



**A Qualitative Inquiry into Practitioners' Experiences of Using
Ibogaine and Other Psychoplastogens in the Treatment of
Substance Misuse.**

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Abstract

This thesis explores the therapeutic potential of Ibogaine, a psychoactive substance, in treating substance misuse disorders. The research is driven by the increasing interest in psychedelic therapies amidst the perceived inadequacies of conventional treatments. The study is divided into two main components: a scoping review of the existing literature on psychedelic-assisted therapies and a qualitative analysis based on semi-structured interviews with experienced Ibogaine treatment providers.

By mapping the broader field of psychedelic research, the scoping review provides context to the specific findings on Ibogaine. It identifies key challenges and opportunities within the field, underscoring the details of trials utilising psychedelics like LSD and psilocybin, alongside Ibogaine and other psychoplastogens in addressing substance misuse.

The qualitative study investigates the experiences and approaches of treatment providers, offering insights into the multifaceted dimensions of Ibogaine administration, including varied dosing strategies, pre-treatment rituals, and post-treatment care. These findings highlight the importance of a holistic, patient-centric approach, which is crucial for maximising therapeutic outcomes in substance misuse treatment.

This thesis contributes to the growing body of knowledge on psychedelic therapies by offering a detailed examination of Ibogaine's role in addiction treatment and situating it within the larger context of psychedelic research. The study advocates for the integration of patient-centric approaches in treatment protocols and calls for further research to explore the synergistic effects of combining Ibogaine with other therapeutic agents. Additionally, it addresses the need for adaptive regulatory frameworks and ethical guidelines to support the safe and effective application of these emerging therapies.

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Author Statement

I hereby declare that this thesis, entitled "A Qualitative Inquiry into Practitioners' Experiences of Using Ibogaine and Other Psychoplastogens in the Treatment of Substance Misuse" is my own original work and has not been submitted in substantially the same form for the award of a higher degree at any other institution. All the research and writing presented in this thesis have been conducted and authored by me independently. No sections of this thesis have been published or submitted elsewhere. This work is submitted in fulfilment of the requirements for the degree of Doctor of Philosophy.

Dedication

To the roots that nourished me, the branches that grew alongside me, and the countless fellow travellers who've shared in the sacred song of being.

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Finally, I dedicate this thesis to all current and future Ibogaine treatment providers. This research would not have been possible without your existence and unconditional participation. Thank you for your commitment to this important work.

Glossary

Abbreviation	Full Term
5-MeO-DMT	5-methoxy-N,N-dimethyltryptamine
5-HT2A	5-Hydroxytryptamine 2A
AA	Alcoholics Anonymous
AASE	Alcohol Abstinence Self-Efficacy Scale
ACP	Addiction Care Practice
AE	Adverse Event
ARCI	Addiction Research Center Inventory
ASI	Addiction Severity Index
AUDIT	Alcohol Use Disorders Identification Test
BAC	Blood Alcohol Content
BDI	Beck Depression Inventory
BMI	Body Mass Index
BPS	British Psychological Society
CADSS	Clinician Administered Dissociative Symptoms Scale
CBT	Cognitive Behavioural Therapy
CBQ	Craving Beliefs Questionnaire
CHIME	Connectedness, Hope, Identity, Meaning, and Empowerment
CIWA-Ar	Clinical Institute Withdrawal Assessment for Alcohol
CNS	Central Nervous System
COWS	Clinical Opiate Withdrawal Scale
CR	Critical Realist
DAST-10	Drug Abuse Screening Test-10
NN-DMT	N,N-Dimethyltryptamine
DOS	Dutch Opiate Scale
DPT	Dipropyltryptamine
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
ECG	Electrocardiogram
EPIC	Enhancing Patient Involvement in Clinical Trials
EU	European Union
FHM	Faculty of Health and Medicine
FHMREC	Faculty of Health and Medicine Research Ethics Committee
GABA	Gamma-aminobutyric acid
GAD-7	Generalized Anxiety Disorder 7-item scale
G.E.D.	General Educational Development
GDNF	Glial cell line-derived neurotrophic factor
GITA	Global Ibogaine Therapy Alliance
HAM-D	Hamilton Depression Rating Scale

HCL	Hydrochloride
HHS	U.S. Department of Health and Human Services
HRS	Hallucinogen Rating Scale
ICEERS	International Center for Ethnobotanical Education, Research, and Service
IM	Intramuscular
KAT	Ketamine-Assisted Therapy
KEP	Ketamine Enhanced Psychotherapy
KPT	Ketamine psychedelic therapy
LCS	Life Crisis Scale
LSD	Lysergic acid diethylamide
MAO	Monoamine oxidase
MAPS	Multidisciplinary Association for Psychedelic Studies
MD	Methadone
MDMA	Methylenedioxymethamphetamine
MEQ	Mystical Experience Questionnaire
MESH	Medical Subject Headings
MET	Motivational Enhancement Therapy
MMPI	Minnesota Multiphasic Personality Inventory
MS	Multiple Sclerosis
NA	Narcotics Anonymous
NCT	Nicotine Craving Test
NIHR	National Institute for Health Research
NMDA	N-methyl-D-aspartate
O.H.R.P.	Office for Human Research Protections
ONS	Office for National Statistics
OOWS	Objective Opiate Withdrawal Scale
OPCS	Office of Population Censuses and Surveys
OST	Opiate Substitution Therapy
PACS	Psilocybin-Assisted Cognitive-Behavioural Smoking Cessation
PEP	Psychiatric Evaluation Profile
PHE	Public Health England
PHQ-9	Patient Health Questionnaire-9
PIS	Participant Information Sheet
PLT	Periodic Level of Tension
POI	Personal Orientation Inventory
POMS	Profile of Mood States
PPI	Patient and Public Involvement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PTA	Purified Total Alkaloid

QSU	Questionnaire of Smoking Urges
RCT	Randomized Controlled Trial
REM	Rapid eye movement
RQ	Research Question
RRQ	Reasons for Relapse Questionnaire
SA	Self-Assessment
SARA	Scale for the Assessment and Rating of Ataxia
SAS	Self-Rating Anxiety Scale
SCID I	Structured Clinical Interview for DSM-IV Axis I Disorders
SDT	Scopolamine Detoxification Technique
SF-12	Short Form Health Survey-12
SIP-2R	Short Index of Problems
SMH	Self-Medication Hypothesis
SOC	Sense of Coherence
SOCQ	Subjective Outcome of the Cognitive Therapy
SOCRATES 8A	Sociocultural Attitudes Towards Substance Use Scale
SOWS	Subjective Opiate Withdrawal Scale
TA	Total Alkaloid
TLFB	Timeline Follow-Back
TQD	Target Quit Date
U.K.	United Kingdom
U.S.	United States
VAS	Visual Analogue Scale

1. Introduction

This chapter aims to introduce the role of Ibogaine and other psychedelics in the treatment of substance misuse, highlight the importance of the social context in understanding their effectiveness, building an argument for the main aims of the thesis.

1.1 Substance Misuse: A Growing Concern

1.1.1 Definition

Substance misuse, a term that encapsulates the inappropriate consumption of both legal and illicit substances, has become a pressing concern in recent years. Such misuse affects the brain's reward, motivation, and memory systems, leading to compulsive or obsessive behaviours without consideration of potential consequences (Koob & Volkow, 2016; Everitt & Robbins, 2016). The repercussions of substance misuse are vast, ranging from personal health issues to wider societal, political and economic challenges.

1.1.2 Prevalence

In 2022, 2.6% of adults aged 16 to 59 in England and Wales were identified as frequent drug users (defined by the Office for National Statistics as having taken an illicit drug more than once a month in the last year). (Office for National Statistics, 2022). Furthermore, between April 2021 and March 2022, the number of adults in the UK seeking help from drug and alcohol services rose to 289,215 compared to 275,896 the previous year, continuing a gradual upward trend observed in recent years. (UK Government, 2022a; UK Government, 2022b). This surge in numbers is especially alarming considering that 4,359 drug poisoning-related deaths were reported in England and Wales in 2021 alone (Office for National Statistics, 2021a). Furthermore, Scotland's drug-induced death rate is the highest in Europe at 27.7 per 100,000, almost three times higher than the next highest country, Ireland (Royal College of Psychiatrists, 2024).

1.1.3 Challenges

The challenges inherent in treating substance misuse are multifaceted and require careful consideration to ensure effective treatment strategies. High relapse rates and limited alternative treatments mean that current interventions often require multiple sessions and continuous monitoring (Koob & Volkow, 2010). Singular, short-term treatments are generally considered unconventional. Moreover, the complexities in treating substance misuse have led to the exploration of various treatments, including Opiate Substitution Therapy (OST). OST involves replacing illicit opiate substances with safer and medically controlled variants and it is often seen as a maintenance treatment. However, despite their

popularity, treatment can be challenging as it has been associated with adverse events, logistical issues, and the requirement of abstinence (Adrian, 2013). This approach can also be dangerous when combined with other sedatives, especially benzodiazepines, alcohol and (tricyclic) antidepressants (Connock et al., 2007).

Before exploring the potential of psychedelics, it is important to contextualise the current landscape of addiction treatment. Standard care in the UK for substance use disorders often involves a combination of psychosocial support and pharmacotherapy. For opioid use disorder, Opiate Substitution Therapy (OST) using methadone or buprenorphine remains the primary treatment approach. For alcohol use disorder, medications such as naltrexone, acamprosate, and disulfiram are used to help manage cravings and prevent relapse (National Institute for Health and Care Excellence [NICE], 2011). While these treatments can be effective, they often require long-term adherence, can have significant side effects, and relapse rates remain a challenge, highlighting the ongoing need for novel therapeutic approaches.

1.2 Psychedelic and Psychoplastogen Substances

1.2.1 Nature and History

The use of psychedelics and psychoplastogens can be traced back to ancient practices (Principe, 2023). Psychedelics and psychoplastogens are a class of substances that can potentially induce rapid structural and functional neural plasticity (Vargas et al., 2021; Olson, 2018), and their therapeutic potential has been explored since the 1960s (Liemer, 2014; Smart et al., 1966). However, after their initial exploration, many of these substances were criminalised and heavily restricted globally. Despite this, there is an abundance of studies investigating the therapeutic potential of these substances for treating substance misuse. However, challenges such as small sample sizes, methodological inconsistencies, and the absence of long-term follow-up data raise important questions about the long-term impact of these interventions (Muthukumaraswamy et al., 2023; Olson et al., 2022; Szegedi et al., 2023).

1.2.2 Therapeutic Potential

Psychedelics are a class of psychoactive substances that produce profound changes in perception, mood, and thought, primarily by acting as agonists at serotonin 5-HT_{2A} receptors. The use of psychedelics and psychoplastogens can be traced back to ancient practices (Nichols, 2016). Since the early 2010s, scientific interest has been resurgent regarding the therapeutic applications of psychedelic substances. Psychedelics belongs to a wider category of psychoplastogens—molecules known to induce structural and functional neural plasticity swiftly. This category encompasses not only psychedelics but also compounds such as ketamine, scopolamine, methylenedioxymethamphetamine (MDMA), and other newly identified fast-acting antidepressants (Olson, 2018). The therapeutic application of these

psychoplastogenic compounds could represent a paradigm shift in neuropsychiatry. Recognising past efforts, including the varied strategies and outcomes from previous trials, is crucial.

Present trials also utilise diverse methods and measures, such as neuroimaging techniques, behavioural assessments, clinical rating scales, patient-reported outcomes, and the analysis of neuroplasticity biomarkers like BDNF and neuroinflammatory markers. Thus, pinpointing the most effective approach for broad implementation is imperative (Vargas et al., 2021).

Numerous psychedelics and psychoplastogen substances have been explored for their potential therapeutic benefits in treating substance misuse. This range of substances underscores the exploratory nature of the field and the continuous endeavours to identify the most efficacious substances for various addiction types. It's noteworthy that double-blind randomised controlled trial designs were utilised in studies assessing the efficacy of LSD for alcohol misuse treatment (Krebs & Johansen, 2012). These studies revealed that a single dose of LSD was associated with a statistically significant decrease in alcohol misuse compared to placebo or other treatments. However, it's important to acknowledge that these findings should be interpreted cautiously due to the limited number of trials and potential methodological limitations.

Preliminary clinical trials integrating psychedelics with psychotherapy for substance misuse treatment have shown promising results (Krebs & Johansen, 2012; Rothberg et al., 2021; Johnson et al., 2017). Among these substances, Ibogaine, a naturally occurring psychoactive alkaloid derived from the Iboga plant, has attracted considerable interest for its unique, putative anti-addictive properties, particularly its potential to interrupt opioid withdrawal symptoms and cravings after a single administration (Brown & Alper, 2018; Alper et al., 2008). Early research, including ethnographic analyses by Alper et al. (2008) of over 3,000 Ibogaine users and their treatment settings, and retrospective reviews of adverse events in 305 individuals (Alper et al., 2006), has begun to explore its effects. Alper & Lotsof (2007) conducted an open-label case series with 14 opioid-dependent individuals, demonstrating Ibogaine's potential to rapidly reduce withdrawal symptoms. This aligns with Alper et al. (2008), who conducted 12-month observational study of 14 opioid-dependent individuals, which found that a single Ibogaine treatment significantly reduced opioid withdrawal symptoms, measured using the Subjective Opiate Withdrawal Scale (Handelsman et al., 2005) and led to either opioid cessation or sustained reduction in use for most participants.

While these studies, along with Lotsof & Alexander's (2001) review of preclinical and clinical data, suggest potential efficacy in reducing cravings and relapse, methodological limitations persist. These

include small sample sizes, such as the 14 participants in both the Alper & Lotsof (2007) and Alper et al. (2008) studies, and a lack of control groups in some instances. This limits the generalisability of findings and the ability to definitively attribute observed effects to Ibogaine. Furthermore, Alper et al. (2006) highlighted safety concerns, including cardiac complications, associated with Ibogaine administration.

Despite these early insights, the need for more robust research is echoed by Brown and Molinari (2021). Their systematic review of 24 studies on Ibogaine and its derivative, Noribogaine, found only two randomised, double-blind, controlled clinical trials. This scarcity of rigorous trials, also highlighted by the limited sample size (20 participants) of a recent clinical trial in Spain testing a novel Ibogaine protocol for opioid dependency (ICEERS, 2023), underscores the need for further investigation. Rigorous, large-scale

clinical trials with appropriate control groups and comprehensive safety monitoring are crucial to definitively establish Ibogaine's efficacy and safety as a treatment for substance use disorders.

Therefore, while the existing evidence suggests Ibogaine's potential, further rigorous research is needed to definitively establish its efficacy and safety for treating opioid addiction. This need for further investigation strengthens the rationale for pursuing a PhD in this area, as it highlights the opportunity to contribute significantly to the understanding and development of Ibogaine as a potential treatment option.

1.3 A Conceptual Bio-Psycho-Social Framework for Substance Misuse and Psychedelic Use

1.3.1 The Biopsychosocial Model: A Holistic Approach to Substance Misuse

The recovery approach has become the most influential paradigm shaping Western mental health policy and practice (Slade et al., 2014; Braslow, 2013). Emerging from the anti-psychiatry and survivor movements of the 1960s and 1970s, it was firmly established as a 'vision' in the 1990s. The concept of 'recovery' is grounded in two distinct traditions (Slade, 2009). The medical model interprets distress as a "disorder," viewing it as an incurable deviation from 'typical' brain functioning, with a focus on 'clinical recovery,' which is defined by symptom remission and a return to a functional baseline as measured by 'standardised' outcome measures (Braslow, 2013). In contrast, the psychosocial personal recovery model emphasises a process leading to a meaningful, fulfilling, and hopeful life despite ongoing or fluctuating distress (Slade et al., 2014; Anthony, 1993). This understanding of personal recovery aligns with the biopsychosocial model of substance misuse treatment, which acknowledges the interplay of biological, psychological, and social factors in addiction and recovery. By emphasizing individual empowerment, social connection, and the development of meaningful life goals, the personal recovery approach addresses all three domains of the biopsychosocial model. However, it is important to note that the concept of "recovery" in the substance misuse field may differ somewhat from its application in mental health. While mental health recovery often focuses on managing symptoms and improving overall well-being, recovery from substance use may involve complete abstinence, harm reduction, or a combination of approaches, depending on the individual's goals and needs. This distinction highlights the importance of person-centred care and individualized definitions of recovery in the substance misuse field, as emphasised by Brophy, Dyson, & Katherine (2023). Their concept analysis underscores that recovery from substance use is defined by the affected individual, who sets goals and objectives for

life improvements that may include managing substance use but also encompass broader aspects of well-being.

The Self-Medication Hypothesis (SMH) (Khantzian, 1985) was initially considered as a theoretical lens for this thesis because of its focus on how individuals with psychiatric disorders or emotional distress use drugs or alcohol to alleviate symptoms or cope with painful emotional states. The SMH suggests that individuals do not choose substances randomly; rather, their choice is influenced by the specific psychopharmacological effects of the drug that best addresses their psychological struggles. For example, opiates may be preferred by those dealing with aggression and rage due to their calming effects, while cocaine may be chosen by individuals experiencing depression or hyperactivity for its stimulating properties (Tronnier, 2015). However, while the SMH provides valuable insights into the psychological motivations behind substance use, it is somewhat subsumed by the biopsychosocial model, which offers a more comprehensive framework by accounting for not only psychological factors but also biological and social influences that contribute to addiction and recovery. There is little consensus on the 'model' of personal recovery (Andresen, Oades & Caputi, 2011). One such model is CHIME (connectedness, hope, identity, meaningfulness, and empowerment: Leamy et al., 2011) which synthesizes 'personal recovery processes' documented in the literature. Mental health services adopting the recovery approach promote these processes by helping service users achieve personal recovery goals such as positive relationships, meaningful work, and cultural or spiritual perspectives. The recovery approach has been praised for providing an alternative to coercive, deficit-based mental health practices (Jacob, 2015). However, it has been criticized as being 'conceptually fuzzy' (Roberts & Wolfson, 2004), possessing an individualistic worldview (Adeponle et al., 2012) and being manipulated by governments and mental health professionals to align with biomedical discourse (Harper & Speed, 2014; Hunt & Resnick, 2015; Rose, 2014).

A key criticism is that 'recovery' is almost always defined at an individual level (Topor et al., 2011), with the responsibility for recovery resting solely on the individual while ignoring the social, material, and political contexts (Adeponle et al., 2012; Harper & Speed, 2014; Duff, 2016; White, 2005). This is despite social and structural determinants such as healthcare provision, family support, education attainment, and progressive workplace arrangements being some of the strongest predictors of positive mental health outcomes (Allen et al., 2014; Furlong, 2013).

1.3.2 Biological Mechanisms of Substance Misuse and Psychedelics

Psychedelics belong to a wider category of psychoplastogens—molecules known to induce structural and functional neural plasticity swiftly. Their interaction with neurotransmitters and brain structures offers potential therapeutic benefits in treating substance misuse (Olson, 2018; Carhart-Harris & Friston, 2019; Vargas et al., 2021). Ibogaine, a naturally occurring psychoactive substance, is posited to exert its therapeutic effects by modulating brain chemistry and inducing alterations in consciousness, thereby fostering increased self-awareness of thought patterns and behaviours (Alper, Lotsof & Kaplan, 2008).

Specifically, Ibogaine is believed to act on multiple neurotransmitter systems in the brain in a way that differs from other psychedelics. It acts as an agonist at a variety of serotonin, dopamine, and gamma-aminobutyric acid (GABA) receptors. Ibogaine also interacts with multiple opioid receptors, which is thought to be responsible for its quick opioid withdrawal relief and anti-addiction properties.

Furthermore, it has been found to modulate the release of glutamate and acetylcholine, which are involved in neuroplasticity and neurogenesis (Popik & Skolnick, 1999). This suggests that Ibogaine may be neuroprotective, potentially allowing for long-term changes in neuronal organization and function. The neurobiological effect of Ibogaine is believed to have multiple actions in the brain such as MAO inhibition, agonism on 5-Hydroxytryptamine 2A (5-HT_{2A}), opioid kappa, sigma-1 and sigma-2 receptors, modulation of ligand binding to the mu-opioid receptor, antagonism on dopaminergic and 5-HT transporters, and antagonism on N-methyl-D-aspartate (NMDA) and nicotinic receptors (Popik & Skolnick, 1999). Preclinical research on Ibogaine has displayed effects such as lessening of withdrawal symptoms in alcohol-dependent rats (Svetic, Paškulin & Bresjanac, 2014). Moreover, tests showed Ibogaine and its by-product, Noribogaine, had antidepressant effects in rats without changing their activity levels. Noribogaine worked quickly but briefly, tied to its high level in the brain, while Ibogaine had longer-lasting effects (Rodríguez-Cano et al., 2020). In contrast to other psychedelics, Ibogaine appears to not only interact with 5-HT_{2A} receptors, which are thought to be responsible for the “psychedelic” effects of drugs such as LSD and psilocybin. This may explain why Ibogaine does not produce the same type of “trip” as other psychedelics but instead, it is described to produce a more dream-like state.

Furthermore, Ibogaine may stimulate neuroplasticity, the brain's capacity to reorganise and create new neural connections, potentially through the upregulation of glial cell line-derived neurotrophic factor (GDNF) and its associated signalling pathways (Svetic, Paškulin, & Bresjanac, 2014). The neuroplasticity effect is vital for recovering from brain injuries and addiction-related brain changes (Cherian et al.,

2023). A study on U.S. Special Operations Veterans with combat-related traumatic brain injury showed that Ibogaine treatment was linked to better cognitive performance. The study used neuropsychological assessments like the Hopkins Verbal Learning Test (Brandt & Benedict, 2001) and Wechsler Adult Intelligence Scale (Wechsler, 2008) to evaluate various areas of cognitive function (Cherian et al., 2023).

1.3.3 Psychological Impacts: Beyond the Trip

Given its effects on numerous neurotransmitters and neuroplasticity, Ibogaine is believed to have the potential to induce transformative experiences, which can play a crucial role in promoting mental well-being and addressing substance misuse issues (Brown, Noller, & Denenberg, 2019). The psychological impacts of these substances, both during and after the "trip", can offer therapeutic benefits when integrated with proper therapeutic guidance. Researchers have reported Ibogaine as an "addiction interrupter" due to its potential to diminish drug cravings and withdrawal symptoms, especially in opioid addiction (Mash, 2023; Luz & Mash, 2021). The powerful psychoactive effects of Ibogaine can create a profound and transformative psychological experience, which may lead to changes in perspective and behaviour that support recovery (Cherian et al., 2023). This effect has been described as "profoundly spiritual and deeply meaningful", contributing to a more positive outlook on life (Popik, 1996).

Psychedelics and psychoplastogens are thought to amplify emotional experiences and induce changes leading to altered states of consciousness that can be profoundly therapeutic (Johnson et al., 2014; Palhano-Fontes et al., 2019). Psychedelics can facilitate a sense of openness and connectedness with oneself, with others, and with the world at large (Carhart-Harris et al., 2014; Dos Santos et al., 2016). This can lead to an increased awareness of one's thought patterns and behaviours, facilitating an opportunity to make changes in their lifestyle through mechanisms like relaxed beliefs, psychological flexibility, and self-motivation, it could improve behavioural change in various disorders and lifestyle issues, and boost numerous psychotherapeutic methods (Teixeira et al., 2022).

1.3.4 Set and Setting: Importance of Social Context in Substance Misuse and Psychedelic Treatments

In psychedelic therapies, efficacy extends beyond the pharmacological impact to encompass the broader therapeutic milieu, including the 'set' (the mindset of the user) and 'setting' (the environment in which the substance is consumed) providing further support to the Biopsychosocial lens (Hartosoghn, 2016). This holistic approach underscores the importance of the social context in which these treatments are administered, suggesting that the therapeutic potential of psychedelics is intricately linked to how they are used, thereby impacting their effectiveness (Kroupa and Wells, 2005; Lotsof and Wachtel, 2003).

The administration of Ibogaine, for instance, varies widely from medically supervised settings to more informal environments, reflecting a spectrum of practices that all aim to harness its potential in treating opioid dependence and other substance misuse disorders. This diversity in practice settings highlights the importance of the therapeutic environment and the role of knowledgeable practitioners in facilitating the treatment process. The practitioners' understanding of the interplay between the therapeutic setting and individual experiences and their ability to conduct integration sessions where insights from the psychedelic experience are discussed is crucial in achieving therapeutic outcomes (Lotsof & Alexander, 2001).

This integrative approach to recovery, which combines the individual's internal psychological journey with the external support available to them, is mirrored in the application of psychedelic treatments like Ibogaine. The 'set and setting'—a concept that is both psychological and inherently social—plays a pivotal role in determining the outcome of the psychedelic experience.

In essence, the social context and the therapeutic setting are not merely background factors but are central to the effectiveness of psychedelic treatments. Understanding this interplay is vital for practitioners and researchers alike, as it opens pathways to potentially more effective and holistic approaches to addiction recovery, where the psychological insights gained from the psychedelic experience are integrated within a supportive social framework. This perspective aligns with the broader thesis that the potential of psychedelics in addiction treatment is maximised within a carefully curated set and setting, emphasizing the need for further research and a detailed understanding of these factors.

1.4 Critique of the Literature

1.4.1 Lack of Sufficient Evidence

A primary criticism of psychedelic treatments for substance misuse is the insufficiency of empirical evidence supporting their efficacy. A comprehensive review spanning studies from 2000 to 2021 revealed that although some research indicated favourable outcomes in areas such as abstinence, substance consumption, psychological and psychosocial results, craving, and withdrawal, the evidence was limited, especially when considering a broad spectrum of addictions like opioid, nicotine, alcohol, cocaine, and unspecified substances (Sharma, Batchelor, & Sin, 2023). This review emphasised the need for more robust research methodologies, larger participant groups, and extended follow-up periods.

1.4.2 Inherent Biases in Research

Psychedelic research has faced criticism for inherent biases, particularly in its treatment of 'mystical experiences' linked to positive mental health outcomes. The term 'intrinsic bias' refers to biases embedded within the research methodology, influencing study design, execution, and interpretation. Critics argue that the conceptualisation of 'mystical experiences' lacks historical and cultural context, leading to a bias that predominantly reflects Christian and perennialist perspectives, which suggest a universal mystic truth across all religions (Mosurinjohn, Roseman, & Girn, 2023). This critique highlights a methodological bias where the research framework may inadvertently favour certain cultural or religious viewpoints, thus restricting the universality of the findings. Moreover, this bias can manifest in various forms, including selection bias in participant recruitment or researcher backgrounds, performance bias in the setting and guidance provided during psychedelic sessions, detection bias in the assessment and interpretation of experiences, attrition bias due to challenging experiences or cultural dissonance, and reporting bias in the emphasis on positive outcomes and selective publication of findings (Carter et al., 2021; Phillips et al., 2022).

Addressing these criticisms requires a broader consideration of methodological biases in psychedelic research. A more inclusive approach is necessary, one that recognises the diverse cultural and historical backgrounds of mystical experiences. Such an approach would enhance the understanding of psychedelics' psychological impacts, ensuring research outcomes are broadly applicable and free from unrecognised cultural or religious biases. Future research should aim to incorporate a variety of perspectives and methodologies, to fully capture the range of experiences induced by psychedelics and other psychoplastogens substances. This includes building diverse research teams, employing culturally sensitive methodologies, incorporating qualitative research, encouraging reflexivity among researchers, and promoting open science practices.

1.4.3 Ethical Concerns

The administration of psychedelics in research settings raises ethical concerns, particularly regarding their legality, adequacy of testing, and potential harm to participants. Outside of approved research, these substances are often illegal to possess under legislation like the UK's Misuse of Drugs Act 1971, and are typically classified as Schedule 1 drugs under the Misuse of Drugs Regulations 2001, indicating they are perceived to have no therapeutic value and cannot be lawfully possessed or prescribed. This legal status, combined with the fact they are sometimes inadequately tested, pose risks that necessitate careful ethical consideration. Concerns about researchers' personal use include the compromise of positionality, exploitation of research participants, or biased reporting. The Office for Human Research

Protections (OHRP) at the U.S. Department of Health and Human Services (HHS) emphasizes the need to address these ethical, legal, and practical considerations to maintain the rights, welfare, and well-being of participants and ensure scientific validity and integrity. Addressing both the administration of psychedelics and researchers' personal use is crucial for upholding ethical standards in psychedelic research (Kious, Schwartz, & Lewis, 2023).

1.4.4 Barriers to Psychedelic Research

The current landscape of psychedelic research is marked by legal and regulatory barriers, as many psychedelics are classified under strict drug control laws. This classification hampers the ability to conduct research freely, affecting everything from obtaining substances for study to securing funding. Practical challenges in research methodology, particularly in ensuring proper blinding in trials, arise from the distinct psychoactive effects of psychedelics, which can make it obvious to participants whether they have received the drug or a placebo. This undermines the blinding process, a cornerstone of experimental design meant to reduce bias. Additionally, the overrepresentation of participants with previous psychedelic experiences poses a challenge because their prior exposure could influence their expectations and psychological responses, potentially skewing study results and limiting the applicability of findings to the general population. These factors highlight the complexities of conducting methodologically sound and unbiased psychedelic research.

1.5 Aims and Objectives of Research

The escalating need for innovative treatments for substance misuse is a global concern. While the opioid crisis in the US is widely publicised, the UK and Europe face their own significant challenges, including some of the highest drug-related death rates in Europe—particularly in Scotland—and the recent emergence of highly potent synthetic opioids such as nitazenes (European Monitoring Centre for Drugs and Drug Addiction [EMCDDA], 2023). This international landscape underscores the urgent importance of exploring the therapeutic potential of novel interventions like psychedelic and psychoplastogen-assisted therapies, notably Ibogaine. For research in this area to be robust, it needs a strong methodological and analytical approach, which this thesis seeks to provide.

While previous studies have focussed on the pharmacological facets of these substances, and *what* is administered, there is a crucial gap in understanding the variety of *ways* in which the substances are delivered, and the rationale behind this. This research aims to illuminate the nuanced treatment procedures and dosing strategies, as well as the rationale behind them, to provide clarity on their pragmatic application. Such insights could pave the way for further research on the relative

effectiveness of different treatment paradigms, ensuring future treatment is designed to be maximally effective and aligned with a holistic approach to substance misuse recovery.

A key part of this exploration is assessing the myriad supplementary therapies utilised alongside Ibogaine, such as talking therapies and other substances. This could offer a roadmap for patients, providers, and policymakers in amalgamating complementary therapies, ensuring a well-rounded recovery journey.

The overarching aim of this study is to provide an in-depth exploration of the application and implications of psychedelic and psychoplastogen-assisted interventions, with a spotlight on Ibogaine, within the landscape of substance misuse treatment. To encapsulate this, the thesis revolves around four synthesised research questions:

1. How are psychedelic and psychoplastogen substances, including Ibogaine, employed in clinical trials addressing substance misuse, and what are the key design and intervention characteristics?
2. What are the perspectives, roles, and practices of Ibogaine treatment providers, and how do they navigate the intricacies of substance misuse recovery?
3. How are supplementary therapies, both conversational and pharmacological, integrated with Ibogaine treatments, and what are their perceived synergies and outcomes?
4. How is the variety and availability of Ibogaine treatments understood by treatment providers, and what reasoning underpins the choice of specific treatments?

2. Methodology

This methodology chapter provides a rationale for adopting a Critical Realist (CR) position. To answer the research questions, we used scoping reviews, in-depth individual interviews, and a qualitative Reflexive Thematic Analysis (TA) approach.

2.1 Rationale for Methodology

The qualitative approach adopted for the main empirical study was deemed appropriate as it enhances understanding of human experiences and processes. The research question requires eliciting the detailed perspectives of treatment providers and understanding how their broader context influences their working practices. Furthermore, because Ibogaine is a lesser-studied psychedelic substance, and there is a scarcity of empirical studies on the topic, the use of standardised measures would limit the depth of exploration and opportunity to discover factors that the researcher might not be aware of at

the outset and therefore would fail to measure. Combining a pre-interview survey with various questions (rating, open-ended etc.) and using cross-sectional qualitative interviewing, the methodology will elicit rich and detailed accounts from treatment providers regarding their experiences with Ibogaine in the treatment of addiction (Barbour, 2013). The pre-interview survey allowed specific factual details to be captured that helped contextualise the more in-depth exploratory interviews.

2.1.1 Epistemological and Ontological Position

According to Willig (2012), researchers must first acknowledge the assumptions in their research questions and their role in shaping the study before defining data collection and analysis. This study adopts a Critical Realist (CR) perspective, which is ontologically realist—accepting that an external reality exists—and epistemologically relativist, recognising that people interpret reality differently. CR distinguishes between three domains: the empirical, actual, and real. This study focuses on the empirical and actual domains. The empirical domain captures observed experiences, such as treatment providers' narratives about Ibogaine. The actual domain explores the events and processes—like treatment practices and decision-making—that shape these experiences. By examining these domains, the study uncovers how Ibogaine is applied in substance misuse recovery and how treatment practices are structured and enacted. This focus allows the research to explore not only what treatment providers perceive (empirical) but also the mechanisms and practices they engage with (actual). While the findings aim to shed light on Ibogaine treatment, they are shaped by both the providers' accounts and the researcher's interpretation, reflecting CR's layered approach to understanding reality.

Data, according to a CR perspective, provides information about reality. However, it does not function as a direct mirror - instead, it should be interpreted to reveal the underlying structures of reality. Thus, although an objective reality exists, it cannot be precisely comprehended (Archer et al., 2012). The data obtained through the consultation (which is affected by interview-related demand characteristics) reveals the individual's perspective. The analysis represents the researcher's interpretation based on their understanding, experience, and knowledge.

2.2 Rationale for Design

2.2.1 Design choices

The research design was meticulously chosen to ensure a comprehensive exploration of the topic. The decision to employ a scoping review was deliberate, primarily due to the nature of the primary studies the research aimed to encompass. Traditional systematic reviews often focus narrowly on specific types

of primary studies, potentially excluding considerable portions of the available literature. Given the broad nature of the research question, a traditional systematic review (and meta-analysis) would have been too restrictive. Scoping reviews, as outlined by Arksey and O'Malley (2005), are adept at examining the extent, range, and nature of primary research in each area. They allow for the summarisation and dissemination of research findings from primary studies and are instrumental in identifying gaps in the current literature.

Furthermore, the choice of a qualitative semi-structured interview for the empirical study was rooted in the desire to capture the intricate nuances and complexities inherent in the experiences of treatment providers. Whilst quantitative methods might provide statistical insights, they often miss the depth and richness of individual experiences. Additionally, it would have been difficult to reach a powered sample given the limited number of practitioners globally. Qualitative research, especially semi-structured interviews, is well-suited for eliciting in-depth, detailed, and nuanced data. This method allows for a profound exploration of participants' experiences, beliefs, and perceptions, offering a holistic view of the topic at hand (Thelwall & Nevill, 2021).

2.2.2 Research Setting

In the primary study, participants were recruited globally, predominantly from the Americas, without excluding any countries, to ensure a broad spectrum of experiences in treating substance misuse. The focus was specifically on Ibogaine, due to its notable application in the treatment of substance misuse, mainly opiates. Thus, this research deliberately concentrated on substance misuse treatment, excluding broader mental health issues to maintain a targeted investigation.

2.2.3 Participant Recruitment

For the primary study, participant recruitment was a critical resource. Practitioners specialising in Ibogaine treatment were targeted to ensure a comprehensive understanding of its application in addiction treatment. The use of convenience sampling, complemented by the snowballing technique, was chosen over other sampling methods for its practicality in creating under-researched samples based on accessibility and availability.

2.3 Reflexivity statement

According to Clarke & Braun (2013), the experiences, values, assumptions, and beliefs of a researcher affect their connection with the literature and interview data, influencing how they read the data and interpret it. The term reflexivity describes a transparent and insightful approach to pre-existing

relationships with the subject matter pertinent to the credibility of the analysis and research process (Willig, 2013). The use of a CR approach necessitates reflection, as the CR approach challenges objectivity and recognises that participant and researchers' subjectivity is important (Willig, 2013; De Vaujany, 2008).

