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The perceptions of cancer health-care practitioners in New Zealand and the USA toward psychedelic-assisted therapy with cancer patients: A cross-sectional survey

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Abstract

Objectives. A resurgence of research investigating the administration of psychedelic compounds alongside psychotherapy suggests that this treatment is a promising intervention for anxiety, depression, and existential distress in people with cancer. However, psychedelic treatment that induces a mind-altering experience potentially poses barriers to vulnerable cancer patients, and health-care practitioners may have concerns about referring their patients to trials investigating this approach. The aim of the current study was to investigate the perceptions of cancer health-care practitioners based in New Zealand and the USA related to psychedelic-assisted therapy.

Methods. This study utilized a cross-sectional survey of cancer health-care practitioners in New Zealand and the USA via convenience sampling to identify their perceptions about the concept of conducting psychedelic-assisted therapy with cancer patients.

Results. Participants perceived that (1) psychedelic-assisted therapy has the potential to provide benefit for cancer patients, (2) research in this area across a variety of domains is important, (3) work should consider spiritual and indigenous perspectives of health, and (4) there was willingness to refer patients to trials in this area, especially patients with advanced disease who were no longer going through curative treatment. Participants in the USA had greater awareness of psychedelics than the New Zealand sample; however, New Zealand participants more strongly believed that spiritual/indigenous factors should be considered in psychedelic-assisted therapy. Significance of results. Cancer health-care practitioners in our sample considered research investigating the potential for psychedelic-assisted therapies to be important and may be more open to studies that start in palliative and end-of-life contexts.

Introduction

Cancer is associated with high rates of psychological dysfunction including depression and anxiety (Mitchell et al. 2011). Such difficulties impact quality of life (Smith et al. 2003) and are related to poorer treatment outcomes (Arrieta et al. 2012). Despite recommendations that psychological support is available for patients across the cancer trajectory (National Comprehensive Cancer Network 2003), practical barriers limit the feasibility of many interventions. These challenges are exacerbated during advanced stages where patients can be physically unwell and are managing numerous medical appointments (Henry et al. 2008). Interventions in this context need to be timely and effective. An approach that appears to offer promise and is generating interest in cancer contexts is psychedelic-assisted therapy (PAT). Given the key role that cancer health-care practitioners have in provision of treatment and referral to research for people with cancer, the current study aimed to investigate the perceptions of this stakeholder group.

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In recent years, there has been a revival of research investigating the therapeutic potential of psychedelic agents. Reviews of first- and second-wave trials investigating psychedelics in cancer and serious illness settings have suggested that guided psychedelic experience alongside psychotherapy can produce rapid and sustained improvements in both psychiatric and existential distress, with some initial evidence for physical symptom control (Maia et al. 2022; Ross 2018; Ross et al. 2022). One study found that a single high dose of a psychedelic (psilocybin) produced sustained reductions in existential distress (depression, anxiety, and fear of death) and increases in quality of life in people with cancer with long-standing depression and/or anxiety (Griffiths et al. 2016). These antidepressant and anxiolytic effects appear to be partially mediated by "mystical-type experiences" perceived by participants as highly meaningful and spiritual. Another study of psilocybin-assisted therapy in cancer patients found that approximately 4 years post administration, 60-80% of participants met criteria for a clinically significant antidepressant or anxiolytic response (Agin-Liebes et al. 2020). Additionally, another trial demonstrated rapid antidepressant effects among participants with treatment-resistant depression within 1 day of a single psychedelic dose of another psychedelic (ayahuasca) (Truu 2019). Such fastacting and effective responses are particularly relevant in the context of life-limiting illness where timeliness is a priority.

However, there appear to be considerable barriers to psychedelic intervention in the cancer context. Cancer patients are vulnerable and often have complex competing personal and medical commitments. People participating in trials investigating psychedelic experiences need to spend many hours preparing, having the psychedelic experience, and engaging in post-treatment psychotherapy. Furthermore, psychedelic compounds are classified as Schedule 1 illegal drugs in the USA and NZ based on 3 criteria: first, that they are deemed to have a high potential for abuse; second, they are considered to have "no therapeutic value" even in medical contexts; and lastly that there is a lack of accepted safety for use (Nutt et al. 2013). These classifications broadly remain, despite a lack of scientific consensus to support them. However, some jurisdictions in the USA have recently decriminalized possession of psychedelics or legalized medical use (Psychedelic Alpha 2022). Despite these recent developments, treating health practitioners may still be wary about referring patients to trials investigating psychedelic therapies, especially given that, at high doses, psychedelics have been associated with transient episodes of psychological distress (Griffiths et al. 2016).

The perceptions of health-care practitioners are consistently shown to influence the uptake of therapeutic innovations (Garján et al. 2012). Understanding the perceptions of this stakeholder group is an important first step in developing clinical trials. Qualitative research with a small number of cancer health-care practitioners in New Zealand (NZ; N=12) provides preliminary evidence that this group supports research in the area (Reynolds et al. 2021). However, quantitative research with a larger sample and in another country is required to determine the generalizability of these qualitative findings and allow comparison among nations where psychedelic compounds have different cultural acceptability and legal statuses.

The current study

The primary aim of this work was to quantify perceptions among cancer health-care practitioners identified in previous qualitative work (Reynolds et al. 2021). The project had 3 objectives:

- 1. To assess cancer health-care practitioners' perceptions about PAT for cancer patients and their likelihood to refer to trials investigating this approach.
- 2. To assess whether there are differences in perceptions among practitioners in 2 countries that have different legal and cultural contexts (NZ and USA).
- 3. To identify predictors of perceptions regarding PAT in cancer health-care practitioners.

