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RESEARCH SUBMISSION

Patient perspectives on research gaps in cluster headache

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Abstract

Objective: This study was undertaken to identify gaps in cluster headache management, highlight patient-prioritized research needs, and assess patient interest in, and preferences for, clinical trial participation.

Background: Many people with cluster headache still lack effective treatment options to control or prevent attacks. There is a critical need for more studies, particularly clinical trials, in this field. To design and conduct successful trials, it is essential to identify priority research areas, allocate resources effectively, and ensure patient engagement and support.

Methods: This study was an online survey conducted among Australian adults with self-reported cluster headache. Participants were recruited using a multi-channel approach, including direct outreach by clinicians, support from patient advocacy groups, and broad social media distribution. It collected data on demographics, treatment experiences, and perspectives on future research, including research priorities, and preferred outcomes and interventions. Additionally, participants' interest in joining clinical trials was assessed to help identify potential candidates for future studies.

Results: Of the 219 individuals who began the survey, 17 (8%) were excluded due to providing no responses beyond demographic data or reporting no cluster headache diagnosis by a healthcare professional. The final sample consisted of 202 participants, with an average age of 46 years, 77% aged 25–54 years, 55% male, 72% had been living with cluster headache for more than 10 years, and 29% reported attacks occurring almost every month throughout the year.

A quarter of participants had not followed up with a healthcare provider for cluster headache management when they completed the survey. Among those who sought care ($n = 145$ [72%]), general practitioners were the most frequently consulted (86%),

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Abbreviations: AUD, Australian dollar; CGRP, calcitonin gene-related peptide; LSD, lysergic acid diethylamide; NSAIDS, non-steroidal anti-inflammatory drugs; nVNS, non-invasive vagus nerve stimulation.

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followed by neurologists (66%). Treatments were considered "not at all effective" or "somewhat ineffective" by 35% of all participants, while 27% reported only partial effectiveness. The main treatment challenges were ineffectiveness (74%), side effects (54%), cost (53%), and difficulties with access (39%).

Among the 202 participants, 126 (62%) indicated interest in participating in future cluster headache trials, while 26 (13%) responded with "maybe." Psilocybin was the highest-ranked treatment in terms of participants who were "very interested," with 66% selecting this option. The combined proportion of participants who were "very interested" or "interested" was 84% for combination therapies, 82% for psilocybin, 71% for medical devices, and 66% for anti-CGRP treatments.

Conclusion: Participants with reported cluster headache highlighted inadequate treatment options, emphasized the need for further research, and expressed interest in future clinical trials, particularly those involving psilocybin or combination therapies.

Plain Language summary

Cluster headache is one of the most severe pains a person can experience, yet effective treatment options are lacking, and research on the condition remains insufficient. Using an online survey, we asked 219 people with cluster headache about their experiences with the disease and available treatments, their opinions on future research, their interest in joining clinical trials, and their preferred types of interventions. Among participants, 35% found treatments "not at all effective" or "somewhat ineffective," 27% reported only partial effectiveness, and 62% expressed interest in future clinical trials, particularly if the trials involved psilocybin or combination therapies.

KEYWORDS
cluster headache, gaps, headache, research, survey

INTRODUCTION

Cluster headache is recognized as one of the most excruciating forms of pain a human can experience[1] and has a prevalence of approximately 1 in 1000 individuals.[2] The mean annual cost per patient is estimated at 11,000 euros (approximately 20,000 AUD) based on data from tertiary centers,[3] reflecting the significant economic burden, which is further compounded by the condition's impact on quality of life, disability, job-related challenges, and sleep disturbances.[3,4]

While various medications are available for cluster headache, issues such as limited efficacy, availability, cost, contraindications, and safety persist.[3] Among the acute treatments, oxygen therapy and triptans are the most effective options.[3,5,6] While there are strong guideline recommendations for initial preventive treatments, including verapamil, preventive options remain inadequate, with limited high-quality evidence for patients who do not respond to or cannot tolerate first-line therapies.[3,5,6] The management of cluster headache is still largely trial and error, with a substantial unmet need for more effective and accessible treatments.[3] Furthermore, significant obstacles in cluster headache research include recruiting adequate numbers of participants for clinical trials.[7] Together, this highlights a clear need to research and develop more effective treatments.

Despite the lack of clinical options, there are treatments, such as psychedelics including psilocybin, that many patients report using and consider effective. For example, in the Clusterbusters survey, 36% of participants reported using psilocybin, with approximately 40% finding it completely effective and 30% moderately effective.[8] However, despite this promising anecdotal evidence, psilocybin remains under-researched and is not currently recommended in clinical guidelines. To address current challenges and inform the development of more effective solutions, targeted research that incorporates the perspectives and priorities of people living with cluster headache is essential.

This study aimed to identify gaps in cluster headache research and management from the patient perspective, assess interest in clinical trial participation, and determine patient preferences for trial involvement in Australia. The findings of this study will provide essential insights to inform the development of future clinical trials, ensuring they are aligned with patient needs and priorities. By identifying important gaps and understanding what matters most to patients, this study represents an important step toward designing patient-centered trials on cluster headache in Australia.

METHODS

Study design and participants

This study was an online survey that included individuals aged 18 years or older with a self-reported diagnosis of cluster headache who lived in Australia. Participants were excluded if they did not complete any questions beyond the demographic section or if they reported that a doctor had not diagnosed their condition. It recruited participants from February 2024 to October 2025.

The study evaluated the experiences of individuals with cluster headache, including their management approaches, perspectives on future research, and interest in participating in clinical trials, particularly those involving psilocybin. Additionally, we gathered patients' opinions on the design of future trials and suggestions for making them more feasible.