I am a 30-year-old cisgender male from North Cyprus; I speak Turkish and English and have lived in London for six years. My education includes a Bachelor's in Psychology, a Master's in Neuropsychology, and I am currently working towards a PhD in Mental Health. I have worked in substance misuse clinics for more than two years as a drug and alcohol practitioner. During my first year in the substance misuse sector, I became aware of the struggles associated with using opiate substitute medications due to the time and motivation required to detoxify from methadone and buprenorphine, the substances used to taper people away from more harmful substances. Most of my caseload also liked to use other substances besides their prescribed opiate, which was highly dangerous and actively discouraged. I am a firm believer in psychedelic treatments for mental health and substance misuse. At the start of my research, I possessed surface-level information on Ibogaine available widely on drug information sites and psychonaut websites such as Reddit and Bluelight.

Initially, I had heard numerous anecdotes from talking with people who have experienced many years of recovery/sobriety after a single Ibogaine administration and began exploring avenues to become an Ibogaine treatment provider myself. However, during this time, I quickly became aware of the lack of depth and clarity of information surrounding Ibogaine administration for substance misuse and addiction, both for those seeking to educate themselves and those undergoing treatment. With psychedelic research experiencing a resurgence, LSD and psilocybin are being discussed more frequently in medical circles, both for the potential benefits of microdosing and for their therapeutic effects demonstrated in recent clinical trials (Nutt, 2019; Reiff et al., 2020).

I decided to undertake a study with Ibogaine, not with the users but with the practitioners, to explore their views and reasonings and clarify the practices and the treatment variety in the Ibogaine treatment sector. As treatments with Ibogaine have been provided worldwide since the 1960s, different clinics and treatment providers offer a variety of treatments. In my dealings with treatment providers before the thesis, I found previous 1-2-1 audio/verbal conversations more efficient for extracting information and learning more about their views on the treatment they provide than exchanging emails. Similarly, this

particular interest in the range of Ibogaine administrations led to an interest in observing treatment characteristics – the range of substances, dosing practices, pre/after treatment approaches, etc. This led to the scoping review element of my thesis. A reflexivity journal is also used to note how the study topic affected my thoughts and decisions during the research process, and vice versa, and to explain how the codes and patterns within the raw data were interpreted and combined to form themes. I wanted to be as transparent as possible, so I preferred an inductive approach complemented with reflexivity. See the quality of the research section for more details.

Changes in opinions and decisions were noted and reflected upon in the reflective journal. For example, initially, only legal clinics would be included in the sample; after contacting an independent treatment provider (working without a clinic), the scope of the study was expanded. This was in response to realising the importance of understanding how Ibogaine treatments are provided without a clinic, as this is also a common practice. After this experience, I applied for an ethics amendment and explained the reasons behind the change in the inclusion criteria. At the start of the PhD research, the expectation was more on exploring the drugs and the treatments modalities offered, as the variety of different practices were both intriguing and concerning.

It is acknowledged that a researcher's prior experiences and beliefs can influence their engagement with the literature and data interpretation (Clarke & Braun, 2013). For the integrity of the analysis and the research process, transparency, and self-awareness regarding any pre-existing affiliations with the topic are essential (Willig, 2013). Such self-awareness is crucial when adopting a critical realist approach, as it is not entirely objective; it is enhanced when both the participants' and researcher's subjectivities are recognised (Berger, 2015; Finlay, 2002). Hence, an initial reflexive statement was written at the start of the project, and a reflexive journal maintained throughout. This ensured all decisions were done with awareness through this reflexive lens. Furthermore, reflexivity also guided the integration of stakeholder feedback into the scoping review, ensuring that the research questions and methodologies were aligned with the needs and insights of those directly involved in substance misuse treatment.

2.4 Rationale for using Reflexive Thematic Analysis

Reflexive thematic analysis is a qualitative research method that was chosen for this thesis due to its suitability for exploring complex patterns of meaning within data, particularly in the context of mental health and addiction (Clarke & Braun, 2013; Braun & Clarke, 2019). This method is characterised by its flexibility and its emphasis on the active role of the researcher in the knowledge production process,

which aligns well with the critical realist approach adopted in this study. Reflexive thematic analysis involves an iterative process, where the researcher continuously moves between the data, coding, and theme development, allowing for a rich and nuanced analysis. Unlike more rigid approaches, such as grounded theory or interpretative phenomenological analysis, reflexive thematic analysis is adaptable to a variety of theoretical frameworks and research questions, making it particularly useful for exploratory studies. The method's focus on reflexivity is also crucial, as it acknowledges the influence of the researcher's own experiences and assumptions on the analysis, thus enhancing the depth and transparency of the findings (Clarke & Braun, 2013; Braun & Clarke, 2019). Despite its advantages, reflexive thematic analysis can be time-consuming and labour-intensive due to its iterative nature, and there is a potential for subjectivity in the interpretation of data if reflexivity is not properly addressed (Nowell et al., 2017). However, its ability to capture both latent and manifest meanings within the data, combined with its flexibility, makes it an ideal method for this research, allowing for a comprehensive exploration of the subjective experiences and perceptions central to the study. This approach not only complements the theoretical lens of the research but also aligns with the study's aim to uncover deeper insights into the complex phenomena under investigation.

2.5 Public Patient Involvement

2.5.1 Patient and Public Involvement (PPI) in Research

Patient and Public Involvement (PPI) has emerged as a cornerstone of health research, ensuring that studies are designed to be relevant, participant-centric, and ethically robust. The significance of PPI is underscored by its potential to elevate the relevance and quality of clinical research (Buck et al., 2014; Simpson, Cook & Miles, 2014). Furthermore, PPI initiatives have been lauded for their empowering nature, often bolstering the confidence and personal growth of contributors. Notably, researchers who have engaged in PPI programmes have attested to a transformative shift in their perspectives, underscoring the value and importance of such involvement (Mockford et al., 2012).

2.5.2 PPI in the Current Study

In the context of this study, the PhD candidate actively sought to embed PPI principles by forging connections with a diverse array of stakeholders, including Ibogaine treatment providers (both within and outside legal frameworks), researchers, and NGOs dedicated to harm reduction in substance misuse. The specific focus on Ibogaine was driven by feedback from these contributors, who emphasised

the novelty and relevance of focusing on Ibogaine treatment providers, a group that has historically been underrepresented in research.

While initial interactions with these stakeholders were overwhelmingly positive, subsequent engagements unveiled the complexities and challenges of researching this domain. For instance, professionals in the Ibogaine realm highlighted potential hurdles in participant recruitment and the intricacies of divulging treatment protocols. To ease the process, the PhD candidate engaged the participants via email reminders on processes of recruitment starting with debriefing the informing sheet, to checking-in the day with an email reminder ahead of the interview.

The iterative feedback from these stakeholders was crucial in refining the research tools. A notable example of this is the alteration of the adverse event rating question in the questionnaire. Stakeholders highlighted the inherent difficulties in accurately documenting adverse events linked to Ibogaine use. These invaluable insights informed further versions of the questionnaire and interview questions, ensuring they were better aligned with the objectives of the study. Consequently, upon stakeholders emphasising the diversity of treatment approaches and modalities, the research adopted a more qualitative approach. It shifted focus from attempting to quantify the severity of adverse events based on their frequency, to exploring the various events that could occur during treatments and examining ways in which they might be prevented or mitigated. Similarly, this knowledge was also responsible for the information extraction of the scoping review study. Notably, these refinements were undertaken in strict adherence to ethical guidelines, with all modifications receiving the requisite approvals from the ethics committee.

2.4.3 The Ideal PPI Framework and Limitations

In an ideal scenario, supported by adequate funding, the research would benefit immensely from establishing a dedicated PPI group. This group would be a mosaic of diverse stakeholders, including Ibogaine treatment providers, representatives from harm-reduction charities, seasoned research professionals, and individuals who have either undergone or about to undergo Ibogaine treatment for addiction. Regular interactions with this group, such as through monthly meetings, would serve as a crucible for refining research decisions, ensuring they are both relevant and impactful, and providing a sounding board for the analysis and interpretation of the data.

However, it is imperative to acknowledge the constraints faced by the PhD candidate. Members of PPI groups should be paid for their time and any out-of-pocket expenses (National Institute for Health and

Care Research, 2023). Since the research is self-funded, establishing such an extensive PPI framework remains aspirational. Despite these limitations, the candidate remains unwavering in their commitment to the PPI ethos, striving to make informed research decisions based on continuous engagement and consultation with the aforementioned stakeholders.

2.6 Quality of Research

2.6.1 Trustworthiness

Conducting qualitative research demands a rigorous and systematic approach to yield meaningful and relevant results (Attride-Stirling, 2001). The term 'trustworthiness' in qualitative studies is pivotal, suggesting that the outcomes are deserving of attention (Lincoln & Guba, 1985). Lincoln and Guba (1985) further elaborated on 'trustworthiness' by introducing criteria such as credibility, transferability, dependability, and confirmability. Nowell et al. (2017) offered a guideline for these criteria to ensure 'trustworthiness' throughout each segment of TA, which was utilised in this research.

2.6.2 Credibility

Credibility pertains to the believability of the research outcomes based on the evidence presented, such that it resonates with the reader (Guba & Lincoln, 1989). In this investigation, credibility was ensured through the application of the six steps of thematic analysis as outlined by Braun and Clarke (2006, 2019) extended immersion in the data, continuous observation of data collected from the interviews and scoping review, consultations with the researcher's supervisor, and by cross-referencing initial outcomes with the primary data, as recommended by Lincoln and Guba (1985).

2.6.3 Transferability

Transferability considers whether the research outcomes can be applied in other contexts. In qualitative research, it is not always evident where the findings might be applicable. Therefore, detailed descriptions of themes, how they were developed, and from what kinds of participants, are essential, allowing those who wish to consider the relevance of the findings elsewhere to do so with confidence (Lincoln & Guba, 1985).

2.6.4 Dependability

Dependability emphasises that the research process should be coherent, transparent, and well-documented (Tobin & Begley, 2004). A comprehensive record, detailing the researcher's decisions related to theoretical and methodological concerns, is essential (Koch, 1994). This study maintained

meticulous documentation, including original data, observational notes, transcriptions, systematic coding (Appendix C7), and a reflective diary, aiding in the organisation and cross-referencing of data (Halpern, 1983).

2.6.5 Confirmability

Confirmability is concerned with ensuring that the researcher's conclusions are directly drawn from the data (Tobin & Begley, 2004). It is achieved when credibility, transferability, and dependability are all met (Guba & Lincoln, 1989). In addition, regular meetings with research supervisors to present and discuss the development themes offered an opportunity for reflection and challenge on the researcher's interpretations to ensure these could be justified by the data.

3. The Research Design and Intervention Characteristics of Trials Using Psychedelics and Other Psychoplastogens for Addiction Treatment: A scoping review

This chapter undertakes a comprehensive scoping review of clinical trials employing psychedelics and psychoplastogens in substance misuse treatment. It aims to map the research design and intervention characteristics of these trials, highlighting the diverse approaches, methods and substances used. By analysing these aspects, the review seeks to identify gaps and inconsistencies in the existing literature, thereby informing future research directions and contributing to the development of treatment frameworks for psychedelic-assisted therapies in substance misuse.

3.1 Introduction

Owing to the complexities in effectively treating substance misuse, psychedelics have been explored as potential therapies since the 1960s (Liester, 2014; Smart et al. 1966). After their initial exploration, many psychedelic substances were criminalised and heavily restricted globally due to shifting perceptions, legal classification, and concerns about their societal and individual effects (Brooks Dollar, 2022). These restrictions limited controlled research and were influenced by broader political and social factors. Nonetheless, there is a renewed scientific interest in the present day. Preliminary clinical trials integrating psychedelics with psychotherapy for substance misuse treatment have shown encouraging outcomes. Various studies have examined the efficacy of LSD, ketamine, psilocybin, and ayahuasca for addiction treatment, each with distinct doses, treatment modalities, and measures (Krebs & Johansen, 2012; Rothberg et al., 2021; Thomas et al., 2013; Johnson et al., 2014).

Psychedelics belong to a wider category of psychoplastogens—molecules known to induce structural and functional neural plasticity swiftly. This category encompasses not only psychedelics but also compounds such as ketamine, scopolamine, methylenedioxymethamphetamine (MDMA), and other newly identified fast-acting antidepressants (Olson, 2018).

Numerous psychedelics and psychoplastogens, such as LSD and ketamine, have shown promise in treating alcohol misuse through rigorous double-blind randomised controlled trials. LSD demonstrated efficacy in reducing alcohol misuse in a meta-analysis (Krebs & Johansen, 2012), while ketamine, particularly when combined with psychotherapy, showed potential benefits for achieving abstinence and managing alcohol use disorder (Grabski et al., 2022). These findings highlight the evolving exploration of these substances in addiction treatment. Even within studies focusing on identical

substances, there is a discernible variance in the doses administered and other contextual factors such as differing dosing strategies, additional support and setting of administration. This inconsistency across studies poses challenges in determining an optimal dose for psychoplastogenic treatments in substance misuse. The field of psychedelic science currently faces methodological challenges that impede conclusive determinations regarding the efficacy of these interventions in substance misuse treatments. While abundant clinical trials explore the potential of these substances, issues such as small sample sizes, methodological inconsistencies, site and session variability, absence of long-term follow-up data, and neglect of overall quality-of-life measures raise questions about the genuine impact of these interventions (Olson et al., 2022). This argument is consistent with the views expressed by several researchers in the field of psychedelic studies. The challenges mentioned, including small sample sizes, methodological inconsistencies, and lack of long-term follow-up data, are highlighted in multiple sources as significant concerns in psychedelic research (Muthukumaraswamy et al., 2023; Olson et al., 2022; Szigeti et al., 2023).

Muthukumaraswamy et al. (2023) specifically point out that psychedelic studies often suffer from low-powered studies and a strong selection bias in participant inclusion, which threatens external validity. They also emphasise the lack of long-term treatment effects as a threat to construct validity. Olson et al. (2022) discuss the methodological challenges in psychedelic clinical trials, including the difficulty of masking participants to their treatment condition and the influence of media hype on participants' expectations. They argue that these factors can lead to large placebo and nocebo effects, potentially clouding our understanding of the source of clinical improvements in psychedelic studies. Szigeti et al. (2023) further support this argument by highlighting the need for properly powered studies and the inclusion of long-term outcomes (≥ 12 months) in psychedelic research. They also stress the importance of addressing multiple testing issues and publication bias, which can inflate effect sizes and threaten statistical conclusion validity.

Furthermore, recent studies underscore the importance of understanding the interplay between the therapeutic setting and individual experiences, as well as the role of integration sessions in amplifying therapeutic outcomes (Hartogsohn, 2024; Davis, Barrett & Griffiths, 2020). For instance, Gründer and Jungaberle (2021) emphasised the necessity of a unified framework for treatment durations and follow-ups, addressing the variability observed across studies. They argue that psychedelic-assisted psychotherapy not only represents a new treatment paradigm in psychopharmacology but also necessitates a redefinition of psychotherapeutic processes and the contextualisation of

psychopharmacological interventions within a new treatment infrastructure. They identified key areas crucial for future practice and research in the field, including (1) informed patient referral and co-treatment practices, (2) appropriate patient screening, (3) dosing preparation sessions, (4) the structure of assisted dosing sessions, and (5) after-care procedures such as psychological integration. Additionally, they stress the importance of (6) supporting the development of structured patient communities. Defining future treatment delivery infrastructures and establishing requirements for therapist training are further challenges for both research and practice. Finally, Gründer and Jungaberle argue that the implementation of psychedelic-assisted psychotherapy in routine mental health care must be embedded in public communication about the potential and risks of these innovative therapeutic approaches.

In response to these challenges, this scoping review endeavours to offer a thorough evaluation of the evidence supporting the use of psychedelic and psychoplastogen-assisted interventions in substance misuse treatment. By examining the diverse methodologies and outcomes of past trials, the aim is to comprehend the various therapeutic applications of these substances. The primary goal of this scoping review is to highlight the existing gaps and inconsistencies in the literature, providing a foundation for future research. Addressing these issues can identify under-served areas needing further exploration in the domain of addiction treatment using psychedelics and psychoplastogens.

3.2 Materials and Methods

3.2.1 Study design and protocol

A scoping review was considered the most acceptable strategy based on the study's goal. The goal was too broad to be addressed through a traditional systematic review (and meta-analysis) and could be better addressed by examining the extent, range, and nature of research in this area, summarising and disseminating research findings to date, and identifying research gaps in this area; all of which are common scoping review purposes (Arksey & Malley, 2005). Unlike other secondary review methodologies, a scoping review is typically an iterative process that allows adjustments when new information about the evidence base is gained regarding the inclusion and exclusion criteria, research topics, and analytical methodologies (Munn et al., 2018). A scoping review also permits the inclusion of a wide variety of study designs, giving a more thorough picture of the research field. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension for the scoping reviews checklist (Additional File 1) (Trico et al., 2018). It adopted an established five-stage scoping review protocol developed by Arksey & O'Malley (2005) and expanded by Levac, Colquhoun &

O'Brien (2018). A five-step scoping review methodology was used to collect, evaluate, and present the analysed literature:

- Step 1: Identifying the research question(s);
- Step 2: Identifying relevant studies;
- Step 3: Study selection;
- Step 4: Charting the data;
- Step 5: Collating, summarising, and reporting the results.

3.2.2 Aims and Research Questions

This review aimed to examine the evidence for psychedelic and other psychoplastogen-assisted interventions for the treatment of substance misuse to understand the range of ways in which these substances have been used to treat substance misuse and to highlight gaps in the current literature to inform future research.

The objectives of this review are to:

- i. Examine the design characteristics of studies and interventions in clinical trials to describe psychedelic and psychoplastogen treatments.
- ii. Describe intervention characteristics and measures used to assess the impacts of psychoplastogens to treat substance misuse.

Specifically, this study sought to answer the following research questions:

- What were the design and intervention characteristics of trials that used psychedelic and psychoplastogen substances to treat substance misuse?
- What were the measures used to evaluate the impacts of these substances? What were the measures used before/during/after the intervention?

3.2.3 Identifying the relevant studies

Three electronic databases (Psycinfo, Embase and Medline) were systematically searched for relevant published trials of psychedelic and other psychoplastogen-assisted interventions for substance misuse. The above databases were chosen due to their focus on psychology, pharmacology, and mental health studies.

This scoping review search was specific to psychedelic and other psychoplastogen substances used in human trials to treat substance misuse disorders. The first concept was substance misuse which has been characterised by use of illegal substances such as heroin and cocaine, as well as prescription and legal substances such as alcohol and tobacco misuse.

The second concept was psychedelics and other psychoplastogens, including Ibogaine, psilocybin, LSD and Ayahuasca/DMT. Mescaline, as well as other psychoplastogens such as ketamine, scopolamine and MDMA, were under the scope of this review. Novel psychoplastogens arising from the search (e.g: scopolamine derivative Hab-o Shefa) have also been included in the review.

The third concept was controlled trials, which filter into open-label and double-randomised control trials. Even though there are an increasing number of observational/retrospective studies, this review was interested in observing the characteristics and measures used in trials as retrospective or survey designs are more prone to biases and less reliable.

3.2.4 Study selection and search concepts

A comprehensive search approach (Appendix 1) was used to locate published and unpublished studies. To find studies related to the concepts, the PhD candidate ran a subject/MESH terms or a thesaurus search for each database with keywords. These keywords were amalgamated from previous studies on psychedelic and psychoplastogen substances (LSD meta-analysis, Ibogaine, psilocybin papers), which the PhD candidate has been reading for primary research looking at Ibogaine treatment for substance misuse. Most substance misuse terminology comes from PhD candidates' experience working in the substance misuse sector for over two years. There was also combined support from the faculty library Information Specialist and supervisor (HR) in refining the search terms. The subject terms in each database were tested and selected initially. The following generic search strings were used to search for abstracts and titles:

Table 1*Search Strings Used in the Review*

Concept	Keywords
S1: Substance misuse	S1: ("Substance misuse*" or "Drug addict*" or "Opioid misuse*" or "Substance Withdrawal Syndrome" or "Heroin" or "Heroin Dependence" or "Opiate Dependence" or "Morphine Dependence" or "Alcoholism" or "Alcoholic*" or "Substance Abuse Treatment Center*" or "Tobacco addiction" or "Nicotine addiction" or "Detox*" or "Drug-Seeking Behavior" or "Drug Misuse" or "Abstinence" or "Alcohol Abstinence" or "Substance Abuse*" or "Drug Rehabilita*")
S2: Psychedelics and other psychoplastogens	S2: ("Lysergic Acid Diethylamide" or "LSD" or "Ergolines" or "2,5-Dimethoxy-4-Methylamphetamine" or "Psilocyb*" or "Magic Mushroom*" or "Ayahuasca" or "Harmala Alkaloids" or "Mescaline" or "PCP" or "phencyclidine" or "Indole Alkaloids" or "N,N-Dimethyltryptamine" or "Dihydroxytryptamines" or "Tryptamines" or "Banisteriopsis" or "Tabernaemontana" or "Iboga*" or "Bufotenin" or "Hallucinogens" or "Ketamine" or "Phencyclidine" or "Mitragyna" or "N-Methyl-3,4-methylenedioxyamphetamine" or "MDMA" or "DMT" or "5-Meo-DMT" or "Scopolamine" or "Mescaline" or "Hab-o shefa" or "Hab* " or "psychoplastogen*" or "psychedelic*" or "lysergamide" or "Kratom" or "Ayahuasca" or "5-Meo-DMT" or "NN-DMT")
S3: Human trials	S3: ("Control Groups" or "Non-Randomized Controlled Trial*" or "Randomised Controlled Trial*" or "Non-Randomized Controlled Trials" or "Pilot study" or "Clinical Trials" or "Single-Blind Method" or "Double-Blind Method" or "Longitudinal Studies" or "Placebo control*" or "Neuropsychological Tests" or "Psychological Test*" or "Human trials" or "RCT" or "Open-label" or "off-label")

3.2.5 Inclusion criteria

Reviews were not included but were used to identify other relevant articles. Any additional papers that met the criteria but may have been missed in the electronic search were captured by backwards and forwards chaining. A title/abstract was eligible for full-text screening if it:

- a. Referred to adults with problematic substance use (including alcohol, cannabis, tobacco, stimulant, and opioid use).
- b. Was about administering psychedelics or other psychoplastogens to treat addiction or substance misuse.
- c. Was set in a health-oriented context (including inpatient or outpatient hospital settings, emergency departments, community-based or primary care health settings, and any specialised drug treatment or low-threshold agencies and programmes).
- d. Was conducted before 31 July 2022.
- e. Was published in a peer-reviewed journal.
- f. Included a trial to test the effectiveness of the intervention. Given the scarcity of studies and the exploratory nature of this review, there were no limits on the types of trials to include. Both double-randomised, as well as open-label trials, were included to consider different aspects of measuring intervention outcomes.

3.2.6 Exclusion criteria

- a. Not in the English language
- b. Retrospective/case studies
- c. Duplicate publication
- d. Opinion pieces (not a research study)
- e. No outcomes measured
- f. Recreational use, or microdosing

3.3 Data charting and extraction

Rayyan online software was used for screening and selecting studies. Additionally, duplications were removed, records screened, assessed for eligibility and included or excluded from the full-text review. The primary reviewer read the full text of selected studies and extracted data using an original data extraction tool. The data extraction tool was developed based on previous reviews investigating trials with psychedelic substances for the treatment of substance misuse (Krebs & Johansen, 2013; Winkelman, 2014).

To ensure the reliability of the screening process, a secondary reviewer independently screened 20% of the retrieved papers against the inclusion and exclusion criteria. An initial comparison of decisions showed a high level of agreement. The few discrepancies that arose were resolved through discussion between the two reviewers. This process was instrumental in clarifying the nuances of the selection criteria, which were refined accordingly. Following this iterative discussion and clarification, 100% consensus was achieved for the final inclusion of studies for full-text review. A data-charting form was developed. The PhD candidate independently charted the data, discussed the results and process of the research with supervisors and continuously updated the data-charting form in an iterative process. The authors of included papers were only contacted, if necessary, to obtain missing or supplementary information. Out of four authors contacted, none responded back. See Table 2 below for the topic areas that were extracted.

Table 2

Extracted Topic Areas from The Review

Topics	Content to be extracted
Study characteristics	Sample size, study design, primary substance of abuse
Intervention characteristics	Aim of intervention (detox/rehab/detox+rehab), substance and dose (solution, mg/kg, frequency) treatment/administration setting (clinic, university hospital etc), available support (counselling, breathwork etc.). Treatment program (approximate length in days), Preparation for administration, treatment during administration, aftercare after administration
Intervention measures	Outcomes measured and timepoints (before/during/after treatment)

3.3.1 Risk of bias assessment

A risk of bias assessment on the included studies was deemed necessary due to the inclusion of papers spanning several decades, the use of open-label trials, and the nature of drugs used leading to participants recognising their treatment as being controlled or not. The Cochrane Risk of Bias Tool is widely used in systematic reviews and meta-analyses to assess the methodological quality and potential biases in randomised controlled trials (RCTs) (Higgins & Green, 2011). Higgins and Green (2011) have highlighted the importance of rigorous methodology in ensuring the validity of trial results in their Cochrane Handbook for Systematic Reviews of Interventions. The included studies often deal with subjective experience, and due to the visible effects some active drugs had on participants, even double-blind studies were not free from personal bias. This must be taken into consideration when analysing data, as emphasised by O'Connor et al. (2021) in their methodological review.

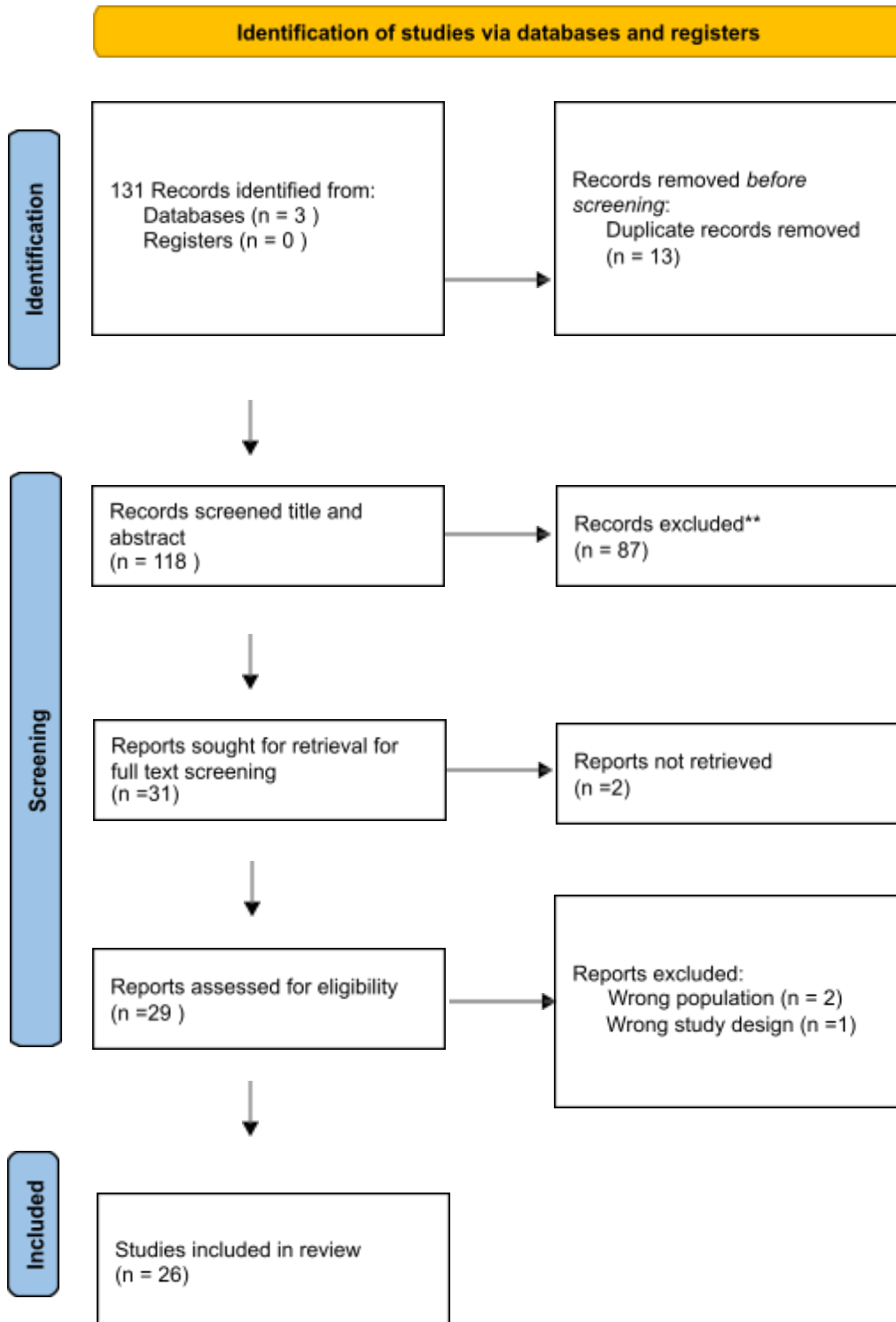
The Cochrane Risk of Bias Tool included criteria such as "adequate sequence generation", "allocation concealment", "blinding", "concurrent therapies similar", "incomplete data addressed", "uniform and explicit outcome definitions", "free of selective outcome reporting", "free of other bias", and "overall risk of bias". The indications used were red for high risk of bias, orange for moderate risk, and green for low risk of bias (Monti et al., 2014; Catillon, 2019). Open-label trials were automatically labelled as high risk for "adequate sequence generation", "allocation concealment", and "blinding", as open-label trials are inherently incapable of concealing treatment, as noted by Higgins and Green (2011). Similarly, Johnson and Griffiths (2021) specifically addressed the challenges in assessing the risk of bias in open-label trials, especially those involving psychedelic-assisted therapies.

3.4 Results

3.4.1 Search results

Figure 1

Prisma Flow Chart Illustration of the Identification, Screening and Inclusion of Trials.



3.4.2 Risk of bias assessment findings

Several blinded trials received a moderate risk for "allocation concealment" due to the use of psychedelic-inducing active substances. This heightens the chances for participants, practitioners, or both to recognise the effects of the active substance, leading to a higher risk of bias. "Concurrent therapies similar" is relevant only for studies including more than one group. Single-arm studies were therefore excluded from this criterion. Just one trial was labelled as high risk for bias in the "free of other bias" section, as it was a replication study. "Overall risk of bias" was assessed through the simple rule of the majority. Eldridge et al. (2021) discussed the unique considerations in cluster randomised trials, emphasising the importance of a comprehensive risk of bias assessment. Studies including two or more high-risk labels were considered as having a moderate risk of overall bias. Studies including a minority of green labels were regarded as having a high risk on "overall risk of bias". Of the 26 studies included in the risk of bias assessment, 8 had a low risk of overall bias, 17 had a moderate risk, and 1 had a high risk of bias (Kolp et al., 2006).

Figure 2*Risk of Bias Assessment of Identified Trials*

Adequate sequence Generation																									
Allocation concealment																									
Blinding																									
Concurrent therapies similar																									
Incomplete outcome data addressed																									
Uniform and explicit outcome definitions																									
Free of selective outcome reporting																									
Free of other bias																									
Overall risk of bias																									
	Alper et al. (1999)	Bogenschutz et al. (2015)	Bogenschutz et al. (2022)	Dakwar et al. (2022)	Garcia-Romeu et al. (2015)	Glue et al. (2016)	Grabski et al. (2022)	Grof et al. (1973)	Hollister et al. (1969)	Holzer et al. (2001)	Hull et al. (2022)	Johnson et al. (2014)	Johnson et al. (2017)	Jovašša et al. (2006)	Knuijver et al. (2022)	Kolp et al. (2006)	Krupitsky et al. (2002)	Liu et al. (2013)	Mash et al. (2018)	Moosavzadeh et al. (2020)	Ramsey et al. (1963)	Rothberg et al. (2021)	Savage et al. (1973)	Sessa et al. (2021)	Smart et al. (1996)

3.4.3 Design characteristics**Timeline of Trials**

The clinical trials under review spanned from 1963 (Hollister et al., 1969; Jensen & Ramsay, 1963) to 2022 (Bogenschutz et al., 2022; Grabski et al., 2022; Hull et al., 2022; Knuijver et al., 2022), illustrating the enduring interest and evolving perspectives on the therapeutic potential of these substances over the decades.

Geographical Distribution

The research landscape is geographically diverse, with studies conducted in various nations. Most studies were conducted in Western countries, with the majority in the United States of America (n=14); (Bogenschutz et al., 2015; Hull et al., 2022), followed by other countries such as Canada (n=1) (Smart et al., 1966), the United Kingdom (n=1) (Grabski et al., 2022), Russia (n=1) (Krupitsky & Grinenko, 1997),

China (n=1) (Liu et al., 2013), Lithuania (n=1) (Jovaiša et al., 2006), Iran (n=1) (Moosavizadeh et al., 2020), and New Zealand (n=1) (Glue et al., 2016). See Appendix B, Table 3 for a detailed breakdown.

Trial Designs

Across trials, the design was either Randomised Controlled Trials (RCTs) (n = 19) or Open-label designs (n= 10) across all research periods. In specific exploratory or pilot studies, especially when confronted with the complexities of methodological blinding, researchers favoured single-arm open-label designs (n = 9), as seen in studies by f-Romeu et al. (2014) and Johnson et al. (2014). It's noteworthy to highlight the diverse blinding techniques utilised across these trials. A major proportion employed a rigorous double-blind approach, aiming to mitigate potential biases, as demonstrated in studies by Bogenschutz et al. (2015), García-Romeu, Griffiths, & Johnson (2014), Grabski et al. (2022), Johnson et al. (2014), and Smart et al. (1966). Several studies employed single-arm open-label trial designs (n= 9), including those by Garcia-Romeu et al. (2014) and Johnson et al. (2014). RCTs (n= 19) prominently featured as a research methodology in seminal studies, the stringent criteria and rigour associated with RCTs resulted in fewer such trials, such as those by Smart et al. (1966), Bogenschutz et al. (2015), and Grabski et al. (2022), in comparison to open-label trials.

Sample Sizes

Studies sampled a diverse range of participants, with numbers varying from 4 (Sessa et al., 2021) to 1247 in an open-label trial (Hull et al., 2022) (Appendix B, Table 4). No discernible trend in sample sizes across the studies was observed. Hull et al. (2022) utilised Mindbloom to conduct a large-scale, open-label trial where participants received sublingual ketamine tablets in their homes under remote supervision. This approach allowed for a broader reach and greater accessibility to treatment, particularly during the COVID-19 pandemic when in-person treatment options were limited.

Active Compounds and Their Dosages

Among the psychedelics, LSD and psilocybin emerged as recurrent substance of interest. Smart et al. (1966) administered an 800-µg dose of lysergide, while Bowen et al. (1970) and Hollister et al. (1969) opted for doses of 500-µg and 600 µg of LSD-25, respectively. Psilocybin, another psychedelic, were a focal point in multiple studies. Bogenschutz et al. (2015 & 2022) administered doses adjusted to body weight, ranging from 0.3 mg/kg to 40 mg/70 kg. Johnson et al. (2014 & 2017) consistently used doses of 20mg/70kg and 30mg/70kg across sessions. Notably, LSD appeared to be the most frequently examined

substances however majority of these studies were compared before 2000s. Psilocybin was a more recently studied psychedelic substance making more frequent appearance following 2000s.