Method

Study design and participants

An anonymous, cross-sectional, online survey was conducted with cancer health-care practitioners aged 18+ in NZ and the USA in accordance with the Declaration of Helsinki (Code of Ethics of the World Medical Association). NZ data were collected from February to April 2021 and US data were collected between December 2021 and April 2022. Across NZ, convenience sampling of medical, cancer care, and palliative networks was combined with snowball sampling via social media (Facebook, LinkedIn, and Twitter) to recruit doctors, nurses, and allied health-care practitioners. In the USA, the survey was sent to the American authors' social networks at large health-care centers, primarily located in California, Florida, Kentucky, Massachusetts, Michigan, and Ohio, while further disseminated on cancer, palliative care, and health-care practitionerfocused forums on Reddit, as well as to the memberships of the Organization of Psychedelic and Entheogenic Nurses and the Academy of Oncology Nurse & Patient Navigators. Because the survey was anonymous, we are unable to provide information about the proportions of responses coming from these different sources. Interested participants were sent study information and a link to the online survey hosted by Qualtrics. NZ participants were offered the opportunity to enter a prize draw for an iPad mini, while no participation incentive was offered to US participants. Only participants who fully completed the survey were included in analyses.

Measures

The survey was designed by a team of cancer health-care practitioners and academic researchers (authors L.M.R., B.B., J.W., E.M., A.S., N.L., N.H., F.S., and A.A.) experienced in questionnaire design and was piloted before being finalized. Survey instruments for NZ and US participants were essentially identical apart from different answer choices for race/ethnicity and slight modifications in wording to adjust for variations in English between the 2 countries. For example, the NZ version stated "How many years has it been since you qualified for your profession?" and the US version asked "How many years has it been since you completed training for your profession?"

Demographic/professional characteristics

The survey began with questions about demographic and professional characteristics including age, gender, ethnicity, professional practice, years since qualification, years working with cancer patients, average number of patients per week, patient population, and involvement in previous research.

Awareness of psychedelic drugs and PAT

Awareness of psychedelic drugs and PAT were assessed in 2 ways. Participants were asked to indicate their awareness of PAT on

Table 1. Confirmatory factor loadings based on maximum likelihood extraction with direct oblimin rotation for the Perceptions of Psychedelic-Assisted Therapy (POPAT) scale

		Warrants research	Potential benefits	Spiritual/ indigenous
1	It is important to consider how psychedelic-assisted therapy might fit alongside medical cancer treatment	0.856		
2	I am comfortable with research in this area as long as studies are well designed and follow rigorous safety protocols	0.802		
3	I am supportive of psychedelic-assisted therapy if it helps with a patient's depression or anxiety	0.914		
4	Psychedelic-assisted therapy warrants further research as a potential treatment for anxiety and depression in patients with cancer	0.596		
5	The administration of psychedelic compounds could increase the risk of mental health issues in patients with cancer			
6	Research should start by investigating psychedelic-assisted therapy at low doses (microdoses) before researching higher doses which induce a psychedelic experience			
7	Psychedelic-assisted therapy could be helpful in treating anxiety and depression in patients with cancer		0.577	
8ª	Psychedelic-assisted therapy could be helpful in alleviating spiritual distress in patients with cancer			
9	Psychedelic-assisted therapy could help reduce fear of dying in patients with cancer		0.705	
10	Psychedelic-assisted therapy could be more effective than current treatments in treating depression and anxiety		0.572	
11	It is important to consider spirituality in the use of psychedelic-assisted therapy in patients with cancer			0.774
12 ^b	It is important to consider how psychedelic-assisted therapy fits with traditional indigenous healing practice			1.013

Loadings of less than 0.5 are suppressed.

a scale from 0 ("I'd never heard of psychedelic-assisted therapy before today") to 10 ("I'd heard a lot about psychedelic-assisted therapy before today"). Participants were also asked which compounds they had heard of out of 8 psychedelic compounds. The sum of compounds (score of 0–8) was added to the awareness of PAT rating score (score of 0–10) to give a total awareness score out of 18. The reliability of this score was adequate (Cronbach's $\alpha=0.73$).

Perceptions of PAT

A scale to assess perceptions of PAT was developed for the study based on prior qualitative research (Reynolds et al. 2021). The Perceptions of Psychedelic-Assisted Therapy (POPAT) scale included 12 items covering a range of perceptions related to potential benefits and considerations for future research (Table 1). Participants indicated how much they agreed or disagreed with statements using a scale from -10 ("strongly disagree") to 10 ("strongly agree") with a mid-point score of 0 ("neutral"). Exploratory factor analysis was conducted by first assessing the Kaiser-Meyer-Olkin score (0.87), which indicated that the sample in the current study (N = 245) was adequate for factor analysis and Bartlett's test of sphericity ($\chi^2 = 1,562.15$, p < 0.001) met the homogeneity of variance assumption. Item 8 was removed to minimize multicollinearity due to correlations >0.8 with other items. Maximum likelihood extraction and direct oblimin rotation revealed 2 components with eigenvalues over 1; however, a third component with a loading of 0.97 was retained following examination of the scree plot, item loadings, and face validity of how the items fit together. Items 5 and 6 were culled because loadings were less than 0.5. The overall model fit was significant χ^2 (25) = 61.29, p < 0.001, and the 3-component solution explained 72.86% of the variance. The first factor, "warrants research," included items calling for well-designed trials that investigate the safety and efficacy of PAT. The second factor, "potential benefits," included items describing the potential for PAT to benefit anxiety, depression, and fear of dying. The final factor, "spiritual/indigenous considerations," contained 2 items related to broader perspectives of health including consideration of spiritual and indigenous healing practice. The scales had good reliability ("warrants research": $\alpha = 0.88$, "potential benefits": $\alpha = 0.89$, and "spiritual/indigenous considerations": $\alpha = 0.86$). Mean scores were calculated for all scales.

Likelihood of referring patients

Participants were asked to indicate the likelihood of referring cancer patients to a trial investigating (1) the safety and (2) efficacy of PAT on a sliding scale from -10 (very unlikely) to 10 (very likely); the mean of these items provided a "likelihood to refer" score. Next, to understand whether there were differences in the likelihood of referral across various contexts, participants were asked to indicate the likelihood of referring a patient to a trial if the patient was going through different cancer treatments (Figure 2) and at various stages of treatment (Figure 3).