The online survey (Supplementary S1) was designed using the Qualtrics XM Platform (www.qualtrics.com) and comprised three main sections:

1. *Demographic information*: This section included age, gender, Aboriginal and/or Torres Strait Islander origin, and place of residence.
2. *Treatment experience*: Participants were asked whether their treating doctor made the diagnosis or if they self-diagnosed. They were also asked whether they currently visit healthcare professionals, any challenges they face, disease duration and attack frequency, comorbid mood disorders such as stress, anxiety, and depression, current treatments and their reported efficacy rated on a five-point rating scale (very effective, somewhat effective, about equal times effective vs. not effective, somewhat ineffective, and not at all effective), and any challenges related to treatment including cost, effectiveness, access, and side effects.
3. *Future research and needs*: This section explored participants' views on what should be studied, their preferred outcomes to be evaluated, their interest in joining clinical trials (especially on psilocybin), preferred interventions to be explored, how often they could attend trial sessions each month, and their comfort level with placebo treatments.

Upon following the survey link, detailed information on the survey was provided, and consent was collected before participants completed a brief checklist to confirm their eligibility.

Recruitment for the study utilized multiple methods to maximize outreach. First, medical professionals on our team, including neurologists, informed eligible patients using approved recruitment materials such as flyers, email content, and e-posters. Additionally, patient advocacy groups such as Migraine and Headache Australia, and Clusterbusters, and the Australian and New Zealand Headache Society helped share the study's ethics-approved materials and survey link with their audiences. The survey link was also distributed through social media platforms like Twitter (X), Facebook, and Instagram. Paid promotion for the survey was not used.

Data analysis

The study did not involve comparing groups or calculating effect sizes; therefore, a formal sample size calculation was not required. However, since the original goal was to generate supporting data for future clinical trials, we aimed to collect data from a sufficient number of participants to reflect the sample size we would anticipate in a potential future trial. As such, our target was to recruit at least 90 participants who expressed interest in joining future trials through the survey. This number was based on power calculations for a trial, indicating that 90 participants would provide approximately 80% power at a two-sided α of 0.05 to detect a clinically meaningful difference of 2.5 attacks per week, assuming a standard deviation of 4.5 attacks per week, a moderate effect size ($d \approx 0.55$), and allowing for a 15% dropout rate.

Missing data are indicated in each section.

Categorical variables were summarized as numbers and percentages. For multiple-choice questions, the percentage of participants selecting each answer was reported. Age was collected as a categorical variable; therefore, the mean age was estimated by assigning the midpoint value of each category and calculating the weighted mean across categories. Analyses were conducted using IBM SPSS Statistics software (Version 29).

Ethics and data management

Data were collected using the Qualtrics XM Platform and stored on The George Institute for Global Health's password-protected OneDrive. The study was approved by the University of New South Wales Human Research Ethics Committee (iRECS0806).

RESULTS

A total of 219 individuals began the survey. Seventeen (7.8%) out of 219 participants were excluded from the analysis: Nine provided no responses after consenting, seven only entered demographic data, and one reported not being diagnosed with cluster headache by a healthcare professional. Therefore, 202 participants were included in the final analysis (Figure S1). Participant characteristics are shown in Table 1. The mean weighted age of participants was 45.6 years, with the majority ($n = 154$, 77%) aged 25–54 years, and 111 (55%) identified as male. Among the participants, 9 (5%) were Aboriginal and/or Torres Strait Islander, and 132 (66%) resided in urban areas, while 68 (34%) lived in rural or regional areas. Although exact participant-level data were not collected, observationally, the most effective recruitment methods appeared to be the Migraine and Headache Australia newsletter and targeted posts in relevant Facebook groups. This conclusion is based on the immediate increase in the number of new participants recorded in the survey following each newsletter distribution and targeted post.

TABLE 1 Characteristics of participants in the survey ($N = 202$).

Characteristic	N (%)
Age (years)	
18–24	0
25–34	44 (21.9%)
35–44	52 (25.9%)
45–54	58 (28.9%)
55–64	32 (15.9%)
65 or older	15 (7.5%)
Missing data[a]	1 (0.5%)
Sex?	
Man	111 (55.2%)
Woman	89 (44.3%)
Non-binary	1 (0.5%)
Missing data[a]	1 (0.5%)
Aboriginal and/or Torres Strait Islander origin	
No	192 (95.5%)
Yes–aboriginal	9 (4.5%)
Yes–Torres Strait Islander	0 (0%)
Missing data[a]	1 (0.5%)
Area of residency	
Rural	13 (6.5%)
Regional	55 (27.5%)
Urban	132 (66.0%)
Missing data[a]	2 (1.0%)

Note: Percentages are calculated based on the number of participants who answered each specific question.

[a] Missing data were excluded from the percentage calculations in other sections.

Experience with cluster headache and its treatment

Data on participants' experiences with cluster headache and its treatment are shown in Table 2. All participants reported being diagnosed with cluster headache by a doctor, and 145 (72%) had experienced cluster headache for more than 10 years. While 138 participants (69%) reported having headache during only certain months of the year—58 (29%) with predictable timing occurring in the same months each year, and 80 (40%) with an inconsistent or unclear pattern— 58 (29%) reported attacks occurring almost every month throughout the year. Notably, most participants ($n = 171$, 85%; missing data for five participants) reported experiencing at least one mental health condition, which they themselves attributed/related to cluster headache, with many reporting multiple conditions. The most commonly reported conditions were stress ($n = 139$, 71%), anxiety ($n = 135$, 69%), and depression ($n = 118$, 60%), followed by insomnia ($n = 101$, 51%) and panic attacks ($n = 48$, 24%) (Table 2). Only 30 respondents (15%) reported no mental health impacts.

Participants also provided information about their experiences engaging with healthcare services (Table 2). A total of 145

TABLE 2 Characteristics of cluster headache and treatment experiences among study participants ($N = 202$).