Transitioning to psychoplastogens, ketamine treatment potential was repeatedly tested in trials, Dakwar et al. (2020) administered a dose of 0.71 mg/kg, while Grabski et al. (2022) opted for 0.8mg/kg infusions. Grof et al. (1973) explored the effects of 15 mg/cm³ of DPT. Scopolamine, another psychoplastogen, was investigated by Liu et al. (2013) at dosages between 0.03–0.05 mg/kg. Krupitsky and Grinenko (1997) contrasted hallucinogenic and non-hallucinogenic doses of ketamine, highlighting the substance's versatility in research. Psilocybin was identified as a particularly prominent psychedelic, and ketamine emerged as a frequently researched psychoplastogen (Appendix B, Table 5). See *Appendix B, Table 6* for active and control substances used in trials.

3.4.4 Intervention characteristics

Routes of Administration

The routes through which these psychoactive substances were administered in clinical trials appeared to be judiciously chosen, keeping in mind both the pharmacokinetics and the anticipated therapeutic outcomes. LSD, for instance, was predominantly administered via the intramuscular route, as showcased in Smart et al. (1966), ensuring swift systemic absorption. Psilocybin was typically favoured for oral administration, as demonstrated in the trial of Bogenschutz et al. (2015). However, for compounds such as DPT, the specific route remained unspecified, as per the data from Grof et al. (1973). MDMA was primarily administered orally, as observed in the study by Sessa et al. (2021). The route for Scopolamine remained unspecified in the research by Liu et al. (2013). Both oral and intravenous administration of drugs were used across studies, depending mainly on the active drug administered, (Appendix B, Table 7). LSD, for example, was primarily administered orally, whereas ketamine was administered intravenously. Most papers do not report why they preferred their method of administration.

Substances of Misuse and Their Treatments

The primary substances of misuse or target conditions addressed in these studies encompass alcoholism (Smart et al., 1966; Bowen et al., 1970; Grof et al., 1973), alcohol dependence (Bogenschutz, et al., 2015; Dakwar et al., 2020; Grabski et al., 2022), tobacco addiction (Garcia-Romeu et al., 2014). For treatments, the landscape of clinical research witnessed the administration of an eclectic range of psychoactive compounds. Regarding LSD, research, such as that by Smart et al. (1966) and Bowen, Soskin, Chotlos (1970), ventured into a spectrum of dosages, ranging from 25µg to 800µg. Psilocybin, dosages exhibited

variation, with Bogenschutz et al. (2015) administering amounts from 0.3 mg/kg to 0.4 mg/kg, and Johnson et al. (2017) probing a range between 10mg to 30mg/70kg. The therapeutic exploration of Ketamine was characterised by dosages such as 0.71 mg/kg, as documented in Dakwar et al. (2020), and 0.8mg/kg as presented by Grabski et al. (2022). Furthermore, a plethora of substances, including DPT, MDMA, and Scopolamine, were at the forefront of rigorous clinical investigation, each administered in unique dosages across diverse studies (Grof, Soskin, Richards, & Kurland, 1973; Liu, Li, Shen, et al., 2013; Sessa et al., 2021) (Appendix B, Table 8).

Intervention Settings: Treatment Administration and Setting

The settings in which psychedelics and related substances were administered varied widely, reflecting the diverse approaches researchers had taken to ensure participant safety, comfort, and optimal therapeutic outcomes; it was not always explicit whether this was intentional or a result of convenience. Sixteen studies used controlled environments, such as hospitals or treatment facilities (Bogenschutz et al., 2022; Bowen et al., 1970; Dakwar et al., 2020; Glue et al., 2016; Grabski et al., 2022; Grof et al., 1973; Hollister et al., 1969 ; Johnson et al., 2021; Jovaiša et al., 2006; Knuijver et al., 2022; Liu et al., 2013; Mash et al., 2018; Moosavizadeh et al., 2020; Rothberg et al., 2021; Savage & McCabe, 1973 ; Sessa et al., 2021; Smart et al., 1966). For instance, Smart et al. (1966) conducted their research within the confines of a psychiatric ward at the Toronto Western Hospital, Canada, ensuring a structured yet clinical backdrop for their study. Similarly, Bowen et al. (1970) and Hollister et al. (1969) both opted for hospital settings, with the latter emphasising a room specifically furnished to provide a homelier ambiance than the typical clinical environment.

In contrast, five studies took a different approach, curating environments that emulated more comfortable living spaces. Bogenschutz et al. (2015) and Johnson et al. (2014) were notable examples, with their studies taking place in rooms specially prepared to resemble a living-room, ensuring participants felt at ease during the therapeutic process. Other studies ventured outside traditional clinical settings: Hull et al. (2022) and Kolp et al. (2006) adopted an outpatient approach, allowing participants to undergo therapy in the familiarity of their own homes, while Alper et al. (1999) conducted their research within hotel rooms or apartments.

Furthermore, academic institutions have also been utilised as settings for research, as seen in the study by Bogenschutz et al. (2022), which took place across two academic centres in the US. This choice underscores the importance of rigorous scientific oversight in psychedelic research. The varied settings

chosen for these studies highlight the adaptability and flexibility of psychedelic therapy, with researchers prioritising both the safety and comfort of participants. Whether in a clinical hospital ward, a homely room, or an academic institution, the primary focus remains on creating an environment conducive to positive therapeutic outcomes.

Available Support

Psychedelics were the focal point of numerous therapeutic studies, with their administration often accompanied by a range of support mechanisms to enhance the therapeutic process. Smart et al. (1966) conducted their study in a psychiatric ward of a general hospital, specifically the Toronto Western Hospital, and incorporated a therapeutic community approach, offering both group and individual therapy in conjunction with LSD administration. Bogenschutz et al. (2015 & 2022) provided a comprehensive psychosocial intervention, encompassing Motivational Enhancement Therapy, preparation sessions, and debriefing sessions. Cognitive-behavioural therapy (CBT) was used to support for participants in the study by Garcia-Romeu et al. (2014).

Breathwork, interactive classes, lectures, yoga, meditation, cooking classes, guided imagery/meditation, and journaling were all integrated into the therapeutic regimen by Kolp et al. (2006). Some studies, like that of Rothberg et al. (2021), focused on Motivational enhancement therapy, while others, such as Savage et al. (1973), emphasised psychotherapy and familiarisation with the psychotherapist. The diversity in support mechanisms underscored the holistic approach often taken in psychedelic therapy, ensuring participants are well-supported throughout their therapeutic journey. Dakwar et al. (2020) incorporated relaxation and mindfulness-based exercises, aiding participants in achieving a calm state of mind. Lastly, the encouragement for participants to maintain journals, as seen in the study by Grabski et al. (2022), provided them with a space to reflect on and process their experiences (Appendix B, Table 9).

Preparatory measures

Research studies included in this review employed a diverse range of preparatory techniques tailored to their specific objectives. While some older studies, like Smart et al. (1966), opted for providing brief orientation, often with little or no description of the possible effects of LSD, more recent studies have tended towards more comprehensive approaches. For example, Bogenschutz et al. (2015, 2022) and Johnson et al. (2017) incorporated multiple psychotherapy sessions, ranging from 1 to 15 sessions, to prepare participants. Psychotherapy, Motivational Enhancement Therapy (MET), CBT, and mindfulness exercises were the most common preparatory measures. MET is a collaborative, person-centred

counselling approach designed to enhance an individual's motivation to change problematic behaviours (Miller et al., 1992). It focuses on exploring and resolving ambivalence about change. These techniques, used in studies like those by Dakwar et al. (2020) and Grabski et al. (2022), often combined psychological support with medical treatment. Although not always correlating with better outcomes, studies incorporating psychological support generally reported higher abstinence success rates compared to control groups with minimal preparation. This suggests that while preparation has an important role in psychedelic research, further investigation is needed to identify the most effective techniques for different substances and participant populations.

Additionally, several studies emphasised the importance of well-being and abstinence prerequisites in psychedelic-assisted therapies. For example, Bogenschutz et al. (2015) and Grabski et al. (2022) required participants to abstain from alcohol before treatment, while Hull et al. (2022) extended these requirements in a sublingual ketamine study. Controlled treatment environments were also preferred in some studies, such as Hollister et al. (1969), which used a specialised detox room. Physiological preparations were prominent in studies like Jovaiša et al. (2006) and Mash et al. (2018), who transitioned patients to morphine sulphate before detoxification, highlighting the multifaceted nature of preparatory measures in such trials. See Appendix B, Table 10 for a breakdown of preparatory measures used in trials.

During the experience

Studies investigating substance use disorder treatments employed a range of approaches during the administration of both conventional and psychedelic substances. For instance, Smart et al. (1966) incorporated a 3-hour interview without continuous observation during LSD therapy. In contrast, Bogenschutz et al. (2015, 2022) provided a controlled environment for psilocybin administration, where participants lay on a couch with eyeshades and headphones playing music, under supervision for up to 8 hours. Bowen et al. (1970) emphasised non-verbal introspection during LSD sessions, while Dakwar et al. (2020) integrated a ketamine infusion with a motivational enhancement session.

Further variations in treatment protocols were observed in Grabski et al. (2022), where participants listened to instrumental relaxational music during a 40-minute ketamine infusion. Hollister et al. (1969) ensured patients remained in the treatment room for eight hours post-LSD administration, including meal provisions. Holze et al. (2021) followed a structured 24-hour observation period post-LSD, with meals at set intervals.

Some studies, such as Hull et al. (2022), adapted telehealth approaches for ketamine sessions, allowing patients to prepare their home environments. Knuijver et al. (2022) focused on patient observations during the night following Ibogaine administration, while Kolp et al. (2006) combined ketamine therapy with existential and transpersonal group therapy. Krupitsky et al. (2002) employed a 2-hour ketamine session supported by music and psychotherapy, and Mash et al. (2018) encouraged participants to narrate their experiences during Ibogaine administration. Alper et al. (1999) recommended patients lie in a quiet, dimly lit room post-Ibogaine treatment, and Savage and McCabe (1973) integrated psychotherapy following high-dose LSD administration (Appendix B, Table 12).

After the experience

Post-administration care varied significantly across studies, reflecting diverse strategies to support participants following substance use treatments. Smart et al. (1966) encouraged outpatient or social-recreational contacts with the clinic. Bogenschutz et al. (2015, 2022) combined family support, where participants were escorted home by a friend or family member, with subsequent psychosocial interventions. Dakwar et al. (2020) provided immediate medical coverage for up to three hours post-infusion, followed by psychiatric evaluation, referrals, and a six-month follow-up.

Garcia-Romeu et al. (2014) used facilitator-led discussions to reinforce CBT techniques post-psilocybin sessions, while Johnson et al. (2014, 2017) scheduled follow-up meetings ranging from the day after the session to up to 30 months later. Hull et al. (2022) employed a telehealth model integrating journaling, video meetings, and continuous symptom monitoring. Jovaiša et al. (2006) offered participants the choice of enrolling in various aftercare programmes, including abstinence-based or naltrexone-supported outpatient counselling (Appendix B, Table 13).

Additional approaches included continued human relations training (Bowen et al., 1970), integration interviews (Grof et al., 1973), and structured outpatient treatment (Liu et al., 2013; Mash et al., 2018). Grabski et al. (2022) and Sessa et al. (2021) provided post-administration therapy sessions to help integrate treatment experiences into broader therapeutic goals, underscoring the importance of aftercare in enhancing the efficacy of substance use disorder treatments (Kolp et al., 2006; Krupitsky & Grinenko, 1997; Rothberg et al., 2021).

3.4.5 Measures used in trials

Treatment Duration and Follow-Up Assessments

Treatment programmes ranged from 3 days to 8 months, with follow-up assessments commonly conducted at 3, 6, and 12 months post-treatment. These follow-ups provided insights into the longevity of treatment effects, often revealing a declining success rate over time in abstinence. For detailed information on programme durations, refer to Appendix B, Table 14.

Pre-Treatment Baseline Measures

Prior to intervention, studies employed various baseline assessments to establish a foundation for evaluating the impact of psychedelic and psychoplastogen treatments. Common tools included the Timeline Follow-Back (TLFB) method, utilised by Garcia-Romeu et al. (2014) and Johnson et al. (2014, 2017) to measure substance use patterns pre-treatment. Biological markers, such as urine drug screens, were employed by Bogenschutz et al. (2015) and Grabski et al. (2022) to corroborate self-reported substance use. The Addiction Severity Index (ASI), used by Knuijver et al. (2022) and Mash et al. (2018), offered detailed insights into participants' addiction severity. Physiological assessments, including heart rate and blood pressure monitoring, became increasingly common in trials conducted after 1973. For a comprehensive list of outcomes measured before treatment, see Appendix B, Table 15.

Measures During Treatment

During intervention sessions, various physiological and psychological parameters were monitored to capture the acute effects of treatments. Heart rate and blood pressure were frequently recorded, as noted in studies by Bogenschutz et al. (2015, 2022) and Holze et al. (2021). The TLFB remained a critical tool for real-time assessment, particularly in studies such as Johnson et al. (2014, 2017), where it was supplemented with biological markers like exhaled carbon monoxide. Psychedelic experience scales, including the Hallucinogen Rating Scale (HRS) Intensity subscale and the 5-Dimensional Altered States of Consciousness (5D-ASC), were employed by Bogenschutz et al. (2015) and Garcia-Romeu et al. (2014) to assess subjective experiences. Continuous electrocardiography was used in studies like Liu et al. (2013) and Knuijver et al. (2022) to monitor cardiac responses during drug administration. For detailed information on outcomes measured during treatment, refer to Appendix B, Table 16.

Post-Treatment Measures and Longitudinal Effects

Post-treatment evaluations varied widely, with some studies focusing on behavioural changes and others on physiological or psychological outcomes. For example, Smart et al. (1966) assessed alcohol-

related behaviours, including morning drinking, while Bogenschutz et al. (2015, 2022) employed comprehensive questionnaires and biological markers such as ethyl glucuronide in hair samples. The TLFB was also used post-session by Garcia-Romeu et al. (2014) and Johnson et al. (2014, 2017) to track substance use and daily behaviours. Psychological assessments included tools like the Beck Depression Inventory (BDI) and Hamilton Depression Rating Scale (HAM-D), as seen in Grabski et al. (2022), and the Adjective Mood Rating Scale, employed by Holze et al. (2021).

Grof et al. (1973) utilised a robust pre- and post-treatment framework, comparing psychological test results, including the Minnesota Multiphasic Personality Inventory (MMPI), Personal Orientation Inventory (POI), Raven Progressive Matrices, Psychiatric Evaluation Profile (PEP), and Benton Visual Retention Test, to evaluate personality and cognitive changes. Other studies also incorporated similar pre- and post-treatment measures. For instance, Bogenschutz et al. (2015, 2022) and Johnson et al. (2014, 2017) used TLFB assessments at both stages to measure the impact of interventions. For a summary of outcomes measured before, during, and after treatment, refer to Appendix B, Tables 16,17 and 18.

3.4.6 Findings from the trials

In recent decades, academic attention has pivoted towards the potential therapeutic applications of psychotropic substances in treating substance dependence. Some initial studies, such as Smart et al. (1966), found limited evidence for LSD's efficacy in reducing alcohol consumption, with no significant differences observed between treatment and control groups in terms of abstinence or drinking behaviour. Contrastingly, research conducted by Bogenschutz et al. (2015, 2022) demonstrated significant reductions in alcohol consumption and increased abstinence with psilocybin-assisted psychotherapy, with effects lasting 32–36 weeks. The 2015 pilot study showed promising short-term effects, while the larger 2022 study confirmed medium-term efficacy, maintaining low rates of heavy drinking days throughout. These findings suggest psilocybin, combined with psychotherapy, holds the potential for sustained alcohol use reduction, though long-term effects require further investigation. These studies highlighted sustained gains at follow-ups extending to 36 weeks and noted a strong correlation between the intensity of psilocybin sessions and positive changes in drinking behaviour and abstinence self-efficacy.

Shifting focus to ketamine, studies by Dakwar et al. (2020) and Grabski et al. (2022) underlined its potential in increasing the likelihood of abstinence and extending sobriety, especially when integrated with motivational enhancement therapy or psychological support. Both studies reported that ketamine

not only reduced measures of drinking but also extended the period of sobriety, with Grabski et al. (2022) noting a positive impact at 6-month follow-up.

The role of mystical-type experiences in treatment efficacy was emphasised by Garcia-Romeu et al. (2014) and Rothberg et al. (2021), who found that the profundity of these experiences correlated with better therapeutic outcomes, such as smoking cessation and reduced at-risk drinking. These findings suggest that the subjective quality of the psychedelic experience may be as important as the pharmacological effects in achieving long-term benefits.

However, the potential risks associated with these treatments should not be overlooked. For example, Knuijver et al. (2022) highlighted that Ibogaine, while showing promise in treating opioid use disorder, carries cardiovascular risks, such as reversible QTc prolongation and bradycardia. Despite these risks, the broader landscape of studies, including those by Sessa et al. (2021), underscores the transformative potential of these compounds, particularly when administered within structured therapeutic environments. Sessa et al. (2021) found that MDMA-assisted psychotherapy significantly improved psychosocial functioning and reduced alcohol consumption post-detoxification, highlighting the importance of comprehensive therapeutic support in maximising treatment efficacy. See Appendix Table 4 for a breakdown of trial findings.

Table 4*Extracted Topic Areas from The Review*

Study (Author, Year)	N	Substance & Dose	Target Condition(s)	Study Design	Key Findings
Alcohol Use Disorder					
Bogenschutz et al. (2022)	93	Psilocybin (25-40 mg/70 kg)	Alcohol Use Disorder	Double-blind RCT	Significant reduction in heavy drinking days in the psilocybin group vs. active placebo.
Grabski et al. (2022)	96	Ketamine (0.8mg/kg)	Alcohol Use Disorder	RCT	Ketamine group had significantly more days of abstinence from alcohol at 6-month follow-up.
Kolp et al. (2006)	95	Ketamine (0.2-2.0 mg/kg IM)	Alcoholism	Open-label	Ketamine Enhanced Psychotherapy showed effectiveness; authors noted ketamine alone was not sufficient.
Bogenschutz et al. (2015)	10	Psilocybin (0.3-0.4 mg/kg)	Alcohol Dependence	Open-label pilot	Abstinence increased significantly post-psilocybin administration; gains maintained at 36-week follow-up.
Dakwar et al. (2020)	40	Ketamine (0.71 mg/kg)	Alcohol Dependence	RCT with active placebo	Increased abstinence likelihood and delayed relapse in the ketamine group compared to midazolam.
Sessa et al. (2021)	4	MDMA (187.5mg)	Alcohol Use Disorder	Open-label exploratory	Significant improvement in psychosocial functioning and a drastic reduction in alcohol consumption.
Grof et al. (1973)	60	DPT (15 mg/cm ³)	Alcoholism	Open-label	Post-DPT sessions showed significant improvement in depression and global adjustment scales.
Hollister et al. (1969)	12	LSD (600 µg) vs Dextroamphetamin e	Alcoholism	Controlled Trial	LSD-treated patients fared better at 2 months, but by 6 months differences between treatments disappeared.
Bowen et al. (1970)	120	LSD (500 µg)	Alcoholism	Controlled Trial	No significant difference in adjustment between the LSD and control groups after 1 year.
Smart et al. (1966)	58	LSD (800 µg)	Alcoholism	Controlled Trial	No significant difference in abstinence or drinking behaviour between groups.
Jensen & Ramsay (1963)	28	LSD (Dose not specified)	Alcoholism	Open-label	LSD treatment led to increased social and religious values in patients affiliated with A.A.
Opioid & Narcotic Use Disorders					
Knuijver et al. (2022)	30	Ibogaine-HCl (10 mg/kg)	Opioid Use Disorder	Open-label observational	Demonstrated detoxification potential but identified significant cardiovascular risks (QTc prolongation).
Krupitsky & Grinenko (1997)	74	Ketamine (2.0 mg/kg vs 0.2 mg/kg)	Heroin Addiction	Controlled Trial	High-dose ketamine showed significantly better abstinence rates and reduced cravings compared to low-dose.

Moosavyzadeh et al. (2020)	40	Hab-o Shefa (500mg capsules)	Opioid Dependence	RCT	Hab-o Shefa was more effective than placebo in preventing opioid relapse and reducing craving.
Savage & McCabe (1973)	78	LSD (300-450 µg)	Narcotic Addiction	Controlled Trial	LSD therapy enhanced the probability of better community adjustment compared to the control group.
Alper et al. (1999)	33	Ibogaine (6-29 mg/kg)	Opioid Dependence	Observational	Reduction in opioid withdrawal symptoms was observed, but the study had a limited framework.
Glue et al. (2016)	24	Noribogaine (60-240 mg)	Opioid Dependence	RCT	Non-statistically significant trend toward decreased opioid withdrawal ratings.
Jovaiša et al. (2006)	30	Ketamine (0.5 mg/kg/h)	Opioid Dependence	RCT	Effective in acute opioid withdrawal management, but showed no long-term effects on dependence.
Liu et al. (2013)	114	Scopolamine (0.03-0.05 mg/kg)	Opioid Dependence	Controlled Trial	Scopolamine considerably reduced heroin withdrawal symptoms and had better outcomes than conventional detox.
Cocaine Use Disorder					
Mash et al. (2018)	191	Ibogaine HCl (8–12 mg/kg)	Opioid & Cocaine Use	Open-label	Self-reported craving for cocaine was reduced one month post-discharge.
Tobacco Addiction					
Johnson et al. (2017)	15	Psilocybin (20-30mg/70kg)	Tobacco Addiction	Open-label follow-up	Confirmed earlier findings, showing sustained long-term smoking abstinence at a mean of 30 months.
Garcia-Romeu et al. (2014)	15	Psilocybin (20-30mg/70kg)	Tobacco Addiction	Open-label pilot	High rate of smoking cessation (80% at 6 months). Strong positive correlation with mystical experience scores.
Mixed / General					
Hull et al. (2022)	1247	Ketamine (300-450mg sublingual)	Anxiety & Depression	Open-label effectiveness trial	At-home, telehealth-based ketamine showed significant antidepressant and anxiolytic effects.
Holze et al. (2021)	24	LSD (25-200 µg)	Healthy Volunteers	RCT	Characterized dose-dependent subjective effects and confirmed the crucial role of 5-HT2A receptors.
Johnson et al. (2014)	~440k	Naturalistic Psychedelic Use	General Substance Use	Online Survey	Naturalistic use was associated with decreased or ceased use of other substances, particularly alcohol and cannabis.
Rothberg et al. (2021)	45	Ketamine (Dose not specified)	At-Risk Drinking	RCT with active placebo	Ketamine-induced mystical-type experiences mediated its impact on reducing at-risk drinking.

3.5 Discussion

This scoping review synthesised findings on psychedelic and psychoplastogen-assisted interventions for substance misuse, illustrating both the promise and the complexity of this emerging therapeutic field. While evidence supports the efficacy of certain psychedelics in promoting abstinence and reducing substance cravings, methodological limitations and regulatory challenges temper these results. Achieving clinical relevance will necessitate more rigorous research designs, along with a clearer understanding of the neurobiological and psychological mechanisms underpinning these interventions (Carhart-Harris & Friston, 2019).

3.5.1 Methodological Evolution and Design Characteristics

The renewed interest in psychedelic-assisted therapy for substance misuse, particularly in the last decade, reflects evolving perspectives on addiction treatment and neuroplasticity. Recent studies demonstrate a diverse range of designs, from rigorous randomised controlled trials (RCTs) to open-label studies. RCTs, such as those conducted by Bogenschutz et al. (2015, 2022), offer higher validity by mitigating bias through blinding and placebo controls, yet are less common due to logistical and ethical constraints in psychedelic research (Gasser et al., 2014). Open-label studies, while lacking the control necessary to attribute effects exclusively to the intervention, provide practical insights and foundational data essential for hypothesis generation in novel treatments (Garcia-Romeu et al., 2011). The variety of trial structures in psychedelic research suggests an evolving field, wherein flexibility in design is often essential to accommodate the unique requirements of psychedelic interventions (Carhart-Harris et al., 2018).

However, methodological diversity complicates cross-study comparisons and hinders efforts to consolidate evidence systematically. The limited sample sizes characteristic of many studies, such as the four-participant study by Sessa et al. (2021), impede the reliability and generalisability of findings. Nichols (2016) advocates for larger, multi-site trials that standardise protocols across populations, a strategy that would support more meaningful meta-analyses and contribute to a robust evidence base. Future research should consider innovative methodologies to address sample size limitations, such as telehealth-enabled trials seen in Hull et al. (2022), though these approaches must be carefully managed to control for selection biases and socio-economic disparities.

3.5.2 Neurobiological Mechanisms and Psychoplastogenic Potential

Emerging evidence suggests that the efficacy of psychedelics in treating substance misuse may be due to their ability to promote neuroplasticity and disrupt maladaptive brain patterns associated with addiction (Carhart-Harris & Friston, 2019; de Vos, Mason & Kuypers, 2021). Psilocybin and LSD, two of the most

studied psychedelics in this review, appear to influence the brain's default mode network (DMN), potentially allowing for the "resetting" of habitual thought patterns and addictive behaviours (Carhart-Harris et al., 2014). This mechanism aligns with findings by Bogenschutz et al. (2015, 2022), where psilocybin, combined with psychotherapy, facilitated lasting behavioural changes by promoting introspection and emotional reconnection, leading to reduced alcohol use.

In addition to classic psychedelics, ketamine—a psychoplastogen with distinct pharmacological properties—has gained traction as an adjunctive therapy for addiction. Unlike serotonergic psychedelics, ketamine primarily targets NMDA receptors, promoting synaptogenesis and rapid plasticity that may support emotional regulation and resilience against relapse (Dakwar et al., 2020; Grabski et al., 2022). de Vos, Mason and Kuypers (2021) argue that ketamine's rapid onset and distinct pharmacodynamics make it particularly suitable for patients needing immediate therapeutic intervention. Nevertheless, studies such as those by Dakwar et al. (2020) indicate that ketamine's efficacy is optimised when combined with motivational and cognitive-behavioural therapies, suggesting that psychoplastogenic effects alone may be insufficient without a structured therapeutic framework.

3.5.3 Bias and Methodological Limitations

One of the central limitations across the studies reviewed is the high risk of bias, particularly related to allocation concealment and blinding. Given the noticeable psychoactive effects of psychedelics, achieving effective blinding is challenging, potentially leading to expectancy effects that influence both patient and clinician assessments of efficacy (Nichols, 2016). Open-label designs, while valuable for preliminary exploration, heighten these risks, as exemplified by high rates of subjective improvement in non-blinded studies like Bogenschutz et al. (2022). Eldridge et al. (2021) stress the need for meticulous bias assessments in trials involving potent psychoactive substances, as even minor biases can significantly skew outcomes in this context. Employing active placebos, as done by Dakwar et al. (2020), represents one potential solution, though it complicates the interpretation of results by introducing non-specific pharmacological effects.

Sample sizes also present a recurring limitation, with many trials constrained by small participant pools that limit statistical power and generalisability. Carhart-Harris et al. (2021) highlights that small-scale studies in psychedelic research, while important for feasibility testing, are unlikely to produce data suitable for clinical guidelines without corroboration from larger, standardised trials. In line with Gründer and Jungaberle (2021), the establishment of multi-site collaborations and harmonised protocols may be critical to overcoming these limitations and enhancing the scalability and validity of psychedelic research for addiction.

3.5.4 Set, Setting, and Contextual Influences

The impact of "set" (mindset) and "setting" (environment) on psychedelic experiences is widely acknowledged as integral to treatment outcomes. Studies reviewed consistently highlight the therapeutic benefits of structured, supportive environments, such as controlled clinics or home-like settings designed to foster introspection and emotional safety (Bogenschutz et al., 2015). Carhart-Harris et al. (2018) argue that the psychedelic experience's therapeutic potential is closely tied to the context in which it occurs, underscoring the importance of setting in facilitating meaningful psychological breakthroughs. This principle is reflected in studies that employed holistic approaches, such as Kolp et al. (2006), which integrated breathwork, meditation, and journaling to support patients' journeys through intense and often challenging psychedelic experiences.

However, while creating conducive environments is valuable, further research is needed to identify the specific elements of set and setting that most directly contribute to positive outcomes in substance misuse treatment. As Hartogsohn (2021) suggests, a better understanding of how mindset and environment interact with individual patient characteristics could enhance the personalisation of psychedelic therapies, potentially improving efficacy and reducing risks of adverse experiences.

3.5.5 Integration and Support Mechanisms Post-Treatment

The importance of integration—support provided after psychedelic sessions to help patients process their experiences—is a recurring theme in the studies reviewed. Integration support, such as follow-up psychotherapy and journaling exercises, appears crucial in translating the acute psychedelic experience into sustained behavioural change. Studies by Johnson et al. (2017) and Bogenschutz et al. (2022) illustrate how structured aftercare enhances the long-term efficacy of psychedelic therapy by helping patients incorporate new insights into their daily lives. This aligns with broader literature on addiction recovery, which suggests that building a coherent, substance-free identity is fundamental to sustained abstinence (McIntosh & McKeganey, 2000).

Furthermore, the use of telehealth for integration, as seen in Hull et al. (2022), offers a promising model for improving accessibility and continuity of care, particularly for individuals in remote areas. However, as Turner et al. (2022) note, telehealth integration may lack the immediacy and depth of in-person support, which can be crucial during the vulnerable post-session phase. Comparative studies on telehealth versus in-person integration could inform best practices and identify optimal support structures for diverse patient populations.

3.5.6 Measures Used in Trials

The trials reviewed utilised a mix of subjective and objective measures to evaluate the effects of

psychedelic and psychoplastogen-assisted interventions for substance misuse. Subjective tools, such as the 5D-ASC and Addiction Severity Index, provide valuable insight into personal behaviours and transformative experiences but are prone to biases from recall inaccuracies and participant expectations (Carhart-Harris et al., 2018). Objective markers, including urine drug screens and physiological metrics, offer verification of substance use changes but often fail to capture the psychological and existential dimensions that are central to psychedelic therapy (Nichols, 2016).

The inconsistent application of these measures, particularly psychedelic-specific tools like the Mystical Experience Questionnaire, highlights a gap in standardising assessments across trials. This inconsistency risks overlooking critical aspects of the therapeutic process, such as the role of set and setting in shaping outcomes (Hartogsohn, 2021). Future research should focus on developing comprehensive, standardised tools that integrate subjective experiences with biological and behavioural outcomes, enhancing both the comparability of findings and the understanding of therapeutic mechanisms (Gründer & Jungaberle, 2021).

3.5.7 Relevance to Stakeholders

This review is pivotal for stakeholders in the field of psychedelic-assisted therapy, spanning clinicians, researchers, policymakers and treatment seekers. The findings elucidate the current landscape of the field, showcasing the promising role of psilocybin in enhancing abstinence from alcohol (Bogenschutz et al., 2015:2022) and the potential of ketamine in augmenting abstinence likelihood (Dakwar et al., 2020; Grabski et al., 2022). However, the inherent risk of bias in open-label trials (Higgins & Green, 2011; Johnson & Griffiths, 2021) and potential cardiovascular risks with substances like Ibogaine (Knuijver et al., 2022) delineate the existing research's limitations. The review accentuates the potential of psychedelic-assisted therapies for various mental health conditions, with the profundity of mystical-type experiences potentially playing a pivotal role in therapeutic outcomes (Garcia-Romeu et al., 2011; Rothberg et al., 2021). The findings could be instrumental in shaping guidelines and policies related to psychedelic use in therapeutic contexts. Recommendations would include prioritising rigorous methodology, integrating structured therapeutic environments, and maintaining vigilance regarding potential risks.

3.5.8 Strengths and Limitations

The review's strengths lie in its systematic approach to data collection and analysis. Utilising three major electronic databases known for their relevance to psychology, pharmacology, and mental health studies ensured a broad spectrum of potential studies. This was further enhanced by the inclusion of both well-known and emerging psychoplastogens. The iterative process of data charting, combined with the

continuous engagement and discussions with supervisors, ensured that the data extraction remained relevant and adaptable throughout the review. The use of Rayyan online software for study selection, paired with the involvement of a secondary reviewer for a portion of the papers, added rigour to the study selection process (Ouzani, Hammady, Fedorowicz, Elmagarmid, 2016).

However, there were limitations to consider. The heterogeneity of the included studies in terms of design and intervention characteristics posed challenges in drawing definitive conclusions, the nature of this challenge was the main reason opting for a scoping review, which elucidates previous heterogeneous evidence. While the review's focus on controlled trials added rigour, the exclusion of retrospective or case studies might have left out valuable insights. The language restriction to English might have omitted pertinent research conducted in other languages. Additionally, the non-response from authors when contacted for supplementary information could have resulted in potential gaps in the data. It's worth noting that while most studies were conducted in Western countries, the geographical context might not be as important given the nature of the subject matter. Lastly, while efforts were made to address potential biases, the inherent risk associated with some studies cannot be entirely discounted.

3.5.9 Future Directions

Considering the findings from this review, several recommendations can be proposed for future research in the field of psychedelic-assisted therapy. Firstly, there is a clear need for more rigorous study designs, including double-blind and placebo-controlled trials, to mitigate the risk of bias and enhance the validity of the findings. Secondly, future research should strive to develop personalised treatment protocols that consider each patient's unique needs and characteristics. This could involve a comprehensive pre-treatment assessment to inform the development of an individualised therapeutic plan. Thirdly, comprehensive assessment tools that capture both the biological and subjective effects of psychedelic-assisted therapies are recommended. This will enable a more holistic understanding of the impact of these therapies. Finally, further research is needed to determine the optimal approach to providing support in psychedelic-assisted therapies. This could involve exploring the comparative effectiveness of different therapeutic modalities and investigating the optimal timing and intensity of therapeutic support.

3.6 Conclusion

The evolution of trials with psychedelics and psychoplastogens has seen notable shifts, particularly in study design characteristics. A research pause between 1973 and 1999, largely due to legal constraints, was succeeded by a revival in the 2010s, predominantly in Western countries (Nichols, 2016; Johnson et al., 2023). Other than four trials (Mash et al., 2018; Moosavizadeh et al., 2020; Hull et al., 2022; Bowen

et al., 1970) sample sizes were smaller than 100 participants for most of the trials in this review. Though with over 1000 participants, Hull et al.'s (2022) telemedicine-based method is distinctive, albeit with potential biases. Interventions range from classic psychedelics like LSD to 'newer' substances such as Ketamine and Ibogaine. The measures to assess these interventions merge biological and subjective metrics, but some studies indicate a decrease in therapeutic benefits over time (Garcia-Romeu et al., 2011). The blend of randomised controlled trials and open-label designs showcases methodological variety, with the choice of placebo in RCTs being pivotal for interpretation. In summary, whilst psychedelics offer promising therapeutic avenues, the field requires rigorous methodologies and standardised treatment approaches.

4. Exploring Current Practices in Substance Misuse Treatment with Iboga and Ibogaine: Insights from Facilitators

This empirical chapter explores the application of Ibogaine, focusing on the experiences of treatment providers. Through addressing three core research questions via interviews with treatment providers, the study aims to uncover the professional backgrounds, treatment methodologies, and the use of adjunct therapies by these providers, aiming to elucidate the practicalities of Ibogaine application for substance misuse treatment. This research is pivotal for shaping future treatment frameworks, informed by the nuanced experiences of those administering Ibogaine.

4.1 Background

Like other nations, Opiate Substitution Therapy (OST) remains the primary treatment route for opioid misusers in the UK (GOV.UK, 2022). This method involves treating opiate users with progressively reduced doses of safer prescribed opioids. However, due to the extended duration required for tapering, OST often takes longer than alcohol detoxification, resulting in higher costs. The typical duration for detoxification using opioid substitution treatment (OST) methods can vary. According to Public Health England (PHE), inpatient detoxification from opioids typically lasts up to 28 days, while outpatient detoxification may extend up to 12 weeks (PHE, 2015). However, the process of tapering off opioids and achieving abstinence is often more complex than these timeframes suggest. Even after completing a tapering schedule within the recommended timeframe, individuals may experience cravings and relapse into opioid use. This is supported by research indicating that approximately 27.6% of individuals who successfully taper off opioids remain abstinent after one year, highlighting the challenges of long-term recovery (Davis, Digwood, Mehta, & McPherson, 2020). Additionally, medications used in OST can be challenging to discontinue due to their addictive properties and have been associated with adverse events when combined with sedative substances (Connock et al., 2007). Many individuals may revert to previous usage patterns due to various psychological and physiological factors, underscoring the need for ongoing support and interventions beyond the initial detoxification period.