^aRemoved due to issues of multicollinearity.

^bNZ wording and US wording differed: NZ wording – "It is important to consider how psychedelic-assisted therapy fits with traditional Māori healing practice (rongoā)"; US wording – "It is important to consider how psychedelic-assisted therapy fits with traditional Indigenous peoples/Native American healing practice."

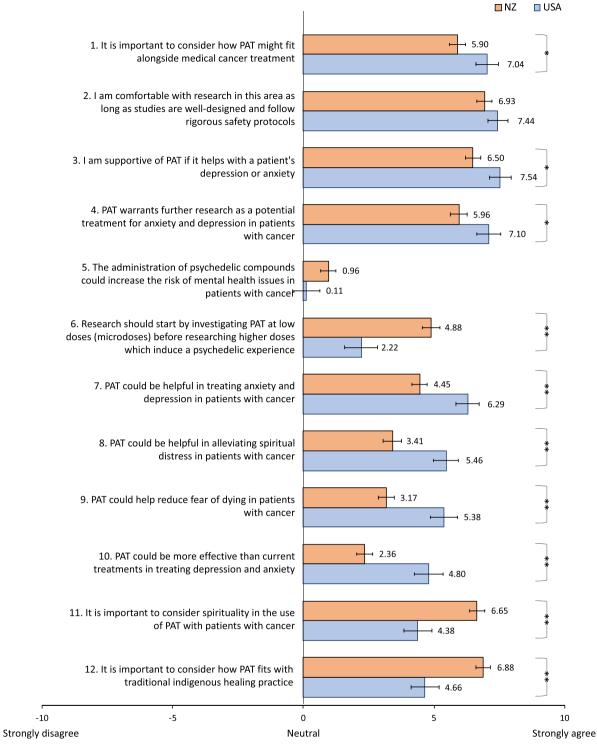


Fig. 1. Bar graph showing mean scores of individual items on POPAT measure with standard error bars where possible scores range from $\neg 10$ (strongly disagree) to 10 (strongly agree) and indicating differences across countries. POPAT = perceptions of psychedelic-assisted therapy, PAT = psychedelic-assisted therapy. *p < 0.05, **p < 0.00.

Statistical analysis

Analyses were conducted with IBM SPSS Statistics v.26 software. All tests were 2-sided at a 5% significance level. Demographic, professional characteristics, and awareness of psychedelics across countries were assessed using t-tests for continuous data and chi-square analyses for categorical data. To assess perceptions

related to PAT, the likelihood of practitioners referring patients to trials, and whether there were differences across countries, mean scores for individual items on the POPAT and likelihood to refer questions were reviewed and *t*-tests assessed differences. To determine predictors of perceptions, bivariate associations among demographic, professional characteristics, and perceptions of PAT were assessed using Pearson's correlations (continuous data) and

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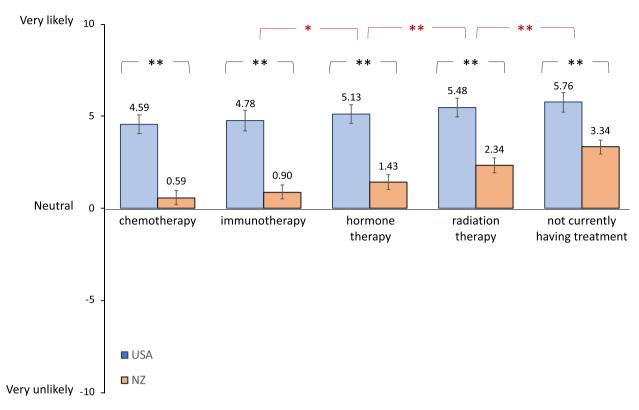


Fig. 2. Bar graph showing mean scores with standard error bars of likelihood of referring patients to a psychedelic-assisted therapy trial when going through various cancer treatments with differences across countries (indicated in black) and differences across various treatments (indicated in red). $^*p < 0.05$, $^{**}p < 0.00$.

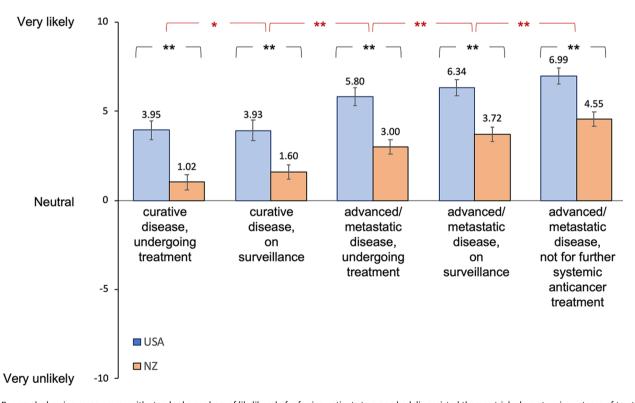


Fig. 3. Bar graph showing mean scores with standard error bars of likelihood of referring patients to a psychedelic-assisted therapy trial when at various stages of treatment with differences across countries (indicated in black) and differences across stages of treatment (indicated in red). *p < 0.05, **p < 0.05.

Spearman's Rho (categorical data). These correlations informed the decision about which variables to include in multivariate analyses. Multivariate regression models assessed the demographic and

professional predictors of POPAT subscales (warrants research, potential benefits, and spiritual/indigenous considerations) and likelihood to refer.

