Clinical Psychedelic Research in Adolescents: Scoping Review and Overview of Ethical Considerations

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Conflicts of Interest Statements:

- KR, KC, JH, NL, EW, IS, MTA, FF have no conflict of interest to declare.
- BDE and DBY are directors of HOPE: The Hub at Oxford for Psychedelic Ethics, which has received an anonymous donation to support conference travel support for under-represented scholars. BDE and DBY do not personally receive any funds in relation to co-directing HOPE.
- EJ receives funding from the Wellcome Trust (award 221152/Z/20/Z)
- DBY receives funding for psychedelic-related research from the National Institute of Health (NCCIH), Steven and Alexandra Cohen Foundation, and Heffter Research Institute.
- IS receives funding from the Wellcome Trust (award 203132/Z/16/Z), National Institute for Health and Care Research (NIHR), and Oxford Health Biomedical Research Centre (award NIHR203316).
- LB received a small honorarium from the Psychedelic Safety Institute for guidance on harm reduction.
- JS is a Bioethics Committee consultant for Bayer and a Bioethics Advisor to the Hevolution Foundation (2022 to present)

Authors' Contributions:

Khaleel Rajwani, Edward Jacobs, Brian D. Earp, Lori Bruce, Elisha Waldman, and Jamila Hokanson conceptualized the original Viewpoint article. Khaleel Rajwani drafted the initial manuscript, integrated critical feedback into the working manuscript, and edited the final revised version. Edward Jacobs and Brian D. Earp contributed to the ongoing development of the article and reviewed initial, working, and final revised manuscripts. Lori Bruce, Elisha Waldman, Jamila Hokanson, Katherine Cheung, Neil Levy, Julian Savulescu, Ilina Singh, and David B. Yaden participated in critical revisions, editing, and proofreading of the manuscript. Khaleel, Edward and Brian revised the manuscript in response to peer-reviewer feedback.

After editorial review, Khaleel Rajwani and Brian D. Earp assembled the research team for developing, executing and integrating the scoping review. Khaleel Rajwani developed the initial outline of the scoping review protocol and provided direction to team members. Melanie T. Almonte, and Faisal Feroz reviewed, edited, and formatted the study protocol and offered strategic guidance on methods, resources, software, and data visualization. Brian D. Earp, Jamila Hokanson, Edward Jacobs, David B. Yaden, Julian Savulescu, and Ilina Singh offered critical feedback during the development of the study protocol. Melanie T. Almonte and Faisal Feroz executed the review,

with Brian D. Earp resolving discrepancies. Melanie consolidated the review results into summaries and tables. Khaleel Rajwani integrated the findings of the scoping review into the revised manuscript.
All authors participated in minor revisions and critical feedback of the revised drafts. All authors approved the final version for submission. All authors attest to their contributions and confirm no others meeting authorship criteria were omitted.

Abstract:

The use of psychedelic-assisted therapies to treat adolescents with mental illnesses has recently generated interest and concern among mental health professionals, researchers, and ethicists. Modern clinical psychedelic research has focused on adults, and adolescents under 18 are routinely excluded due to regulatory, legal, and ethical challenges. Although some historical literature has been critically discussed, it was unclear if any clinical research in the 21st century included adolescents. To address this gap, we conducted a scoping review of clinical studies involving psychedelic drug administration to adolescents under 18 globally from 2000 to 2025. Our review identified 3 clinical trial registrations and 1 trial plan including participants under 18; no studies were completed or published. Reporting of ethical approval and recruitment status was inconsistent. The proposed trials investigated MDMA or psilocybin, delivered with psychotherapy or cognitive behavioural therapy, for adolescents with PTSD, autism with social anxiety, or self-harm. We hold that this lack of research indicates a critical evidence gap that will impede informed clinical decision-making.