Characteristic	N (%)
Duration of years experiencing cluster headache	
Less than 1	1 (0.5%)
1–5	26 (12.9%)
6–10	29 (14.4%)
More than 10	145 (72.1%)
Missing data[a]	1 (0.5%)
Frequency of cluster headache attacks	
Almost every month throughout the year	58 (28.9%)
Occurs during specific months of the year	58 (28.9%)
Occurs some months a year, but the timing is not consistent or clear	80 (39.8%)
Not sure	5 (2.5%)
Missing data[a]	1 (0.5%)
Mental health conditions related to cluster headache	
No mental health condition	30 (15.2%)
Stress	139 (70.5%)
Anxiety	135 (68.5%)
Insomnia	101 (51.3%)
Depression	118 (59.9%)
Panic attacks	48 (24.4%)
Other	17 (8.6%)
Missing data[a]	5 (2.4%)
Currently seeing a healthcare professional for cluster headache	
Yes	145 (71.8%)
No	57 (28.2%)
Reasons for not seeing a healthcare professional[b]	**$N = 57$**
Financial constraints	9 (15.8%)
Access issues	5 (8.8%)
Self-treatment	29 (50.9%)
Time constraints	9 (15.8%)
Not getting expected benefits	22 (38.6%)
Other	25 (43.8%)
Type of healthcare professional visited[c]	**$N = 145$**
GP	124 (85.5%)
Neurologist	96 (66.2%)
Pain specialist	24 (16.5%)
Physiotherapist/chiropractor	21 (14.5%)
Other	8 (5.5%)
Treatment methods used for cluster headache management	
Prescription medications during the pain (e.g., sumatriptan, dihydroergotamine, zolmitriptan)	172 (85.6%)
Over-the-counter pain medications (e.g., paracetamol, ibuprofen)	163 (81.1%)
Oxygen therapy	108 (53.7%)

TABLE 2 (Continued)

Characteristic	*N* (%)
Prednisolone	112 (55.7%)
Nerve block	75 (37.3%)
Prescription medications to prevent the pain (e.g., verapamil, lithium carbonate, divalproex sodium, melatonin, topiramate)	150 (74.6%)
Lifestyle changes (e.g., sleep patterns, diet)	131 (65.2%)
Non-invasive vagal nerve stimulation	23 (11.4%)
Missing data[a]	1 (0.5%)
How effective the treatment was	
Very effective	12 (6.0%)
Somewhat effective	65 (32.3%)
About equal times effective vs. not effective	54 (26.9%)
Somewhat ineffective	48 (23.9%)
Not at all effective	22 (10.9%)
Missing data[a]	1 (0.5%)
Challenges with the treatment	
Cost	104 (52.8%)
Effectiveness	152 (77.2%)
Access	77 (39.1%)
Side effects	107 (54.3%)
Missing data[a]	5 (2.5%)

Note: Percentages are calculated based on the number of participants who answered each specific question; For some sections, the total numbers might exceed 137 due to overlapping answers.

Abbreviation: GP, general practitioner.

[a] Missing data were not included in the calculation of percentages for other sections.

[b] Percentages are calculated based on those who are not currently seeing a healthcare professional.

[c] Percentages are calculated based on those who are currently seeing a healthcare professional.

participants (72%) reported ongoing consultation with a healthcare professional for their cluster headache. Among the 57 (28%) participants who were not currently under physician care, the most commonly reported reasons for not seeing a healthcare professional were self-treatment (*n* = 29, 51%) and not receiving expected benefits from prior care (*n* = 22, 39%), followed by financial constraints (*n* = 9, 16%), time limitations (*n* = 9, 16%), and access issues (*n* = 5, 9%). For participants who visited a healthcare professional, the majority consulted a general practitioner (*n* = 124, 86%), followed by a neurologist (*n* = 96, 66%), a pain specialist (*n* = 24, 17%), and a physiotherapist or chiropractor (*n* = 21, 15%).

Participants reported using a range of treatments to manage their condition (Table 2). The most commonly used treatments were prescription medications for acute pain relief (e.g., sumatriptan, dihydroergotamine, zolmitriptan), reported by 172 participants (86%). This was followed by over-the-counter pain medications (*n* = 163, 81%), and prescription medications to prevent the pain (*n* = 150, 75%). Other methods included lifestyle changes (*n* = 131, 65%), prednisolone (*n* = 112, 56%), oxygen therapy (*n* = 108, 54%), nerve blocks (*n* = 75, 37%), and non-invasive vagal nerve stimulation (*n* = 23, 11%).

Participants reported the effectiveness of current cluster headache treatment in a single, all-inclusive question addressing both acute and preventive therapies. Only a small proportion (*n* = 12, 6%) considered their treatment to be very effective (Table 2). To provide further detail, the most commonly reported response was that treatment was somewhat effective (*n* = 65, 32%). However, a combined 35% (*n* = 70) rated their treatment as either somewhat ineffective (*n* = 48, 24%) or not at all effective (*n* = 22, 11%). The most commonly reported challenges with treatment were concerns with effectiveness (*n* = 152, 77%), side effects (*n* = 107, 54%), cost (*n* = 104, 53%), and access issues (*n* = 77, 39%).

Participant-rated importance of future research areas and needs

Figure 1 presents participants' ratings of the importance of various future research areas in cluster headache. A total of 164 participants (with data missing from 38) provided responses. The areas of research identified most commonly as "very important" were understanding the underlying causes (*n* = 148, 90%), developing more effective medications (*n* = 144, 88%), educating doctors and the public (*n* = 133, 82%), improving diagnostic methods (*n* = 115, 70%), and overall awareness and education (n = 115, 70%).