Furthermore, Scotland's drug-induced death rate remains a significant concern, with the latest data indicating a rate of 27.7 per 100,000, making it the highest in Europe. This rate is nearly three times higher than that of the next highest country, Ireland, reflecting the severe impact of drug misuse in the region (Royal College of Psychiatrists, 2024). The high prevalence of drug-induced deaths in Scotland

underscores the urgent need for enhanced treatment strategies and public health interventions tailored to address the unique challenges faced by affected communities.

Ibogaine, an active alkaloid derived from the psychoactive plant *Tabernanthe iboga*, is renowned for its potential anti-addictive properties (Brown & Alper, 2018). Ibogaine can be consumed in various forms, including rootbark (commonly known as Iboga), extracts, and as Ibogaine HCL (Brown & Alper, 2018). While pure Ibogaine HCL is often preferred for opioid detoxes due to its reduced physical burden on the body (Knuijver et al., 2022), less adulterated forms are favoured for treating other addictions and mental health issues. These forms include Total Alkaloid extract (TA), containing Ibogaine and 11 other alkaloids, and Purified Total extract (PTA), with Ibogaine and three other alkaloids (Tabula Rasa Retreat, n.d.).

Naranjo (1974) classified Ibogaine as an oneirogen, a substance that induces dream-like states while awake. For many individuals undergoing Ibogaine treatment, this manifests as vivid and deeply personal visual experiences, unfolding in a manner akin to dreaming, with a profound emphasis on subjective interpretation. Goutarel et al. (1993) posited that Ibogaine induces a neuropsychological state akin to rapid eye movement (REM) sleep, characterised by heightened neurological and psychological integration, yet experienced with full conscious awareness. This state, they argued, diverges significantly from that produced by classic psychedelic substances, both in terms of subjective experience and the intricate physiological responses it elicits. Contemporary research supports this hypothesis, with rodent studies demonstrating that Ibogaine induces a unique waking state with REM-like features, including distinct gamma oscillations (Gonzalez et al., 2018). This "Ibogaine wakefulness" is characterised by oneirogenic effects, promoting dream-like cognition while maintaining conscious awareness, and is further distinguished from typical psychedelic states by its complex electrophysiological signature and the long-lasting suppression of REM sleep (Castro-Nin et al., 2023). This suggests that Ibogaine may facilitate a unique state of consciousness conducive to introspection and self-reflection, which could explain its purported efficacy in addressing addiction.

Numerous studies have emphasised Ibogaine's ability to alleviate opioid withdrawal symptoms and reduce addictive behaviour with a single administration (Alper et al., 2008; Alper et al., 2006; Alper & Lotsof, 2007; Lotsof & Alexander, 2001). Ibogaine therapy, as outlined by Lotsof and Wachtel (2002), employs a strategic dosing regimen, typically ranging from 15 mg/kg to 20 mg/kg, to address chemical and opioid dependence. The administration is crucially timed to coincide with the onset of withdrawal symptoms, enhancing Ibogaine's efficacy. Adjustments to dosage, based on patient response, and

management of potential withdrawal symptoms underscore the therapy's tailored approach. The experiences following administration, from physical sensations to cognitive evaluations, are integral to the therapeutic process, reflecting Ibogaine's comprehensive impact on addiction treatment (Lotsof & Wachtel, 2002).

4.1.1 History of Ibogaine treatment for substance misuse

Ibogaine has experienced a complex transition from its traditional use in African Bwiti rituals to a potential tool in Western addiction therapy (Fernandez & Fernandez, 2001; Popik & Skolnick, 1999). Discovered to contain 11 psychoactive constituents and chemically related to psychedelics like harmaline, Ibogaine was isolated in 1901, marking the beginning of its scientific exploration (Goutarel, Gollnhofer, & Sillans, 1993).

Howard Lotsof's accidental discovery of Ibogaine's potential to alleviate opioid withdrawal symptoms in the 1960s, was complemented by Dr. Claudio Naranjo's research into its psychotherapeutic benefits. Their work highlighted Ibogaine's unique ability to facilitate introspection and memory retrieval, suggesting its utility in psychotherapy (Naranjo, 1974; Alper et al., 1999). However, the classification of Ibogaine as a Schedule I substance severely restricted further research and clinical application, effectively marginalising its use within both legal and medical contexts.

The response to these restrictions was the formation of underground networks and self-help groups, such as the Junkiebond, a harm reduction activist group formed by heroin users in Rotterdam, Netherlands, in 1981, emerged as pivotal in maintaining access to Ibogaine therapy. This and other small groups, operating in a legal grey zone, have played a crucial role in providing support and treatment options outside conventional medical channels, embodying a grassroots response to the pressing need for effective addiction treatments amidst stringent regulatory environments (Goutarel et al., 1993).

Alper, Lotsof and Kaplan (2008) wrote an important paper titled "Ibogaine medical subculture" where they categorise the various settings in which Ibogaine treatment occurs as distinct "scenes," each reflecting different approaches and philosophies regarding its use. The medical model involves licensed physicians administering Ibogaine in clinical or research environments such as hospitals or accredited facilities, adhering to conventional medical standards like pre-treatment evaluations. This model, rooted in the 1950s, is primarily found in countries like Mexico and Saint Kitts, where experimental treatments are legally supported. In contrast, the lay provider/guide scene involves non-medically credentialed individuals who administer Ibogaine in informal settings, such as private residences or hotels. These

providers, often acting as guides, focus on facilitating the therapeutic process for addiction therapy or psychospiritual growth, while still employing basic safety measures. The activist/self-help scene is characterised by a strong activist stance, where individuals promote the acceptance of Ibogaine, sometimes through civil disobedience. An example is the "Ibogaine underground" in the U.S., where former users assist others in overcoming addiction, reflecting a grassroots, harm-reduction approach. Lastly, the religious/ceremonial scene involves the use of Ibogaine in religious or ceremonial contexts, often inspired by traditional Bwiti rituals. Participants in this setting seek spiritual experiences, personal transformation, or treatment for medical conditions, with this scene present in locations such as Gabon, Europe, and the U.S. These diverse contexts of Ibogaine use, each with its unique practices, benefits, and risks, underscore the ongoing evolution and complexity of Ibogaine treatment (Alper et al., 2007).

Clinical studies show single-dose Ibogaine for detoxification is generally well-tolerated (Mash, 2001, 2018). Common side effects are mild and include ataxia, tremor, and nausea (Mash, 2001, 2018). Hypotension, observed in some cocaine users, is likely due to cocaine-induced volume depletion and resolves with rehydration. Rarely, manic episodes lasting 1-2 weeks, with symptoms like sleeplessness, irritability, and mania, have been reported (Marta, 2015). Life-threatening events, including QT prolongation and respiratory insufficiency, have occurred within days of the first dose, sometimes in patients with opioid use (Paling, 2012). Fatalities have been linked to Ibogaine, particularly in those with comorbidities like cardiovascular disease or concomitant opioid use (Litjens & Brunt, 2016; Maas, 2006; Maciulatis et al., 2008; Papadodima et al., 2013; Vlaanderen, 2014).

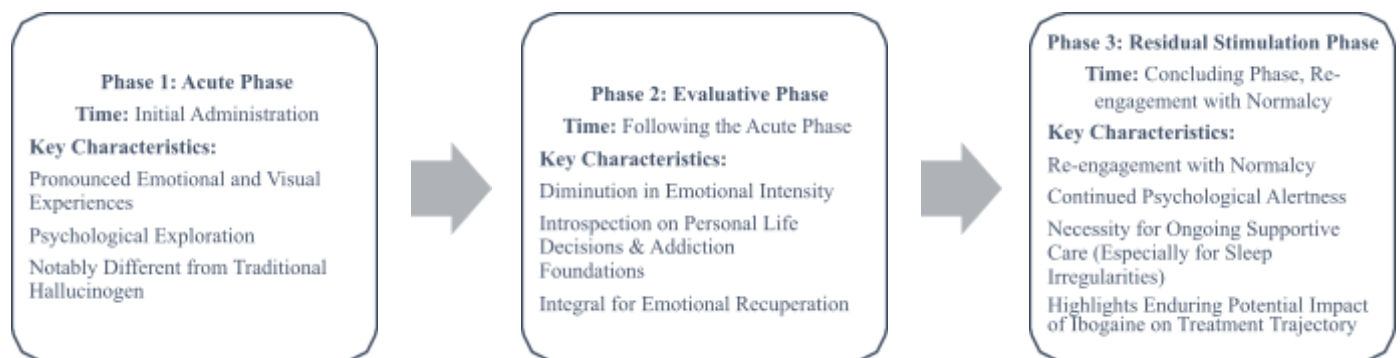
Recent studies have explored the potential of Ibogaine as an alternative treatment for opioid addiction yet, its use poses risks, including severe side effects from undiagnosed conditions or unknown drug interactions (Corkery, 2018). Recent trials have underscored Ibogaine's potential in treating opioid dependency, with ATAI Life Sciences' 2023 Phase 1 trial of DMX-1002 showcasing its safety and tolerability. This study confirmed that DMX-1002, an Ibogaine formulation, was well-tolerated in a controlled clinical setting, with patients experiencing transient hallucinatory states without serious adverse events. Additionally, ICEERS' 2020 Phase II trial further investigated Ibogaine's efficacy in methadone detoxification, demonstrating its ability to reduce withdrawal symptoms and dependency in participants. These findings, supported by ATAI Life Sciences and ICEERS, contribute to the growing body of evidence on Ibogaine's therapeutic benefits (ATAI Life Sciences, 2023; ICEERS, 2020)

4.1.2 Conceptual framework

The Ibogaine treatment process is delineated into three distinct phases, as visually represented in Figure 3. Identified by Alper and Lotsof (2007) and further detailed by Alper et al. (2007). The initial administration phase known as the 'acute' phase, is distinguished by pronounced emotional and visual experiences. These experiences are notably different from those elicited by traditional hallucinogens, offering a unique pathway for psychological exploration (Goutarel et al., 1993). Subsequently, the 'evaluative' phase is characterised by a diminution in emotional intensity, facilitating a period of introspection concerning personal life decisions and the foundational aspects of one's addiction (Mash, 2010). This stage is perceived as integral for the patient's emotional recuperation following treatment. The concluding 'residual stimulation' phase signals a re-engagement with normalcy, albeit accompanied by continued psychological alertness (Alper et al., 2007). This phase highlights the necessity for ongoing supportive care alongside Ibogaine administration, particularly in addressing potential sleep irregularities, thereby illustrating the enduring potential impact of Ibogaine on the treatment trajectory. See *Figure 3* for the summary of Ibogaine experience phases.

Figure 3

Phases of Ibogaine Experience



Ibogaine's impact on addiction involves complex interactions with the Central Nervous System (CNS), notably affecting serotonin and dopamine receptors critical for mood and addiction behaviours. This modulation alters the brain's reward pathways, diminishing the desire for addictive substances (Mash et al., 2000). Ibogaine also modulates opioid receptors, including kappa and mu receptors, potentially reducing both physical withdrawal symptoms and psychological dependence on opioids. This highlights Ibogaine's dual action on the physical and psychological facets of addiction (Glick et al., 2002). The role

of Noribogaine, Ibogaine's metabolite, is important due to its extended half-life and continuous CNS activity, further supporting the sustained reduction of craving and withdrawal symptoms post-Ibogaine metabolism (Mash et al., 1998).

The therapeutic approach for Ibogaine, as developed by Howard Lotsof, is structured around a fourfold approach, distinctly termed the "Lotsof Procedure." This methodology is designed to: 1) establish trust with the patient, 2) ensure their comfort, 3) aid in interrupting chemical dependency, and 4) provide a comprehensive support network for recovery and personal development (Lotsof, 1994). Friedlander (2003) argues this model diverges from traditional addiction treatments by advocating a patient-centered strategy, which does not demand immediate abstinence but rather supports the individual through a process that might lead to cessation of substance use, facilitated by Ibogaine's unique pharmacological profile.

4.2 Objectives and aims

The increasing prevalence of substance misuse in England and the broader UK underscores the urgency for innovative and effective treatment modalities. With the rise in opioid addiction, the healthcare community is actively seeking alternative treatments. Ibogaine, a psychoactive alkaloid, has emerged as a potential contender. However, its application remains a subject of debate, given the stigma associated with psychoactive substances, the anecdotal nature of Ibogaine's efficacy and the absence of standardised treatment protocols. For research in this domain to be credible, a robust methodological and analytical framework is necessary. Previous investigations have predominantly centred on patient accounts or the pharmacological properties of Ibogaine. To the author's knowledge this is only the second exploration of Ibogaine treatment providers since Alper et al. (2007), which seeks to bridge the gap by focusing on the experiential narratives of treatment providers. This is an alternative to interviewing treatment seekers or those who completed treatment as such narratives will not yield information and insight on how the treatment is planned and applied, but rather on the effects of receiving the treatment. This study is guided by three primary research questions:

1. What is the role of Ibogaine and treatment providers in substance misuse recovery?
2. How is Ibogaine used to treat substance misuse?
3. What therapies are used to support Ibogaine treatment?

To answer these questions, this study sets out three primary aims with corresponding objectives.

The first aim, responding to research question one, seeks to investigate the backgrounds, responsibilities, and perspectives of Ibogaine treatment providers. This encompasses elucidating the demographic and professional backgrounds of these providers (Objective 1), gaining insight into their roles and responsibilities in the treatment process (Objective 2), and capturing their perspectives on the potential of Ibogaine as a tool for addiction recovery (Objective 3). Given the historical and cultural importance of Ibogaine being administered by a knowledgeable person, it is important to better understand their experiences and opinions of providing treatment with Ibogaine as well as a comprehensive view of Ibogaine's application in various settings, from legal treatment centres to more informal environments.

The second aim, addressing research question two, intends to explore various treatment procedures and dosing strategies applied in Ibogaine therapy for addiction. This involves investigating the narratives around pre-treatment preparations, the actual Ibogaine administration, and post-treatment support (Objective 1), understanding perspectives on dosing strategies and the factors influencing dosage determination (Objective 2), and examining the reasoning behind these treatment procedures and dosing strategies (Objective 3). By exploring the intricacies of treatment procedures and dosing, this research offers clarity on the practical application of Ibogaine. This knowledge can serve as a foundation for future treatment models, ensuring that they are informed by a rich tapestry of experiences and are aligned with the holistic approach to substance misuse recovery.

The third aim, responding to research question three, endeavours to scrutinise the array of supplementary therapies used in conjunction with Ibogaine, including talking therapies and other substances. Objectives for this aim include exploring the administration, perceived benefits, and considerations of these additional substances used in Ibogaine therapy (Objective 1), understanding the role and importance of talking therapies within the Ibogaine treatment context (Objective 2), and exploring the use and potential synergies of therapies like yoga and meditation with Ibogaine treatments (Objective 3). By identifying potential synergies and understanding the holistic approach to addiction recovery, we can enhance the benefits of Ibogaine. This comprehensive view can guide patients, providers, and policymakers in integrating complementary therapies, ensuring a well-rounded recovery experience that draws from a diverse range of therapeutic modalities.

Ethical approval to conduct the study has been obtained from the Faculty of Health and Medicine Research Ethics Committee (FHMREC) University of Lancaster, Research and Ethics Committee (Ref: 20117) (Appendix A). See Section 2 for a detailed explanation of how ethical issues was addressed.

4.3 Methods

4.3.1 Design

A qualitative, semi-structured interview study was conducted (September 2021) to gain a deeper understanding of addiction treatment with Ibogaine from the perspective of treatment providers. Additionally, a pre-interview survey was also used to gather participants socio-demographic information and contextual data relating to treatment. Ethical approval to conduct the study has been obtained from the Faculty of Health and Medicine Research Ethics Committee (FHMREC) University of Lancaster, Research and Ethics Committee (Ref: 20117).

4.3.2 Participant recruitment

Current practitioners specialising in Ibogaine treatment were recruited from various global regions to ensure a comprehensive understanding of its application in addiction treatment was captured. The study employed a convenience sampling approach, complemented by the snowballing technique, for participant recruitment (Patton, 2007). Convenience sampling, a non-probability sampling method, was chosen for its practicality in creating samples based on accessibility and availability. Given the limited literature on Ibogaine treatment centres at the time of the study, this approach was pivotal in pinpointing practitioners with specific expertise in Ibogaine treatment. The snowballing method leveraged the existing knowledge and networks of participants, enabling the identification of other potential contributors and ensuring a broader representation of the community (Biernacki & Waldorf, 1981). The primary goal was to recruit from a diverse set of countries, but the actual range was influenced by recruitment challenges. In regions where Ibogaine's legal status was ambiguous or stringently controlled (i.e. Canada) potential participants displayed apprehension, which complicated the recruitment process. Organisations and individuals who were identified as being active in their Ibogaine administration practices for opioid misuse were identified through a search of Ibogaine treatment centres; LinkedIn was also used to search for treatment providers. Ibogaine treatment centre websites that promoted their experience and competency in Ibogaine treatment was approached directly via email (Appendix C1) in their "contact us" section. The study was further advertised in online Ibogaine related forums (Appendix C2). A participant recruitment post was shared on psychedelic use-related platforms such as Reddit and Bluelight.org for treatment centres that the researcher might have overlooked. The rules of the websites/forums stated that advertising a scientific study is allowed. Participants indicated whether they would like to participate by emailing the researcher directly. Approached participants also had the opportunity to refer additional suitable participants for the study

by forwarding the Researcher's contact details. Participants had to adhere to the inclusion criteria stated in Table 21.

Table 21

Inclusion and exclusion criteria

Inclusion Criteria	Exclusion criteria
• Aged 18 or older. • Currently providing treatment for addiction with Ibogaine OR having worked independently or in a treatment centre for addiction treatment with Ibogaine for at least one year. • Able to give informed consent	• Self-reported English-speaking level below Intermediate.

4.3.3 Data collection

Participants were initially provided with a Participant Information Sheet (PIS) (Appendix 3) to inform them about the study's objectives, procedures, and their rights as participants. After reviewing the PIS, participants who were willing to participate provided their signed consent (Appendix 4), ensuring their voluntary participation and understanding of the study's scope and purpose.

With consent secured, a pre-interview demographic survey (Appendix 5) was dispatched to the participants. This aimed to capture their demographics, experience, treatment regime, and supplementary therapy. The responses from this survey were instrumental in tailoring the subsequent interview questions to be most relevant to each participant's experience and expertise.

Upon completion of the survey, individual one-on-one interviews were scheduled. These interviews were conducted online via Microsoft (MS) Teams video chat software. The privacy policy of this software was highlighted in the participation sheet to ensure participants were aware of the data handling procedures.

Participant semi-structured interviews were designed to encompass various facets of the treatment process, from admission to aftercare, and the treatment regime, including dose, setting, and adjacent therapies. While the information provided in the pre-interview survey, allowed a deeper exploration of

the contextual factors influencing Ibogaine administration, focusing on participants' backgrounds, views, and opinions on the treatment they provided.

The PhD candidate (AE) conducted semi-structured topic-guided interviews (Table 22) via Microsoft (MS) Teams video chat software. Interviews, guided by the topics derived from the treatment process and pre-interview survey lasted for an average duration of 60 minutes, covering the areas in Table 22, with a range from 45 minutes to 1 hour and 20 minutes. The PhD candidate conducted 1 pilot interview to test the interview questions with a participant who is not a practitioner but is knowledgeable in the area of Ibogaine treatments and learnings from the pilot allowed the PhD candidate to expand the scope of dosing to different approaches and better understanding of the legal and logistical predicaments experienced by participants.

Table 22*Key Topic Areas for Interviews*

Focus Area	Examples of questions and probes
Practitioner responsibilities and background	What is your background? Prompts: Can you explain your responsibilities? How do your background and previous experiences affect your current position? How did you get involved in Ibogaine treatment? Prompts: Have you personally experimented with Ibogaine? Why? Has it affected your practice?
Treatment process and regime	Why do treatment seekers choose Ibogaine treatment? What happens after admission? Prompt: Can you narrate what a service user will go through? Can you describe the treatment setting of your work area (Location, premise, facilities, therapeutic features?) What is the importance of the treatment setting? (Set and Setting) Do you have a preferred Ibogaine dose? What is it (is it the same as indicated in the pre-interview survey)? Prompt: Why? What happens after the initial dose? Can you tell me more about the additional therapies you provide? Prompt: How do they help? Do you offer different treatment options/regimes? (different dosing, selection of therapies, being exempt, pick and mix etc.)? Prompt: Why?
Ibogaine treatment details, benefits, and challenges	What do you think about the role of Ibogaine in the context of the treatment? (Set & Setting) Prompt: How does it work? Why? What are the impacts of Ibogaine treatment for people visiting your center? What do you think is important in generating these impacts? Prompt: How does your treatment protocol lead to people feeling that way? Are there differences in treatment provided for opiate and non-opiate addictions (alcohol/benzodiazepine/cannabis)? What about addictions like sex/gambling? Prompts: Why? How do they differ? What do you think about the role of Ibogaine in the context of the treatment? Prompt: How does it work? Why? As a practitioner, are there challenges in providing addiction treatment with Ibogaine? Prompt: What are those challenges? Why do they arise? Can you overcome them? How? For service users, what are the main benefits of undergoing Ibogaine treatment? Prompt: What causes the effect? What is the significance? Are there factors affecting undergoing Ibogaine treatment and the treatment outcomes? Prompt: If yes, what are those? How? Why? Can you describe the risk mitigations undertaken by the treatment centre ?
Longevity and Post-treatment	What do you think about the longevity of the treatment? Prompt: Are there any factors affecting longevity? Do you offer aftercare/relapse prevention services? Prompts: What is the significance? How? What does it consist of? What do you think the future of Ibogaine treatment will be? Prompts: What makes you say that?
Closure	Is there anything else you would like to add or ask?

Once the participant signed and submitted the consent sheet and pre-interview survey, a timeslot was arranged for the interview. The differences in time zones were managed by sending an electronic invite to the participants. Issues surrounding confidentiality were restated at the start of the interview. The interview audio was captured by placing the Dictaphone near the computer speakers, and the audio was recorded with a password-protected audio recorder. See Figure 4 for a flowchart display of the procedure of recruiting participants.

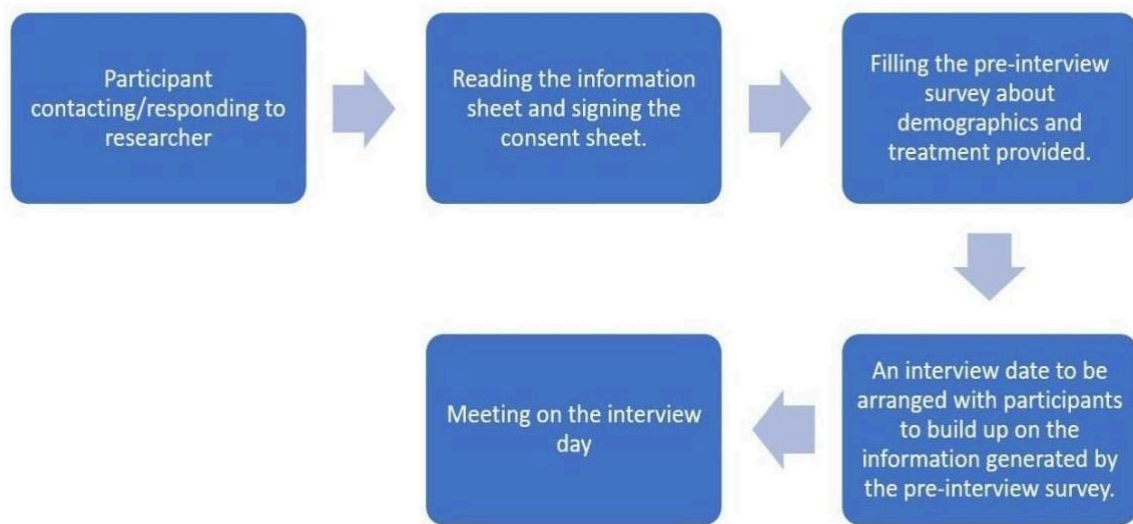


Figure 4

Data collection flowchart

4.3.4 Data analysis

Thematic analysis has become a popular and flexible method in qualitative research over recent years. One approach that stands out is Braun and Clarke's reflexive thematic analysis. Based on their influential work, this method places a strong emphasis on being reflexive, meaning researchers continuously reflect on their role and influence throughout the analysis. A later work by Braun et al. (2021) further elaborates on the importance of this reflexive approach, providing more detailed guidance on how to implement it effectively in research. This emphasis on reflexivity is particularly relevant to the primary research conducted by the PhD candidate, who demonstrates a deep commitment to this approach, recognising its value in providing a detailed and rich understanding of the data.

To analyse the online surveys conducted through Qualtrics, survey data were downloaded and reviewed. Descriptive statistics regarding demographic details and other study-relevant information were thoroughly analysed. For the analysis of interviews, the PhD candidate followed Braun and Clarke's method closely. The first step was getting to know the data, spotting initial patterns and ideas. After that, the PhD candidate started coding the raw data, which means labelling parts of the data that seemed interesting or important in relation to the research questions. Once the coding was complete, the PhD candidate analysed the codes to identify potential subthemes, grouping codes that shared common underlying concepts or patterns. These subthemes were then further examined and organised into broader, overarching themes that captured the main ideas emerging from the data. This iterative process involved constantly comparing and refining the subthemes and themes to ensure they accurately reflected the nuances of the entire dataset. The final step involved providing clear and concise definitions for each theme and subtheme, ensuring clarity and coherence in the analysis.

For analysis, the software NVivo12 was employed by the PhD candidate to systematically organise and analyse the data. A notable observation was the variance in perspectives between participants associated with the treatment centre and those appearing promotional in nature, disproportionately highlighting the benefits and positive sides of such treatment. This necessitated the research to exercise heightened discernment during interviews, particularly when confronted with bold assertions made by the participants. A case in point was a claim suggesting that Ibogaine could entirely modify all addiction-related components of the brain. Such statements, while intriguing, underscored the imperative for the research to align interpretations with well-established scientific knowledge. Throughout the data collection process, the PhD candidate prioritised receptivity to ensure accurate capture of the interviewees' perspectives, irrespective of personal agreement or disagreement. Critical analysis was reserved for the subsequent stages of data analysis, where the collected information was rigorously examined and interpreted.

In the analysis, the PhD candidate adhered to Shenton's (2004) strategies to enhance the trustworthiness of qualitative findings, while closely following Braun and Clarke's reflexive thematic analysis method. Key steps included prolonged engagement with the data to gain a deeper understanding, and the use of triangulation through two approaches: contextualising interview findings within the broader research area in the discussion section, and engaging in in-depth discussions with supervisors.

Additionally, the PhD candidate maintained a reflexive log throughout the process to continuously monitor and reflect on their potential biases, ensuring that interpretations were rooted in the data rather than influenced by personal perspectives. Thick descriptions of the data were provided to enhance the transferability of the findings to other contexts. During the interviews, member checks with participants were conducted to verify the credibility of the themes identified. Collectively, these measures aimed to minimise bias and uphold the study's credibility, dependability, and overall trustworthiness.

4.3.5 Reflexivity

Reflexivity, a cornerstone of Thematic Analysis (TA) as posited by Clarke & Braun (2013), underscores the intricate interplay between a researcher's personal experiences, values, and beliefs and their engagement with the data. This transparent and introspective approach to one's pre-existing relationships with the subject matter is pivotal for the credibility of the analysis and the research process (Willig, 2013). A Critical Realist (CR) approach further accentuates this reflexivity, acknowledging the intertwined subjectivities of both participant and researcher (Willig, 2013; De Vaujany, 2008). See section 2.3 for a detailed breakdown of the reflexive statement.

While my initial knowledge of Ibogaine was gleaned from mainstream drug information sites and forums, my interest in apprenticing with an Ibogaine treatment provider led to interactions that deepened my understanding, prompting a shift in research focus. Recognising the diversity in Ibogaine treatments and the value of direct conversations over written exchanges, I opted for an inductive approach with TA, complemented by rigorous reflexivity. This approach was further enriched by maintaining a reflexivity journal, capturing the evolution of thoughts, decisions, and interpretations throughout the research journey.

4.4 Results

This results section presents the findings of the study, organised around the central research questions (RQs). Starting with the socio-demographic details of participants and expanding on the overarching themes that correspond to each research question, with sub-themes identified through the analysis. These sub-themes explore various aspects of the participants' experiences and perspectives, providing a detailed understanding of the research topics. Participant quotations are integrated throughout to illustrate key points and to give voice to the participants' insights and reflections. This structure ensures a coherent presentation of the results, allowing for a nuanced exploration of the complexities involved

in Ibogaine treatment from the perspectives of practitioners and those who have undergone treatment themselves.

4.4.1 Socio-demographic details of participants

The recruitment process for this study presented initial challenges, as potential participants were hesitant to discuss their experiences with providing treatment using a little-known and illegal substance. However, once a few practitioners (n = 3) agreed to be interviewed and recommended others to participate, recruitment became considerably easier.

Of the 13 participants (n = 13) who took part in the study, the majority were male (n = 10, 76.9%). The median age was 47 years (range: 30 to 75 years). Most participants identified as White (n = 11, 84.6%), while one participant (n = 1, 7.7%) identified with a mixed racial background of White, Black or African American, and Spanish/Mexican/Latin. Another participant (n = 1, 7.7%) classified themselves as 'Other'.

The participants came from a variety of nationalities, with a strong representation from North America (n=5), particularly Canada (n=2) and the USA (n=3). There were also participants from European countries, such as Ireland (n=1), the UK (n=1), and Italy (n=1). See table 23 for a breakdown of participants' demographic details as well as information on languages they speak and the highest degree certification obtained. Even though they had similar responsibilities, in terms of their jobs, participant job titles included Owners, Directors, and Recovery Coaches, among others. They had worked in the field for different lengths, from 2 years up to 25 years.

Table 23*Socio-demographic details and education level of participants via survey*

P#	Gender	Age	Description	Nationality	Native Language	Other Languages	Highest Degree
P1	Male	47	White	Canadian	English		Some college, no degree
P2	Male	34	White	Canadian/Irish	English	Spanish	Bachelor's degree
P3	Male	44	White	American	English	French, Spanish	Bachelor's degree
P4	Male	50	White	British	English	English, Portuguese, Italian, Spanish, French	Bachelor's degree
P5	Male	57	Other	Irish	English	English and Spanish	Bachelor's degree
P6	Male	30	White	Canada, Dutch	English	Dutch, French	Some college, no degree
P7	Male	56	White	English	English	No	High school degree
P8	Male	32	White	USA	English	Spanglish	High school degree
P9	Female	37	White	USA	English		Bachelor's degree
P10	Male	75	White	Italian	English		Associate degree
P11	Female	52	White, Black or African American, Spanish/Mexican/Latin	Born in South Africa; citizen of USA; live in Mexico	Xhosa and English	English, Spanish	Some college, no degree
P12	Female	54	White	USA	English	No	Some college, no degree
P13	Male	36	White	American	English	No	Associate degree

4.4.2 Research Question 1: What is the role of Ibogaine and treatment providers in substance misuse recovery?

Wounded Healers: From Personal Struggle to Professional Purpose

Participants in this study, all with personal experiences of substance use or mental health challenges, often elaborated on both their own treatment experiences using Iboga or Ibogaine and their motivations for pursuing careers in healing professions. One participant noted, "When I found Ibogaine, I mean it's just, like as soon as I got treated, I had said to them do you guys need any help like for me to talk to people so I can explain what happens when you come back?" (Participant 11). This transition from patient to practitioner is not just a professional shift but a deeply personal one, driven by the profound healing they experienced. The influence of personal experience, whether abstaining from cigarettes addiction to heroin use to negative effects of prescribed antidepressants, there was a common theme shared by other participants, who also sought out experienced individuals they could learn from to provide treatment with Ibogaine.

Ibogaine as a Last Resort

Central to the narrative of these "Wounded Healers" is the recognition of Ibogaine as a "last resort" in both personal recovery and professional practice. Most practitioners, having themselves turned to Ibogaine after exhausting other treatment avenues, observe a similar pattern in their patients. They witness first-hand how Ibogaine offers a lifeline to individuals with severe addiction, often heroin, for whom conventional treatments opioid substitute treatments have failed. Participant 2 observed, "For our patients, Ibogaine represents the final attempt after a series of unsuccessful treatments. They tried everything else." Similarly, Participant 9 noted, "Individuals seek Ibogaine treatment out of a sense of last hope, often stating, 'nothing else works like it' [regarding the opiate detoxification effect]," highlighting its effectiveness where other methods have not succeeded.

This perception of Ibogaine as a final option is further cemented by its limited accessibility and awareness. As Participant 5 explains, "It's not a mainstream...doctors in the U.S. most of our clients come from the U.S. doctors in the United States legally are not even allowed to recommend that somebody go do Ibogaine." This lack of mainstream acceptance and legal restrictions contribute to the information scarcity surrounding Ibogaine, making it "a word of mouth thing of doing your research online." Consequently, for many, "even though it should have been the first it's a last resort kind of thing."

Participants characterised Ibogaine as a "interruptor," emphasizing its therapeutic efficacy attributed to its distinctive psychoactive properties which facilitate emotional detachment, thereby enabling introspection into addiction patterns and alleviating physical withdrawal symptoms commonly associated with opiate dependency. On two occasions participant 7 explains the interruption effect as "Because if you're trying to get off opiates, it's hands down the best way to do it. And actually, in many respects, it's a really good way to interrupt any drug use. And it's a powerful addiction interrupter. It's not a silver bullet by any means. However, what it does is it can provide people with the insight and, in many respects kind of like get the monkey off their back for a period of time.". Participant 7 also mentions the effect duration of interruption in his experience with treatment seekers "Okay. I know we prefer to work with people 35 and over, you know, but so, it's a powerful addiction interruption for like three months. And depending on what you had set up, like aftercare working with [name redacted], stuff like that, you know, so that's the kind of curation, and maybe you learned enough during that period that you, that you dropped drugs completely or, you know, and start dealing with that trauma. That's the underlying cause of the drug use."

4.4.3 Research Question 2: How is Ibogaine used to treat substance misuse?

Dosing Strategies and Ibogaine Forms Employed in Treatment

Ibogaine treatment protocols vary, particularly in dosing strategies. Two primary approaches exist: 'flood dosing', which involves a single, large dose aimed at inducing a rapid and intense psychedelic experience, often described as "the trip" or "the hallucination". In contrast, 'extended dosing', uses smaller, repeated doses spread out over a longer period, often several days, to achieve a gradual and controlled effect.

Another important consideration is the form of Ibogaine to be administered as participants often argued different forms of Ibogaine have slightly differing effects, as participant 5 explains "protocol is varied. We have clinics in [country redacted] that do a ... tapering up with a TA or a PTA. Some of them do use HCL that has been extracted or semi-synthesised from vocong. So those effects will be different... So that experience, that side of it is going to contribute to them vastly different experience for people, the medicine that's being used in the first place, but then also the protocol and who's administering care matters, huge, worked with clinics. And some of them, I agree completely with their protocol and some of them, I disagree slightly with the way that they, you know, use the medicine or the protocol that they use. But I worked with all kinds of people because I think that there needs to be that varied."

Despite favouring the variety, some participants reported that the intense flood dose experience comes with risks, notably cardiac complications. Participant 3's experience following seeking Ibogaine treatment for their heroin addiction, resulted in "six cardiac arrests and hospitalisation where they spent two weeks on a pacemaker," illustrates the potential dangers of a poorly managed flood dose.