We offer an overview of the ethical issues that emerge when contemplating the translation of psychedelic therapy research into adolescent contexts. Many medications are prescribed to adolescents despite limited clinical trials, and if psychedelics are approved as medicines, they may be used off-label in adolescent healthcare. This raises ethical questions about whether and how psychedelics should be studied in this population before clinical use. We argue that addressing this gap requires carefully designed studies, beginning with older adolescents facing special circumstances (e.g. terminal illness) to minimize risk while building essential knowledge about mechanisms of action, benefits, and harms. Given the pressing need for effective interventions for difficult-to-treat and treatment-resistant adolescent mental illness, and the risks of proceeding without adequate research, careful investigation of psychedelic-assisted therapies in this population should be considered, alongside robust ethical debate.

Clinical Psychedelic Research in Adolescents: Scoping Review and Overview of Ethical Considerations

The prospect of using psychedelic-assisted therapies to treat adolescents experiencing mental illnesses has recently generated both interest and concern among mental health professionals, researchers, and ethicists.[i] Many medications are prescribed to adolescents despite limited clinical trials, and if psychedelics are approved as medicines, they will likely be used off-label in adolescent healthcare; this raises ethical questions about whether and how psychedelics should be scientifically studied in this population before clinical use.

Table 1: *Scope of Terminology*

Scope of "Psychedelics"
We use the term psychedelics to refer to classic psychedelics, defined as substances that are partial agonists of 5-HT2A receptors which frequently give rise to altered states of consciousness, including changes to affect, cognition, and perception. Notable examples include psilocybin, mescaline, Lysergic acid diethylamide (LSD), and N,N-Dimethyltryptamine (DMT). In our use of the term we also include 3,4-Methylenedioxymethamphetamine (MDMA), which may not meet strict historical pharmacological criteria, but can interact with 5HT2A receptors and is generally included within biomedical psychedelic discourse today. Although many of the ethical considerations we raise likely will apply to a broader set of non-classic psychedelic substances such as ketamine, ibogaine, and cannabis, which can frequently generate altered states of consciousness, we recognize the ways that these substances can differ from classic psychedelics in their pharmacological mechanisms of action, sociocultural contexts of use, and acute subjective effects.
Scope of "Adolescent"
We use the term adolescent to refer to individuals on the spectrum of development between puberty and adulthood. This can fall within a broad chronological age range of 10-24 years, and which individuals are included within the adolescent category is context dependent. Most modern clinical psychedelic research has focused on the treatment of adults, and the preclusion of adolescents under the age of 18 has become a standardized exclusion criterion for psychedelic research in the 21st century. We believe that a cautious approach to adolescent psychedelic research would initially proceed with certain adolescents aged 16 and 17; those whose unique circumstances imply a high net benefit-to-harm ratio. However, we note the critical importance of individual, social, cultural, and legal context rather than strict age limits in making determinations about research inclusion, clinical care, and informed consent.

[i] For discussion on the scope of terminology see Figure 1

Biomedical literature suggests the efficacy of psychedelic-assisted therapies for improving clinical outcomes in some adults experiencing treatment-resistant mental illnesses, such as depression and substance use disorders.[1] Although most modern clinical psychedelic research has focused on the treatment of adults, clinicians and researchers have begun to identify contexts where psychedelic therapies could serve as potentially effective tools for addressing the mental health needs of some adolescents.[2–4] These potential applications include post-traumatic stress disorder (PTSD), difficult-to-treat or treatment-resistant depression and anxiety, refractory obsessive-compulsive disorder, and eating disorders, all conditions that often carry significant morbidity and mortality.[5–9] Psychedelic-assisted therapies could also serve as a potential tool to address existential distress among adolescents related to serious illnesses and terminal diagnoses.[10,11] However, the preclusion of adolescents under the age of 18 has become a standardized exclusion criterion for psychedelic research in the 21st century.[2,3]

Given the global mental health crisis among youth, which has been exacerbated by the COVID-19 pandemic, and the need for safe and effective treatments, some have called for adolescent inclusion in psychedelic therapy research, while highlighting the need for caution, careful evaluation of risks and adverse effects, and robust ethical inquiry.[3]

It is notable that there have been substantial ethical concerns about psychedelic research in adults, including concerns related to study design (including blinding practices and methodologies), underreporting of adverse events, short follow-up periods, expectations about treatments (including hype), and generalizability of findings (including lack of representation of indigenous peoples and ethnic minorities).[12,13] The ethics of psychedelic research in adolescents cannot be considered in a vacuum without paying considerable attention to these broader issues in the field; however, in what follows we focus on the additional ethical concerns that arise if adolescents are included in research.