Results

A total of 245 participants completed the survey including 163 in the NZ and 82 in the US samples (Table 2). Age ranged between 22 and 81 years (median = 55 years) with no difference in ages across countries. There was a difference in the gender split among countries, with the NZ sample being predominantly female (87%), whereas the gender discrepancy in the US group was less (female 60%). Most NZ participants identified as NZ European (67%), with a small percentage identifying as indigenous (NZ Māori, 6%). Similarly, the majority of the US samples were Caucasian/White (77%) with only 4% identifying as indigenous. There was a difference in profession across countries; the US sample was more likely to be medical doctors (40%) or nurses (43%), whereas the NZ sample was more evenly spread across professions. As might be expected given the difference in professions, the US sample was more likely to provide cancer treatment. Importantly in the context of perceptions of PAT, the US sample had a greater total awareness of psychedelics and PAT (means: USA = 11.12 vs. NZ = 6.45) (Figure 1).

Cancer health-care practitioners' perceptions

To understand health-care practitioners' views about PAT, we assessed responses to items of the POPAT scale. Mean scores on all items fell between neutral and strongly agree (Figure 1). Compared to NZ participants, those from the USA rated items on the "warrants research" (items 1, 2, 3, and 4) and "potential benefits" (items 7, 9, and 10) scales significantly higher. The only items where NZ respondents rated higher than US respondents were item 5, suggesting an increased risk of mental health issues, item 6 that research should start by investigating microdoses, and items 11 and 12 urging consideration of spirituality and indigenous healing practice. Notably, the total mean for item 5 (risk of mental health issues) was closer to neutral than other items.

Willingness to refer cancer patients

The mean scores for likelihood of referral were greater than neutral in all scenarios (Figure 2). Of note, there were differences across treatments, with participants least likely to refer a patient during chemotherapy (M = 1.95, SD = 5.21) and most likely to refer a patient not having treatment (M = 4.17, SD = 5.02). Across scenarios of various stages of cancer (Figure 3), the likelihood to refer was greater than neutral in all instances. Referral was least likely when a patient was undergoing treatment for curative disease (M = 2.04, SD = 5.24) and most likely when patients had advanced disease and were not designated for further anti-cancer treatment (M = 5.36, SD = 4.81). Of note, US participants were more likely to refer cancer patients compared to NZ practitioners across all scenarios.

Predictors of perceptions about PAT

Bivariate correlations indicated that awareness was positively associated with each of the outcome measures (Table 3). Those with a greater number of years working with cancer patients were less likely to believe that research was warranted. Being a medical doctor was inversely associated with a view that research was warranted and positively associated with the likelihood of referring patients to a clinical trial. Additionally, practitioners who provide cancer treatment were more likely to perceive benefits of PAT, view research as warranted, and refer patients to a trial. As expected, participants who had previously been a research investigator were also more likely to refer patients to a trial.

Table 2. Demographic and professional characteristics of the sample									
Measure	NZ par- ticipants (N = 163)	US participants (N = 82)	Statistical difference: t -test or χ^2 test						
Age (years), mean (SD)	44.80 (12.75)	42.79 (13.18)	-1.15						
Gender									
Female	141 (86.5%)	49 (59.8%)							
Male	22 (13.5%)	32 (39.0%)	23.15**						
Nonbinary	0 (0%)	1 (1.2%)							
Ethnicity									
NZ sample									
NZ European	109 (66.9%)								
NZ indigenous (NZ Māori)	10 (6.1%)								
Pacific Island	6 (3.7%)								
Asian	11 (6.7%)								
European	18 (11.0%)								
Other	9 (5.5%)								
US sample									
Caucasian/White		63 (76.8%)							
US indigenous (American Indian/Native American, Alaska Native/Native Hawaiian/Pacific Island)		3 (3.7%)							
Asian		12 (14.6%)							
Hispanic/Latino		3 (3.7%)							
Profession									
Medical doctor	37 (22.7%)	33 (40.2%)							
Nurse	60 (36.8%)	35 (42.7%)	15.60*						
Radiation therapy	22 (13.5%)	4 (4.9%)							
Psychosocial support	44 (27.0%)	10 (12.2%)							
Years working with cancer patients (years), mean (SD)	12.76 (10.71)	11.34 (10.38)	-0.94						
Types of clinical work ^a									
Cancer inves- tigation/ diagnosis	59 (36.2%)	34 (41.5%)	0.80						
Cancer treatment	122 (74.8%)	65 (79.3%)	6.01**						
Palliative care	104 (63.8%)	47 (57.3%)	-0.98						
Investigator on research study									
Yes	67 (41.1%)	39 (47.6%)	0.96						
No Awareness of psychedelics, mean	96 (58.9%)	43 (52.4%)	0.00						
(SD)			(Continued)						

(Continued)

Table 2. (Continued.)

Measure	NZ par- ticipants (N = 163)	US participants $(N = 82)$	Statistical difference: t -test or χ^2 test
No. of compounds	3.08 (3.09)	6.17 (3.28)	7.25**
Self-reported score	3.37 (1.98)	4.95 (2.41)	5.49**
Total score	6.45 (4.45)	11.12 (5.15)	7.35**

^aThe total is greater than 100% as many participants worked across several areas of clinical work.

Multivariate analyses of predictors of perceptions

To avoid multicollinearity and maintain power in multivariate models, the following demographic and professional variables were chosen for inclusion as potential predictors:

- 1. Gender (not female = 0, female = 1).
- 2. Number of years working with cancer patients.
- 3. Psychosocial workers (coded 0) versus medical health professionals (doctor/nurse/radiation - coded 1).
- 4. Provider of cancer treatment (no = 0; ves = 1).
- 5. Awareness of PAT.
- 6. Research investigator (no = 0; yes = 1).
- 7. Country (USA = 0; NZ = 1).