Whilst both flood dose and extended dosing were argued to be tailored to the individual's needs, participant accounts highlighted extended dosing to be more personalised due to the increased frequency administration of smaller doses, participant 6 explains "If somebody requires longer, if they're ready for a larger dose sooner, it's just important to give somebody at least a day to two days, load of boosting to lead up to any larger dose you're going to get."

See Table 24 for an overview of Ibogaine form, dose, and frequency of administration based on participant survey responses.

Table 24

Form and Dose of Ibogaine as well as frequency of administration via survey results

Participant	Form and Dose of Ibogaine Administered for Addiction Treatment	Frequency of Administration
1	PTA and TA extracts. PTA 15mg-20mg per kg. TA 35-45mg per kg. Stopped using HCl.	Test dose, then flood dose and booster dose if required. Not extended over 3 days. (Flood)
2	HCl, usually 13mg/kg for detox, or 8-10mg/kg for psychospiritual	For detox, 300mg doses every 30 minutes for flood. For psychospiritual, 8mg/kg at once or in 2 doses 45 minutes apart. (Extended dose)
3	HCl capsules	One dosage in the morning. (Flood dose)
4	TA, PTA and HCl	Dependent on client's weight, physical and mental condition, reaction to test dose, metabolism, and heart monitor readings. (Both)
5	Ibogaine	Depends on the treatment and patient (Both)
6	RA, PTA, HCl, TA and other alkaloid concentrations	1-2 times daily for up to 5 days. Dependent on protocol, 2-4 days of low doses. (Extended dose)
7	Differs by weight of client	Once a day for up to 14 days. Differs between patients. (Extended dose)
8	HCl	One flood, and smaller doses post-treatment. Depends on individual. (Both)
9	Depends on the substance of dependency	Depends on whether a center does flood dosing or low dosing protocols. (Both)
10	HCl (full dose based on weight) - 1000=1200 mg usually.	Once (Flood)
11	HCl and TA (Total Alkaloid, full spectrum extract). Dosages vary per treatment, substance(s), age, career use, comorbidities, etc.	Varies; all client treatments are individually tailored. (Both)
12	HCl & TA	2-3 times in a week (Flood)
13	For normal retreats, use Root Bark and TA. For Detoxes, mostly TA but sometimes Root Bark and Tea. Dose varies based on several factors.	Varies a lot, but spaced out as much as possible within withdrawal window. (Both with mostly extended)

Criticisms of Flood Dosing and the Advantages of Extended Dosing

Participant 8 criticised flood dosing: "Well, I don't agree with flood dosing anymore... hoping for a low-risk positive outcome for someone is I think just incredibly naive... if you don't do a slow, gradual titration with the Boga... it's really difficult for people who overuse the medicine with their clients." They highlighted the risks: "In addition to the potential cardiotoxicity, flood dose renders you completely unable to move," hindering integration of insights. They advocated for extended dosing: "With low dosing, people can still go about their daily life... It's just a better way to integrate the experience. I see a much higher success rate in people going through low dose than the flood dose."

Extended dosing enhances safety, particularly with potent substances like fentanyl. Participant 7 explained: "in the last sort of five or six years, fentanyl has been really taking off... what used to be...a \$50 a day habit now...might be 1200 to 1500 milligrams of morphine." They detailed their approach: "we would start...on a pinky...maybe one or two milligrams per kilogram... then I could see...how they're receiving the medicine. Also...the body doesn't try to reject it and throw it up...electrolytes are pretty important..." Like other participants, this participant also emphasised individual treatment approaches: "Ibogaine...isn't cookie cutter...I'm working with a 72-year-old woman...very slowly over three weeks."

Participant 11 supported extended dosing for high-risk patients: "And so, and we treat a lot of high-risk patients... cardiologically compromised. Ages, obese... These opioids are, they can cause seizures... Dosing is hugely decided by... their ECG... Not just their physical metabolism, but their psychological metabolism. We've given someone a test dose and they had a panic attack... dose and administer the medicine according to the body... Your body will tell us."

Post-treatment Processes in Ibogaine Treatment

Post-treatment support is crucial for both physical and emotional recovery. Participant 7 described the "grey day," a challenging period around five to six days after flood dosing: "Typically occurring around day five or six post flood dose, this phase may involve a temporary emotional downturn." Conversely, the "Ibogaine afterglow," as discussed by Participant 4, can lead to overconfidence: "You see, you got clients that do stimulants like cocaine, methamphetamine? They believe they are cured and they're ready to rule the world again, and then they often want to leave earlier..." While the interviews didn't explicitly differentiate post-treatment support between dosing strategies, flood dosing clinics mentioned structured programs with meditation and group discussions, while extended dosing

providers emphasized one-to-one support to integrate "lessons learned" as participants 6,9 and 11 have mentioned.

Participant Accounts of How Ibogaine Works

Participants described the intense "buzz" or "hum" of the flood dose experience, with Participant 1 noting that "the buzz gets more intense, it starts to turn into a hum...if they don't get nauseous." This suggests a profound impact on sensory perception. Participant 2 vividly described how Ibogaine interrupted the relentless cycle of craving and consumption associated with crack cocaine addiction: "Every part of your mental process when you're addicted to crack...the cravings are 10 out of 10 - 24/7...you can't think about anything else. The high and then you have to get some more...and Ibogaine (makes a "feeiwttt" sound) just cut straight through that." This interruption, he explains, allowed for introspection and self-reflection, facilitating the identification of personal flaws and their origins. Participant 2 highlighted the experience of confronting his "moral cowardice" stemming from childhood trauma following Ibogaine administration and think the confrontation of his traumas helped him overcome his addiction: "In my experience, I got my ass kicked. I got beaten up...when I was a kid...I formed like a moral cowardice...and then I would hate myself secretly, so not standing up for myself or my family..." The supportive environment of the Ibogaine treatment setting fostered the subsequent development of self-esteem. He emphasized the enduring impact of Ibogaine: "...it lasts for a really long time like Ibogaine lasted for like 18 months two years for me. Like everything was a revelation." This period was marked by personal revelations and the development of crucial life skills, effectively enabling his transition to a "functioning member of society."

Participant 7 corroborated the notion of Ibogaine as a powerful "addiction interrupter," stating that "if you're trying to get off opiates, it's hands down the best way to do it." He stressed the importance of Ibogaine as a tool within a broader recovery strategy: "Ibogaine should just be used as one of the tools in somebody's recovery. Not it's all Ibogaine though...people have the tendency [to put] all of their eggs, into the Iboga Ibogaine basket thinking that's gonna do it for them." This participant also acknowledged the adaptive nature of drug use, highlighting the difficulty of addressing deeper emotional problems while actively engaged in addiction with the lack of a support network.

Navigating the Complexities and Challenges of Ibogaine Treatment

The complexities of Ibogaine treatment are compounded by factors like provider expertise and clinic resources. As Participant 5 noted, "The variability in treatment experiences can be alarming, ranging

from transformative to traumatic, largely depending on the practitioner's expertise and the setup." This variability is linked to the lack of standardisation and oversight in the field, which Participant 3 referred to as the "dark void." Adequate staffing and training are crucial, as highlighted by Participant 5: "A lot of the hospitalizations happen when a provider decides that they need a little bit of break to take a nap, and then something pops up when they're not looking... You really need to have like a large, well-trained staff, and most clinics don't have that."

Furthermore, the treatment process is complicated by both controllable factors, such as patient honesty about substance use, and uncontrollable factors, like the quality of Iboga bark and the prevalence of potent substances like fentanyl. Participant 10 emphasized the importance of timing: "Scheduling treatment during periods when emergency services are readily available can greatly enhance patient safety." The prevalence of burnout among Ibogaine providers, who often come from a substance abuse background themselves, adds another layer of complexity. Participant 5 highlighted this issue: "There's a huge issue of burnout that leads to... accidents with the clients as well."

4.4.4 Research Question 3: What therapies are used to support Ibogaine treatment?

Psychological Support for Ibogaine Treatment

Participant accounts reveals a diverse range of approaches, reflecting the individualised nature of the support offered. However, this apparent lack of standardisation raises questions about the theoretical underpinnings and consistency of these interventions.

Several participants, including Participant 7, highlighted the introspective qualities of Ibogaine, suggesting that "Ibogaine does a lot of the awareness work." This perception may explain the absence of clearly defined methodologies for talking therapies within Ibogaine treatment. Participants, such as Participant 5, emphasise providing individualised support, often drawing on personal experiences with addiction, sobriety, and Ibogaine treatment rather than established therapeutic frameworks. Participant 5 describes their approach as "asking questions and listening to the person," facilitating a process of self-discovery rather than imposing external direction. This emphasis on patient autonomy and empowerment contrasts with what Participant 5 perceives as the disempowering and dehumanising nature of mainstream addiction treatment.

Participant 5 mentions that in response to the identified lack of mental health expertise within the Ibogaine community, clinics have begun to integrate trained counselling professionals into their teams.

This shift signifies a growing recognition of the importance of psychological support in conjunction with Ibogaine treatment and explains the reason behind her role “Many of these clinics are run by people who have zero clinical mental health training, and they have they don't know how to support people going through trauma. So a lot of people will call me saying that the clinic essentially just like left them alone, and maybe there was a nice pool or whatever, but there was no real consistent psychological support, so that's a big complaint and also most clinics don't offer like follow up support, they just send you home and say goodbye and which is part of the reason why I do the work I do 'cause I noticed that was a really big issue, so so that's another issue that happens, and then there's the issue of people feeling rushed into treatment when they don't feel completely safe or ready to do it like I was saying earlier about people with fentanyl in their systems. Often people are being pushed to do Ibogaine too soon before it's safe, and the client can feel that, and it makes them feel nervous and unsafe.” However, Participant 5's inability to clearly articulate their methodology or provide concrete examples raises concerns about the consistency and replicability of their approach. This lack of a defined theoretical framework may indicate a reliance on intuition and personal experience rather than evidence-based practice. While flexibility is undoubtedly important in meeting individual needs, the absence of a clear structure may lead to inconsistencies in treatment delivery and hinder replicability.

In contrast to Participant 5's highly individualised approach, Participant 3 and Participant 4 provide insights into more structured aftercare programmes. Both describe an 8-week online programme incorporating group sessions and one-on-one coaching. Participant 4's programme draws inspiration from elements of Narcotics Anonymous and Alcoholics Anonymous, including a "buddy-up system" to foster peer support and connection. These structured programmes offer a more standardised approach to aftercare, potentially addressing the concerns raised about the consistency and replicability of individualised interventions. However, further research is needed to evaluate the effectiveness of these programmes and determine their suitability for diverse populations undergoing Ibogaine treatment.

In conclusion, the provision of talking therapies within Ibogaine treatment settings appears to be highly varied, ranging from highly individualised approaches to structured programmes. While the emphasis on individual needs and patient-centred care is commendable, the lack of clearly defined methodologies and theoretical frameworks for some interventions raises concerns about consistency and efficacy. Further research is needed to establish best practices for talking therapies in Ibogaine treatment and ensure that these interventions effectively support long-term recovery.

Pharmacological Support for Ibogaine Treatment

Some participants mentioned the use of 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) in conjunction with Ibogaine treatment. This was not something the PhD candidate expected to hear before designing the study. 5-MeO-DMT is a naturally occurring psychoactive compound known for inducing intense, albeit short-lived, psychedelic experiences. Participants discussed its strategic application alongside Ibogaine, highlighting its potential benefits in managing anxiety and facilitating the integration of the Ibogaine experience. Many users report experiencing moderate-to-strong mystical-type experiences, including sensations of ineffability, timelessness, and awe or amazement (Davis et al., 2018).

Participant 2 advocates for the pre-emptive use of 5-MeO-DMT, suggesting that "Administering 5-MeO-DMT before Ibogaine can ease initial apprehension and prepare individuals for the profound introspection that Ibogaine induces." Conversely, Participant 7 sees value in its post-treatment application: "Using 5-MeO-DMT after Ibogaine acts as a cementing phase, helping solidify the insights gained from the Ibogaine experience." These contrasting perspectives illustrate the diverse approaches to integrating 5-MeO-DMT within Ibogaine treatment protocols.

However, Participant 6 expresses caution against over-reliance on adjunct substances, asserting that "Ibogaine does not need any other drug to go along with it. It's potent enough. The counselling, the integrative coaching, the ongoing support systems are what truly matters." This perspective highlights the importance of comprehensive support systems and therapeutic interventions alongside the pharmacological effects of Ibogaine.

Beyond 5-MeO-DMT, participants also discussed the use of other substances, such as diazepam and cannabis oil, to manage side effects and promote sleep regulation following Ibogaine administration. Participant 5 clarifies their clinic's protocol: "We sometimes administer 10 mg diazepam if a patient is not sleeping, along with cannabis oil to help with sleep before Ibogaine treatment." This statement clarifies that these substances are used as pre-treatment aids rather than post-treatment interventions.

4.5 Discussion

This research represents the first comprehensive exploration of the backgrounds, practices, and perspectives of Ibogaine treatment providers, offering critical insights into the evolving landscape of substance misuse recovery. The study's findings are the first to shed light on the multifaceted roles that Ibogaine treatment providers play, not only in administering the treatment but also in integrating

supplementary therapies and ensuring comprehensive aftercare. This is essential in understanding Ibogaine's place within broader addiction treatment frameworks, particularly as a last-resort option where other treatments have failed.

The following discussion is structured around the study's three primary research questions, each addressing specific aspects of Ibogaine treatment and its application. First, the backgrounds and experiences of the providers are examined, highlighting the transition from personal recovery to professional practice. Second, the study delves into the varied approaches to treatment procedures and dosing strategies, reflecting the individualised nature of Ibogaine therapy. Finally, the discussion expands to include the range of supplementary therapies and their synergistic potential with Ibogaine, emphasising the importance of holistic care and mental health support in sustaining recovery.

4.5.1 Discussion in relation to research questions

Research question 1 – What is the role of Ibogaine and treatment providers in substance misuse recovery?

The Role of Ibogaine in Transformative Healing: A Dual Perspective from Wounded Healers

The concept of the "wounded healer," first coined by Carl Jung (Smith, 1997), is exemplified in the narratives of participants who transitioned from being patients to practitioners in the Ibogaine treatment community. Participants felt that their dual role as both healers and survivors adds a rich layer of empathy and understanding to their work, embodying the profound impact of personal healing on professional motivations. In their accounts, participants often utilised their history of being a substance misuser as well as their experience of recovery and sobriety, a lot of their treatment support came from this personal history and experience. The phenomenon of individuals who have benefited from Ibogaine moving into roles of advocacy and support is documented in the research by Alper et al. (2008), highlighting a unique aspect of the Ibogaine treatment community. Emphasising the "wounded Healers" phenomenon where many providers have personal recovery experiences.

The efficacy of Ibogaine, particularly in cases deemed as "last resort," is rooted in both personal experiences and professional observations. This belief is supported by broader literature, including studies by Malcolm, Polanca, & Basruglia (2018) and Noller, Frampton and Klosinski (2018), which position Ibogaine as a unique therapeutic agent capable of offering swift alleviation from opiate withdrawal symptoms and cravings. Despite the varied individual explanations about how Ibogaine works, there is a common understanding that it facilitates a psychological detachment allowing

treatment seekers to introspect and better understand their addiction issues, which is how the GITA guidelines summarise Ibogaine's psychological effects (Dickinson et al., 2015). This process not only assists in reducing physical withdrawal symptoms but also provides an anti-depressive effect for the users. However, it was unanimously emphasised among the participants of this study that Ibogaine should not be considered a miracle cure, but rather, it should form part of a more comprehensive, long-term support and treatment plan. This aligns with the consensus among treatment providers about its role and the importance of managing expectations and ensuring comprehensive care beyond the Ibogaine treatment itself.

Research question 2 - How is Ibogaine used to treat substance misuse?

Biopsychosocial Model and Ibogaine Recovery from Participant Accounts

Participant narratives, interwoven with existing literature, suggest that Ibogaine operates through a complex interplay of neurobiological, psychological, and social processes. At a neurobiological level, the intense sensory experiences described by participants during the "flood dose" phase align with Ibogaine's known interactions with various neurotransmitter systems. Its antagonism at μ -opioid receptors likely contributes to the alleviation of withdrawal symptoms and cravings for opioids (Baumann et al., 2001). Furthermore, Ibogaine's modulation of serotonin and dopamine transmission may contribute to its reported effects, including mood improvements, reductions in anxiety, and potential influence on reward pathways disrupted by addiction. Additionally, its long-lasting therapeutic action is linked to the upregulation of GDNF and a positive feedback loop in GDNF expression and signalling. However, the concept of "resetting" reward pathways oversimplifies Ibogaine's complex neurochemical and molecular effects (He & Ron, 2006). While promising, these findings are based on preclinical research and limited human studies, warranting further investigation. The interaction with NMDA receptors may also play a crucial role in reversing opioid-induced neuroadaptations, potentially facilitating a break from addictive behaviours and fostering the sense of clarity described by participants.

The contrasting views on dosing strategies, particularly the vivid experiences shared by Participants 1 and 8, reflect the ongoing debate within the treatment community regarding the balance between efficacy and safety. The intense and immediate effects described by Participant 1 are indicative of the 'flood dose' method's potential for rapid symptom alleviation. However, as Participant 8's shift in stance and Participant 3's adverse experiences illustrate, the cardiac risks associated with this approach can be severe. This aligns with findings by Alper & Lotsof (2007), who note that while effective, flood dosing

must be managed carefully to mitigate health risks, particularly in settings without comprehensive medical monitoring. Extended dosing, as discussed by Participant 6, presents a more gradual approach to Ibogaine administration, which may reduce the likelihood of severe adverse events. This method allows for continuous monitoring and adjustment of dosing, potentially leading to safer and more sustainable outcomes. However, the trade-off in terms of the intensity of the experience and the longer duration of treatment raises questions about cost-effectiveness and patient adherence over longer treatment periods, which would require further investigation.

Beyond its neurochemical actions, Ibogaine appears to catalyse profound psychological processes. Participants described experiences of introspection and self-reflection, enabling their patients to confront deep-seated psychological issues underpinning their addictive behaviours. Participant 2's narrative, for instance, highlights the confrontation of childhood trauma and the subsequent development of self-esteem within a supportive therapeutic environment. These findings underscore the importance of integrating psychological support and therapeutic processing to fully harness the potential of Ibogaine treatment. By fostering a safe space for introspection, Ibogaine may empower individuals to address emotional wounds and develop healthier coping mechanisms. The detailed account by Participant 2 and Participant 4 of the pre-treatment rituals, such as breathwork, meditation, and ceremonial activities, provides insight into the psychological preparation essential for facilitating deep therapeutic work. Research supports that such mindfulness practices can improve outcomes in substance misuse treatments by enhancing self-regulation and emotional management (Chiesa & Serretti, 2014; Garland & Howard, 2018).

Crucially, the present study also illuminates the vital role of social and environmental factors in supporting long-term recovery. While Ibogaine can disrupt addictive patterns and provide a window of opportunity, participants emphasised the need for ongoing support and the development of life skills to maintain sobriety. This resonates with the CHIME model of recovery (Leamy et al., 2011), which emphasises connectedness, hope, identity, meaningfulness, and empowerment as key processes in the recovery journey. From a social perspective, the letter burning before Ibogaine administration and group sessions following Ibogaine administration highlight the communal aspect of these rituals, which is known to contribute to building a supportive network among patients, which is critical in recovery settings (Pennebaker & Smyth, 2016; Alcoholics Anonymous, 2001). Ibogaine treatment, therefore, should be considered a catalyst within a broader framework of recovery, necessitating ongoing engagement with supportive communities and therapeutic interventions. The post-treatment phase in

flood dosing, particularly the 'grey day' phenomenon described by Participant 7, was also reflected in the literature, where the exhaustion and fatigue following Ibogaine administration has also been noted by Lotsof and Wachtel (2002) as well as Kohek et al. (2020). Given Ibogaine is often in a legal grey area and without a regulatory body, such fatigue raises questions about safety when administered in one-to-one, "underground" settings.

Similarly, the 'Ibogaine afterglow' discussed by Participant 9 and Participant 4, underscores the complexity of recovery from substance misuse. Brecksema et al. (2020) systematically reviewed qualitative studies on patient experiences with psychedelics, including Ibogaine. While the review does not explicitly mention overconfidence as a theme, it highlights the importance of post-treatment support systems. Participants frequently mentioned the value of preparatory and integration sessions in helping them process their experiences, manage emotional fluctuations, and sustain therapeutic benefits. These accounts suggest that such support systems play a role in helping individuals maintain the changes achieved during treatment.

The incorporation of holistic and integrative approaches, such as talking therapies, meditation, and yoga, within Ibogaine therapy reflects a broader evolution in substance misuse recovery. This shift goes beyond the sole focus on Ibogaine administration for craving and withdrawal suppression, acknowledging the psychological and social dimensions of addiction. This holistic trend may be attributed to practitioners' personal recovery experiences and a recognition of the multifaceted nature of addiction. However, the observation that such holistic practices are predominantly offered within clinic settings, as opposed to cheaper, underground detoxification-focused treatments, raises the question of commodification.

The structured aftercare programmes, such as the "8-week online programme" described by Participants 3 and 4, which incorporate group sessions and one-on-one coaching, drawing inspiration from elements of 12-step programmes. These structured programmes offer a more standardised approach to aftercare, potentially addressing concerns about the consistency and replicability of individualised interventions. Regardless of the specific approach, the existence of such programmes underscores the importance of ongoing support, echoing Howard Lotsof's emphasis on a supportive and empowering treatment environment (Lotsof, 1994). Further research is needed to evaluate the effectiveness of these programmes and determine their suitability for diverse populations undergoing Ibogaine treatment.

Beaussant et al. (2021) advocate for standardisation across several domains to ensure the safe and effective integration of psychedelic-assisted therapies within healthcare. Firstly, they emphasise the need for clear standards defining the optimal therapeutic environment, encompassing both physical space and interdisciplinary care models. This involves specifying criteria for treatment rooms and integrating psychedelic research into collaborative care approaches involving mental health, palliative care, and other relevant specialists. Secondly, the authors call for standardised research methodologies, including the use of complementary approaches like phenomenology and neuroimaging, to better understand the mechanisms of action of these therapies. Thirdly, they highlight the necessity of standardised education and certification programs for therapists, encompassing curricula, facilitator training, and diversity training. This comprehensive approach to standardisation aims to optimise therapeutic outcomes, enhance research quality, promote equitable access, and ensure the responsible and ethical implementation of psychedelic-assisted therapies.

Regulatory Challenges and the Need for Standardisation

Participant 3's description of the "dark void" of inconsistent treatment practices points to a critical gap in the regulatory framework surrounding Ibogaine treatment. The absence of standardised protocols not only complicate the treatment landscape but also hinders broader acceptance and integration of Ibogaine as a legitimate therapeutic option. Addressing these regulatory challenges by developing clear guidelines and ensuring practitioner compliance could enhance treatment safety and efficacy, contributing to better health outcomes and potentially wider acceptance of Ibogaine in the medical community.

For example, the rigorous pre-admission processes highlighted by Participant 2 and others play a crucial role in safeguarding patient safety and tailoring treatment approaches to individual needs. The comprehensive evaluations of medical and psychiatric histories are vital in anticipating potential complications during Ibogaine treatment. This underscores the necessity of such protocols, which align with broader healthcare practices that prioritise patient safety before the administration of any intensive treatment (Smith et al., 2018).

While the therapeutic potential of Ibogaine in treating substance misuse is evident, the treatment process involves complexities that require careful management. The insights provided by the participants underscored the importance of balanced dosing strategies, rigorous pre-admission screening, and comprehensive post-treatment support to optimise treatment outcomes and patient safety. As the field evolves, ongoing research and dialogue within the medical and regulatory

communities will be vital in refining these approaches and ensuring that Ibogaine treatment can be a safe and effective option for those battling severe addiction.

Research question 3 - What therapies are used to support Ibogaine treatment?

Enhancing Efficacy through Supplementary Therapies and Mental Health Support

As the landscape of Ibogaine treatment continues to evolve, the integration of counselling and mental health support, alongside the judicious application of adjunctive therapies, is likely to become increasingly critical. Ongoing research and clinical observations, such as those by Koslowski et al. (2021) and Rodríguez-Cano et al. (2023), are essential to refine these practices and maximise efficacy and safety.

Koslowski et al. (2021) underscore the vital role of psychotherapy in conjunction with psychedelic treatments like Ibogaine. Their research suggests that integrating psychotherapy can potentiate therapeutic benefits and address the underlying psychological factors contributing to substance use disorders. This implies that Ibogaine treatment should not be viewed as a panacea, but rather as a component of a comprehensive approach encompassing robust psychological support. Furthermore, the establishment of standardised protocols and rigorous training for therapists, as suggested by Beaussant et al. (2021), will be vital in advancing the field towards a more holistic and effective treatment model. However, now, the precise nature and duration of such psychotherapeutic interventions remains an open question, requiring further investigation to optimise efficacy.

Similarly, use of other substances requires further investigation, an unexpected finding of this study was the use of 5-MeO-DMT alongside Ibogaine presents a nuanced approach to enhancing therapeutic outcomes. While some practitioners utilize 5-MeO-DMT to reduce pre-treatment anxiety or to solidify therapeutic gains post-treatment, the need for caution is paramount. Given the literature on the fatiguing effects of an Ibogaine flood dose (Kohek et al., 2016; Lotsof & Wachtel, 2002), Participant 6 is rightfully sceptical about the potential risk of combining these potent psychedelics, which could negate the benefits of the treatment. This stance is supported by research, which suggests that while adjunctive use of substances like 5-MeO-DMT can enhance treatment for conditions such as alcohol addiction, it should be carefully managed to avoid adverse effects.

For instance, Barsuglia et al. (2018) found that the sequential administration of Ibogaine and 5-MeO-DMT showed potential in reducing alcohol cravings and promoting abstinence. Their case study also noted improvements in mood, and reductions in depression and anxiety symptoms. Similarly, Davis et

al. (2023) reported significant reductions in PTSD symptoms, depression, and anxiety in trauma-exposed male Special Operations Forces veterans following Ibogaine and 5-MeO-DMT-assisted therapy. Both studies highlight the potential therapeutic benefits but also underscore the need for careful consideration and further research to fully understand the effects and optimise treatment protocols.

The administration of supplementary substances such as diazepam and cannabis oil to manage side effects and aid sleep regulation during the treatment process is a practice rooted in the need for comfort and stability during recovery. However, as Participant 5 mentioned, these interventions should be used judiciously, ensuring they do not overshadow the primary treatment effects of Ibogaine. Whilst some participants reported having medical staff present on-site, access to pharmaceuticals and applications highlight the grey area in Ibogaine treatments, it is not known how practitioners would source pharmaceutical substances in the absence of psychiatrists on-site or supporting the treatment outside of the clinic via signposting.

4.5.2 Limitations, implications and recommendations

Stakeholders in this Research

The intended stakeholders for this research are practitioners and academics interested in the world of Ibogaine treatments. This research provides valuable insights into the experiences and perspectives of Ibogaine treatment providers, shedding light on the different approaches and challenges of this treatment to substance misuse. It highlights the need for a standardisation to ensure safest and most replicable practice, whilst considering the foundations built by treatment providers.

Role of NGOs, Regulatory Bodies, and Standardised Care

The findings of this study showed the variety of approaches to Ibogaine treatment with a consensus around Ibogaine not being a silver bullet to addiction issues. This highlights the important role of NGOs and regulatory bodies in promoting standardised care in Ibogaine treatment, as observed in this thesis, is a crucial aspect of the evolving Ibogaine treatment landscape. Brown & Alper (2023) highlighted the need for standardised care guidelines to ensure patient safety and treatment effectiveness. The involvement of NGOs within regulatory bodies may contribute to developing and implementing these guidelines. Whilst, the Global Ibogaine Treatment Alliance (Dickinson et al., 2015) periodically has spearheaded the NGO efforts by publishing guidelines and trying to map out treatment providers.

However, the GITA's current inactivity exposes a critical gap. This aligns with this thesis' findings, which reveal that Ibogaine providers often operate in a regulatory vacuum, hindering the establishment of consistent treatment standards and potentially compromising patient safety and treatment efficacy.

A key implication of this research is the urgent need for a regulatory body to oversee Ibogaine treatment, building on the work of organisations like the GITA. This would formalise standards and provide a framework for safe and effective treatment.

By facilitating the establishment of such a body, this thesis could contribute to a safer and more effective Ibogaine treatment landscape. This benefits both; providers, by offering clear guidance and legitimacy, and treatment seekers, by mitigating risks and increasing the likelihood of successful outcomes. Furthermore, a regulatory framework could encourage greater collaboration and knowledge sharing amongst providers, fostering a more robust and unified approach to Ibogaine treatment.

Strengths of This Study

The global recruitment of Ibogaine practitioners captures diverse experiences and perspectives, enhancing the transferability of findings. Lengthy in-depth interviews allow for a rich and detailed data collection, capturing broad overviews and nuanced insights. Braun and Clarke's six-phase reflexive thematic analysis provides a flexible and reflective framework for data analysis, accommodating both inductive and deductive reasoning and mostly semantic and latent coding. The snowball sampling strategy extends the reach of participant recruitment, while the thoughtful navigation of potential legal and accessibility challenges demonstrates an ethical research approach. Lastly, the focus on qualitative data captures the complexities of Ibogaine treatment that might not be reflected in quantitative measures, providing a richer understanding of the experiences and perspectives of Ibogaine treatment providers.

Importance and Implications

By understanding the intricate web of elements of Ibogaine treatments, from the personal experiences of providers to the broader treatment context, stakeholders can play a pivotal role in shaping the future of Ibogaine treatment for substance misuse. By exploring the practitioner accounts behind Ibogaine treatment can guide more effective and safer integration of Ibogaine into substance misuse treatment protocols. It underscores the need for individualised care, considering both the physiological and psychological impacts of the treatment.

Additionally, this research contributes to the growing body of knowledge on psychedelic treatments, bridging personal narratives with the actual reality as the research has observed different empirical point of views coming from participants and analysed commonalities and differences in their accounts. As a result, this research offers a novel perspective, through the lens of critical realism, on how to interpret and understand the treatment process and modalities. The findings highlight the potential of Ibogaine, not just as a substance but as part of a broader therapeutic framework.

Limitations

Whilst the research offers valuable insights, it has limitations. Although designed to capture a broad range of perspectives, the recruitment strategy may not have reached all Ibogaine treatment providers, particularly in countries where the legality of Ibogaine is unclear or strictly controlled. This could limit the transferability of the findings. Additionally, the research relied on self-reported data from 13 practitioners, which, given the sensitive nature of the topic of study, could be limited for transferability. Despite these limitations, the research provides important insights into the current landscape of Ibogaine treatment for substance misuse and sets the stage for further research in this area.

Future Directions

Future research should concentrate on elucidating the benefits and issues with flood and long dosing. As mentioned, there are research on synergistic effects of Ibogaine and 5-meo-Dmt, such research will help practitioners better understand the risks and benefits associated with the combination. Talking therapies or counselling aspect of Ibogaine therapy requires the most research, from the participant accounts most available support is unstructured and not standardised. Often practitioners will support treatment seekers based on their experience of recovery with Ibogaine. Longitudinal studies are crucial to grasp the long-term effects and efficacy, tracking patients throughout their treatment journey.

Standardising Ibogaine treatment protocols, encompassing patient screening, dosing strategies, and post-treatment support, can pave the way for safer and more effective practices.

Additionally, exploring the personal experiences of patients, alongside the perspectives of treatment providers, can offer a holistic view of the treatment process. Given the legal complexities associated with Ibogaine in various countries, investigating the influence of legal and regulatory contexts on treatment practices is essential. This could guide policy discussions and advocacy in the Ibogaine treatment domain. Clinical trials are already probing Ibogaine's immediate effects, but a deeper examination of its long-term physiological and psychological impacts is warranted. Research should also consider the potential benefits of combining Ibogaine with other substances or therapeutic techniques.

By integrating personal narratives with objective outcome measures, we can achieve a comprehensive understanding of Ibogaine's role in substance misuse recovery.

Reflexivity

The PhD candidate worked in the substance misuse field in the UK and has witnessed service users healing with Ibogaine, equally he has seen service users being on long-term opioid substitute therapies (20 years+) due to this he is intrigued by the “instant withdrawal alleviation” effects of Ibogaine treatment. Because of this predisposition, the PhD candidate may have had a positive bias towards Ibogaine treatments. Nonetheless, he is aware of the occasional clandestine treatments and worried about the safety and replicability of findings, so he maintained a critical stance on that. The PhD candidate has also witnessed service users healing with Ibogaine. Equally, the candidate has seen service users remain on long-term opioid substitute therapies (20+ years).

Intrigued by the "instant withdrawal alleviation" effects of Ibogaine treatment, the candidate may have had a positive bias towards this approach. Nonetheless, aware of the occasional clandestine treatments and concerned about the safety and replicability of findings, a critical stance was maintained throughout the research.

During the study, several insights regarding Ibogaine treatment emerged. The candidate observed that Ibogaine, when administered in moderate doses by informed professionals, may not be as perilous as commonly perceived. The diversity in treatment approaches, from setting to dosing, was surprising. Concurrently, ongoing trials in Manchester were exploring Ibogaine's potential for substance misuse treatment, aligning with broader interest in the life sciences. The candidate aspires that the amassed data and generated knowledge will benefit both treatment providers and those seeking treatment. An unexpected revelation was the administration of 5-MeO-DMT in addition to Ibogaine. Initially sceptical due to the anticipated intensity of such a combination, the candidate's perspective shifted after engaging with treatment providers' accounts and after coming across studies investigating such combination.

4.6 Conclusion

Although the small sample size limits the generalisability of the findings, several important findings emerged: First of all, almost all participants in the sample used Ibogaine to treat their or a friend or family member's addiction with Ibogaine and that experience has led them become treatment providers. These providers said treatment seekers often seek Ibogaine treatment as a "last resort",

particularly valued for its effectiveness in alleviating withdrawal symptoms and cravings. However, despite the perceived effectiveness, participants often highlighted that it is not a “silver bullet” and treatment seekers have to be committed to the recovery process. The research underscores the different treatment approaches and different forms of Ibogaine and as a result the importance of standardising treatment and care with Ibogaine. The potential advantages of combining Ibogaine with other substances such as 5-MeO-DMT was mentioned both in treatment provider interviews as well as the recent literature. Additionally, the involvement of NGOs in regulatory boards is deemed crucial for the standardisation of Ibogaine care. While acknowledging potential biases and limitations due to self-reported data, the study highlights Ibogaine's promising role within a broader therapeutic context and underscores the need for further research, particularly given the complex legal landscape surrounding its use.

5. Discussion

This thesis has explored the therapeutic potential of psychedelic and psychoplastogen-assisted therapies, with a specific focus on Ibogaine, in the treatment of substance misuse. Through a scoping review of past and present clinical trials and a primary study exploring the experiences of Ibogaine treatment providers, this research has illuminated the diverse landscape of these emerging treatments, highlighting their potential benefits, challenges, and the potential for standardisation.

One of the key findings of this research is the variability in treatment strategies and protocols, particularly in the use of Ibogaine. While some providers advocate for a "flood dose" approach, aiming for a rapid and intense psychedelic experience, others favour "extended dosing," which involves smaller, repeated doses over a longer period. This lack of consensus underscores the need for standardised guidelines to ensure both the safety and efficacy of Ibogaine treatment.

Furthermore, the research has highlighted the crucial role of adjunct therapies, such as talking therapies and other substances like 5-MeO-DMT, in supporting the Ibogaine experience. However, the integration of these therapies remains largely unstructured and unstandardised, raising questions about their consistent application and effectiveness in promoting long-term recovery.