Clinical Psychedelic Research Involving Adolescents: A Scoping Review of Intervention Studies

While modern clinical psychedelic therapy research has focused on adult populations, adolescents under 18 are routinely excluded from studies due to regulatory, legal, and ethical challenges. Despite growing interest in the intersection of adolescent mental health and psychedelic therapy, it is unclear whether any controlled clinical research has been conducted with adolescents in the 21st century. To address this gap in the literature, we conducted a scoping review of clinical studies involving psychedelic drug administration, including psychedelic-assisted therapy, in adolescent populations.

There exist some observational data and controlled psychedelic research from 1959 to 1974, primarily focusing on the use of LSD to treat children and adolescents with mental illnesses. However, these historical studies do not meet contemporary scientific and ethical standards.[2,4] Major concerns from critical reviewers included bias, inconsistent or invalid psychometric measurements, limited therapeutic options, misreporting of neutral or negative findings, and the absence of standardized ethical principles and regulations for drug research involving human subjects.[4,14] Thus,

our review focused on identifying clinical research in the 21st century, which roughly coincides with the so-called "renaissance" in clinical psychedelic research in Western biomedicine.[15]

Although our review focused on interventions involving classic psychedelics (See table 1) it is important to note that some contemporary research into non-classic psychedelic treatments for adolescents experiencing mental illness is underway. For example, several clinical trials are currently investigating the safety, efficacy, and trajectory of ketamine as a treatment for adolescents with major depressive disorder (MDD) and suicidal ideation.[16]

Summary of Methods

The scoping review followed PRISMA-ScR guidelines, and the study protocol was preregistered.[17,18] The Population, Intervention, Comparator, Outcomes and Study Design (PICOS) framework was pre-specified (Table S1) to include intervention studies that involved the administration of a classic psychedelic to adolescents (aged ≥ 10 to ≤ 17 years) in a clinical setting. Studies were eligible if they included a wider age range, children through to adults, as long as the inclusion age-range also covered adolescents aged 10 – 17 years. A classic psychedelic in this review was defined as a psychoactive substance whose pharmacological mechanism of action primarily involves serotonergic pathways or activation of the 5-HT2A receptor within [18]three classes: tryptamines, phenethylamines, and lysergamides.[19,20] Thus, studies of substances that did not meet these criteria (e.g., ketamine, ibogaine, salvia, scopolamine, cannabis) were excluded. Peer-reviewed publications and grey literature, including clinical trial registrations and study protocols, were included. The combination of variations of keywords was searched in titles and abstracts including "adolescents", "psychedelic", "intervention", and "clinical", adapted to each database (Tables S2 and S3). Searches were limited to studies written in English.

We searched each database for studies registered or published from January 1st, 2000, to April 1st, 2025. By limiting the search from 2000 onwards, we excluded psychedelic research conducted on children before widespread prohibition on psychedelic research as these studies have already been discussed and critically reviewed.[4 17] We extracted data on study characteristics, recruitment status, participant inclusion/exclusion criteria, interventions, and comparators (Table S6). Detailed definitions, database selections, eligibility criteria and data extraction methods are provided in the scoping review protocol.[18]

Summary of Results [ii]

We identified 2335 records through database search and 44 through clinical trial registries. After duplicates were excluded, we screened 1666 titles and abstracts (Figure 1). Of these, 7 full-text records were reviewed. Three were excluded, leaving 4 studies to be included. A list of records excluded at full-text screening (Table S4) and records included (Tables S5 and S6) are provided in the supplementary tables.