All models were significant and, as might be expected, awareness of PAT was a significant predictor in all cases (Table 4). The model assessing predictors of perceiving potential benefits from PAT was significant, $R^2 = 0.49$, F(7,237) = 32.76, p < 0.001. Participants with a greater awareness of psychedelics were more likely to perceive benefits ($\beta = 0.53$, t = 13.22, p < 0.001), as were medical practitioners ($\beta = 0.10$, t = 1.99, p = 0.048). Interestingly, participants who had previously been an investigator on a research trial were less likely to perceive benefits $(\beta = -0.94, t = -2.50, p = 0.013)$. The model assessing predictors that PAT warrants research was significant, $R^2 = 0.32$, F(7,237) = 15.63, p < 0.001 with the only predictor being awareness ($\beta = 0.37$, t = 9.31, p < 0.001). The model assessing predictors of spiritual/indigenous considerations was also significant, $R^2 = 0.27$, F(7,237) = 12.40, p = 0.000. Along with greater awareness ($\beta = 0.31$, t = 6.34, p < 0.001), participants who were female ($\beta = 1.15$, t = 2.01, p = 0.045) and from NZ ($\beta = 3.34$, t = 6.31, p < 0.001) were more likely to believe that spirituality and indigenous healing should be considered. Conversely, having worked for a greater number of years with cancer patients was inversely associated with a view to consider spiritual and indigenous factors ($\beta = -0.04$, t = -2.01, p = 0.046). Finally, the model assessing the likelihood to refer patients to a clinical trial was significant, $R^2 = 0.28$, F(7,237) = 12.84, p < 0.001. Again, greater awareness ($\beta = 0.42$, t = 6.80, p < 0.001) predicted, as did being a medical practitioner ($\beta = 2.70$, t = 3.88, p < 0.001) and an investigator on a previous trial ($\beta = 1.40$, t = 2.45, p = 0.015).

Discussion

The primary aim of this study was to assess the perceptions of cancer health-care practitioners toward PAT in cancer patients. Previous qualitative research in NZ and the USA generally reports

support from palliative care providers toward further research into PAT and notes limitations in current treatments for existential distress. This prior work has also highlighted institutional and systemic barriers that need to be resolved before wider implementation of PAT, for example, the need for further clarity on who will receive training and how this fits into existing treatment structures (Mayer et al. 2021; Niles et al. 2021; Reynolds et al. 2021). Our results extend this previous qualitative work by detailing the views of practitioners toward PAT across 2 countries and extending our understanding to the contexts when practitioners might be willing to refer their patients to clinical trials. Although some participants noted words of caution, there was broad agreement among NZ and US practitioners that PAT has potential to offer benefits to people with cancer. Most participants agreed that well-designed research trials in this area are warranted and that studies should consider how PAT fits alongside medical cancer treatment and traditional healing practices. Practitioners were also willing to refer patients to such trials even during intensive treatments (i.e., chemotherapy) or when patients were undergoing curative treatment. However, willingness to refer was the greatest when patients had advanced disease and were not going through anti-cancer treatment. Finally, multivariate analyses revealed that awareness of psychedelics (unsurprisingly) predicted all outcomes, medical practitioners were more likely to perceive benefits from PAT and refer to a trial, and, interestingly, being a previous investigator on a trial was negatively related to the perception of benefits. Although most differences across countries revealed in bivariate analyses did not hold up against confounder analyses, the NZ sample rated the importance of considering spiritual and indigenous practice more highly than US participants. Below, these findings are integrated with the extant literature, and implications for future research and clinical practice are considered.

First, it is worth emphasizing our finding regarding the relationship between awareness of psychedelics and views about PAT. Greater awareness predicted greater perceptions of benefit, stronger agreement that research is warranted, a greater belief that spiritual and indigenous practices should be considered, and a greater willingness to refer a patient to a clinical trial in the area. Furthermore, awareness was a primary factor explaining differences across countries. That awareness shapes perceptions in medical contexts is well known (Petrie and Weinman 2012), and in recent years there has been increased media coverage on the potential of psychedelics, leading to what some describe as a "cultural shift" (Andrews and Wright 2022). However, it is possible this positive relationship could change as "backlash" stories of negative accounts arise (e.g., Nickles and Ross 2021). Future research would benefit from examining the "awareness-perception" relationship, in particular identifying how and where health professionals gain awareness about PAT, as well as how accurately their understanding reflects the current state of the literature, which was not assessed in the current study.

Our findings that, overall, cancer health-care practitioners perceive potential benefits from PAT align with emerging evidence that suggests promise in this treatment across various domains. Although relevant clinical trials are few, early-stage studies have indicated promise in cancer and palliative contexts in reducing anxiety, depression, and existential distress and improving spiritual well-being (Ross 2018; Ross et al. 2022). However, it would be wise to consider that expectation of benefit is well established as a predictor of placebo responding (Horing et al. 2014) with recent work indicating a trend of increasing placebo response and decreasing treatment effect in psychiatric drug trials

^{*}p < .05 **p < .01.

Table 3. Bivariate correlations among demographics, professional characteristics, awareness, and perceptions of psychedelic-assisted therapy

		POPAT potential benefits	POPAT warrants research	POPAT spiritual/ indigenous	Likelihood to refer
1	Age	-0.11	-0.07	-0.09	-0.11
2	Gender ^{a,b}	-0.10	-0.03	0.19**	-0.20**
3	Medical doctors ^{a,c}	-0.09	-0.15*	-0.31**	0.17**
4	Nurses ^{a,c}	0.13	0.12	0.11	0.09
5	Works in radiation therapy ^{a,c}	-0.11	-0.09	-0.02	-0.16*
6	Psychosocial support workers ^{a,c}	0.04	0.09	0.22**	-0.17**
7	Years working with cancer patients	-0.11	-0.11	-0.19**	0.02
8	Provides cancer treatment ^{a,c}	0.61**	0.49**	0.15*	0.81**
9	Provides palliative care ^{a,c}	0.13*	0.12	0.16*	0.03
10	Research investigators ^{a,c}	-0.09	-0.11	-0.14*	0.17**
11	Country ^{a,d}	-0.27**	-0.17**	0.25**	-0.29**
12	Awareness of PAT	0.68**	0.53**	0.22**	0.43**

 $Pearson's\ correlations\ unless\ otherwise\ indicated.\ POPAT=perceptions\ of\ psychedelic-assisted\ therapy,\ PAT=psychedelic-assisted\ therapy.$