The survey revealed the various measures (outcomes) in a clinical trial that are most important to individuals with cluster headache (Figure 2). A total of 165 participants (with data missing from 37) provided responses. The outcomes most commonly rated as "very important" were pain severity (*n* = 118, 72%), number of attacks (n = 115, 70%), overall well-being (*n* = 111, 67%), and duration of each attack (n = 111, 67%). Measuring the number of medications taken for an attack (*n* = 92, 56%) and the duration of headache-free intervals between attacks (*n* = 85, 52%) was also considered very important by most participants. When participants were asked to provide additional suggestions, they also mentioned items such as measuring the impact on social life, cognitive impact, productivity, work-life balance, and sleep quality.

Participant interest in future trial interventions

Of the 202 participants, 126 (62%) expressed interest in future clinical trials for cluster headache, 26 (13%) responded "maybe," 13 (6%) indicated they were not interested, and 37 (18%) did not respond. For those who selected "maybe," they added that their participation depended on factors such as time, location, type of intervention, route of administration, the ability to continue using

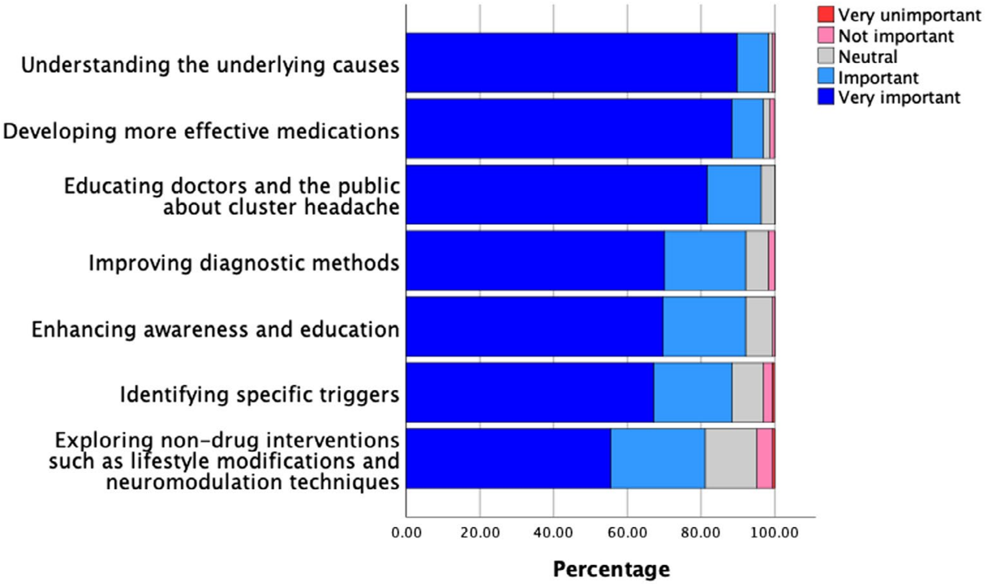

FIGURE 1 Participants' perspectives on important research priorities for cluster headache ($N=164$).

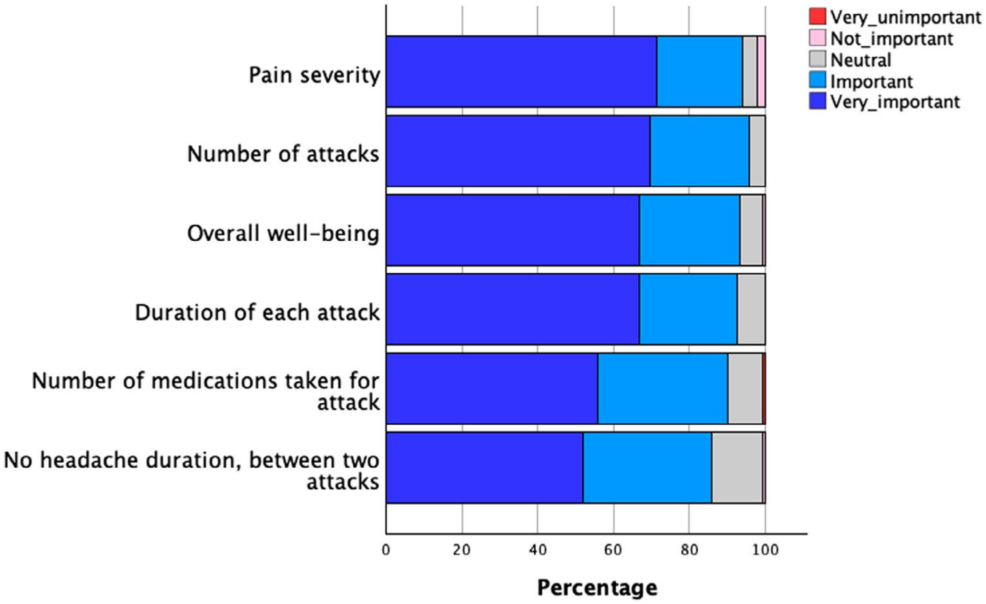

FIGURE 2 The importance of different measures (outcomes) in a trial on cluster headache from the participants' point of view ($N=165$).

their usual cluster headache medications, and concerns about potential side effects.

Figure 3 presents participants' levels of interest in various interventions they would like to see tested in future clinical trials for cluster headache. A total of 158 participants (with data missing from 44) responded. The highest level of interest was for psilocybin, with 105 participants (66%) reporting being “very interested” and 25 (16%) “interested.” Similarly, combination therapies received significant interest, with 73 participants (47%) “very interested” and 58 (37%) “interested.” Interest in anti-calcitonin gene-related peptide (CGRP) medications showed variability, with 61 participants (38%) being “very interested,” 45 (28%) being “interested,” and a notable 32 (20%) being “not interested.” Interest in medical devices like non-invasive vagus nerve stimulation (nVNS) devices, was also relatively high, with 60 (38%) of participants "very interested" and 53 (33%) “interested,” followed by non-medication approaches such as biofeedback and acupuncture (35% “very interested” and 33% “interested”). Lifestyle changes, such as diet and exercise, showed lower levels of interest, with only 46 participants (29%) indicating “very interested” and 46 (29%) indicating “interested.”