[ii] See Table 2

Of the 4 included studies (Table 2), 3 are clinical trial registrations,[21–23] only 1 of which made their full study protocol available on the clinical trial registration platform.[22] The remaining study is an abstract that reported details of a planned clinical trial.[24] All four studies were registered since 2022. Studies were registered in three jurisdictions: USA, UK, and Australia.

The studies target a diverse population of adolescents ranging from those diagnosed with autism and social anxiety (ages 16 – 25)[21], self-harm (ages 16 – 25)[22], and PTSD (ages 16 – 17)[23] and (ages 7 – 17)[24]. The studies investigate two psychedelic drugs: MDMA[21,23,24] and psilocybin[22] delivered alongside psychotherapy or cognitive behavioural therapy, and include comparison to placebo controls in 3 of 4 studies. All studies are in early stages — two are not yet recruiting[21,22], one was withdrawn due to FDA review[23] and one did not report its status [24]. Study designs varied in their target sample size, ranging from 10 to 156 participants, and in their follow-up periods, from 3 to 12 months. Reporting of ethical approval status is inconsistent across studies: one study was reported as pending approval [21], and the status of the remaining three is unknown.

Discussion

Our scoping review affirmed our initial hypothesis that no clinical intervention studies involving psychedelic therapies have been completed in adolescent populations since 2000. Of the 4 clinical trials that have been registered, it could not be confirmed if any have received ethical approval by relevant institutions or proceeded to recruitment. Ultimately our findings suggest that, to date, adolescents under 18 have been excluded from modern clinical psychedelic research globally. Thus, there exists an expansive gap in clinical knowledge regarding how psychedelic interventions would affect adolescents, as we could find no completed studies in this domain.

The review also supported our contention that there is growing interest among clinicians and researchers in using psychedelic-assisted therapeutic interventions to treat adolescent mental illnesses including PTSD, autism with social anxiety, and self-harm, particularly in the age range of 16-17 years. Notably, MDMA-assisted psychotherapy represented the primary intervention in 3 of 4 registered studies included. MDMA-assisted psychotherapy may continue to be a proposed intervention for early adolescent psychedelic therapy research, particularly in jurisdictions such as Australia where the intervention has already been approved for clinical use in adults with certain diagnoses.

Understanding the Safety and Efficacy of Psychedelic Use in Adolescence

It is unknown whether findings from psychedelic research in adults will apply to adolescents. Adolescents are not simply "small adults," and adolescent mental healthcare demands distinct biophysiological and psychosocial considerations. Differences in physiological, cognitive, emotional, and social development may impact psychedelic pharmacokinetics and neurophenomenology, and

may lead to significant differences in clinical outcomes and adverse effects.[2] Furthermore, adolescents may experience limited autonomy within family dynamics and the broader social contexts within which psychedelic therapies take place.[25] Adolescents may have less ability to select, avoid, or modify salient aspects of their social environment which can not only compromise improvements fostered by the treatment, but can amplify the potential for harm when adolescents return to suboptimal environments in a heightened state of sensitivity and vulnerability after their psychedelic experiences.[25,26] However, a family-centered approach to adolescent psychedelic therapy can leverage pre-screening assessments, family resources, psychoeducation, and targeted caregiver support in ways that can improve trajectories and healing outcomes for adolescent participants.[25] Researchers have argued that mature adolescents can possess the requisite emotional regulation and self-awareness and occupy stable social environments, which are essential for the positive integration of psychedelic experiences.[27] Thus, sufficiently mature adolescents within supportive environments could stand to benefit from psychedelic experiences in similar ways to their adult counterparts. [iii]