5.1 Different Treatment Strategies: Ibogaine and Broader Psychedelic Therapies

The primary study highlights Ibogaine as a treatment overwhelmingly described by participants as a "last resort," reflecting gaps in conventional addiction therapies and the urgency often accompanying its use. Ibogaine is commonly administered via flood dosing, a single high-intensity session lasting over 24 hours, aimed at rapidly alleviating withdrawal symptoms through its action on opioid and NMDA receptors and the sustained effects of Ibogaine (Mash et al., 2018). While effective for acute detoxification, this approach is known to carry cardiotoxicity risks, particularly in unregulated settings (Alper et al., 1999). Participants also reported extended dosing—smaller, repeated administrations over several days—as a safer alternative, though it lacks robust research and standardisation.

The scoping review provided a broader lens, examining psychedelics like psilocybin and LSD, typically administered in one or two high-dose sessions within tightly regulated clinical trials. These therapies emphasise long-term psychological transformation through structured protocols and multi-week frameworks (Bogenschutz et al., 2022; Gasser et al., 2014). Psilocybin treatments, for instance, often include extensive preparatory and integration phases to sustain therapeutic insights.

Both studies reveal a shared need for greater standardisation. While Ibogaine’s unregulated use poses safety and variability concerns, the scoping review also notes inconsistencies in methodologies across trials, hindering the consolidation of evidence. Despite their differences, both Ibogaine treatments and broader psychedelic therapies would benefit from standardised frameworks to improve replicability and patient outcomes.

5.2 Pre-Treatment and Post-Treatment Preparation and Integration

The primary study reveals that Ibogaine providers use practices such as a variety of approaches to “prepare” treatment seekers for the Ibogaine experience and offer “integration” to make sense of the experience. Schenberg et al., (2024) also emphasises the importance of patient preparation, including mandatory pre-treatment abstinence and psychological evaluations, and post-treatment follow-up therapy in conjunction to Ibogaine to sustain long-term recovery. However, these methods are inconsistently applied, reflecting the unregulated nature of many Ibogaine treatments. This variability risks leaving patients unprepared for the intensity of their experience, a concern echoed in broader discussions on preparation for psychedelics (Phelps, 2017).

The scoping review underscores the importance of preparation and integration in clinical trials, where protocols ensure consistency through psychological screening, preparatory therapy, and follow-up interventions (Bogenschutz et al., 2022; Johnson et al., 2017). However, even these trials rarely adapt integration practices to individual or cultural needs, despite the personal subjectivity of psychedelic experiences. Bridging these approaches—combining the “personalisation” in Ibogaine treatments with the structured frameworks of clinical trials—could optimise outcomes by addressing both flexibility and standardisation.

5.3 Set and Setting

Set and setting—the psychological and environmental contexts of psychedelic therapies—play a central role in shaping treatment outcomes, as evidenced by both the primary study and the scoping review.

The primary study highlights how Ibogaine providers emphasise environments that foster deep introspection and emotional breakthroughs. Practices such as pre-treatment rituals, ceremonial elements, and the thoughtful arrangement of physical spaces are intended to support patients’ psychological readiness. However, the lack of regulation results in variability, which can affect the consistency of outcomes.

The scoping review describes a more standardised approach to set and setting in psychedelic trials, where controlled environments are carefully curated to ensure patient comfort and minimise anxiety. Facilitators play a key role in these settings, guiding participants through their experiences and helping them process challenging moments. Phelps (2017) underscores the importance of such facilitation, advocating for comprehensive training that equips guides to create psychologically safe and supportive contexts, tailored to patients' needs.

Both studies converge on the critical influence of set and setting in determining the depth and integration of psychedelic experiences. While the primary study reveals how unregulated Ibogaine practices can lead to inconsistencies, the scoping review demonstrates how clinical environments, though standardised, may lack flexibility. As Hartogsohn (2021) suggests, the interplay between set, setting, and individual factors requires careful calibration to optimise therapeutic outcomes. This intersection of set and setting with individual variability aligns with the biopsychosocial model adopted as the theoretical framework for this research. The model acknowledges the interconnectedness of biological, psychological, and social factors in shaping human experiences and behaviours, including the response to psychedelic therapies. The "set," encompassing an individual's mindset, expectations, and psychological state, represents the psychological domain. The "setting," encompassing the physical and social environment, represents the social domain. Individual factors, such as personality, genetics, and cultural background, represent the biological domain. The biopsychosocial model's recognition of the complex interplay between these domains underscores the need for personalised and holistic approaches to psychedelic therapies, where set, setting, and individual factors are carefully considered to optimise therapeutic outcomes.

5.4 Psychedelic and Psychoplastogen Treatments and Talking Therapies

Both the primary study and scoping review highlight the integration of talking therapies within psychedelic and psychoplastogen-assisted treatments, yet their systematic role and implementation remain in formative stages. The primary study reveals that Ibogaine providers often employ counselling practices that are experience-based and informal, rather than adhering to structured therapeutic models. This approach stands in contrast to the more formalised and consistently applied therapeutic frameworks commonly seen in trials of other psychedelic substances such as psilocybin and LSD (Carhart-Harris et al., 2016), and in established evidence-based treatments for substance misuse disorders (SUDs) more broadly (McLellan et al., 2000). This variability in Ibogaine treatment settings,

often outside of regulated healthcare systems, raises valid concerns regarding the consistency and demonstrable efficacy of these informal adjunctive approaches in fostering sustained recovery.

The scoping review further illustrates that in research settings investigating psychedelics like psilocybin, LSD, and ketamine, talking therapies are intentionally incorporated as supplementary, yet crucial, components. For instance, Bogenschutz et al.'s (2015, 2022) studies, examining psilocybin-assisted therapy for alcohol use disorder, integrated motivational interviewing (MI) and psychotherapy. These therapies were designed to actively facilitate the processing of psychedelic experiences and to support the translation of experiential insights into tangible behavioural modifications. These trials demonstrated significant efficacy, with the 2015 study showing a substantial decrease in heavy drinking days at 36 weeks post-treatment in the psilocybin group compared to controls (Bogenschutz et al., 2015), and the 2022 follow-up reinforcing sustained reductions in drinking and improvements in psychosocial functioning over a two-year period (Bogenschutz et al., 2022). Similarly, Dakwar et al. (2020) paired ketamine infusions with manualised cognitive-behavioural therapy (CBT) for cocaine use disorder. This combination aimed to leverage ketamine's rapid-acting antidepressant and psychoplastogenic effects to enhance engagement and effectiveness of CBT. While the Dakwar et al. (2020) study, being a pilot, primarily focused on feasibility and preliminary efficacy, it indicated promising engagement with treatment and reductions in cocaine use, suggesting the potential of this combined approach. These structured approaches across psychedelic research emphasise the growing recognition of talking therapies as not merely secondary to the psychedelic experience, but as integral to maximising therapeutic outcomes and ensuring enduring change.

However, as Phelps (2017) points out, there remains a critical gap in the explicit development and evaluation of therapist competencies essential for psychedelic-assisted therapies. While structured models are valuable, competencies such as therapist empathy, spiritual intelligence, and skill in utilising complementary techniques like mindfulness or somatic experiencing are likely paramount for effective integration of talking therapies within the often profound and emotionally intense context of psychedelic experiences (Johnson & Griffiths, 2017; Richards, 2015). This is not unique to psychedelic-assisted therapy but resonates strongly within the broader substance misuse treatment field, where the therapeutic alliance and therapist qualities are consistently identified as significant predictors of positive outcomes across various modalities (Moyers et al., 2016; Miller & Moyers, 2017).

Both the empirical study and literature review within this thesis underscore existing gaps in the consistent and standardised implementation of talking therapies within psychedelic and psychoplastogen-assisted treatments. Echoing wider trends in substance misuse and healthcare, the primary study's emphasis on personalisation and the scoping review's call for evidence-based, replicable approaches are not mutually exclusive but rather complementary necessities for the field. Looking at established substance misuse treatment modalities, the evolution has consistently moved towards more integrated and personalised approaches (McLellan et al., 2000). For instance, Medication-Assisted Treatment (MAT) for opioid use disorder, considered a gold standard, combines pharmacological interventions with psychosocial support tailored to individual patient needs (NIDA, 2020). This parallels the potential trajectory for psychedelic-assisted therapies, suggesting that the synergistic combination of psychoplastogens with carefully delivered and personalised talking therapies could optimise both acute and long-term therapeutic gains in SUD treatment (Koob & Volkow, 2016). As personalised healthcare gains increasing recognition across medicine (Hamburg & Collins, 2010), the field of psychedelic-assisted therapy must also strive to develop training frameworks and treatment guidelines that carefully balance the need for standardisation and evidence-based practice with the essential flexibility required to meet the diverse and individualistic needs of those seeking recovery from substance misuse through these novel therapeutic avenues. This nuanced approach will be crucial in ensuring that talking therapies effectively support the unique demands and maximise the enduring potential of psychedelic and psychoplastogen treatments for substance misuse disorders.

5.5 Importance and Challenges of Standardisation

Standardisation of treatment regimens and procedures, encompassing administration protocols, supportive therapies, aftercare practices, and potentially even costs, is crucial for ensuring safety, consistency, and replicability in psychedelic and psychoplastogen-assisted therapies. The primary study underscores the variability inherent in unregulated Ibogaine treatments, where dosing strategies, therapeutic settings, and integration practices differ among providers. This lack of standardisation raises safety concerns—such as cardiotoxicity linked to high-dose Ibogaine sessions—and limits the generalisability of treatment outcomes. Participants overwhelmingly highlighted the need for clearer frameworks to legitimise and improve these treatments, particularly in underground settings.

The scoping review reveals that while individual trials involving psychedelics like psilocybin and ketamine follow structured protocols, no universal benchmarks exist across the field. Dosing regimens, therapeutic contexts, and integration practices vary widely between studies, reflecting the nascent and

experimental nature of the field. This fragmentation inhibits cross-study comparability and the development of generalisable guidelines. Phelps (2017) suggests that the absence of unified standards also complicates the training of therapists, who require competencies that span diverse therapeutic approaches and substances.

Both the literature review and the empirical study presented in this thesis emphasise the need for a balance between flexibility and replicability in developing standardised protocols. Efforts like the Global Ibogaine Treatment Alliance (GITA) attempted to address this gap by publishing guidelines and mapping treatment providers, but have stalled due to inactivity, leaving a regulatory void. Future frameworks should aim to harmonise essential components of psychedelic therapies while allowing for personalisation and cultural sensitivity. Standardisation across dosing, preparation, and integration practices is not only critical for patient safety but also for advancing the credibility and scalability of these treatments.

Integrating standardisation into psychedelic therapies presents profound challenges due to the deeply personal, mystical, and often ineffable nature of these experiences. Psychedelic healing frequently involves subjective, non-linear processes that resist the rigid frameworks of modernist and positivist methodologies (Aday, Carhart-Harris, & Woolley, 2023). While standardised protocols are essential for ensuring safety and replicability, they risk oversimplifying the transformative and culturally nuanced elements central to these treatments. Additionally, the illegality of many psychedelics and the restrictive regulatory environment have historically impeded research efforts, making it difficult to establish universal benchmarks or fully explore the cultural and individual dimensions critical to effective psychedelic therapies.

5.6 Holistic Therapies and Complementary Practices

Holistic therapies and complementary practices, such as mindfulness, yoga, journaling, and ceremonial rituals, are frequently observed in psychedelic and psychoplastogen-assisted treatments but lack a robust evidence base to guide their application. The primary study demonstrates the informal yet integral use of these practices in Ibogaine treatment settings, where pre-treatment rituals and activities like breathwork are often tailored to individual patient needs. However, the absence of systematic frameworks and a standardised knowledge base leaves uncertainty about which practices work best, in what combinations, and at which stages of the therapeutic process.

The scoping review highlights the use of structured practices in clinical trials, such as journaling and meditation in ketamine treatments for alcohol misuse (Kolp et al., 2006). Similarly, Johnson et al. (2017) used elements of mindfulness and guided imagery in a trial on psilocybin-facilitated smoking cessation. While these practices enhance psychological integration and emotional processing, they are inconsistently applied and under-researched. Phelps (2017) underscores the need for psychedelic therapist training to incorporate competencies in complementary techniques, such as mindfulness and spiritual intelligence, but this area remains underdeveloped.

Further research is needed to establish the optimal integration of holistic therapies, including their duration, timing, and compatibility with different psychedelics and psychoplastogens. Without this knowledge base, their use risks being anecdotal and fragmented, reducing their potential to enhance outcomes consistently. Hartogssohn (2021) argues that such practices could be vital for fostering the introspection and integration necessary for transformative change, but only if implemented thoughtfully within a structured therapeutic framework. The challenge lies in balancing flexibility to accommodate individual needs with the rigour needed for replicability and broader acceptance in clinical and cultural contexts.

5.6.1 Further Development and Evidence

The exploration of synergistic effects offers a novel perspective on addiction treatment, suggesting that combining substances like Ibogaine with other therapeutic agents may hold the key to unlocking greater efficacy. This is exemplified by Barsuglia et al. (2018), who delved into the potential of non-hallucinogenic psychedelic analogues, finding that the sequential administration of Ibogaine and 5-MeO-DMT in treating alcohol addiction could potentially reduce cravings, promote abstinence, and improve mood while reducing depression and anxiety symptoms. This research aligns with the growing interest in modifying psychedelic compounds to enhance safety and therapeutic potential, as demonstrated by Cameron et al. (2021) in their development of Tabernanthalog, a non-hallucinogenic Ibogaine analogue. Cameron et al. (2021) highlighted the challenges associated with Ibogaine's toxicity and hallucinogenic effects, prompting their investigation into safer alternatives. Their work underscores the importance of "function-oriented synthesis" in identifying key structural elements of therapeutic pharmacophores, ultimately leading to the creation of Tabernanthalog, which has shown promise in preclinical studies for reducing addiction-related behaviours and promoting neural plasticity. This study highlights the potential of combining psychedelics and psychoplastogens to achieve outcomes that individual substances alone may not, providing evidence for the theory that the future of addiction treatment

might not just be about individual substances but about how they can be integrated into comprehensive therapeutic frameworks. Furthermore, the emphasis on set and setting in psychedelic trials underscores the importance of the mind-environment interplay in therapeutic outcomes. This suggests that external factors considerably influence the therapeutic potential of these substances, adding another layer to our understanding of how to optimise treatment interventions.

5.7 Implications and Limitations

Based on the findings from the literature review and the primary study, the following recommendations have been outlined for various stakeholders interested in psychedelic and other psychoplastogens containing treatments for substance misuse.

5.7.1 For Academics

Academics should consider expanding their research frameworks to incorporate more integrated approaches that combine empirical methodologies with ethnographic insights. This would allow for a more comprehensive understanding of the therapeutic implications of psychedelic substances. Additionally, embracing holistic methodologies that consider psychological, sociocultural, and environmental factors is crucial for advancing the field of substance misuse treatment.

5.7.2 For Policy Makers

Policymakers need to revisit and potentially revise regulatory frameworks to accommodate the growing body of evidence supporting the use of psychedelics in therapeutic settings. This includes facilitating safer research environments through more adaptive regulations that balance public safety with the need for scientific exploration. Furthermore, clear ethical guidelines must be established to ensure that research in this domain prioritises participant well-being and maintains the integrity of the academic pursuit.

5.7.3 For Treatment Providers

Treatment providers should adapt to dynamic therapeutic protocols that are flexible and evidence based. The findings on varied dosing strategies for Ibogaine underscore the need for adaptable clinical protocols that can be tailored to individual patient needs. Providers are also encouraged to broaden their therapeutic approaches, incorporating diverse modalities from group interventions to individual counselling, to enhance patient outcomes.

5.7.4 For Those Seeking Treatment

Individuals seeking treatment can benefit from the insights provided into the therapeutic process of Ibogaine. This knowledge can guide them in making informed decisions about their treatment options. Additionally, exploring integrative treatments that combine Ibogaine with other therapeutic agents may offer enhanced outcomes, and patients are encouraged to discuss these options with their providers.

5.8 End of Thesis Reflexive Statement

The research journey has deepened the PhD candidate's understanding of psychedelic modalities, affirming their immense potential in substance misuse treatment. Ibogaine, in particular, shows promise not only as a detoxification tool but also as a catalyst for introspection and behavioural change. However, this exploration has highlighted the urgent need for standardisation. While standardised protocols could improve safety, replicability, and acceptance, they must account for the ineffable and personal nature of psychedelic experiences, which resist positivist frameworks and demand a balance between structure and individualisation.

The absence of uniformed training frameworks further complicates this process, leaving practitioners with varying levels of expertise and patients vulnerable to inconsistent care. For instance, taking Ibogaine in a Bwiti shamanistic ceremony differs significantly from a clinical trial setting or poorly regulated treatment by an untrained practitioner. This realisation has prompted the PhD candidate's growing interest in the Bwiti tradition, recognising that any attempt to standardise Ibogaine must consider its origins and traditional use. Initially excluded from the study, this perspective now appears essential to shaping more holistic approaches. This logic extends to the shamanistic and ritualistic use of other psychedelics, such as ayahuasca and psilocybin, as understanding their traditional applications could inform modern therapeutic practices.

This research has also shifted the candidate's view of pre-modern practices. The historical use of substances like Ibogaine by the Bwiti and ayahuasca by Amazonian tribes offers valuable lessons in healing frameworks that emphasise community, ritual, and meaning making. Integrating these insights into modern practices could enrich treatments, ensuring cultural respect while leveraging contemporary scientific knowledge. As psychedelic research progresses, drawing parallels between traditional and modern approaches may help bridge these worlds, fostering more effective and holistic therapies.

Ultimately, the potential of psychedelic and psychoplastogen therapies will only be fully realised through integrating historical practices, rigorous research, and thoughtful standardisation that respects

the transformative nature of these substances. This synthesis of tradition and science represents a key frontier for the candidate's future work.

6. Conclusion

6.1 Principal insights

This thesis reports mainly five new or novel concepts to the literature:

1) The Role of Personal Ibogaine Experience in Treatment Provision

This study highlights the prevalence of Ibogaine treatment providers who have personal experience with Ibogaine and the recovery process. This first-hand knowledge allows for a deeper understanding of the treatment process, enabling them to better support individuals seeking treatment. They can more effectively aid in preparation, guide individuals through the experience, and facilitate the interpretation of their Ibogaine experiences for personal growth and understanding.

2) Diverse Approaches to Ibogaine Administration

This research explores the diverse approaches to Ibogaine administration and their impact on treatment. Ibogaine treatment exists on a spectrum, ranging from 'flood dosing' (a single high dose) to 'extended dosing' (multiple lower doses over an extended period). Beyond dosing, factors such as the form of Ibogaine (hydrochloride, total alkaloid, purified total alkaloid) and even the extraction source influence the experience. While individual preferences vary, practitioners have observed that Ibogaine hydrochloride may be more effective in managing withdrawal, while TA and PTA extracts may promote more vivid visionary experiences in flood doses.

3) Emerging Practice: Combined Use of 5-MeO-DMT and Ibogaine

This study reveals the emerging practice of combining 5-MeO-DMT with Ibogaine. Four participants reported using 5-MeO-DMT either before or after their Ibogaine experience, and many demonstrated awareness of this practice. While perspectives on this combined use varied, this finding contributes valuable nuance and insight to the growing body of literature exploring the potential synergies between these substances.

4) Managing Expectations and Emphasising Ongoing Commitment

Treatment providers observe that individuals often consider Ibogaine as a last resort when other treatments have failed, drawn to its perceived efficacy in managing withdrawal and cravings. However, they emphasise that Ibogaine is not a cure-all, and that long-term success requires ongoing commitment to the recovery process.

5) The Need for Standardised Protocols in Psychedelic-Assisted Therapies for Substance Use Disorder

This thesis also examines the broader landscape of psychedelic-assisted therapies for substance misuse, highlighting the variety of substances (LSD, ketamine, etc.), dosing regimens, and outcome measures used in research since the 1960s. The use of both biological and subjective metrics, along with varying methodological approaches, underscores the need for further research to establish standardised protocols and optimise treatment strategies for psychedelic-assisted therapies within the context of substance misuse.

6.2 Conclusion

This PhD critically analysed the therapeutic approaches with psychedelic and psychoplastogen-assisted therapies, with a focus on substance misuse. Through a scoping review and primary qualitative study, it examined diverse treatment frameworks, identifying both transformative potential and substantial gaps in practice. Psychedelic substances, including Ibogaine, psilocybin, and ketamine, show promise not only in alleviating withdrawal symptoms but also in fostering deep psychological insights and long-term behavioural change. However, the absence of universal standards across the field presents significant barriers to consistency, safety, and efficacy, particularly in the case of unregulated treatments.

A notable finding was the variability in therapeutic strategies, preparation, and integration practices, which remain fragmented and largely dependent on individual practitioner knowledge rather than an evidence-based framework. While clinical trials offer standardised environments, the field lacks overarching protocols to harmonise approaches across substances, settings, and cultural contexts. Furthermore, the study emphasised the need for a deeper understanding of the historical and shamanistic uses of these substances. Integrating insights from traditional practices, such as the Bwiti use of Ibogaine, could enhance modern frameworks, provided they are adapted rigorously to contemporary ethical and scientific standards.

This research concludes that while the potential of psychedelic therapies is profound, realising their clinical utility requires interdisciplinary collaboration, standardisation efforts, and the careful incorporation of cultural and individual dimensions. Such a synthesis is essential for advancing their safe and effective application within modern substance misuse treatments.

7. References

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8. Appendices

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Appendix A: Ethics Application and Approval Letter

Appendix A1

Faculty of Health and Medicine Research Ethics Committee (FHMREC), Lancaster University

Application for Ethical Approval for Research

Title of Project: Addiction and Ibogaine Treatment Centres: An Exploratory Study with Practitioners

Name of applicant/researcher: Ahmet Enginsoy

ACP ID number (if applicable)*:

N/A

Funding source (if applicable)

N/A

Grant code (if applicable): N/A

***If your project has *not* been costed on A.C.P., you will also need to complete the Governance Checklist [\[link\]](#).**

Type of study

- ☐ Involves existing documents/data only, or the evaluation of an existing project with no direct contact with human participants. **Complete sections one, *two* and four of this form**
- ☐ Includes *direct* involvement by human subjects. **Complete sections one, *three* and four of this form**

SECTION ONE

1. Appointment/position held by applicant and Division within F.H.M.

PhD Student

2. Contact information for applicant:

Email aenginsoy@gmail.com

Telephone: 07733707450 (please give a number on which you can be contacted at short notice)

Address: Flat 1, 35A Topsfield Parade, Crouch End, London N8 8QA, United Kingdom`

3. Names and appointments of all members of the research team (including degree where applicable)

Ahmet Enginsoy – PhD candidate (A.E)

Professor Fiona Lobban – Primary supervisor (F.A.L)

Doctor Heather Robinson – Secondary supervisor (H.R) (currently on maternity leave)

Doctor Abigail Morris – Temporary secondary supervisor (A.M)

3. If this is a student project, please indicate what type of project by marking the relevant box/deleting as appropriate: (please note that U.G. and taught masters projects should complete **FHMREC form UG-tPG**, following the procedures set out on the [FHMREC website](#))

P.G. Diploma ☐
☐

Masters by research

PhD Thesis
☐

PhD Pall. Care
☐

PhD Pub. Health
☐

PhD Org. Health & Well Being
☐

PhD Mental Health
☐

MD ☐

DClinPsy S.R.P. ☐ [if S.R.P. Service Evaluation, please also indicate here:
☐

DClinPsy Thesis
☐

• **Project supervisor(s), if different from applicant:**

Professor Fiona Lobban

Doctor Heather Robinson

Doctor Abigail Morris

• **Appointment held by supervisor(s) and institution(s) where based (if**

applicable): Professor Fiona Lobban – Professor, Lancaster University

Doctor Heather Robinson – Lecturer, Lancaster University

Doctor Abigail Morris – Lecturer, Lancaster University

SECTION THREE

Complete this section if your project includes *direct* involvement by human subjects

1. Summary of research protocol in lay terms:

According to the U.K. Focal Point Annual Report (2018), heroin users make up most of the population receiving structured drug treatment in the United Kingdom. In 2016, 57 673 individuals reported an

opioid to be their primary problem substance. Like other countries, opiate substitution therapy (methadone, buprenorphine etc.) is currently the primary treatment route for opioid misusers in the U.K. Ibogaine treatment is argued to be an alternative intervention for opioid and substance misuse in general (Alper et al., 2008). Ibogaine is a psychoactive plant known for its anti-addictive properties. According to Alper et al. (2008), Ibogaine alleviates opioid withdrawal symptoms within one administration. Numerous treatment centres have been providing Ibogaine treatment for addiction with medical supervision and continuous monitoring. However, the available literature is somewhat anecdotal and is limited with unfinished Randomised Control Trials with human-subjects. Due to the little research, treatment packages are unclear. To explore the practitioners' treatment details and opinions, the proposed research will undertake topic-guided interviews with Ibogaine treatment providers about the treatment they are providing and their professional opinions. Research objectives are to: Objectives of the proposed thesis are; to (1) identify different treatment regimens and associated benefits and challenges; (2) to determine the variety of supplementary therapies (for example, psychotherapy, meditation, breathwork etc.) provided by treatment centres; (3) to explore practitioner opinions, backgrounds, and their role in the treatment. We aim to explore:

- How do Ibogaine practitioners understand the role of Ibogaine treatment in helping people overcome addiction?
- How do Ibogaine practitioners understand the role of context in effective Ibogaine treatment?

Twenty-two participants currently working as practitioners in various clinics will be recruited by convenience sampling. Participants will be recruited by email invitations (Appendix 1) or forum posts (Appendix 2) in Ibogaine-related online communities. Topic guided interviews will last around 45 minutes. The interview transcripts will be analysed with Thematic Analysis in NVivo 12. This study's findings will increase the understanding of Ibogaine treatment for substance misuse. For more information, please see the study proposal (Section2).

2. Anticipated project dates (month and year only)

Start date: 03/2021

End date: 01/2023

Data Collection and Management

For additional guidance on data management, please go to [Research Data Management](#) webpage, or email the R.D.M. support email: rdm@lancaster.ac.uk

3. Please describe the sample of participants to be studied (including maximum & minimum number, age, gender):

Practitioners worldwide be recruited to acquire a wide range of knowledge related to addiction treatment using Ibogaine. Staff from various treatment clinics will be interviewed to present the variety of treatment methods across various treatment centres. An approximate of 22 participants is desired for the study. Due to the scarcity of treatment centres, every treatment centre will be limited with three practitioners. A minimum of 20 and a maximum of 24 Ibogaine treatment providers are desired for the study. After receiving the consent sheets, individuals may be denied participation if there are already too many participants from one centre, and there are other potential participants available who can help bring perspectives of other centres. It will be ideal for including experienced practitioners from various treatment centres and countries. However, the PhD candidate acknowledges that the sample range will depend on ease of recruitment. See the table below for full inclusion and exclusion criteria.

4. How will participants be recruited and from where? Be as specific as possible. Ensure that you provide the *full versions* of all recruitment materials you intend to use with this application (eg adverts, flyers, posters).

The proposed study is interested in Ibogaine practitioners working in clinics. Suitable organisations and individuals will be identified through a web search of treatment centres, and treatment providers will also be searched on LinkedIn. Clinic websites that provide treatment with Ibogaine will be approached via email (Appendix 1) in their "contact us" section. The study will also be advertised in online Ibogaine related forums (Appendix 2). A participant recruitment post in Ibogaine will use related forums such as Reddit (r/Ibogaine & r/Iboga) and Blue light (both websites allow participant recruitment). Practitioners can indicate whether they would like to participate by contacting the email account provided (a.enginsoy@lancaster.ac.uk). The study will employ snowballing by enabling participants to refer other suitable practitioners to the study by forwarding the participation email.

Participants from illegal countries will be also able to participate, see Ethics section below for safety measures taken for anonymity, data safety and dealing with distress for treatment providers in illegal countries. According to a treatment provider who wants to remain anonymous, most Ibogaine clinics are based in Mexico, so we expect to have a higher number of participants from Mexico. Materials will not be translated for the different languages we recruit due to this study's budget and scope. This will be communicated to participants via the information sheet. Treatment centres are in Mexico, but practitioners are not Mexican; they are primarily American and European citizens residing in Mexico. Furthermore, treatment seekers are often English speakers, and treatment centre websites are usually in English (Barber et al., 2020). It would be ideal to interview the most experienced practitioner in every treatment centre, regardless of their position.

Those wishing to participate will receive an online version of the information (Appendix 3) and consent sheet (Appendix 4) following the initial contact. To ease the recruitment process, forms will be created on QUALTRICS, and participants will receive a link to the documents. Participants will be given time to consider the information sheet (for at least 24 hours) and have the opportunity to ask questions about the study before signing and emailing the consent sheet to the research team.

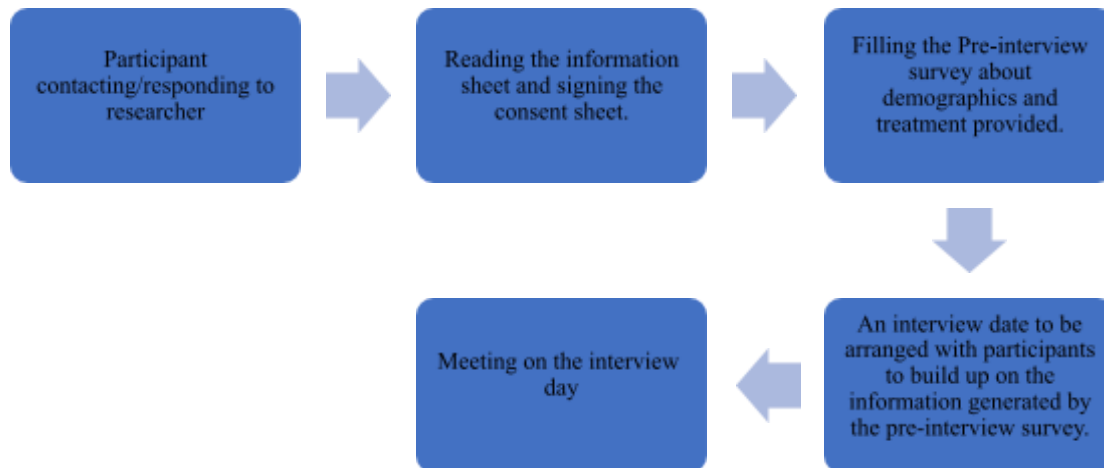


Figure 1: Recruitment flowchart

5. Briefly describe your data collection and analysis methods and the rationale for their use.

A pre-interview survey will enquire about participants' demographics, experience and treatment regime and supplementary therapy. The treatment regime consists of questions about dose, setting and additional therapies. Upon completing the survey, an interview will be arranged. Interviews will seek to expand on the information given in the survey (Appendix 5), focusing on participants' views and opinions on how Ibogaine works and the importance of various facets of the treatment. The PhD candidate (AE) will conduct topic-guided interviews (Appendix 6) via Microsoft (M.S.) Teams video chat software. The privacy policy of this software (<https://docs.microsoft.com/en-us/microsoftteams/security-compliance-overview>) will be presented in the participation sheet. The meetings will last around 45 minutes and cover the following areas:

- (a) Practitioner Backgrounds and Responsibilities
- (b) Treatment process (from admission to aftercare) and regime (dose, setting and adjacent therapies)
- (c) Ibogaine treatment details, benefits, and challenges.
- (d) Post-treatment and longevity

The PhD candidate will transcribe the recorded interview conversations into Microsoft Word and import them into NVivo 12 software for analysis to describe and interpret the

practitioners' thoughts, opinions, and beliefs. The PhD candidate and research team will review the qualitative data. Following the detailed procedure, the PhD candidate will conduct the thematic analysis, which involves analysing the transcripts line by line, coding each portion of the transcript and then structuring those codes into preliminary themes. Themes will be established through the transcripts focusing on mutual understandings, contradictions, and a variety of views, beliefs, and attitudes. The data will be evaluated, considering the research objectives.

Participants can only offer what they are prepared to share regarding their experience, but the topic-guided framework grants versatility and should be viewed reflectively. Furthermore, thematic analysis is valuable when exploring people's experiences, identifying parallels and disparities, and creating unforeseen observations (Braun et al., 2019).

6. What plan is in place for the storage, back-up, security, and data (electronic, digital, paper, etc.)? Note who will be responsible for deleting the data at the end of the storage period. Please ensure that your plans comply with General Data Protection Regulation (GDPR) and the (U.K.) Data Protection Act 2018.

Data will be handled in compliance with the E.U. General Data Security Policy (Voigt et al., 2018) and the (U.K.) Data Protection Act of 2018. Interviews will be audio-recorded using a password-protected voice recording device. Lancaster University's Research Data Management Policy and OneDrive will be used as a digital storage tool for archive purposes. The audio files will be stored in the University password-protected OneDrive. Files will be transferred to the OneDrive and deleted from the dictaphone immediately after the interview. Audio recordings will be kept in the drive until the research project has been examined. The participants' names and contact information will not be included in transcripts.

Identifying details will be anonymised by referring to participants with their participation order number (1st participant etc.). Both identifiable and de-identifiable documents will be kept separately in a password-protected form. Personal contact information will be destroyed after the interview. In case of not completing the PhD programme, the researcher will destroy all collected data before leaving the University. The data will not be distributed to any party other than the student supervisors for the project's course. Anonymised interview and survey data will be retained, and for ten years in the relevant data archive and repository, the PhD candidate will be using Lancaster University's PURE. After ten years, the data will be destroyed by the PhD supervisor. Quotes could identify participants; therefore, stored data will be only accessible via request. Any quotes used in publications will be anonymised by removing any references to location and changing pronouns etc., as required. The participant information sheet (Appendix 3) will provide an upfront overview of where and how results will be communicated and disseminated.

7. Will audio or video recording take place? ☐ no ☐ audio ☐ video

a. Please confirm that portable devices (laptop, USB drive etc.) will be encrypted where they are used for identifiable data. If it is not possible to encrypt your mobile devices, please comment on the steps you will take to protect the data.

Yes, the audio of interviews will be recorded using a password-protected dictaphone. All data will be stored on the dedicated University OneDrive Audio files deleted from the password-protected voice recorder immediately after transferring to the University Drive.

b. What arrangements have been made for audio/video data storage? At what point in the research will tapes/digital recordings/files be destroyed?

Audio recordings will be kept securely in the University OneDrive until the research project has been examined. Then it will be destroyed by either the PhD candidate or the supervisor.

Please answer the following questions *only* if you have not completed a Data Management Plan for an external funder

8a. How will you share and preserve the data underpinning your publications for at least ten years e.g. PURE?

Interview and survey data will be retained and stored for ten years in the relevant data archive and repository; in this project, it would be Lancaster University's PURE.

8b. Are there any restrictions on sharing your data?

Quotes could identify participants; therefore, stored data will be only accessible via request.

9. Consent

a. Will you take all necessary steps to obtain the voluntary and informed consent of the prospective participant(s) or, in the case of individual(s) not capable of giving informed consent, the permission of a legally authorised representative in accordance with applicable law?

b. Detail the procedure you will use for obtaining consent?

All potential participants will be emailed with an online participant information sheet (Appendix 3) following initial contact, along with the participant consent sheet (Appendix 4). This sheet will inform participants about the study as well as the handling of confidentiality status. Additionally, recording, management of interview data and other ethics points will be clarified in the information sheet. Participants will be given time to digest the information sheet (for at least 24 hours) and will have the opportunity to ask any questions. These online forms were created on QUALTRICS to ease the participant recruitment process. Participants will provide their explicit consent by completing the consent sheet, and only then will they be eligible to participate in the study. After filling the signed consent sheet, the researcher then will email a link to the pre-interview survey. Participants will be reminded of the consent policy and their right to withdraw at any point before, during and up to two weeks after the interview.

10. What discomfort (including psychological e.g. distressing or sensitive topics), inconvenience or danger could be caused by participation in the project? Please indicate plans to address these potential risks. State the timescales within which participants may withdraw from the study, noting your reasons.

