin-facilitated Experience on the Psychology and Effectiveness of Professional Leaders in Religion") and concluded that the following must be reported to all journals and disclosed in all publications where data related to this study may be published: (1) There were two unapproved study team members, one who was also a study funding sponsor, directly engaged in the research. (2) There was an additional approved study team member whose role as a funding sponsor of the study was not disclosed to the IRB and who directly led the qualitative analysis. (3) Conflicts of interest related to the two individuals who were engaged in the research and also served as funding sponsors were not appropriately disclosed nor managed. (4) The funding sponsorship for this study was not disclosed to the JHM IRB.

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The mission statements of the funding organizations are provided, as some are relevant to the content of the study. They are as follows:

- ***The CSP Fund*** is managed by the San Francisco Foundation, a 501(c)(3) public charity, and is advised by R.J. It is the successor to the Council on Spiritual Practices, a 501(c)(3) public charity convened by R.J. as "a collaboration among spiritual guides, experts in the behavioral and biomedical sciences, and scholars of religion, dedicated to making direct experience of the sacred more available to more people." The CSP Fund received contributions for this study from the RiverStyx Foundation, MST 1998 Trust FBO T C Swift, the Turnbull Family Foundation, Carey and Claudia Turnbull, and Dr. Bronner's. R.J. was involved in the conception and design of this study and in the preparation of this article.
- ***Turnbull Family Foundation*** is a 501(c)(3), further classified as a private foundation within the meaning of Section 509(a). It is required to file a Form 990-PF return of private foundation annually. It has no mission statement. It has donated exclusively to other 501(c)(3)'s, solely awarding grants for scientific research.
- ***The RiverStyx Foundation*** is a 501(c)(3) charitable organization co-directed by T. Cody Swift. Its mission statement indicates that it "works to provide a bridge to the relinquished parts of ourselves, our society, and our ecology by funding and initiating projects that demonstrate the potential for healing when life is embraced in its fullest expression."

Supplementary Material

Supplementary Data S1
Supplementary Data S2
Supplementary Data S3
Supplementary Data S4
Supplementary Table S1
Supplementary Table S2
Supplementary Table S3
Supplementary Table S4
Supplementary Table S5

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