Table 4. Multiple regression models showing the multivariate predictors of perceptions of psychedelic-assisted therapy

	POPAT potential benefits			POPAT warrants research		POPAT spiritual/indigenous			Likelihood to refer			
Predictors	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value	β	SE	<i>p</i> -Value
Constant	-0.83	0.97		3.34	0.96		1.66	1.17		-2.97	1.48	
Gender ^a	0.67	0.48	0.159	0.62	0.47	0.187	1.15	0.57	0.046**	0.41	0.72	0.569
Years working with cancer patients	-0.00	0.02	0.849	-0.01	0.02	0.717	-0.04	0.02	0.046**	0.01	0.03	0.815
Medical health professionals ^{b,c}	0.91	0.46	0.048**	0.14	0.45	0.758	-0.41	0.55	0.456	2.70	0.69	0.000***
Awareness of PAT	0.53	0.04	0.000***	0.37	0.04	0.000***	0.31	0.05	0.000***	0.42	0.06	0.000***
Provide cancer treatment ^b	-0.40	0.43	0.358	-0.40	0.43	0.348	-0.22	0.52	0.676	0.71	0.66	0.283
Research investigators ^b	-0.94	0.38	0.013**	-0.63	0.37	0.091*	-0.45	0.45	0.326	1.40	0.57	0.015**
Country ^d	0.20	0.44	0.652	0.58	0.44	0.186	3.34	0.53	0.000***	-0.55	0.67	0.415

 ${\tt POPAT} = {\tt perceptions} \ \ {\tt of} \ \ {\tt psychedelic-assisted} \ \ {\tt therapy}, \ {\tt SE} = {\tt standard} \ \ {\tt error}, \ {\tt PAT} = {\tt psychedelic-assisted} \ \ {\tt therapy}.$

(Gopalakrishnan et al. 2020). It is noteworthy that participants who had previously been an investigator in research studies were less likely to perceive benefits. Feedback from open-ended comments in this study suggests that these participants were more inclined to consider the scientific evidence before coming to a view, for example, "I simply have no knowledge about the promise of such therapy" and "I do not know enough about the process to have an informed opinion." Enthusiasm for potential benefits should also be contained in noting that previous studies in the area have been challenged by methodological difficulties including problems with blinding, expectancy effects, and self-selection bias (Muthukumaraswamy et al. 2022). Nevertheless, the fact that

our sample were generally positive about the idea of conducting trials in this area, saw the potential for benefits of psychedelic-assisted therapies, and were willing to refer patients to trials, is an important factor in the development of research that will ultimately inform evidenced-based clinical practice.

Cultural differences were apparent, with NZ participants being less aware of PAT, less likely to perceive potential benefits, less likely to refer patients to a clinical trial, but *more* likely to consider spirituality and indigenous practices than US participants. After correcting for potential confounders via multivariate modeling, only the finding that NZ participants were more likely to believe that spiritual/indigenous factors should be considered remained

^aSpearman's Rho correlations.

 $^{^{}b}$ Given that one participant affiliated as nonbinary, gender is coded as 0 = not female and 1 = female.

 $^{{}^{}c}\text{Coded}$ as 0 = no and 1 = yes.

 $^{^{}d}$ Coded as USA = 0 and NZ = 1.

p < 0.05

 $^{^{\}star\star}p < 0.01.$

 $^{^{}a}$ Coded as 0 = not female and 1 = female.

 $^{^{\}mathrm{b}}\mathrm{Coded}$ as $0=\mathrm{no}$ and $1=\mathrm{yes}$. $^{\mathrm{c}}\mathrm{Medical}$ doctor or nurse or radiation therapist versus psychosocial worker.

 $^{^{\}rm d}$ Coded as USA = 0 and NZ = 1.

^{*}p < 0.10
**p < 0.05

^{***}p < 0.001.

statistically significant. Although we cannot conclusively attest why our NZ and US samples differed, we suspect that an increasing focus in NZ health providers to uphold the principles of the founding treaty (Te Tiriti o Waitangi) between the indigenous people (Māori) and British colonizers may be a factor (Ministry of Health 2014). Additionally, NZ has been rated as having less social hostilities involving religion than the USA (Pew Research Center 2018), which may reflect greater respect of spiritual beliefs of indigenous groups. It is also worth noting that participants from both countries gave feedback about the importance of respecting indigenous practice through comments about the importance of cultural humility and that work in this area should include input from spiritual leaders and indigenous stakeholders (Mayer et al. 2021; Niles et al. 2021).

Clinical and research implications

Cancer health-care practitioners are critical gatekeepers to research participants, and our findings suggest willingness to refer patients to trials investigating PAT. There was a notable pattern where willingness to refer increased as cancer treatments became less intensive and in patients with advanced disease. These findings suggest that it may be prudent for clinical trials to begin with research among palliative groups.

Our finding that cancer health-care practitioners recognize that research is warranted across various domains provides a mandate for conducting research in the area. Given the stigma of "psychedelics" and the exaggeration of dangers of such substances (Andrews and Wright 2022), including the unfounded claim that psychedelics can cause cancer (Barnett et al. 2022), we suspect research may need to build a strong evidence base before health practitioners are willing to recommend such treatments to patients. Research should follow a phased approach starting by assessing safety, feasibility, and patient acceptability, before moving to trials comparing PAT to control conditions. Recent publications in this area provide support for this phased approach and make additional recommendations for future research. PAT has numerous potential therapeutic applications, suggesting a need to clarify these indications and work toward developing therapeutic protocols that are standardized. Further work is also required to understand mechanism of action and contextual factors such as set and setting. Importantly, research is needed to clarify how we educate health professionals about PAT and train or certify practitioners involved in the delivery of this treatment (Beaussant et al. 2021; Mayer et al. 2021; Niles et al. 2021). Clinical guidance for practitioners is already being developed, and it will be beneficial to keep these recommendations updated as further evidence is produced (Rosa et al. 2022).