Even though the study does not deal with traumatic issues, interviews may bring up negative memories, and participants may feel uneasy for various reasons. Participants will be informed that they can pause or end the interview when they prefer. Participants will also be offered a follow-up call to check-in with the researcher the day after the interview. The information sheet also contains information on mindfulness exercise for mild distress and international organisations to contact for further assistance in the information sheet and at the end of the interview. The interview sheet will also contain contact information in case the participants are dissatisfied with the study. Participants can withdraw their participation before, during and up to two weeks after the interview.

11. What potential risks may exist for the researcher(s)? Please indicate plans to address such risks (for example, noting the support available to you; counselling considerations arising from the sensitive or distressing nature of the research/topic; details of the lone worker plan you will follow, and the steps you will take).

In case the PhD candidate feels distressed/uncomfortable after hearing malpractice. First, the supervisors will be informed, and the PhD candidate will practice mindfulness meditation and seek further support from the calm zone hotline provided for participants if needed.

12. Whilst we do not generally expect direct benefits to participants as a result of this research, please state here any that result from the completion of the study.

Increased information on Ibogaine treatment centres in the scientific community may lead to a better understanding of treatment packages and better inform those intending to deliver Ibogaine treatment for addiction and those who want to attend these centres.

13. Details of any incentives/payments (including out-of-pocket expenses) made to participants:

Interviews will be conducted via M.S. teams video chat software. Therefore, we are not anticipating travel or out of pocket expenses.

14. Confidentiality and Anonymity

a. Will you take the necessary steps to assure the anonymity of subjects, including in subsequent publications?

b. Please include details of how the confidentiality and anonymity of participants will be ensured and the limits to confidentiality.

Identifying features will be removed in transcripts, and an identification number will be given for thesis excerpts to ensure the privacy of treatment centres and practitioners. Recordings will be destroyed once anonymised transcripts are stored on OneDrive. Only the supervisors and examiners will have access to complete anonymised transcripts. The participation order number will be kept in a password-protected document in a separate folder to the transcripts.

Confidentiality will be breached if the researcher has questions about the unethical practice or if the participant discloses risk to self/others. Participants will be informed of this possibility in the information sheet. If and when it does occur, they will also be informed about what is happening.

The PhD candidate explored options to report however there is not a body to report since Ibogaine is not a legal or acknowledged medication. The Global Ibogaine Therapy Alliance (GITA) is an independent not-for-profit advocacy body and their website has a "report an adverse event" section which seemed to be an ideal place to report low risk events, however GITA is not operating anymore and the PhD candidate's messages did not receive a response. Therefore, this study will breach confidentiality in case of high risk/criminal situations.

For criminal disclosures, police authorities will be contacted; these criminal disclosures are inclusive but not limited to intentional harm, false imprisonment, or unreported death of a service user. Participants will also be recommended to contact Calmzone international mental health support if they disclose harm, self-harm, and suicidal ideation. These sources will be presented in the information sheet.

15. If relevant, describe the involvement of your target participant group in the *design and conduct* of your research.

The researcher has consulted the owners and managers of treatment centres regarding the legality of Ibogaine treatment, the estimated number of treatment seekers and the variety of services provided. The insight gained from these conversations has influenced the design of the interview questions.

16. What are the plans for the dissemination of findings from the research? If you are a student, include here your thesis.

This study's findings will be submitted to Lancaster University in the form of a PhD thesis and disseminated through presentations, poster presentations at related conferences, and, where appropriate, publication in a peer-reviewed journal. The researcher also anticipates creating an overview of results, which could be more accessible to participants and therapy seekers.

17. What particular ethical considerations, not previously noted on this application, do you think there are in the proposed study? Are there any matters about which you wish to seek guidance from the FHMREC?

Appendix B: Tables from Scoping Review

Table B3

Location of studies

Country	# of studies conducted
United States of America	14
Canada	2
United Kingdom	2
China	1
Iran	1
Lithuania	1
the Netherlands	1
New Zealand	1
Russia	1
St. Kitts, West Indies	1
Switzerland	1

Table B4

Number of participants

# of participants	# of studies
<50	13
50 – 100	9
100 – 200	3
>200	1

Table B5*Active Substances*

Active Substance	Count
Psilocybin	7
Ketamine	6
Lysergic Acid Diethylamide (LSD)	5
Ibogaine	3
Noribogaine	1
Dipropyltryptamine (DPT)	1
Scopolamine	1
Hab-o Shefa	1
3,4-Methylenedioxymethamphetamine (MDMA)	1

Table B6*Active and Control Substances Used in Trials*

Author(s). (Year)	Active substance and dose (solution, mg/kg, frequency)	Control substance and dose (solution, mg/kg, frequency)
Smart et al. (1966)	Group 1: "lysergide group" received a single dose of 800-µg lysergide. Group 2: "ephedrine group" received a 60-mg dose of ephedrine sulphate	Group 3: Control group exposed to all procedures and therapies given to the drug groups except for the drug session
Bogenschutz et al. (2015)	First session: Psilocybin dosed at 0.3 mg/kg. Second session: Psilocybin dosed up to 0.4 mg/ kg	Not applicable
Bogenschutz et al. (2022)	Session 1: psilocybin, 25 mg/70 kg Session 2: psilocybin, 30-40 mg/70 kg	Session 1: diphenhydramine, 50 mg Session 2: diphenhydramine, 100 mg
Bowen, et al. (1970)	Group 1: LSD 500-µg Group 3: LSD 500-µg	Group 2: Control group, no placebo Group 4: Placebo dose of LSD (not specified) of 25-µg Group 5: Control group, no placebo
Dakwar, E., et al. (2020)	Ketamine (0.71 mg/kg)	Active control midazolam (0.025 mg/kg)
Garcia-Romeu, et al. (2014)	Moderate (20mg/70kg) and high (30mg/70kg) dose psilocybin sessions	Not applicable

	occurring in weeks 5 and 7 with an optional third high dose session in week 13 and in a 15 week treatment period	
Glue et al. (2016)	3 ascending-dose levels (60, 120, and 240 mg). Dosing began with the lowest Noribogaine dose, and subsequent cohorts received the next highest dose after the blinded safety	Matching placebo (60, 120, and 240 mg). In the week before Noribogaine/placebo dosing, methadone was replaced by oral controlled-release morphine capsules (M-Eslon)
Grabski et al. (2022)	Group 1: ketamine (0.8mg/kg, 40 minutes) plus psychological therapy Group 2: three ketamine infusions (0.8mg/kg, 40 minutes) plus alcohol education	Group 3: three saline infusions (0.9%, 40 minutes) plus psychological therapy Group 4: three saline infusions (0.9%, 40 minutes) plus alcohol education
Grof et al. (1973)	15 mg of substance (DPT) per cm ³	Not applicable
Hollister et al. (1969)	Group 1: LSD-25, 600 µg Group 2: dextroamphetamine, 60 mg	Not applicable
Holze et al.(2021)	25 µg LSD, 50 µg LSD, 100 µg LSD, 200 µg LSD, and 200 µg LSD 1 h after ketanserin 40 mg administration over six 25 h test sessions	Mannitol prepared in identical capsules
Hull et al. (2022)	300 mg to 450 mg dose of sublingual, rapidly dissolving ketamine tablets	Not applicable
Johnson et al. (2017)	First dose: Psilocybin (20mg/70kg) in week 5 Second dose: Psilocybin (30mg/70kg) in week 7 Optional third dose: Psilocybin (30mg/70kg) in week 13	Not applicable
Johnson et al. (2014)	First dose: Psilocybin (20mg/70kg) in week 5 Second dose: Psilocybin (30mg/70kg) in week 7 Optional third dose: Psilocybin (30mg/70kg) in week 13	Not applicable
Jovaiša et al. (2006)	Subanaesthetic ketamine infusion of 0.5 mg/kg/h	Normal saline
Knuijver et al. (2022)	Ibogaine-HCl 10 mg/kg	Not applicable
Kolp et al. (2006)	KEP (Ketamine Enhanced Psychotherapy) (0.2 mg/kg IM - 2.0 mg/kg IM)	Not applicable
Krupitsky & Grinenko (1997)	Hallucinogenic ("psychedelic") dose of ketamine (2.0 mg/kg im)	Non-hallucinogenic (non-psychedelic), dose of ketamine (0.2 mg/kg im)

Liu et al. (2013)	Scopolamine hydrobromide 0.03–0.05 mg/kg and chlorpromazine hydrochloride 0.6–1.0 mg/kg for 3-4 days	Methadone, initial dose between 30 and 60 mg. Those in the MD group then underwent a 10-day gradual dose reduction of 10% per day regimen (days 4–13)
Mash, et al. (2018)	lbogaine HCl (8–12 mg/kg)	Not applicable
Moosavyzadeh et al. (2020)	Hab-o Shefa, 500mg capsules/day, with a daily increase of 500mg until 3 capsules on day three	"Powdered sugar dosed and prepared in capsules of the same shape and weight as the active capsules "
Alper et al. (1999)	lbogaine (form unstated) 19.3 ± 6.9 mg/kg (range of 6 to 29 mg/kg).	Not applicable
Jensen & Ramsay (1963)	One single dose of d-lysergic acid diethylamide (LSD-25), amount not mentioned	Not applicable
Rothberg et al. (2021)	Ketamine, dose not mentioned	Midazolam, dose not reported
Savage et al. (1973)	One high-dose (300µg to 450/ig) LSD.	Control group, not exposed to drug
Sessa B, et al. (2021)	2 sessions with MDMA (187.5mg each session divided into two doses, 125 and 62.5 respectively)	Not applicable

Table B7

Route of Administration Used in the Study

Route of administration	# of studies
Oral	11
Intravenous	6

Table B8

Primary Target Conditions in Trials

Primary substance/target condition	# of studies
Alcohol	12
Opioids	6
Heroin	2

Tobacco/nicotine	3
LSD	1
Narcotics	1
Non-substance related	1

Table B9

Available support during the study

Available support	# used
Individual therapy/CBT	9
Group therapy	3
Psychosocial intervention (motivational enhancement therapy, interpersonal skills training, etc.)	5
Mindfulness/breathwork/meditation/guided imagery/yoga	5
Other (cooking classes, journaling, info sessions etc.)	5

Table B10

Preparatory process

Author(s). (Year)	Preparation for Administration
Smart et al. (1966)	Brief orientation.
Bogenschutz et al. (2015)	Required to be afebrile, non-hypertensive, non-tachycardic, abstinent from alcohol for at least 24 hours, without evidence of withdrawal
Bogenschutz et al. (2022)	4 psychotherapy sessions.
Bowen et al. (1970)	Psychological support before, during, after. Group lectures
Dakwar et al. (2020)	6 motivational therapy sessions over 5 weeks. Counselling to reduce drinks. Abstain from alcohol for 24 hours before infusion. Fast after midnight
Garcia-Romeu et al. (2014)	15 weekly meetings by 2 to 3 facilitators. TQD set for week 5 concurrent with the first psilocybin session
Glue et al. (2016)	Single-dose Noribogaine in patients seeking to discontinue methadone OST from 24 hours prior to dosing until 72 hours post dose

Grabski et al. (2022)	Prepared for potential experiences. Relaxation or mindfulness techniques. Abstinence for at least 24 hours
Grof et al. (1973)	A series of drug-free interviews
Hollister et al. (1969)	Initial treatment at detoxification. Breakfast of clear liquids. Treatment given at 8:30 a.m in a special room
Holze et al. (2021)	A screening visit
Hull et al. (2022)	Eligibility questionnaire, intake paperwork, standardized medical and psychiatric evaluation through video. 40-60 min intake session
Johnson et al. (2017)	4 weekly preparatory meetings integrating CBT
Johnson et al. (2014)	4 weekly meetings with smoking cessation CBT. Imagery exercises. Smoking diary
Jovaiša et al. (2006)	General anaesthesia on day 3
Knuijver et al. (2022)	Before Ibogaine, subjects admitted to clinic and converted from OST to oral morphine sulphate for 8 days
Kolp et al. (2006)	Orientation, discussing body, mind, and soul needs
Krupitsky & Grinenko (1997)	10 hours of psychotherapy, possible effects explained, confidence creation between therapist and participant
Liu et al. (2013)	Received methadone during days 1–3, pre-medicated with omeprazole 1 hour before induction
Mash et al. (2018)	Opioid patients switched to morphine sulphate for opioid withdrawal control before Ibogaine detoxification
Moosavizadeh et al. (2020)	Complete description of research. Detoxification over 10–14 days. Morphine urine test and NCT with naloxone
Alper et al. (1999)	Ingest last substances the night before treatment. Received Ibogaine 8-10 hours later. Last methadone dose 24 hours before Ibogaine
Jensen & Ramsay (1963)	2 weekly sessions of group psychotherapy, 3 A.A. meetings a week, work therapy, individual psychotherapy
Rothberg et al. (2021)	Decide on treatment day a week prior. Refrain from eating 24h prior to infusion. Relaxation and mindfulness exercises
Savage et al. (1973)	Preparatory psychotherapy
Sessa et al. (2021)	60-minute outpatient non-drug psychotherapy sessions delivered by two clinicians

Table B11*Preparatory measures implemented*

Preparation measures	# used
Medical-related abstinence/detoxification	11
Psychotherapy/psychological support	10
Orientation	6
Mindfulness	4

Table B12*Treatment during administration*

Author(s). (Year)	Treatment during administration (active substance and blind control groups)
Smart et al. (1966)	3h interview and no fulltime observation
Bogenschutz et al. (2015)	Participants took the capsule followed by 4 ounces of water, lied down on a couch wearing eyeshades and headphones.
Bogenschutz et al. (2022)	Administered in two 8-hour sessions, psychotherapy, required to stay in the session room.
Bowen et al. (1970)	Supportive reassurance; emphasis on non-verbal introspection
Dakwar et al. (2020)	An additional motivational enhancement session provided 24 hours after infusion
Garcia-Romeu et al. (2014)	Not reported
Glue et al. (2016)	Not reported
Grabski et al. (2022)	Infusions administered at visits, therapist present, listened to instrumental music...
Grof et al. (1973)	Patient's therapist and nurse in attendance, patient reclined with eyeshades and headphones...
Hollister et al. (1969)	Patient remained in room for next eight hours under constant attendance, lunch provided
Holze et al. (2021)	Ketanserin or placebo administered, measures assessed for 24h, standardized meals provided, subjects never alone for first 16h

Hull et al. (2022)	Prior video meeting, confirmed abstinence, asked to hold ketamine tablets, then lie down with music.
Johnson et al. (2017)	Not reported
Johnson et al. (2014)	Guided imagery exercises, monitored blood pressure, wore an eye mask, and listened to music
Jovaiša et al. (2006)	Not reported
Knuijver et al. (2022)	Subjects left sleeping during evening and night after dosing
Kolp et al. (2006)	Existential and transpersonal group psychotherapies
Krupitsky & Grinenko (1997)	Anaesthesiologist present, subject reclined with eyeshades, music preselected, psychotherapy conducted.
Liu et al. (2013)	MD group underwent a 10-day gradual dose reduction, SDT group underwent SDT-based light anaesthesia.
Mash et al. (2018)	A licensed therapist provided support, subjects narrated their experience after receiving doses
MoosavYZadeh et al. (2020)	Not reported
Alper et al. (1999)	Instructed to lie down in a dimly lit room in a quiet location
Jensen & Ramsay (1963)	A treatment session with lysergic acid diethylamide (LSD-25)
Rothberg et al. (2021)	Relaxation and mindfulness-based exercises if discomfort or anxiety emerged during infusions
Savage & McCabe (1973)	Administration of LSD dose, followed by psychotherapy
Sessa et al. (2021)	Acute anxiety was managed primarily psychologically, sedative medication (oral lorazepam) was available

Table B13*Adoption of Orientation and Mindfulness Approaches Following Treatment*

Author(s). (Year)	Aftercare after administration (active substance and blind control groups)
Smart et al. (1966)	Patients were encouraged to maintain outpatient or social-recreational contacts with the clinic.
Bogenschutz et al. (2015)	Participants were escorted home at the end of the session by a family member or friend, who stayed with the participant overnight. Psychosocial intervention of 12 sessions previously elaborated.
Bogenschutz et al. (2022)	4 psychotherapy sessions in the months following the second medication session.
Bowen et al. (1970)	Continued Human Relations training programme.
Dakwar et al. (2020)	Medical coverage was provided for up to 3 hours post infusion, and a brief psychiatric evaluation was conducted before discharge. Provided with referrals at the end of the trial; telephone follow-up was conducted 6 months after the trial.
Garcia-Romeu et al. (2014)	"Study treatment facilitators met with participants to discuss psilocybin session experiences, encourage and socially reinforce the use of CBT techniques, and provide support for smoking abstinence."
Glue et al. (2016)	Outpatient and telephone assessments until 35 days postdose.
Grabski et al. (2022)	A therapy or alcohol education session about 24 hours after administration of the drug.
Grof et al. (1973)	Several subsequent drug-free interviews for the integration of the session.
Hollister et al. (1969)	At 4:30 p.m., the patient was taken to his regular bedroom or resumed ward activities, and was encouraged additional self-examination. A minimum of 24 hours elapsed following the treatment prior to discharge.
Holze et al. (2021)	After drug administration, and the investigator was in a room next to the subject for up to 24 h. The subjects were sent home the next day at 9:15 a.m. One end-of-study visit.
Hull et al. (2022)	1h post-dose, patients journal for 30 min and then join a 30 min video meeting with their guide. 1-2 days following the first medication session, patients meet again with their prescribing clinician by video for 20 to 30 min to assess the initial reaction and establish a treatment plan.

Johnson et al. (2017)	Follow-up meetings at 6 and 12 months after first sessions, and invited back for a retrospective interview probing potential mechanisms of the study treatment at a mean of 30 months after the first session.
Johnson et al. (2014)	Study staff met with participants the day after each psilocybin session, and weekly after the first dose to discuss session experiences and provide support for smoking cessation, for a total of 19 in-person meetings. A staff member made brief daily phone calls to participants.
Jovaiša et al. (2006)	Enrolment in aftercare programme of their choice: abstinence-based, naltrexone-supported outpatient counselling, or residential rehabilitation programmes.
Knuijver et al. (2022)	Participants received a magnesium bolus infusion of 2 g in 10 minutes, followed by 2 g of magnesium over the next 10 hours for myocardial stabilisation. If necessary, subjects could be transferred to the coronary care unit (CCU) for continuous cardiac monitoring.
Kolp et al. (2006)	Journaling, guided meditation, breathwork, grounding, one-year follow-up with patients.
Rupitsky et al. (2002)	5 hours of psychotherapy, discharged within 3 to 5 days
Liu et al. (2013)	Outpatient treatment twice weekly for 8 weeks, during which participants underwent weekly, manual-guided relapse prevention psychotherapy.
Mash et al. (2018)	Referral to aftercare programmes and community support groups (12-step programmes)
Moosavizadeh et al. (2020)	Not reported
Alper et al. (1999)	Not reported
Jensen & Ramsay (1963)	Not reported
Rothberg et al. (2021)	Referrals for further treatment
Savage & McCabe (1973)	One additional week of therapy
Sessa et al. (2021)	Participants were seen the morning after each drug-assisted session for an integration psychotherapy session.

Table B14*Program length*

Program length	# of studies
>1 month	6
1 - 3 month	11
3 – 6 months	7
6 months – 1 year	2

Table 15: Outcomes measured before treatment

Author(s). (Year)	Outcomes Measured Before Treatment
Smart et al. (1966)	Drinking History Questionnaire, Abstinence (6 months), Maudsley personality inventory, Haigh-Butler Q, Rorschach, Wechsler Adult Intelligence Scale
Bogenschutz et al. (2015)	Urine drug screens (negative for cocaine, psychostimulants, and opioids), Breath (negative for alcohol), Medical history and physical examination, ECG, Liver function tests, Complete blood count, Blood chemistries, Urinalysis, Serum pregnancy test, BMI, CIWA-Ar for alcohol withdrawal
Bogenschutz et al. (2022)	The Short Index of Problems (SIP-2R) at intake
Bowen et al. (1970)	Not reported
Dakwar et al. (2020)	Blood pressure, Heart rate, Blood oxygen saturation during infusion
Garcia-Romeu et al. (2014)	Two biomarkers of recent smoking: Breath carbon monoxide (CO) using a Bedfont Micro III Smokerlyzer, Daily cigarette consumption over past 30 days with TLFB, QSU data, and SASE data
Glue et al. (2016)	Blood for pharmacokinetic assessments predose, ECG recordings, Pharmacodynamic assessments (pupillometry, oximetry, capnography), Pulse oximetry and capnography data, Pupil diameter, SOWS, OOWS, COWS ratings
Grabski et al. (2022)	Reading of 0.0 on breath alcohol test, Negative urine screen for all drugs (except cannabis and benzodiazepines)
Grof et al. (1973)	Physical and psychiatric examination, Pretreatment psychological tests (MMPI, POI, PEP, Raven Progressive matrices, Benton visual retention test), Social history, Blood samples for chromosomal abnormalities
Hollister et al. (1969)	Behaviour during the previous six months
Holze et al. (2021)	Urine sample for drug screening and pregnancy test, VASs 1 hour before drug administration, AMRS used 1 hour before drug administration

Hull et al. (2022)	Screeners for suicide, alcohol use, substance use, and depression and anxiety symptoms at baseline
Johnson et al. (2014)	Two measures of recent smoking, exhaled carbon monoxide (CO) and urinary cotinine level were assessed at intake, Timeline Follow-back, Questionnaire on Smoking Urges, Smoking Abstinence Self-efficacy Scale, Visconsin Smoking Withdrawal Scale, Visual Effects Questionnaire. Mysticism Scale were administered at intake
Johnson et al. (2017)	TLFB at intake
Jovaiša et al. (2006)	Cardiovascular response (blood pressure, pulse), respirations, renal output and gastrointestinal output as well as cortisol levels were measured. Subjective and Objective Opiate Withdrawal Scales (SOWS and OOWS) were assessed during the early post-anaesthetic period. Abstinence rates at 4 months were also secondarily assessed
Knuijver et al. (2022)	Substance use and addiction severity were assessed using the Addiction Severity Index (ASI). K ⁺ Ca ²⁺ and Mg ²⁺ were checked to be within normal ranges prior to Ibogaine administration
Kolp et al. (2006)	Ensures participants satisfied the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV; American Psychiatric Association, 1994), criteria for alcohol dependence
Krupitsky & Grinenko (1997)	ZDS, SAS, VASC, SA, MMPI, LCS, CTA, and PLT. Formal psychiatric examination, complete medical examination (blood chemistry panel, urine analysis, HIV-test, pregnancy test, and EKG) review of previous medical and psychiatric records
Liu et al. (2013)	Heroin craving, depression and anxiety, assessed using a visual analogue scale (VAS), the Beck Depression Inventory (BDI), the Self-Rating Anxiety Scale (SAS) and Working memory and attention, assessed using the Digit-span test and the d2 test on day 0
Mash et al. (2018)	Addiction Severity Index, and Structured Clinical Interview for DSM-IV Axis I Disorders (SCID I)
Moosavyzadeh et al. (2020)	Hamilton Rating Scale for Depression and Hamilton Anxiety Scale. CBQ, a self-report scale for craving substances, was also administered.
Alper et al. (1999)	Opioid Withdrawal Symptoms observed by authors
Jensen & Ramsay (1963)	Allport-Vernon-Lindzey Study of Values which has six scales based on Spranger's classification of interests: theoretical, economic, esthetic, social, political and religious a day or two before the LSD treatment
Rothberg et al. (2021)	Not reported
Savage & McCabe (1973)	Urine monitoring, weekly group therapy
Sessa et al. (2021)	Physical health check comprising an electrocardiogram, routine blood tests, blood pressure, heart rate and physical examination

Table B16*Outcomes measured during treatment*

Author(s). (Year)	Outcomes measured during treatment
Smart et al. (1966)	Not reported
Bogenschutz et al. (2015)	Self-report scales (7 hrs after drug), monitor ratings (0–6 hrs after drug), HRS Intensity subscale, 5D-ASC, ARCI, Monitor Session Rating Form, TLFB, SIP, BAC, SOCRATES 8A, AASE, PACS, POMS, vital signs every 30 mins for first 2 hrs, then hourly next 4 hrs
Bogenschutz et al. (2022)	Blood pressure and heart rate every 30-60 mins for first 6 hrs, MEQ, States of Consciousness Questionnaire post-medication session
Bowen et al. (1970)	Chwelos Scale, timing of LSD treatment
Dakwar et al. (2020)	Timeline followback, arousal (visual analogue scale), withdrawal (Clinical Institute Withdrawal Assessment), self-efficacy (AASE, Drug-Taking Confidence Questionnaire), perceived stress (modified Perceived Stress Scale), mindfulness (Five Facet Mindfulness Questionnaire), impulsivity (Barrett Impulsiveness Scale), urine samples for toxicology
Garcia-Romeu et al. (2014)	Two biomarkers of smoking (15 weeks), TLFB, QSU, SASE (weekly post-TQD), HRS (7 hrs post-capsule), Mysticism scale (specific session), SOCQ (post-session)
Glue et al. (2016)	Physical exams, adverse events, lab tests, vital signs, ECG telemetry (-2 to 6 hrs), 12-lead ECG, continuous ECG recordings
Grabski et al. (2022)	Blood pressure, heart rate, blood oxygen saturation, side effects rating at various intervals, ketamine blood concentration
Grof et al. (1973)	Observations and ratings of the therapist, patient's subjective account, psychedelic experience questionnaire
Hollister et al. (1969)	Mental status evaluation
Holze et al. (2021)	LSD blood concentrations, blood pressure, heart rate, tympanic body temperature
Hull et al. (2022)	Side effects, adverse events and dissociation (post 2nd and 4th medication sessions), blood pressure during sessions
Johnson et al. (2017)	Self-reported daily cigarette consumption using the TLFB, 143-item questionnaire (on changes in attitudes, moods, behaviour, and spirituality) 1 week after first dose. Mystical Experience Questionnaire (MEQ30) 7 hours after administration

Johnson et al. (2014)	Two measures of recent smoking, exhaled carbon monoxide (CO) and urinary cotinine level assessed weekly. States of Consciousness Questionnaire
Jovaiša et al. (2006)	Cardiovascular, respiratory, renal, and gastrointestinal responses during anaesthesia phase. Plasma cortisol concentrations as stress-response markers
Knuijver et al. (2022)	Blood pressure, heart rate, SARA for cerebellar side effects, DOS for psychomimetic effects at intervals for 24h after dose. ECGs every half hour for the first 12 hours
Kolp et al. (2006)	Not mentioned
Krupitsky & Grinenko (1997)	Not reported
Liu et al. (2013)	Continuous electrocardiography, pulse oximetry, blood pressure monitoring, and oesophageal temperature probe. The SOWS daily during inpatient phase. Retention during inpatient and outpatient phases
Mash et al. (2018)	Physical exams, physician ratings of AEs, safety lab tests, vital signs, 12-lead ECG and telemetry from -1 h to 24 h
Moosavizadeh et al. (2020)	Evaluation at four time points: Before treatment, 4 weeks, 8 weeks, and 12 weeks after treatment onset
Alper et al. (1999)	Opioid Withdrawal Symptoms observed by authors
Jensen & Ramsey et al. (1963)	Change in religious value and transcendental experiences during drug effectiveness period
Rothberg et al. (2021)	Deficits like craving, confidence to maintain abstinence, and withdrawal assessed at each visit. Urine toxicology and self-reported drug use using TLFB. CADSS and Hood Mysticism Scale at conclusion of infusion
Savage & McCabe. (1973)	Urine monitoring, weekly group therapy
Sessa et al. (2021)	Physiological changes, observer and subject ratings of distress (SUDS) and intensity of MDMA's psychoactive effects throughout the drug-assisted session

Table B17

Outcomes measured after treatment

Author(s). (Year)	Outcomes measured after treatment and timepoints
Smart et al. (1966)	Self-reported morning drinking, blackouts, drinking on job, or preoccupation with alcohol
Bogenschutz et al. (2015)	7 hours after drug administration: participants completed questionnaires and assessments, brief clinical interview, mental status exam
Bogenschutz et al. (2022)	Timeline followback at weeks 8, 12, 24, and 36. Hair or fingernail samples at week 24 (ethylglucuronide concentration). The Short Index of Problems (SIP-2R) at weeks 12, 24, and 36.
Bowen et al. (1970)	Interview with social worker 1 year after treatment, 8-point adjustment scale
Dakwar et al. (2020)	After the infusion: participants completed a subjective-effects assessment battery
Garcia-Romeu et al. (2014)	Two biomarkers of recent smoking from end of treatment (week 15). TLFB self-report data on daily cigarettes since last visit. Questionnaire on Smoking Urges (QSU) and Smoking Abstinence Self-Efficacy Scale (SASE) at 6-month follow-up. Mysticism scale and others at the end of each session and week 15.
Glue et al. (2016)	Blood for pharmacokinetic assessments at multiple timepoints. Pharmacodynamic assessments: pupillometry, oximetry, capnography. Time to resumption of OST. Subjective, Objective, and Clinical Opioid Withdrawal Scales (SOWS, OOWS, COWS) ratings at various timepoints.
Grabski et al. (2022)	Participants rated side effects at various times post-infusion. Self-reported percentage days abstinent and alcohol relapse at 3 and 6 months. Other measures like BDI, HAM-D, SF-12, Psychotomimetic States Inventory, and more at various timepoints.
Grof et al. (1973)	Between 3 and 5 days after completion: re-administered initial psychological test battery. Two additional blood samples for post-session chromosome analyses.
Hollister et al. (1969)	A Drinking Behavior Scale in areas of drinking habits, social behaviour, and occupational adjustment. Behaviour outcomes at 2 months, 6 months, and 12 months post treatment.
Holze et al. (2021)	Subjective effects assessed repeatedly using VASs at multiple timepoints. The Adjective Mood Rating Scale, 5D-ASC scale, Mystical experiences, and Plasma BDNF levels assessed at various timepoints.
Hull et al. (2022)	Alcohol use with AUDIT. Substance use by DAST-10. Patient Health Questionnaire (PHQ-9) for depression, and the Generalised Anxiety Disorder scale (GAD-7) for anxiety.
Johnson et al. (2017)	Breath carbon monoxide (CO) measured. Urine samples for recent smoking, complete self-report questionnaires, and meeting with study staff at 10 weeks and 12 months. 143-item questionnaire (on changes in attitudes, moods, behaviour, and spirituality) at 12 months follow up.
Johnson et al. (2014)	Two measures of recent smoking, exhaled carbon monoxide and urinary cotinine level were assessed at 6-month follow-up. Timeline Follow-back, Questionnaire on Smoking

	Urges, Smoking Abstinence Self-efficacy Scale, Visconsin Smoking Withdrawal Scale, Visual Effects Questionnaire, Mysticism Scale, and Persisting Effects Questionnaire were also administered during follow-ups.
Jovaiša et al. (2006)	Anaesthetic effects and early postanaesthetic effects within 48 hours. A questionnaire based on Addiction Severity Index was administered 4 months after the procedure.
Knuijver et al. (2022)	Withdrawal was measured using the clinical opioid withdrawal scale (COWS). The SARA and COWS were assessed at 2, 6, 10, and 24 hours after administration of Ibogaine. The DOS scale was assessed every hour for the first 12 hours after administration of Ibogaine.
Kolp et al. (2006)	Abstinence rate was assessed after one year.
Krupitsky & Grinenko (1997)	ZDS, SAS, VASC, SA, MMPI, LCS, CTA, SCS, HRS, and PLT were administered in the week after treatment. ZDS, SAS, and VASC were administered also at 1, 3, 6, 12, 18, and 24 months after treatment. Urine drug testing was conducted at 1, 3, 6, 12, 18, and 24 months after completion of therapy.
Liu et al. (2013)	Heroin use during the outpatient phase was determined by qualitative urine toxicology screens of supervised urine samples obtained twice weekly. Heroin craving, depression, and anxiety were assessed using a visual analogue scale (VAS), the Beck Depression Inventory (BDI), and the Self-Rating Anxiety Scale (SAS) after detoxification (day 15). Working memory and attention were assessed using the Digit-span test and the d2 test (day 15). The reasons for heroin relapse were determined using the Reasons for Relapse Questionnaire (RRQ) when each participant's urine sample was positive.
Mash et al. (2018)	Physical examinations, physician ratings of adverse events, safety laboratory tests, vital signs, 12-lead ECG, and ECG telemetry were monitored from -1 hour to 24 hours after treatment. Whole blood concentrations of Ibogaine and Noribogaine were measured. The current level of craving for cocaine or opioids was determined using questions from the Heroin and Cocaine Craving Questionnaires 1 month following discharge.
Moosavizadeh et al. (2020)	Monthly examination was conducted and rated for symptoms pertinent to pharmacologic side effects of Hab-o Shefa. Vital signs, including blood pressure, temperature, pulse rate, and respiration rate, were recorded monthly.
Alper et al. (1999)	Opioid Withdrawal Symptoms were observed by authors.
Jensen & Ramsay (1963)	The Allport-Vernon-Lindzey Study of Values, which has six scales based on Spranger's classification of interests: theoretical, economic, aesthetic, social, political, and religious, was administered a day or two after the LSD treatment.
Rothberg et al. (2021)	Post-treatment drinking behaviour was measured at 1 and 3 months post-study.
Savage et al. (1973)	Evaluative assessments of the treatment and control groups were conducted 6 and 12 months after release to the community.
Sessa et al. (2021)	Participants were telephoned daily for six days to assess changes in mood, suicidal risk factors using the C-SSRS, and quality of sleep using the Leeds Sleep Evaluation Questionnaire. Outcomes regarding drinking behaviour, quality of life, and

psychosocial functioning were evaluated. At nine months post detox, the average units of alcohol consumption by participants were compared.