When asked specifically about their interest in participating in trials involving psilocybin, 103 participants (64% of respondents) indicated a yes, 17 (8%) said maybe, and 19 (9%) stated they would not participate; 36 (18%) did not answer this question.

Participants' willingness to attend in-person trials was investigated. Among respondents ($n=157$), 117 (75%) reported that they

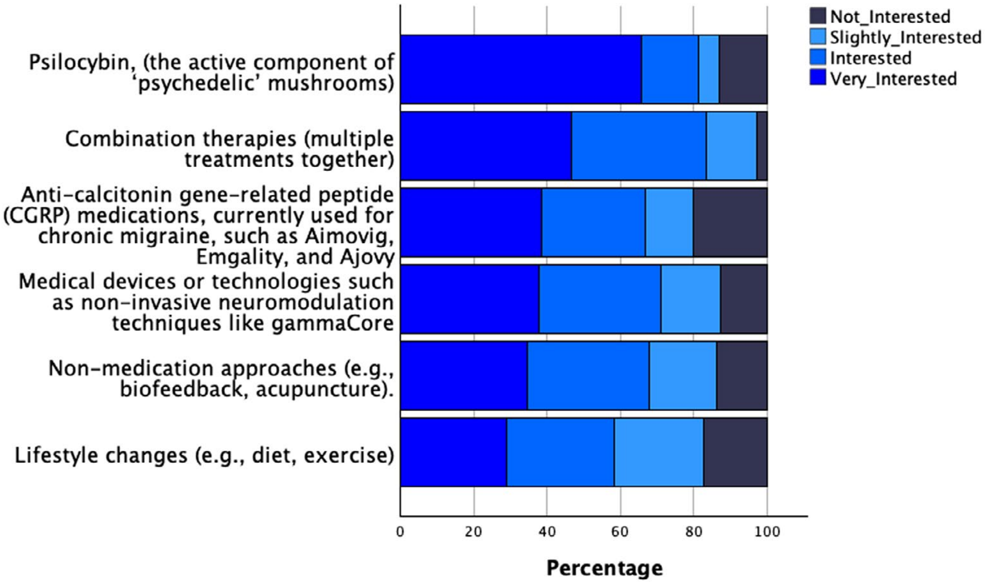

FIGURE 3 The level of interest in different interventions to be tested in trials for cluster headache from the participants' point of view ($N=158$).

could join an in-person trial, and 30 (19%) indicated that they might participate depending on factors such as proximity to trial sites, the number of required visits to the center, and financial support.

When the participants ($N=152$) who showed interest or selected "maybe" regarding participation in future trials were asked how often they would be able to travel to a clinic to receive treatment during a 2- to 3-month study period with travel expenses covered, among the respondents ($n=150$), 62 (41%) indicated they could travel "as many times as needed." Others preferred less frequent visits: 3 (2%) three times per week, 6 (4%) twice per week, 23 (15%) weekly, 22 (15%) every 2 weeks, and 34 (23%) monthly.

When participants' feelings about participating in a clinical trial that involves receiving a placebo (inactive treatment) were queried, among the respondents ($n=156$), the most common response (54, 35%) was being "comfortable with it." Another 53 (34%) reported they would consider it, given the opportunity to try the real treatment at a later point. Twenty-nine (19%) expressed concerns but might still consider participating, while 20 (13%) reported they would not be comfortable with it.

DISCUSSION

This survey of Australians with cluster headache found that, although most participants were engaged in ongoing medical care and frequently used treatments, the reported effectiveness was low—only 6% rated their current regimen as very effective. Participants identified clear priorities for future research, including understanding the underlying causes of cluster headache, developing more effective treatments, and improving clinician and public awareness. Interest in future clinical trials was high, particularly for psilocybin and combination therapies, with many participants expressing willingness to participate in studies even including a placebo arm.

Our findings, indicating treatment inadequacy, align with those of an online medication use survey by Clusterbusters, which reported that approximately 25% of participants (122 out of 493) found no treatment to be effective.[9] A Danish survey[10] involving 400 participants evaluated patient-reported treatment efficacy and found complete response rates of 30% for oxygen, 55% for injectable triptans, and 30% for oral triptans among acute treatments. For preventive therapy, verapamil showed a complete response rate of 15%—only half of those on preventive treatments experienced at least a 50% response rate.[10] Although we did not assess the reported efficacy of individual treatments separately, we found that most participants did not consider their treatment effective—only 6% reported it as very effective. About 32% rated it as somewhat effective. Other studies have reported varying levels of satisfaction with treatments; however, preventive treatments were generally reported as less effective. Among individuals with cluster headache in Norway ($n=196$), the median effectiveness score was 8 out of 10 for acute treatments and 6 out of 10 for preventive treatments.[11] In an online population-based survey conducted in the United States ($n=789$), approximately 80% of participants who met the criteria for cluster headache reported that sumatriptan was effective, while 75% found oxygen beneficial. For preventive treatments, verapamil was rated effective by 58% and lithium by 50%.[12]

We found that most participants used triptans, and half used oxygen for the management of acute pain. Regarding preventive treatments, most use prescription medications such as verapamil or divalproex sodium. These patterns are broadly consistent with previous research, which found high usage and effectiveness ratings for oxygen (80%) and psilocybin (30%) as abortive treatments.[8] Triptan injections, used by 60% of participants, had the highest satisfaction rate, with about 80% rating them as completely or moderately effective.[8] Together, these data highlight the reliance on a limited range of treatments, the need for more effective and accessible options, and the emerging interest of patients in alternatives like psilocybin. Supporting these reports, a systematic literature review conducted in 2022 revealed that oxygen and subcutaneous triptan injections were the most effective abortive treatments, whereas psilocybin and lysergic acid diethylamide (LSD) were the most frequently mentioned as effective preventive options by people with cluster headache.[13]