While some of our participants viewed psychedelic research like any other clinical trial, we are mindful of the indigenous tradition in this area and recognize that colonization has resulted in disconnection of indigenous peoples to their land, communities, and traditional medicinal or religious practices (George et al. 2019). Furthermore, people of color have suffered the repercussion of the "war on drugs" to a much greater degree than White counterparts facing higher penalties and much higher rates of incarceration for drug-related crimes (Forman 2012). It is therefore possible that research in this area may not be perceived as being "safe" to engage with by such communities (George et al. 2019). Contemporary application of psychedelics needs to acknowledge this history, as well as traditional and cultural origins of this practice, while also

ensuring indigenous peoples are not only recognized but also benefit from ongoing research (Fotiou 2020). Indigenous groups are often in greatest need of health interventions, and western medical approaches have not historically well served these groups (Beaussant et al. 2021; Michaels et al. 2018; Rosa et al. 2022; The Lancet 2016). Researchers must act in accordance with the United Nations declaration of indigenous rights (United Nations 2017), and taking an equity approach would necessitate interventions developed in true partnership with indigenous researchers and communities, including engaging in co-design, collaboration, and genuine consultation at every stage of research endeavors. This approach to diversifying psychedelic medicine highlights the importance of researchers in understanding cultural humility and cultural safety (Curtis et al. 2019; George et al. 2019)

Study limitations

Although the current work offers insight into the views of a key group of cancer stakeholders, there are limitations worth noting. First, the study was conducted across 2 countries, and there were demographic and professional differences across these samples. Compared to NZ, the US sample had a more even distribution of gender, had a greater proportion of medical doctors, was more likely to work in cancer treatment, and, perhaps most importantly, had greater awareness of PAT. To control for these differences, we entered country against these other variables into multivariate models, and it remained a significant predictor in one instance (spiritual/indigenous considerations). As noted earlier, legislative and regulatory differences by states in the USA may impact perceptions and awareness of PAT, and without access to geographical data from our US sample, it is not possible to infer what effect this may have had on the data. Additionally, there was a 10-month difference in data collection across the 2 sites, and it is possible that this timing impacted awareness. Additionally, US participants were not offered an incentive to participate, while NZ participants were. As with all cross-sectional work, there may also be a "third" variable that we did not measure that explains differences. Whether there might be differences across other countries seems likely and could be a focus of further investigation. Finally, these data are from a nonrandom sample, with limited diversity, and due to the possibility of self-selection bias, responses may not necessarily align with the perceptions of cancer health-care professionals more generally.

Conclusions

The current work presents findings from a cross-sectional survey investigating perceptions of cancer health-care practitioners toward PAT in NZ and the USA. Overall, participants perceived that (1) PAT has potential to provide benefits for cancer patients, (2) research across a variety of domains is important, (3) work in this area should consider spiritual and indigenous perspectives, and (4) participants were willing to refer their patients, especially those with advanced disease, to trials in this area. Notably, NZ participants were more likely to believe in the importance of considering spirituality and how PAT fits with traditional indigenous healing. Overall, our findings suggest that there is an imperative for clinical trials of PAT in patients with cancer to be developed.

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Conflicts of interest. None declared.

Ethical standards. Ethical approval was obtained in NZ from the Auckland Health Research Ethics Committee (AHREC) on 9 March 2021 for 3 years (No. AH22139) and in the USA from the Cleveland Clinic Institutional Review Board (Protocol No. 21-648) on 3 June 2021.

References

- **Agin-Liebes GI, Malone T, Yalch MM**, *et al.* (2020) Long-term follow-up of psilocybin-assisted psychotherapy for psychiatric and existential distress in patients with life-threatening cancer. *Journal of Psychopharmacology* **34**(2), 155–166. doi:10.1177/0269881119897615
- Andrews T and Wright K (2022) The frontiers of new psychedelic therapies: A survey of sociological themes and issues. Sociology Compass 16(2), 1–16. doi:10.1111/soc4.12959
- Arrieta Ó, Oñate-Ocaña LF, Macedo EO, et al. (2012) Association of depression and anxiety on quality of life, treatment adherence, and prognosis in patients with advanced non-small cell lung cancer. Annals of Surgical Oncology 20(6), 1941–1948. doi:10.1245/s10434-012-2793-5
- Barnett BS, Ziegler K, Doblin R, et al. (2022) Is psychedelic use associated with cancer?: Interrogating a half-century-old claim using contemporary population-level data. *Journal of Psychopharmacology* **36**(10), 1118–1128. doi:10.1177/02698811221117536
- Beaussant Y, Tulsky J, Guérin B, et al. (2021) Mapping an agenda for psychedelic-assisted therapy research in patients with serious illness. *Journal of Palliative Medicine* 24(11), 1657–1666. doi:10.1089/jpm.2020.0764
- Curtis E, Jones R, Tipene-Leach D, *et al.* (2019) Why cultural safety rather than cultural competency is required to achieve health equity: a literature review and recommended definition. *International Journal for Equity in Health* 18(1), 174. doi:10.1186/s12939-019-1082-3
- Forman J, Jr. (2012) Racial critiques of mass incarceration: Beyond the new Jim Crow. New York University Law Review, 87, 101–146.
- Fotiou E (2020) The role of Indigenous knowledges in psychedelic science. Journal of Psychedelic Studies 4(1), 16–23. doi:10.1556/2054.2019.031
- Garján FJ, Azparren A, Vergara I, et al. (2012) Adoption of new drugs by physicians: A survival analysis. BMC Health Services Research 12(1), 1–8. doi:10.1186/1472-6963-12-56
- George JR, Michaels TI, Sevelius J, et al. (2019) The psychedelic renaissance and the limitations of a White-dominant medical framework: A call for indigenous and ethnic minority inclusion. *Journal of Psychedelic Studies* 4(1), 4–15. doi:10.1556/2054.2019.015
- Gopalakrishnan M, Zhu H, Farchione TR, et al. (2020) The trend of increasing placebo response and decreasing treatment effect in schizophrenia trials continues: An update from the US Food and Drug Administration. *The Journal of Clinical Psychiatry* 81(2), 14594. doi:10.4088/JCP.19R12960
- Griffiths RR, Johnson MW, Carducci MA, et al. (2016) Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. Journal of Psychopharmacology 30(12), 1181–1197. doi:10.1177/0269881116675513
- Henry DH, Viswanathan HN, Elkin EP, et al. (2008) Symptoms and treatment burden associated with cancer treatment: Results from a cross-sectional national survey in the U.S. Supportive Care in Cancer 16(7), 791–801. doi:10.1007/s00520-007-0380-2
- Horing B, Weimer K, Muth ER, et al. (2014) Prediction of placebo responses: A systematic review of the literature. Frontiers in Psychology 5(Oct), 1079. doi:10.3389/FPSYG.2014.01079/BIBTEX
- The Lancet (2016) Indigenous health: A worldwide focus. The Lancet 388(10040), 104. doi:10.1016/S0140-6736(16)31020-0
- Maia LO, Beaussant Y and Garcia ACM (2022) The therapeutic potential of psychedelic-assisted therapies for symptom control in patients