Table B18

Outcomes measured

Outcomes measured before, during, and after	# used
Medical markers (blood pressure, heart rate, urine samples, liver functioning, etc)	38
Self-report scales (Hallucinogen rating, self-efficacy, daily urges, etc)	38
Medical/psychological history	12

Table 19

Support post-trial

Support post-trial	# used
Referral/continued contact with clinic/therapist	19
Medical monitoring	4
Mindfulness/journaling	2
Enlisted support from familiar contact (family, friends)	1

Table 20

Trial findings

Author(s). (Year)	Findings
Smart et al. (1966)	Simple analyses of variance showed no differences between the lysergide, ephedrine, and control groups in percentage gain in total abstinence or in their longest period of abstinence. No significant effect of lysergide on the number of drinking occasions.
Bogenschutz et al. (2015)	Abstinence did not increase significantly before psilocybin administration but increased post-administration. Gains largely maintained at 36-week follow-up. Strong correlation between psilocybin session intensity and changes in drinking, craving, and abstinence self-efficacy.
Bogenschutz et al. (2022)	Psilocybin showed blood pressure increase and higher heart rate initially. Psilocybin group had a lower percentage of heavy drinking days and daily alcohol consumption. Psilocybin combined with psychotherapy decreased heavy drinking days.
Bowen et al. (1970)	Both studies combined did not show a significant difference in adjustment between LSD and control groups after 1 year.
Dakwar et al. (2020)	Ketamine increased abstinence likelihood, delayed relapse, and reduced heavy drinking days compared to midazolam. Ketamine infusion improved measures of drinking in individuals with alcohol dependence undergoing motivational enhancement therapy.
Garcia-Romeu et al. (2014)	Abstainers at 6 months had higher scores on psilocybin occasioned mystical experiences. Mystical-type effects were pivotal for smoking cessation.
Glue et al. (2016)	Noribogaine showed a nonstatistically significant trend toward decreased total score in opioid withdrawal ratings, most evident at the 120-mg dose.
Grabski et al. (2022)	Treatment with three infusions of ketamine was well tolerated and associated with more days of abstinence from alcohol at 6-month follow-up. Psychological therapy added potential benefits to ketamine treatment.
Grof et al. (1973)	Post-DPT sessions showed significant improvement in depression, social introversion, insight, self-actualising value, and other parameters. Dramatic improvement seen in abstinence, global adjustment, and interpersonal scales.
Hollister et al. (1969)	At two months, LSD-treated patients fared better than dextroamphetamine-treated ones. By six months, differences between treatments had disappeared. While many remained problem drinkers, their impairment had significantly reduced.
Holze et al. (2021)	LSD effects at varying doses were examined. The 200 µg dose induced more ego dissolution but also more anxiety than the 100 µg dose. Ketanserin largely negated the effects of a 200 µg LSD dose, highlighting 5-HT _{2A} receptors' crucial role in LSD's effects.
Hull et al. (2022)	The telemedicine platform study showed that at-home KAT treatment had significant antidepressant and anxiolytic effects consistent with clinic-

	administered treatments. Remote monitoring ensured low levels of adverse events.
Johnson et al. (2017)	Psilocybin holds considerable promise in promoting long-term smoking abstinence when used within a structured treatment programme.
Johnson et al. (2014)	The open-label design does not permit definitive conclusions; however, findings suggest psilocybin might be a potentially efficacious addition to current smoking cessation treatment models.
Jovaiša et al. (2006)	Ketamine helped better control opioid withdrawal symptoms beyond its infusion period. It was effective in acute opioid withdrawal management, but showed no long-term effects on opioid dependence treatment.
Knuijver et al. (2022)	Ibogaine treatment in patients with opioid use disorder may induce reversible QTc prolongation, bradycardia, and severe ataxia.
Kolp et al. (2006)	Ketamine, combined with other therapies, replicated previous findings in effectively treating alcoholism and other conditions. Alone, ketamine was not sufficient.
Krupitsky & Grinenko (1997)	High dose Ketamine Psychotherapy (KPT) showed better results in heroin addicts' abstinence rates and reduced cravings for up to two years compared to low dose KPT.
Liu et al. (2013)	Scopolamine Detoxification Technique (SDT) considerably reduced heroin withdrawal symptoms and had better outcomes on heroin craving, depression, and anxiety than conventional detox methods.
Mash et al. (2018)	Ibogaine showed promise in transitioning opioid and cocaine users to sobriety and had therapeutic benefits as an adjunct to psychotherapy.
Moosavyzadeh et al. (2020)	Hab-o Shefa was more effective than placebo in preventing opioid relapse, craving, depression, and anxiety.
Alper et al. (1999)	Observational study found reduction in opioid withdrawal symptoms with Ibogaine but had a limited framework.
Jensen & Ramsay (1963)	LSD-25 treatment led to increased social and religious values in alcoholics affiliated with an A.A. programme.
Rothberg et al. (2021)	Ketamine induced mystical-type experiences which mediate its impact on at-risk drinking, emphasizing the role of such experiences in addiction treatment.
Savage & McCabe (1973)	LSD therapy enhanced the probability of better adjustment in opioid addicts. Abstinence was a strong indicator of outcome.
Sessa et al. (2021)	MDMA-assisted psychotherapy improved psychosocial functioning and drastically reduced alcohol consumption post detox.

Appendix C: Supporting Primary Research Documents

Appendix C1

Participation Invitation (Email)

Subject: Ibogaine study participation request

To whom it may concern,

My name is Ahmet Enginsoy. I am a PhD student at Lancaster University's Mental Health programme. I am kindly requesting your participation in a doctoral research study that I am conducting titled: Addiction and Ibogaine Treatment Centres: An Exploratory Study with Practitioners.

This research aims to capture the treatment provided in the treatment centre and the practitioners' opinions. As treatment centre staff, you are in an ideal position to give us valuable first-hand information from your perspective. The interviews are informal and will take around 45 minutes. Calls will be conducted over M.S. teams.

Your responses to the questions will be kept confidential. All transcripts will be anonymised. Each interview will be assigned a number code to ensure that personal identifiers are not revealed during the analysis and write-up of findings.

There is no compensation for participating in this study. However, participation will be a valuable addition to the research. Moreover, the findings could create a greater public understanding of Ibogaine treatment for addiction and Ibogaine treatment centres' role.

If you are willing to participate, please read the information sheet, consider your participation, ask questions, and if you wish to take part, please read the information and consent sheet attached to the [link](#). You will then be sent another link for the pre-interview survey to inquire about demographic data and experience details. If you have any questions, please do not hesitate to ask.

If you are aware of any other experienced Ibogaine treatment staff working in your centre or various treatment centres, I would be very grateful if you could forward this invite to them too. I am keen to interview a range of people.

Yours sincerely,

Ahmet Enginsoy

PhD Student

Lancaster University

The United Kingdom

Appendix C2

Participation Invitation (Forum Post)

Calling for Ibogaine Treatment Centre Staff

I am a PhD student at Lancaster University's Mental Health programme. I am looking for Ibogaine Treatment Centre Staff for my doctoral research study. My research is titled: Addiction and Ibogaine Treatment Centres: An Exploratory Study with Practitioners.

The study aims to capture the treatment provided by Ibogaine treatment centres and the practitioners' opinions. Treatment centre staff are in an ideal position to provide valuable first-hand information from their perspective. The interviews are informal and will take around 45 minutes. Calls will be conducted over M.S. teams.

If you are willing to participate, please read the information sheet, consider your participation, ask questions, and if you wish to take part, please read the information and consent sheet attached to the [link](#). You will then be sent another link for the pre-interview survey to inquire about demographic data and experience details. If you have any questions, please do not hesitate to ask.

Your responses to the questions will be kept confidential. All transcripts will be anonymised. Each interview will be assigned a number code to ensure that personal identifiers are not revealed during the analysis and write-up of findings.

There is no compensation for participating in this study. However, participation will be a valuable addition to the research. Moreover, the findings could create a greater public understanding of Ibogaine treatment for addiction and Ibogaine treatment centres' role.

If you are aware of any other experienced Ibogaine treatment staff working in your centre or various treatment centres, I would be very grateful if you could forward this invite to them too. I am keen to interview a range of people.

Email address: a.enginsoy@lancaster.ac.uk

Yours sincerely,

Ahmet Enginsoy

PhD Student

Lancaster University

The United Kingdom

Appendix C3

Participant Information Sheet

Addiction and Ibogaine Treatment Centres: An Exploratory Study with Practitioners

For further information about how Lancaster University processes personal data for research purposes and your data rights, please visit our webpage: www.lancaster.ac.uk/research/data-protection

My name is Ahmet Enginsoy, and I am conducting this research as a student of the Mental Health PhD programme at Lancaster University, Lancaster, United Kingdom.

What is the study about?

This study aims to explore how treatment providers understand the role of Ibogaine treatment in helping people overcome addiction. The interviews will seek to explore:

- Practitioner responsibilities and background
- Treatment process and regime
- Ibogaine treatment details, perceived benefits and challenges
- Treatment longevity and post-treatment.

Why have I been approached?

You have been approached because the study requires information from people who are/have provided treatment with Ibogaine for addiction, independently or in clinics.

You would not be able to take part in the study if you are:

- Younger than 18 years old
- If your experience as a treatment provider in a clinic or independently is less than one year.
- If you are/were involved in treatment of conditions other than addiction.
- Not fluent in English (English speaking level less than intermediate).

Do I have to take part?

No. It is entirely up to you to decide whether you take part in the study. During the study, you will have the chance to pause or end the interview if you want. You can ask or email to withdraw your interview information during and up to two weeks after the interview.

What will I be asked to do if I take part?

Suppose you decide that you would like to participate; you will need to sign the consent form following this information sheet. In that case, you will be asked to complete a pre-interview survey about yourself (gender, age, country, experience level) and treatment provided (treatment process, number of clients treated, treatment setting, additional treatments, Ibogaine administration regime – dosage, timing, etc.). Then you would be asked to take part in an interview via Microsoft Teams video chat software (see below for privacy policy), which may take around 45 minutes. We will talk about the treatment process and details and your opinions about the treatment you have been providing.

Will my data be confidential?

All your data is confidential.

We will store a written transcription of the interview but with your name and any identifying details (e.g. Centre name) anonymised. Quotes from the interviews may be used in publishing the research, but they will not be linked to any individuals and/or treatment centres. We will remove any identifiable details and may change pronouns where appropriate.

The data collected for this study will be stored securely in secure cloud storage approved by the University, and only the research team conducting this study will have access to this data:

- The audio files and transcripts will be encrypted (that is, no one other than the research team will access them), and the University OneDrive itself will be password protected.
- Audio files will be deleted from the password-protected voice recorder as soon as they are transferred to the University OneDrive.
- Audio recordings and transcribed anonymised interviews will be kept securely in the University OneDrive until the research project has been examined.
- All your personal data will be confidential and will be kept separately from your interview responses.

There are some limits to confidentiality: If what is said in the interview makes me think that you, or someone else, are at noteworthy risk of harm, I will have to break confidentiality and contact the authorities. If possible, I will tell you if I must do this. Police authorities will be contacted for high-risk disclosures, such as intentional harm, false imprisonment, or unreported service user death.

What will happen to the results?

Findings of this study will be submitted to Lancaster University in the form of a PhD thesis and disseminated through presentations, poster presentations at related conferences, and, where appropriate, publication in a peer-reviewed journal.

Are there any risks?

There are no risks anticipated from participating in this study. If you experience distress following participation, please inform the researcher and contact the resources at the end of this sheet.

Are there any benefits to taking part?

There are no direct benefits in taking part; however, you may find participating interesting.

Who has reviewed the project?

This study has been reviewed and approved by the Faculty of Health and Medicine Research Ethics Committee at Lancaster University.

Where can I obtain further information about the study if I need it?

If you have any questions about the study, please contact the primary researcher:

Ahmet Enginsoy a.enginsoy@lancaster.ac.uk

Complaints

If you wish to make a complaint or raise concerns about any aspect of this study and do not want to speak to the researcher, you can contact:

Fiona Lobban: -

Title: Professor

Email: [f.lobban @lancaster.ac.uk](mailto:f.lobban@lancaster.ac.uk)

Faculty of Health and Medicine

Health Innovation One

Sir John Fisher Drive

Lancaster University

Lancaster

LA1 4AT

If you wish to speak to someone outside of the Mental Health Doctorate programme, you may also contact:

Dr Laura Machin:-

Chair of FHM REC

Tel: +44 (0)1524 594973

Email: l.machin@lancaster.ac.uk

Faculty of Health and Medicine (Lancaster Medical School)

Lancaster University

Lancaster

LA1 4YG

Thank you for taking the time to read this information sheet.

Resources in the event of distress

Should you feel distressed either due to taking part or in the future, the following resources may be of assistance.

Mindfulness meditation

Participants who feel slightly distressed by the interviews can use the following source for mindfulness meditation. It is widely known that mindfulness meditation helps to deal with negative feelings.

<https://www.mindful.org/mindfulness-meditation-anxiety/>

Mental health charities for further help

Additionally, below you can find a link to a list of international mental health charity hotlines to contact if further assistance is needed following the interview.

<https://www.thecalmzone.net/2019/10/international-mental-health-charities/>

M.S. Teams Privacy Policy

<https://docs.microsoft.com/en-us/microsoftteams/security-compliance-overview>

Appendix C4

Consent Sheet



Consent Form

Study Title: Addiction and Ibogaine Treatment Centres: An Exploratory Study with Practitioners

Before you consent to participate in the study, we ask that you read the participant information sheet and mark each box below with your initials if you agree. If you have any questions or queries before signing the consent form, please speak to the principal investigator, Ahmet Enginsoy (a.enginsoy@lancaster.ac.uk).

Please initial the box after each statement.

1. I confirm that I have read the information sheet and fully understand what is expected of me within this study.	
0. I confirm that I have had the opportunity to ask any questions and to have them answered.	
0. I understand that my interview will be audio-recorded and then made into an anonymised written transcript.	
0. I understand that audio recordings will be kept until the research project has been examined.	
0. I understand that my participation is voluntary and that I am free to withdraw from the interview without giving any reason.	
0. I understand that once my data have been anonymised and incorporated into themes, it might not be possible for it to be withdrawn two weeks after the interview.	
0. I understand an anonymised transcript will be made to extract my data, and all data will be latest destroyed 10 years after the upload date by the PhD candidate or supervisor.	
0. I understand that the information from my interview will be pooled with other participants' responses, anonymised and may be published; all reasonable steps will	

be taken to protect the anonymity of the participants involved in this project.	
0. I consent to anonymised information and quotations from my interview being used in reports, conferences and training events.	
0. I understand that the researcher may/will discuss data with their supervisor as needed.	
0. I understand that any information I give will remain confidential and anonymous unless it is thought that there is a risk of harm to myself or others, in which case the principal investigator will need to share this information with their research supervisor or police authorities.	
0. I consent to Lancaster University keeping written transcriptions of the interview for ten years after the study has finished.	
0. I consent to take part in the study.	

Name of Participant _____ Signature _____ Date _____

Name of Researcher _____ Signature _____ Date _____

Appendix C5
Pre-interview Survey

1 What is your gender?

- Male (4)
- Female (5)
- Other (6) _____
- Prefer not to say (7)

2 What is your age?

3 How would you describe yourself? Please select all that apply.

- White (1)
- Black or African American (2)
- American Indian or Alaska Native (3)
- Asian (4)
- Native Hawaiian or Pacific Islander (5)
- Other (6) _____

4 What is your Nationality?

5 What is your native language?

6 Do you speak more than one language fluently? Please list.

7 What is the highest degree or level of school you have completed?

- Less than a high school diploma (1)
- High school degree or equivalent (e.g. G.E.D.) (2)
- Some college, no degree (3)
- Associate degree (e.g. A.A., AS) (4)
- Bachelor's degree (e.g. B.A., BS) (5)
- Master's degree (e.g. M.A., MS, MEd) (6)
- Doctorate or professional degree (e.g. M.D., D.D.S., PhD) (7)

10 What is the title of your role?

11 How long have you been working in Ibogaine treatment? Answer in year and months please.

12 How long have you been working as an Ibogaine treatment provider? Answer in year and months, please.

13 How many patients have you treated throughout your practitioner experience?

14 How many clients do the treatment center host annually?

16 What is the form (TA, PTA, HCl, bark shavings, tincture etc.) and dose(s) of Ibogaine administered for addiction treatment?

17 How frequently is it administered (Please answer in X times a day, over Y many days)?

19 Do you offer other substances in conjunction or after Ibogaine administration? If Yes, please list the substances (E.g. diazepam, D.M.T. etc.)

20 Please describe the solution, dose, and frequency (Please answer in X times a day, over Y many days) of these substance(s).

20 Can you rate the adverse events below in below in terms likelihood? (1 least likely - 5 most likely).

_____ Cardiac Disorders (1-2-3-4-5)

_____ Triggering Psychosis (1-2-3-4-5)

_____ Aggression towards staff (1-2-3-4-5)

_____ Neurotoxicity (1-2-3-4-5)

_____ Respiratory Disorders (1-2-3-4-5)

_____ Other (Please specify) (1-2-3-4-5)

21 Can you rate the adverse events below in below in terms severity of impact? (1 least likely – 5 most severe).

_____ Cardiac Disorders (1-2-3-4-5)

_____ Triggering Psychosis (1-2-3-4-5)

_____ Aggression towards staff (1-2-3-4-5)

_____ Neurotoxicity (1-2-3-4-5)

_____ Respiratory Disorders (1-2-3-4-5)

_____ Other (Please specify) (1-2-3-4-5)

22 Do you provide counselling/psychological support/meditation? If yes, what? Please list.

24 Is there a safety protocol/ risk management protocol? It would be much appreciated if you can email it to a.enginsoy@lancaster.ac.uk or post a link below.

Appendix C6

Interview

Schedule

- My name is Ahmet Enginsoy; I am a PhD candidate at Lancaster University.
- These interviews aim to explore and describe the different treatment regimes and procedures, and analyse practitioner accounts to better understand the reasons behind the methods they administer Ibogaine treatment.
- This interview will take around 45 minutes.
- During the interview, you can ask me to stop or repeat a question anytime you want.
- During the interview, you can ask to quit the study any time you want.

Focus Area	Examples of questions and prompts
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Appendix C7:

Participant 5's example coded data

- R Well, wow. Oh, that's bad. I think that is very super bad. Uhm, yeah, you know when we had. The lag I put it on pause and didn't, oh that's bad. I will just continue with the interview and maybe try and capture overtime or briefly go through the things that we just talked. Now I know it I can just ask the questions, but I'll just continue and I'll come back to this later on. Sorry for that, that was lesson learned for me to not trust any device ever again. So I'm paranoid now will keep an eye on it anyway, so continuing with, why do treatment seekers choose Ibogaine treatment?
- P5 Uh, because well, especially for opioid users, it's the only drug in the world that allows you to skip part of the detox part of the withdrawal, which is quite miraculous. There's nothing else in the world that offers that, so I think that's a huge part of it. A lot of it is because people like myself have been through mainstream addiction treatment, which is incredibly traumatizing and ineffective for the most part. So Ibogaine is something that's kind of found after the mainstream things don't work, usually and also, unfortunately Ibogaine getting sold as this kind of like miracle magic pill thing, which is which it's not. It's kind of Ibogaine is a great door opener, but it's only the beginning of walking down the path of healing. The real work comes afterwards and so unfortunately it's being sold as like a cure quote unquote, which that word should never be used with Ibogaine, in my opinion, so that's a lot people come to it because they're looking for a miracle and it doesn't. **Ibogaine to me is the best treatment, but it's not a miracle cure so.**
- R Yeah, yeah, that was a great time so I I know you work with different clinics and I forgot to record some of that bit. But next question is about what happens after admission. Obviously I'm I'll formulate this question different for you. So when you work with a client, can you tell me how you prepare them and have they go through treatment?
- P5 How am I preparing people before they go to a clinic 'is that wahat you are asking?
- R Yep Yep Yep. And if you support them during their time in the clinic in any case.
- P5 Well, the first thing that I do when I'm working with people is I kind of evaluate what their systems of support are and what their daily life is like. So we start talking about how to set their life up for. Afterwards. We have healthy community around them. We start talking about like daily habits. Daily life patterns that are going to be healthy. So like a morning ritual. Making time to do things that are just enjoyable so it's not all about productivity, for example. Just setting up some like healthy practices you know with also exercise and things like that. So I like to start talking about that beforehand so it's not so overwhelming afterwards. We also, of course, discuss any fears or issues they're having with every treatment, 'cause it's quite nerve wracking. Before Ibogaine, you don't know what to expect and we start talking about. Goals and intentions for the process. Yeah, and another thing I do is I start to try and introduce these concepts of harm reduction before I begin because often people are quite traumatized by the philosophies of the 12 step program that tell you you have a disease and you're going to be sick forever and then you don't know any better and you have to just submit to some kind of

program. So often I I work with people to get away from this. I I try and support the goals. Uh, that each person has not. I don't push abstinence only. I support whatever people want to do, whether that be just reducing their drug use or only using certain drugs. And so we start off talking about that and and talking about what like what do they want, not what their family wants, not what society wants, but what they want for themselves, yeah, so yeah, a lot of what I'm doing is kind of like, uh, internal decolonization from oppressive system. Uh, because drug users get treated as second class human beings and so I start off working with people to help them feel connected to their own internal power rather than latching on to some external system.

R Yeah, and and then?

P5 During the treatment I stay in touch with people just to check in about any big emotional issues that coming up. Any kind of like overwhelming stress or worry that they have and. You know, usually they have some kind of support at the clinic, but I keep myself available in case anything comes up and then most of my sessions start really start after the treatments and and so then we're just working with the like emotional issues that are coming up any kind of memories that come up during Ibogaine, but also just dealing with the triggering things that are in family life. 'cause many people haven't even been existing in a daily basis without some kind of substance in their system. So like there's a flood of emotions that come after Ibogaine. So a lot of it is just about supporting people and processing that and supporting people in learning how to listen to their intuition and trusting that. Because a lot of us have thought to not trust their own. Intuition, so I'll just continue from where you mentioned and when when you deal with them after the treatment will look what is the program like then. That that's what I was just describing in the end after.

R OK OK OK but that makes perfect sense and and so I'll I'll just because I've kind of missed the recording. I will just ask you if you can just repeat the bit about the flood dosing versus low dosing, and if you just can keep it brief, I'll be happy so I don't trouble you with lots of additional details again.

P5 OK, so flood dosing is when there's one large dose given in a single night. How they administer the largest dippers plant clinic. But usually there's a small test dose that's giving in the beginning and maybe two or three more larger doses. Giving over a four ish hour period to get people to that completely gone fully immersed Ibogaine states. So usually if that's done in one night, that's a flood dose. Low dosing was something completely pioneered by Claire Wilkins at Pangea Biomedics. She came up with this procedure after seeing hospitalizations and deaths because of how dangerous split dosing instructor people and low dosing involves much smaller doses of Ibogaine given on a daily basis for two to five weeks, depending on what the person needs and what substances they're dealing with. The amount and frequency of the dosing depends on the person's EKG, blood pressure, pulse, and other health conditions and how they wrapped the medicine. So it's the very intensive process of monitoring the person for weeks, it's it's really. It's a stressful job to have to do this and and if someone coming off of opioid involved giving up. Morphine at one time of day. And then giving up again another time. Stay far enough away from each other that they don't conflict and gradually the morphine is lowered and the aggregate amount is raised until they slowly step off of it. The benefits of this

method is that people, unlike with the flood dose which renders you completely unable to move with low dosing. People can still go about their daily life and the the the medicine is still doing its work, so the lessons and insights are still coming up. But you're it's easier to integrate them because they're slowly coming up. It's it's much more gentle, and so the. The realizations that you get with the flood dose are it's? It's more gradual and it's. It's just a better way to integrate the experience. I see a much higher success rate in people going through low dose than the flood dose.

R I see great that that was a great answer. You summarized it perfectly. It makes me feel a lot better about it now. I mean, anyway I, I mean about losing recording. But like you know, like because you yeah, you did it justice. That was very good. Thank you. And just to pick up on the 5-meo-DMT side of things, you know in the survey you said that you are. You advise against psychedelics use after the experience? Or can you just repeat that again for me please?

P5 Yeah, no problem. So Ibogaine is the strongest psychedelic in the world. It's an incredibly jarring and exhausting and sometimes re traumatizing experience for people who've been through a lot of trauma. You do not need to take more psychedelics afterward, especially not other one. And there have been cases of hospitalizations and psychosis. Induced by 5 MEO DMT after Ibogaine there's also been 2 deaths that I know. One, from someone doing Ayahuasca a week after I -Ibogaine, it's just not necessary. I begin turns into Noribogaine your liver and Noribogaine stays in your system up to three months. Post Ibogaine and so there is enough work happening in your body with Ibogaine that you do not need to be adding other things and you do not need to be putting people mental stability at risk when it's can be often in a very fragile place. After Ibogaine, 5 MEO is quite violent in my opinion and that it rips you out of reality and those people back in in a matter of 10 to 15 minutes. I think if you know people may be giving a small there's some mushrooms a week after that would be much safer. Although I don't think that's necessary either. I think 5 or meet the really poor choice and it's really putting people's mental stability and mental health at risk and and also what they're going to say. Oh, and Gabon bwiti will tell you we keep practitioners will tell you. That after Iboga do not take other psychedelics for three years. So yeah, there's just there's. There's many reasons why it's a bad idea.

R You did that. Great summary again. Many thanks and again moving forward. What do you think about the role of Ibogaine in the context of treatment?

P5 Right?

R What is the role of Ibogaine in the context of Ibogaine treatment?

P5 Yeah. Yeah, for yeah for substance misuse or any kind of, you know addiction, addictive disorders. So I think that Ibogaine is one of the best tools we have but it is not a miracle cure. It's not cute, shouldn't even be used with this medicine. It's an amazing door opener, but it's only the beginning of walking down the path, appealing, and really the hardest work comes afterwards. So that's super important to keep in mind, but for me, after going through traditional rehab, methadone, Suboxone, foster programs, I began with above and beyond 100 times the better route for me, because it addresses the neurochemical imbalances that are the result from many years of drug use. Traditional rehab does not address the serotonin dopamine deficiency

issue. Whereas after Ibogaine, you feel like completely refreshed and renewed and inspired and connected to a purpose. You know, maybe, maybe not everybody has this complete experience, but most people that I work with have this experience of feeling reconnected to life. And I can tell you, after you get off opioids in our traditional detox. You do not feel excited about life. You do not feel inspired. I even six months later, if you manage to stay away from drugs, you still feel like shit. So this is the big shortcoming of traditional drug treatment is it does not. Yes, the neurochemical issues which I've been done, so I think it's an amazing tool, but it needs to be used in conjunction with long term follow-up support. Long term community support psychotherapy, somatic practices. It's it's a long journey, so I also don't want to settle this in a sensationalist way.

That is another great answer. Thank you and so what do you think about? I mean, you mentioned about the set about preparing people, but what do you think about the setting again in the context of treatment with Ibogaine.

P5 Yeah, the setting the setting is complicated and it varies a lot from place to place. You know there's clinics that completely resemble being a hospital. Full heart monitors ID bags crash cart which makes it super super safe but it makes it also very very sterile. Then on the other end of the spectrum. There's places like in, especially in Costa Rica, that claim to be. We keep practicing spaces and they offer it more in a retreat style with rituals and the traditional music that accompanies like Iboga ceremonies and all of that. I think that there's not just one right way to do it. I think that if you want to have the more traditional aspects, you have to also find a way for the medical aspects to be there to make it safe. So I think the halfway meeting point between that, like, maybe you can have some of the bwiti traditional aspects and the medical aspects. Or you know, maybe not even the Bwiti aspects. Maybe you're working just in a place in a supportive environment that feels comfortable, but that also does have an EKG machine and a heart monitor. For example, so I think kind of having a little bit of both sides of the spectrum involved is important. A lot of the clinics ferry hospital like and I personally would not want to do a psychedelic and then those kinds of scenes, although I also want the safety aspect, so it's about finding the halfway point in between.

R Yeah, so now I will ask you, I will. Ask you about the impacts that you observe in the people that you see before and after the treatment and that you do to follow up with. But before that, can you just rehash your background and have you involved in Ibogaine treatment and the impacts it had on new, so I can just tie it up to that first bid?

P5 Sure, so I was a heroin and opioid dependent person for seven years from when I was 20 to 27. I went through traditional rehab Suboxone methadone 12 step programs traditional detox and none of that was helpful or effective for me. So I found Ibogaine treatment in 2011 and although it completely worked for me and I never use opioids again, I also, the people treating me were not following clinical safety protocols whatsoever and I had the cardiac side effects associated with Ibogaine, which led to six cardiac arrests and two weeks on a pacemaker in an ICU in Guatemala City. So I woke up my treatment in a hospital, and so, although, I felt completely excited and inspired and connected to my passion, which I realized was working with drug users and Ibogaine treatment and my experience also made me very focused on safety protocols and the importance of that. Upon learning about the cardiac side

effects, but also very focused on the issues of dangerous and unstable practitioners that will ramp it in the community. So then I started working in clinics. I trained in three different Ibogaine clinics. After a while realized that wasn't completely my calling and so eventually evolved to be working in operation and integration with clients, but I also work supporting people who are arriving in providers as well because it's one of the most stressful, exhausting jobs of all time giving having treatment. So so yeah, I also work on. The safety issues in the community and supporting people who work with it.

R Yeah yeah, and I also just remembered that you were involved in receiving complaints and all, which I'm just saying for the record again, great stuff since we were talking about the challenges I'll actually take you to a different topic and ask you about the challenges that people experience when they're going through the treatment and again this is not about the clinics associated with you, but the wider clinics available worldwide.

P5 The challenges that people face often there is a complete lack of appropriate psychological support. Many of these clinics are run by people who have zero clinical mental health training and they have they don't know how to support people going through trauma. So a lot of people will call me saying that the clinic essentially just like left them alone, and maybe there was a nice pool or whatever, but there was no real consistent psychological support, so that's a big complaint and also most clinics don't offer like follow up support, they just send you home and say goodbye and which is part of the reason why I do the work I do 'cause I noticed that was a really big issue, so so that's another issue that happens, and then there's the issue of people feeling rushed into treatment when they don't feel completely safe or ready to do it like I was saying earlier about people with fentanyl in their systems. Often people are being pushed to do Ibogaine too soon before it's safe, and the client can feel that, and it makes them feel nervous and unsafe.

R Yeah yeah, that is great answer. And what about the challenges that treatment providers and practitioners experience?

P5 Yeah, well there's a lot with with working and being you're basically in charge of somebody's life for 24/7. While they're with you and people are coming in with years and years of trauma, they might project their issues onto you. They might get angry with you. They might say this didn't work. I want my money back. Uhm, I I've heard of clients trying to like to destroy clinics reputations because they didn't. 'cause their treatment didn't go how they wanted it to go. Uhm, there's also just the risk that a cardiac incident can happen at any time. A lot of the hospitalizations happen when a provider decides that they need a little bit of break to take a nap, and then something pops up when they're not looking so. You really need to have like a large, well trained staff and most clinics don't have that. Uhm, it's usually like a cluster of white men who have gotten off drugs themselves with Ibogaine decide that they have some kind of like special shamanic power to work with people when they actually don't, and they start working together in a clinic with no clinical training. No trauma training and zero idea of how to support women going through the process. Yeah, so we have probably I would say on average one Ibogaine provider in the community dies per year. Uhm, somebody just died a month ago because Ibogaine providers do not take care of themselves. There's relapses. There's many incidents of Ibogaine providers relapsing on their previous drug of choice and continuing to give

treatments, while they're high, that actually happens all the time. There's also providers that get super burnt out and end up. Crashing in a car and dying. That's what happened to my Ibogaine provider. Eventually there's been multiple car accidents with writers dying.

R Oh wow.

P5 Overdoses I it's. It's a really stressful job and you need to be able to know your boundary with when you need to take a break and because most Ibogaine providers are coming from a substance abuse background and they started working and Ibogaine treatment too soon after getting off drugs themselves, they have zero idea of how to take care of themselves. And how to have boundaries with themselves? They haven't worked on their own trauma, they have. They have no idea how to care for themselves in any real way, so they don't take enough breaks. They don't hire enough people on their staff, so there's a huge issue of burnout that leads to, you know, decimal providers, but it also leads to accidents with the clients as well.

R That is great, thank you and so I'll be moving on. I'm moving on to the more positive stuff and what are the main benefits and changes that you observe in people that you see before and after their treatment?

P5 Back to work day. Uh, one of the one of the main things that I see is before treatment. People are feeling super hopeless, super disconnected from their source from their passion. They feel a lot of guilt for what they've done. A lot of shame for where they are in their lives, and then after Ibogaine, suddenly people see their situation from a new perspective. They're able to see meaning and the difficult things that they've been through often people suddenly. Realize, Oh my gosh, I'm actually really passionate about doing this and I want to do this or I want to move and I want to go back to school and it kind of reinvigorates people and connects them to like a source of like passionate inspiration. It's it's actually it's quite rewarding to do this work with people because I'm constantly seeing these 180 degree transformations come in just a couple of days, so yeah, that's one of the main things where I see, and of course for opioid users, people are always amazed that they aren't sick after Ibogaine. In generally people skip around 70 to 80% of opioid withdrawal. they might have some residual stuff, but most of the time people are super excited that they don't have to go through the withdrawal afterwards. That's another big benefit. And yeah, I had mostly

R So just actually, yeah. I was going to ask whilst you were mentioning about opioid and all that stuff. And what about non chemical addictions? Do you work with people who have may have eating disorders or gambling etc.

P5 Yeah, people do like being for all different reasons, not just addictions. Also from PTSD and depression. I also see people like that who are able to look at their circumstances from a completely new perspective who also find like a new source of inspiration and motivation after Ibogaine and also I just want to mention sometimes these beneficial effects don't kick in immediately. Sometimes it takes a few weeks for people to get to this place. It kind of really depends upon the person. But yeah, I, I think probably when I was working in clinics, probably 50% of the people I worked with were not even substance dependency. It was other mental health issues.

- R I see can you give me a bit of an example? What kind of mental health issues were they?
- P5 PTSD trauma depression usually.
- R OK great, I'm moving on so would you say that? Would you think that they are in it?
- P5 Oh, I just want to like that. OK. Short, yeah. I just want to. Say hey I have to go. In 5 minutes I'll let you know.
- R Sure, OK, cool I'll, I'll ask them. The significant important question, which is, what do you think the future of Ibogaine treatment will be?
- P5 Uh, you know I, I really don't know, uh, we're kind of at a dangerous point in the psychedelic therapy world where there's a lot of excitement and urgency around it. A lot of sensationalization of the benefits, and not enough focus on the risks and you can see. So I'm kind of concerned about what the direction I begin is going in. A lot of people are really into this clinical trial aspect. I personally feel very concerned about live again being put into the medical system in the United States because we have a terrible medical system that's racist, it's financially inaccessible zero understanding of spiritual psychic issues so. I don't know I'm I'm. I think that we're going to just see. The issues that we have in the Community. We kind of. Uhm, enhanced. Once we bring it into more of the mainstream place, yeah. My focus personally is making the underground slash international. I think even community safer and and that hopefully that will bleed into the above ground community in the United States. Once that happens, if it does happen, I don't know the future of Ivy treatment. Kind of depends on the legislative stuff that's being worked on right?
- R I see and just something I've got like little time to ask this. Do you think there are any factors that help people undergoing hypergate treatment and their treatment outcomes? Why is that factor or factors?
- P5 The first factor is that people are doing it of their their own decision 100% with no coercion and no pressure from family members or loved ones. It has to be completely just the decision of the person has to be their motivation and their initiative to do. But one of the big things is I have moms calling me all the time saying my son needs treatment right now and it. It's like, wait a minute it's not gonna work. This is incredibly hard work. You have to be ready and willing to do it and work hard if you're doing it for someone else. It's not gonna work out, so it it has to be completely up to the person I the the people that I see most accessible have already been doing work on themselves with therapists and with other modality needs. Before Ibogaine treatment.
- P5 The people that come in who are been on like vendors for a few weeks before going to Ivy and they generally have a harder time because they have no idea how to sit and be present with themselves and how to actually put in the work on themselves. That I begin requires so it takes a good amount of readiness and also what I see as being beneficial is people who really just feel like they're tired of drug use, you know? So like before I went to treatment I had, I was living somewhere where I had unlimited access to opioids and I got to the point where it wasn't enjoyable at all. In fact, it was really depressing, so it was kind of like I squeezed opioids dry until there was nothing good left to come out and I was just over it. Ready to move on? That's when

Ibogaine works the best. If somebody is still kind of like you know, drawn to whatever drugs they're doing in some kind of way, they'll usually go back to the drugs that they were using and so they're tired a bit. So it really works best when you're over it.

R That is great. Thank you very much, I'm I'm done. I mean, I've got. I don't know how much I can on the record. Is there anything you would like to ask? I'm happy to answer via email if you don't have the time.

P5 Uhm, I can't dig anything right now. If there's anything that that got missed or lost in the time sthat didn't get recorded like I'm happy to jump on a call again later on.

R Oh yeah, that that would be great. If there's anything, I'll let you know, but I think I've captured quite well. Well, going to brag (anxious laugh). Thank you very much again

P5. It's been, it's been really, really, really helpful you you gave like such a different perspective. What I've been hearing so far and it's really, really insightful. Thank you very much.

P5 Yeah, I really want. I really want to encourage you to talk to as many women as possible in the Community because we have mostly men speaking up and and the safest people working in the Community are women and the men generally have a very macho szymonik conflict.

R Yes, yes, you're correct.

P5 Very egotistical place that they're working from, so I'm going to send you the name of a lot of women working in the community for you so that you could have a a properly represented study results here.

R That will be amazing.Yeah, yeah, and the perspective is so different. What I've been hearing from you, amazing, thank you very much again

P5 this is great. Have a good day.

R No problem. You too bye.

P5 Bye bye.