Participants in our study expressed interest in various interventions, with the highest level of interest in psilocybin. According to previous reports, some participants had already tried psilocybin and other illicit substances. Lorenzo et al. conducted an Internet-based survey in Italy and reported that 89% of participants ($n=54$) had tried at least one preventive treatment, and all of them expressed dissatisfaction with conventional treatments and had tried illicit drugs, including 34% using cannabinoids, 24% using cocaine, and 33% using psilocybin.[14] About half of the participants reported illicit drugs as safer than conventional therapies.[14] In another study, among preventive medications, psilocybin was used by 35% and LSD by 15%, both showing the highest satisfaction rates, with over 70% of users finding them completely or moderately effective. Verapamil had a lower effectiveness rate, with about 10% reporting it as completely effective and 30% as moderately effective, totaling approximately 40%.[8] Regarding other treatment methods, a study by Rossi et al., based on a headache clinic survey of 100 participants, found that approximately 30% of participants reported using complementary and alternative medicine, such as acupuncture, homeopathy, and chiropractic, for managing cluster headache. However, only 8% found it effective, and 28% reported partial effectiveness.[15]

Mood disorders are commonly reported among people with cluster headache. In our study, the majority (~85%) of participants reported at least one mental health symptom. A substantial proportion experienced stress and anxiety symptoms during attacks, which aligns with previous research indicating that approximately 45% of individuals reported such symptoms during cluster headache attacks.[16] These findings come from a large, multi-country survey ($n=1012$) conducted in the United States, United Kingdom, and Germany. Notably, 60% of our participants reported depression associated with their attacks, which is more than double the rate observed in a Danish study, where around 30% reported depression.[17] The difference may be due to variations in data collection methods. In our study, we only asked participants whether they had depression, whereas the Danish study used a 362-question questionnaire and conducted interviews to establish the diagnosis for different comorbidities. Although our study did not assess suicidal thoughts directly, previous research from the United States involving 1134 individuals with cluster headache found that more than half of individuals with cluster headache have reported experiencing them,[18] underscoring the severe psychological burden of the condition. These findings highlight the urgent need for integrated care approaches that address both the physical and mental health impacts of cluster headache.

Many participants expressed a strong desire for more research on cluster headache and showed interest in being involved in future studies. Of the 202 respondents, 62% were willing to participate in clinical trials, particularly those testing psilocybin and combination therapies (defined in the survey as multiple treatments together). There has been no prior research documenting the willingness of patients with cluster headache to participate in clinical trials. Our study uniquely highlights this interest, showing that most respondents were eager to enroll, with many providing their contact information. This emphasizes that, although cluster headache is a rare condition, individuals affected by it are highly engaged and eager to support clinical research. Regarding the use of a placebo, most participants in our study were comfortable receiving one, although about half of those who expressed comfort noted that this was conditional on having the opportunity to receive the active intervention afterward. Supporting our findings, although not assessed for a trial setting, the clinical use of placebo has been reported as acceptable among patients in a general outpatient clinic.[19]

Emerging research suggests that psilocybin has therapeutic potential for a range of psychological disorders, including anxiety, depression, and addiction.[20] Although these indications involve very different mechanisms and treatment contexts, there is also growing evidence supporting psilocybin's potential in treating headache disorders, including migraine and cluster headache. For example, an exploratory double-blind study revealed that a single dose of psilocybin significantly reduced the number of migraine days per week.[21] Similarly, evidence from clinical trials supports the therapeutic effect of psilocybin on cluster headache.[22,23] Based on anecdotal data, more than half of the people with cluster headache have reported that psilocybin is effective as both a preventive and acute treatment.[8,24,25]

Psilocybin, a serotonin 2A receptor agonist, is hypothesized to help manage cluster headache through its interaction with the serotonergic system and by reducing hypothalamic activity, which has been shown to increase during cluster headache attacks.[22,26] A small trial showed psilocybin's ability to modulate the hypothalamus-diencephalic neural pathway, with participants tolerating the dosing well, experiencing positive effects, and showing a willingness to use it again.[22] Beyond these preliminary findings, it is essential to investigate psilocybin more rigorously, as many individuals with cluster headache are already interested in and may access this drug independently of medical supervision, raising important concerns given its potential for adverse effects. As many individuals with cluster headache already seek out this intervention, it is essential to determine through well-designed randomized clinical trials whether psilocybin is both effective and safe and if it is, to determine a scientifically valid dosing regimen.

Despite consulting healthcare professionals, many still struggled with treatment effectiveness, side effects, access issues, and cost – highlighting the limitations of current management options. The strong interest in participating in clinical trials, particularly those investigating novel therapies such as psilocybin or combination treatments, reflects a pressing unmet need for more effective and accessible interventions. Importantly, participants also expressed clear preferences regarding trial design, including outcome measures, visit frequency, and geographic accessibility. These findings underscore the value of incorporating patient perspectives in shaping future clinical research to ensure it aligns with the needs and priorities of those most affected.

Strengths and limitations

This study holds several limitations. First, the diagnosis of cluster headache was self-reported, which may have influenced the results by introducing misclassification bias. Secondly, compared to previous epidemiological studies,[2] our sample included a higher proportion of individuals who reported attacks occurring almost every month throughout the year—consistent with chronic cluster headache[27]—which may reflect the greater motivation of this group to participate in research. Thirdly, the primary recruitment methods—through specialist clinics and patient advocacy groups—may have resulted in a sample disproportionately composed of individuals with more refractory disease. This recruitment bias could limit the generalizability of the findings to the broader population of people with cluster headache, who may present with a wider spectrum of disease severity. However, the method we used demonstrated our ability to reach a large number of potential participants for future trials and gain their support.