A recent observational study investigated the psychological effects of psychedelic use in adolescents, pooling self-reported survey data from one day, two weeks, and four weeks after self-initiated planned psychedelic experiences.[2] Researchers found that older adolescents (age 20.4 ± 2.2 years) and adults (36.5 ± 9.7 years) experienced "equivalent improvements in psychological wellbeing and secondary measures related to mental health, such as depression, suicidality, self-esteem, and emotional stability."[2] However, subjective experiences of ego-dissolution were found to be less beneficial among older adolescents than among adults, suggesting "age-related differences in the mediational role of ego-dissolution on subsequent mental health outcomes."[2] The older adolescents reported higher mean scores on the Challenging Experiences Questionnaire, a validated instrument that measures difficult psychological aspects of psychedelic experiences across seven dimensions: grief, fear, death, insanity, isolation, physical distress, and paranoia (22.3 ± 17.2; 95% CI: 20.97–23.6 compared with adults: 18.0 ± 15.7; 95% CI: 16.8–19.2). They also reported a higher prevalence of adverse effects four weeks after the experience, including visuo-perceptual alterations and symptoms of hallucinogen-persisting perception disorder (50% compared with 22.4% of adults).[2] The authors argued that the preliminary evidence implied favorable results for safety and efficacy, with "some elevated risk for psychedelic-use in populations under the age of 25."[2] The adolescents within this study were older (age 20.4 ± 2.2 years), more likely to be male (76.1%), and had previous experience with psychedelics and other substances (96.8%). These characteristics may minimize the degree to which they encounter challenging experiences compared to younger adolescents or otherwise influence the generalizability of their outcomes to younger adolescents. Other researchers have suggested that whereas the reported difficulty of psychedelic experiences tends to be correlated with positive outcomes on well-being in adults, challenging psychedelic experiences in adolescence may impact trajectories of cognitive and social development, which heightens psychological risks.[27]

[iii] Definitions of "sufficient" maturity can vary widely in context, and clinicians should use validated capacity assessment tools that apply within their medical, social, legal contexts.

Within the limited literature on the effects of psychedelic use in adolescence, there is a consensus that additional observational and controlled research on safety and efficacy is needed, given "our limited understanding of the differential effects of psychedelic use during critical periods of development."[2]

The Need for Adolescent Drug Research

Due to practical, ethical, and commercial concerns, few medicines are tested on adolescents in clinical trials before receiving regulatory approval.[28–31] Adolescent clinical drug trials may be prohibitively expensive for commercial interests with limited capital, and may be perceived as too risky by cautious researchers and ethicists – particularly as the threshold of "minimal risk" is often applied to paediatric research.[32] However, there are initiatives by regulatory bodies like the European Medicines Agency and the Federal Drug Administration to counteract this tendency.[33]

A significant amount of drug prescription in child and adolescent psychiatry occurs off-label, and research confirms the need to generate safety data for drugs prescribed off-label in paediatric care.[28–30,34] Although off-label prescription may be efficacious and evidence-based, increased access to psychiatric medications only tested in adults has led to safety concerns and clinical ethical issues in paediatric contexts.[28,31] Additionally, psychiatric drug trials in paediatric populations have sometimes been criticized on scientific and ethical grounds; for example, initial trials of selective serotonin reuptake inhibitors (SSRIs) in paediatric contexts gave rise to allegations of methodological limitations, selective reporting of efficacy outcomes, and misrepresentation of treatment-emergent suicidal events.[35,36] While subsequent research, including comprehensive meta-analyses, has helped clarify many safety questions, debates about optimal SSRI use in adolescents continue as off-label prescription rises. This trajectory highlights the importance of robust initial research in paediatric populations to avoid similar patterns of uncertainty with new therapeutic approaches.[37,38]

While researchers, ethicists, and regulators reasonably seek to protect adolescents from immediate risks and adverse effects related to clinical trials, adolescents seeking clinical care may encounter long-term harms including lack of age-specific dose and safety data, and lack of effective medications for many mental illnesses.[28] Given this context there is an ethical imperative to responsibly research the tolerability, safety profile, efficacy, and real-world effectiveness of psychedelic-assisted therapies before they are potentially made available to adolescents in clinical settings.