- diagnosed with serious illness: A systematic review. *Journal of Pain and Symptom Management* **63**(6), e725–e738. doi:10.1016/j.jpainsymman.2022. 01.024
- Mayer CE, LeBaron VT, and Acquaviva KD (2021) Exploring the use of psilocybin therapy for existential distress: A qualitative study of palliative care provider perceptions. *Journal of Psychoactive Drugs* **54**(1), 1–12. doi:10.1080/02791072.2021.1916659
- Michaels TI, Purdon J, Collins A, et al. (2018) Inclusion of people of color in psychedelic-assisted psychotherapy: A review of the literature. BMC Psychiatry 18(1), 1–14. doi:10.1186/S12888-018-1824-6/TABLES/3
- Ministry of Health (2014) The Guide to He Korowai Oranga: Māori Health Strategy. Wellington: Ministry of Health.
- Mitchell AJ, Chan M, Bhatti H, et al. (2011) Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: A meta-analysis of 94 interview-based studies. *The Lancet Oncology* 12(2), 160–174. doi:10.1016/s1470-2045(11)70002-x
- Muthukumaraswamy S, Forsyth A, and Sumner RL (2022) The challenges ahead for psychedelic 'medicine'. Australian and New Zealand Journal of Psychiatry. doi:10.1177/00048674221081763
- National Comprehensive Cancer Network (2003) Distress management. Clinical practice guidelines. *Journal of the National Comprehensive Cancer Network* 1(3), 344. doi:10.6004/jnccn.2003.0031
- Nickles D, and Ross LK (2021) Cover story: Power trip. New York Magazine. https://www.thecut.com/2021/11/cover-story-podcast-goes-into-world-of-psychedelic-therapy.html (accessed 22 October 2022).
- Niles H, Fogg C, Kelmendi B, *et al.* (2021) Palliative care provider attitudes toward existential distress and treatment with psychedelic-assisted therapies. *BMC Palliative Care* **20**(1), 1–14. doi:10.1186/s12904-021-00889-x
- Nutt DJ, King LA and Nichols DE (2013) Effects of Schedule I drug laws on neuroscience research and treatment innovation. *Nature Reviews Neuroscience* 14, 577–585. doi:10.1038/nrn3530
- Petrie KJ and Weinman J (2012) Patients' perceptions of their illness: The dynamo of volition in health care. *Current Directions in Psychological Science* **21**(1), 60–65. doi:10.1177/0963721411429456
- Pew Research Center (2018) Global uptick in Government restrictions on religion in 2016, June 21 https://www.pewresearch.org/religion/2018/06/21/global-uptick-in-government-restrictions-on-religion-in-2016/ (accessed 27 October 2022).
- **Psychedelic Alpha** (2022) Psychedelics legalization & decriminalization tracker https://psychedelicalpha.com/data/psychedelic-laws (accessed 27 October 2022).
- Reynolds LM, Akroyd A, Sundram F, et al. (2021) Cancer healthcare workers' perceptions toward psychedelic-assisted therapy: A preliminary investigation. International Journal of Environmental Research and Public Health 18, 1–14. doi:10.3390/ijerph18158160
- Rosa WE, Sager Z, Miller M, et al. (2022) Top ten tips palliative care clinicians should know about psychedelic-assisted therapy in the context of serious illness. *Journal of Palliative Medicine* **25**(8), 1273–1281. doi:10.1089/jpm.2022.
- Ross S (2018) Therapeutic use of classic psychedelics to treat cancer-related psychiatric distress. *International Review of Psychiatry* 30(4), 317–330. doi:10.1080/09540261.2018.1482261
- Ross S, Agrawal M, Griffiths RR, et al. (2022) Neuropharmacology psychedelic-assisted psychotherapy to treat psychiatric and existential distress in life-threatening medical illnesses and palliative care. Neuropharmacology 216, 109174. doi:10.1016/j.neuropharm.2022.109174
- Smith EEM, Gomm SA and Dickens CMC (2003) Assessing the independent contribution to quality of life from anxiety and depression in patients with advanced cancer. *Palliative Medicine* 17(6), 509–513. doi:10.1191/0269216303pm7810a
- **Truu M** (2019) Dying patients to be given "magic mushrooms" at Melbourne hospital. *SBS News.* https://www.sbs.com.au/news/dying-patients-to-be-given-magic-mushrooms-at-melbourne-hospital (accessed 27 October 2022).
- United Nations (2017) United Nations Declaration on the rights of indigenous peoples: United Nations for indigenous peoples. United Nations Department of Economic and Social Affairs. https://www.un.org/development/desa/ indigenouspeoples/declaration-on-the-rights-of-indigenous-peoples.html.