Additionally, we did not collect data on participants' prior experience with psychedelic medicines or their previous participation in clinical trials. Including such information could have provided useful context for interpreting participants' attitudes and interest in future studies. This limitation should be considered when interpreting the findings. We also did not collect detailed information on the specific types of NSAIDs and triptans used, their routes of administration, or the techniques employed for nerve blocks. Finally, the data we collected on participants' perspectives regarding the efficacy of their treatments were general, and we did not collect separate information on their views of acute versus preventive treatments. Although such data would have been valuable, we aimed to keep the survey focused and easy for participants to complete within a reasonable time frame.

CONCLUSION

This survey demonstrated that people with self-reported cluster headache report substantial gaps in the management of cluster headache in Australia, with more than half of participants not regularly engaging with specialist neurological care. Furthermore, whereas most patients had tried prescription medications for both acute and preventative management, evidence-based treatments like oxygen were not being widely utilized. The need for new therapeutic options is emphasized by the fact that most patients expressed the need for further clinical trials for cluster headache. The majority of participants expressed interest in participating in future clinical trials, particularly for interventions such as psilocybin or combination therapies. This provides promising insight into the feasibility of conducting future trials with strong support from individuals living with cluster headache.

AUTHOR CONTRIBUTIONS

Faraidoon Haghdoost: Conceptualization; investigation; writing – original draft; methodology; validation; visualization; writing – review and editing; software; formal analysis; data curation; resources; project administration. **Dilara Bahceci:** Conceptualization; investigation; methodology; validation; visualization; writing – review and editing. **Candice Delcourt:** Conceptualization; methodology; validation; writing – review and editing; supervision. **Tissa Wijeratne:** Conceptualization; methodology; validation; supervision; writing – review and editing. **Rigmor H. Jensen:** Conceptualization; methodology; writing – review and editing; supervision. **Carl Cincinnato:** Conceptualization; methodology; validation; writing – review and editing. **Susan Tomlinson:** Conceptualization; investigation; writing – review and editing; methodology. **Bob Wold:** Conceptualization; investigation; writing – review and editing; methodology. **Vince Polito:** Conceptualization; investigation; writing – review and editing; methodology. **Cheryl Carcel:** Conceptualization; investigation; supervision; writing – review and editing; methodology. **Usman Ashraf:** Conceptualization; investigation; methodology; validation; visualization; writing – review and editing. **Bronwyn Jenkins:** Conceptualization; investigation; methodology; writing – review and editing. **Anja Sofie Petersen:** Conceptualization; investigation; methodology; validation; writing – review and editing; visualization. **Jason C. Ray:** Conceptualization; investigation; methodology; writing – review and editing. **Emmanuelle A. D. Schindler:** Conceptualization; investigation; writing – review and editing; methodology. **Benjamin Tsang:** Conceptualization; investigation; methodology; writing – review and editing. **Chris Gianacas:** Conceptualization; investigation; methodology; writing – review and editing; supervision. **Anthony Rodgers:** Conceptualization; methodology; investigation; supervision; validation; visualization; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

Rigmor H. Jensen received a restricted research grant (for institution) from Lundbeck pharma, Treatment trial for IIH (for institution) from Novo Nordisk Foundation, and for Cluster Headache from Lundbeck Pharma (for institution). Advisory board for Lundbeck Pharma (for institution), Personal fee for educational and teaching activities from Pfizer, Teva, Novartis, Abbvie, Lundbeck, and Eli-Lilly, Chair of Master of Headache Disorders, Director of Danish Headache Center, and unpaid activities as Director in Lifting The Burden. **Bronwyn Jenkins** has received fees for being on advisory boards for Novartis (Aimovig [erenumab]), Teva (Ajovy [fremanezumab]), Lilly (Emgality [galcanezumab]), AbbVie (Botox [onabotulinum toxin A]), and Pfizer (Nurtec ODT [rimegepant]). Bronwyn previously received honoraria from Care Pharmacy, Healthed, and General Practice Conference and Exhibition for invited lectures. **Anja Sofie Petersen** has received a restricted research grant (payment to the institution) and personal fees from Pfizer for teaching activities. **Jason C. Ray** reports in the past 36 months he has received honoraria for educational presentations for Abbvie, Novartis, and Viatris. He has served on medical advisory boards for Pfizer, Viatris, and Lilly. His institution has received funding for research grants, clinical trials, and projects supported by the International Headache Society, Brain Foundation, Lundbeck, Abbvie, Pfizer, and Eon. **Emmanuelle A. D. Schindler** has received research funding from National Headache Foundation, Wallace Research Foundation, Ceruvia Lifesciences, Heffter Research Institute, Clusterbusters, and the US Department of Veterans Affairs. She serves on the scientific advisory boards for OptoSom and Clusterbusters and previously served as a consultant for Ceruvia Lifesciences and PureTech Health. She is named inventor on the following patent related to psychedelics in headache disorders: US20210236523A1. E.A.D.S. is an employee of the US Department of Veterans Affairs; any opinions, findings, and conclusions, or recommendations expressed in this material are her own and do not necessarily reflect the views of the US Department of Veterans Affairs. **Cheryl Carcel** received funding from the National Health and Medical Research Council Australia (APP 2009726) and from Bayer for serving on a diversity and inclusion committee. **Vince Polito** has received research funding from Mydecine Innovations Group and Woke Pharmaceuticals. **Faraidoon Haghdoost, Dilara Bahceci, Candice Delcourt, Tissa Wijeratne, Carl Cincinnato, Susan Tomlinson, Bob Wold, Vince Polito, Usman Ashraf, Benjamin Tsang, Chris Gianacas**, and **Anthony Rodgers** declare no conflict of interest.