Major Ethical Considerations

Many ethical issues emerge when contemplating the translation of psychedelic therapy research into adolescent contexts. Except for a few early contributions, there has been little coordinated bioethics work to develop general principles for ethically assessing proposed psychedelic research in

adolescent contexts.[2,3,27,39] We offer an overview of important ethical considerations for proposed psychedelic research in adolescent contexts.

Relative Risk Profile of Psychedelic-Assisted Therapies

Unaddressed psychopathology during adolescence can lead to persisting functional impairment and lifelong mental health challenges.[40] When considering psychedelic research in adolescents, researchers must assess the risk profile of psychedelic-assisted therapies relative to available pharmacotherapies, standards of care, and burdens of untreated, difficult-to-treat, or treatment-resistant mental illnesses in adolescent populations.

Classic psychedelics have a substantially more favourable risk profile than previously believed.[41,42] While they carry important risks, including the potential for acute psychological distress and challenging experiences, psychedelics are considered to be physiologically non-toxic even at high doses, and are not generally considered drugs of dependence.[42,43] Psychedelic research, particularly in clinical contexts shows a low incidence of serious adverse effects, but psychedelic use can trigger long-term adverse effects such as derealization and depersonalization.[41–44] In a study of 608 adults with post-trip difficulties, in "approximately one-third of the participants, problems persisted for over a year, and for a sixth, they endured for more than three years."[43] Further, psychedelics can worsen pre-existing symptomology; for example they may alleviate anxiety or PTSD or bring on personal meaning, but they may also precipitate anxiety or PTSD symptoms, or "plunge [users] into existential confusion."[43,44] Similarly, evidence finds that psychiatric medications currently prescribed to adolescents may provide relief, but may also pose significant health risks. For example, SSRIs may reduce suicidality and psychiatric symptoms, or increase the likelihood of suicidality and precipitate short- and long-term adverse effects.[35,36] Evidence for the efficacy of SSRIs for the treatment of MDD remains open to interpretation and critcism.[29,35,36,45] However, researchers and clinicians continue to investigate SSRIs in adolescent populations, for instance to understand which individuals are more likely to experience benefits versus harms. Thus, psychedelic research has similarities with current adolescent drug research in terms of both positive and negative prospective outcomes and should not be exceptionally stigmatized or rejected.[46] Although psychedelic therapies have distinctive features that need to be considered, treating them as fundamentally unique or exceptional compared to other medical treatments may impede the application of established ethical and evidentiary standards that help ensure rigorous, responsible clinical research.[46]

There is also a clear need for safe and effective interventions for adolescents experiencing treatment-resistant mental illnesses. For example, nearly 40% of adolescents remain depressed after initial treatment, and roughly one third of adolescents with MDD will not improve with standard care treatments involving medication and psychotherapy.[47] As in adult contexts, treatment-resistant MDD in adolescents may present an appropriate target for initial psychedelic therapy research, as MDD is associated with significant morbidity and mortality, and effective treatments are urgently needed.[28,47]

Psychedelic Drug Use in Adolescence

Clinicians, researchers, and ethicists must account for the risks of using psychedelic drugs at earlier stages of physiological, cognitive, and social development. Currently, these risks are largely unknown – a fact which must be disclosed in informed consent practices with adolescents and their parents. Clinical psychedelic studies to date have included participants aged 18 to 24 who represent various stages of physiological, cognitive, and social development; since this group includes older adolescents, they could provide a starting point for understanding the effects of psychedelics during later periods of adolescence. However, even if psychedelic therapy involves risks of developmental harms, we should first consider research in cases where the ethical tradeoffs are less ambiguous – for example in older adolescents receiving palliative end-of-life care, where alleviating existential distress is paramount, and longer-term developmental concerns are less applicable. Or, as has occurred in existing research[2], beginning research with those who would otherwise use psychedelics recreationally or socially. Preliminary research ought to be conducted on adolescent populations with the least to lose and most to gain. This is a "harm reduction" approach (see below).