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REFERENCES

1. Burish MJ, Pearson SM, Shapiro RE, Zhang W, Schor LI. Cluster headache is one of the most intensely painful human conditions: results from the international cluster Headache questionnaire. *Headache*. 2021;61:117-124.
2. Fischera M, Marziniak M, Gralow I, Evers S. The incidence and prevalence of cluster Headache: a meta-analysis of population-based studies. *Cephalalgia*. 2008;28:614-618.
3. Lund NLT, Petersen AS, Fronczek R, et al. Current treatment options for cluster headache: limitations and the unmet need for better and specific treatments—a consensus article. *J Headache Pain*. 2023;24:121.
4. Kim SA, Choi SY, Youn MS, Pozo-Rosich P, Lee MJ. Epidemiology, burden and clinical spectrum of cluster headache: a global update. *Cephalalgia*. 2023;43:03331024231201577.
5. May A, Leone M, Afra J, et al. EFNS guidelines on the treatment of cluster headache and other trigeminal-autonomic cephalalgias. *Eur J Neurol*. 2006;13:1066-1077.
6. Ray JC, Stark RJ, Hutton EJ. Cluster headache in adults. *Aust Prescr*. 2022;45:15-20.
7. Petersen AS, Lund N, Goadsby PJ, et al. Recent advances in diagnosing, managing, and understanding the pathophysiology of cluster headache. *Lancet Neurol*. 2024;23:712-724.
8. Schindler EA, Gottschalk CH, Weil MJ, Shapiro RE, Wright DA, Sewell RA. Indoleamine hallucinogens in cluster Headache: results of the Clusterbusters medication use survey. *J Psychoactive Drugs*. 2015;47:372-381.
9. Schindler EAD, Cooper V, Quine DB, et al. "you will eat shoe polish if you think it would help"-familiar and lesser-known themes identified from mixed-methods analysis of a cluster headache survey. *Headache*. 2021;61:318-328.
10. Petersen AS, Lund N, Jensen RH, Barloese M. Real-life treatment of cluster headache in a tertiary headache center—results from the Danish cluster Headache survey. *Cephalalgia*. 2021;41:525-534.
11. Bekkelund SI, Ofte HK, Alstadhaug KB. Patient satisfaction with conventional, complementary, and alternative treatment for cluster headache in a Norwegian cohort. *Scand J Prim Health Care*. 2014;32:111-116.

12. Klapper JA, Klapper A, Voss T. The Misdiagnosis of cluster headache: a nonclinic, population-based, internet survey. *Headache*. 2000;40:730-735.
13. Rusanen SS, De S, Schindler EAD, Artto VA, Storvik M. Self-reported efficacy of treatments in cluster Headache: a systematic review of survey studies. *Curr Pain Headache Rep*. 2022;26:623-637.
14. Di Lorenzo C, Coppola G, Di Lorenzo G, Bracaglia M, Rossi P, Pierelli F. The use of illicit drugs as self-medication in the treatment of cluster headache: results from an Italian online survey. *Cephalalgia*. 2016;36:194-198.
15. Rossi P, Torelli P, Di Lorenzo C, et al. Use of complementary and alternative medicine by patients with cluster headache: results of a multi-centre headache clinic survey. *Complement Ther Med*. 2008;16:220-227.
16. Cotton S, Andrews JS, Nichols RM, et al. Clinical characteristics and treatment patterns of patients with episodic cluster headache: results from the United States, United Kingdom and Germany. *Curr Med Res Opin*. 2023;39:1637-1647.
17. Lund N, Petersen A, Snoer A, Jensen RH, Barloese M. Cluster headache is associated with unhealthy lifestyle and lifestyle-related comorbid diseases: results from the Danish cluster Headache survey. *Cephalalgia*. 2019;39:254-263.
18. Rozen TD, Fishman RS. Cluster headache in The United States of America: demographics, clinical characteristics, triggers, suicidality, and personal burden. *Headache*. 2012;52:99-113.
19. Ortiz R, Chandros Hull S, Colloca L. Patient attitudes about the clinical use of placebo: qualitative perspectives from a telephone survey. *BMJ Open*. 2016;6:e011012.
20. Johnson MW, Griffiths RR. Potential therapeutic effects of psilocybin. *Neurotherapeutics*. 2017;14:734-740.
21. Schindler EAD, Sewell RA, Gottschalk CH, et al. Exploratory controlled study of the migraine-suppressing effects of psilocybin. *Neurotherapeutics*. 2021;18:534-543.
22. Madsen MK, Petersen AS, Stenbæk DS, et al. CCH attack frequency reduction after psilocybin correlates with hypothalamic functional connectivity. *Headache*. 2024;64:55-67.
23. Schindler EAD, Sewell RA, Gottschalk CH, et al. Exploratory investigation of a patient-informed low-dose psilocybin pulse regimen in the suppression of cluster headache: results from a randomized, double-blind, placebo-controlled trial. *Headache*. 2022;62:1383-1394.
24. de Coo IF, Naber WC, Wilbrink LA, Haan J, Ferrari MD, Fronczek R. Increased use of illicit drugs in a Dutch cluster headache population. *Cephalalgia*. 2018;39:626-634.
25. Sewell RA, Halpern JH, Pope HG Jr. Response of cluster headache to psilocybin and LSD. *Neurology*. 2006;66:1920-1922.
26. Courault P, Demarquay G, Zimmer L, Lancelot S. Cluster headache: state of the art of pharmacological treatments and therapeutic perspectives. *Fundam Clin Pharmacol*. 2021;35:595-619.
27. Headache Classification Committee of the International Headache Society (IHS). The International classification of Headache disorders, 3rd edition. *Cephalalgia*. 2018;38:1-211.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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