As more evidence on developmental risk becomes available, researchers and ethicists can better account for these in their assessment of proposed research. However**,** the possibility of unknown risks of psychedelic use during adolescence is not a complete argument against investigating safety and therapeutic potential in adolescent participants. Assessing the specific context of each study proposal, instead of accepting fixed age limits, provides a more flexible approach to investigating the potential benefits and risks of psychedelic therapies for adolescents with serious unmet healthcare needs and limited treatment options.

Autonomy and Consent

While capacity varies widely with age and maturity, adolescent participants may be capable decision-makers with sufficient autonomy to give informed consent, especially with parental support. Adolescents weigh risks and benefits in their everyday decisions, including choices about personal drug use, sexual activity, transportation, and sports – and may be held criminally liable for their actions.[48] In healthcare contexts, capable adolescents make decisions about treatments that have substantial short- and long-term risks and benefits, such as in the cases of cancer treatments and abortion. Research has shown that clinical competency assessments for paediatric psychiatric treatment and hospitalization may be passed as early as 12 years of age.[49] However, principles and policies governing the competency of adolescents to make healthcare decisions can vary significantly across jurisdictions and contexts (e.g. Gillick competence in England and Wales and the mature minor doctrine in the United States of America).

Although psychedelic-assisted therapies may involve effects and experiences that are difficult to communicate or appreciate beforehand, capable adolescents can engage in "enhanced" informed

consent conversations that address the particular risk-benefit profile of psychedelic therapies and the potential for challenging and transformative experiences.[3] In many cases, shared decision making supports the autonomy of adolescents by involving parents and healthcare providers, helping tailor decisions towards participant goals and preferences through consensus-building. [31] A precautionary approach to adolescent psychedelic research should first involve the oldest and most competent adolescents and may progress to younger age bands as the safety profile becomes better established.

The Adolescent "Matrix"

In psychedelic medicine, the "matrix" refers to the multifaceted psychosocial ecosystem to which a participant returns after a psychedelic experience.[50] Relative to typical adults, adolescent participants may have limited autonomy and agency within their social contexts. As in adults, heightened neural plasticity immediately following psychedelic experiences may render adolescents more susceptible to environmental influences -both harmful and beneficial- though adolescents' ability to shape or distance themselves from adverse environmental influences remains constrained. Everyday living space, parental attachment, family functioning, and peer influences count among the features of the environment known to influence mental health treatment trajectories in adolescence.[25] Given the plasticity-enhancing quality of psychedelics, this socioecological context must be considered when determining whether an adolescent is a suitable candidate for a psychedelic-assisted intervention and strategizing about post-experience integration.

Harm Reduction

Adolescents often lack access to appropriate healthcare, leading some to self-medicate by using drugs like MDMA to cope with negative life experiences including trauma, emotional distress, social stigma, discrimination, and stress.[51] However, self-medication and unsupervised use carries serious risks, such as the cross-contamination of street drug supplies with synthetic opioids like fentanyl, which has contributed to the rise in fatal opioid overdoses globally.[52] Additionally, due to criminalization, young people using psychedelic drugs – especially racialized youth – face severe consequences including police violence, imprisonment, and exclusion from school or work, which often have negative impacts on their mental and physical health and social well-being.[53]

The principles of harm reduction support observational studies of current adolescent users of psychedelic drugs to gain awareness of benefits and harms of psychedelics within a naturalistic setting. The harms of unsupervised adolescent psychedelic use may also be mitigated through expanded access to supervised clinical research, which may include participants with a history of psychedelic drug use outside of clinical settings.

Power Dynamics in Psychedelic Caregiving

The power differential between adolescent participants and adult therapists in psychedelic contexts may be significantly amplified compared to adult participants and therapists. Adolescent contexts warrant a higher degree of precaution, for example when considering therapeutic touch. It might be preferable, where practicable, to offer adolescents the opportunity to have a trusted figure present during psychedelic experiences, while ensuring they can refuse this opportunity without repercussions.[54] The presence of a close friend or relative in the therapeutic environment could increase trust, support, safety, and ethical accountability in adolescent care contexts.[54] However, this remains a matter of ethical debate, as in some cases a companion could change therapeutic dynamics by introducing stigma or interpersonal conflict within the healing space.[54]

Social Stigma & Privacy

Adolescents may have different privacy concerns surrounding psychedelic therapy than adults. Young people experience stigma associated with both mental illness and drug use. Parents may denounce or stigmatize psychedelic-assisted therapy for adolescents.[39] For instance, parents surveyed about MDMA-assisted therapy for adolescents initially expressed concerns about MDMA's negative stigma as a dangerous party drug, and believed adolescent use of MDMA should be avoided at all costs, even for therapeutic purposes.[39] However, parental views shifted positively after education and engaged conversation.[39]

The informed consent process should ensure that family expectations, stigma, and judgement around psychedelic drug use are addressed through conversation and education; family support is essential to post-experience integration. Clinicians should discuss confidentiality rights that are relevant to the adolescent and convey empathy and nonjudgement regarding the choice to participate in psychedelic therapy.

Conclusion

If psychedelics are approved as medications, they may be used off-label in adolescent populations before adolescent clinical trials are conducted; other medications have historically followed this trajectory. Including adolescents in cautious, well-designed studies with sound clinical rationale is a critical part of generating knowledge about the potential benefits and harms of adolescent psychedelic therapy. Considering the possibility that psychedelic-assisted therapies may improve mental health and reduce the suffering of adolescents experiencing difficult-to-treat and treatment-resistant mental illnesses, this research should be considered. Researchers must disclose the unknowns associated with adolescent outcomes given the dearth of adolescent studies, the potential for higher rates of challenging experiences and long-term adverse events, and other potential heightened risks in adolescent populations – and comprehensive support must be offered to those who do suffer long-term adverse effects. Research should commence on those with the least to lose – those with terminal clinical conditions and those who would otherwise use psychedelics recreationally. If adolescent psychedelic research begins, bioethical inquiry and interdisciplinary

dialogue between clinicians, researchers, ethicists, adolescents, parents, and other stakeholders will be essential.

Table 3: Summary of Ethical Concerns in Adolescent Research involving Psychedelics

Ethical Concerns	Key Insights
⇒ Many medications are prescribed to adolescents despite limited clinical trials, and if psychedelics are approved as medicines they will likely be used off-label in adolescent healthcare	⇒ Research on the safety and efficacy of psychedelic-assisted therapies for adolescents should be conducted responsibly before they are made clinically available
⇒ There is a clear need for safe and effective interventions for adolescents experiencing difficult-to-treat and treatment-resistant mental illnesses	⇒ The risks of psychedelic-assisted therapies should be compared to existing therapies, standards of care, and the impact of untreated mental illnesses in adolescence
⇒ There are known and unknown risks related to psychedelic use in adolescence, including developmental risks and higher rates of adverse effects and challenging experiences than in adults	⇒ Preliminary adolescent psychedelic research should be conducted on populations with the highest benefit-to-harm ratio ⇒ Comprehensive support should be offered to adolescent research subjects who do suffer adverse effects
⇒ Adolescent participants may have limited autonomy and agency within their medical and social contexts compared to their adult counterparts	⇒ Capable adolescents can make autonomous decisions and provide valid consent or assent to participate in research, especially with parental support ⇒ The socioecological context must be considered when determining whether an adolescent is a suitable candidate for a psychedelic-assisted therapy ⇒ Informed consent practices should address family support, stigma, and judgment about drug use through education and engaged conversation
⇒ Self-medication and unsupervised psychedelic use by adolescents carry serious risks	⇒ Harm reduction principles support observational studies of adolescent users of psychedelic drugs as well as expanded access to supervised clinical research
⇒ The power imbalance between adult therapists and adolescent participants in psychedelic therapy may be greater than with adult participants, increasing the potential for abuse	⇒ Adolescent contexts warrant a higher degree of precaution, for example when considering therapeutic touch ⇒ The option to include a close friend or relative in the therapeutic environment could increase trust, support, safety, and ethical accountability in adolescent care contexts

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