Drug-Centered or Drug-Assisted? Epistemic Perspectives and Methodological Tensions in Psychedelic Psychotherapy

Karen Yan*, Christina Ni, Yun-Ying Kuo, Mu-Hong Chen

The first and corresponding author: Karen Yan, karenyan@nycu.edu.tw

Abstract

This paper distinguishes the drug-centered view of psychedelics (DCP) and the drug-assisted view of psychedelics (DAP). While these approaches differ conceptually, both rely on the methodology of evidence-based medicine, using randomized controlled trials to validate therapeutic efficacy. Using MDMA-assisted psychotherapy as a case study of DAP, we reconstruct the causal reasoning underlying its proposed therapeutic effects, identify two key causal assumptions, and critically examine them. Our analysis shows that the DAP community's reliance on evidence-based medicine is not merely methodological, but also reflects questionable epistemological assumptions inherited from the empirically supported therapy tradition. We conclude by proposing value-based practice as a complementary methodology better suited to the relational and value-laden dimensions of DAP.

Keywords: psychotherapy, psychedelic-assisted psychotherapy, evidence-based medicine, value-based practice, empirically supported therapies, randomized controlled trials

1. Introduction

Psychedelic-assisted psychotherapy is a new[1] form of therapy currently under a heated debate in both clinical and bioethics contexts. This includes debates about the necessity of subjective experience for therapeutic efficacy (Olson 2020; Yaden & Griffiths 2020), ethical concerns about patient vulnerability and autonomy during altered states (Villiger & Trachsel 2023; Barber & Dike 2023; Jacobs 2023), and calls for specialized ethical frameworks and regulatory oversight (Poppe & Repantis 2024; Villiger 2024). Additional discussions focus on the professionalization

[1] The therapeutic exploration of psychedelics has undergone significant transformation since its early days. Between the 1920s and 1960s, psychiatrists conducted experimental research with psychedelic compounds, investigating their potential therapeutic applications (Langlitz, 2021, pp. 26-30). However, this early experimental framework differed significantly from contemporary biomedical research protocols. One major factor is that the FDA established the structured clinical trial phases (Phase I-IV) and mandated drug manufacturers to prove safety and efficacy through well-controlled studies before market approval via the Kefauver–Harris Amendment in 1962. This significantly changes how researchers design psychedelic therapy or psychotherapy. We thus call our research target psychedelic-assisted psychotherapy as a new form of therapy based on how it is designed and validated under a contemporary experimental context.

of psychedelic therapy and the training of therapists (Kinahan & Wilson 2025), sociocultural critiques of medicalization and cultural appropriation (Langlitz & Gearin 2024), and warnings against premature clinical adoption without sufficient empirical grounding or safeguards (Barnett, Mauney & King 2025).

This paper addresses the question of which clinical methodologies are best suited to evaluate the epistemic and ethical dimensions of psychedelic-assisted psychotherapy. In Section 2, we will clarify the ambiguity regarding psychedelic-assisted (psycho)therapy and psychedelic drug therapy/treatment. The ambiguity is sharpened by introducing a contrast between the drug-centered view of psychedelics (DCP) and the drug-assisted view of psychedelics (DAP). Our goal is to examine how psychedelic-assisted psychotherapy is evaluated and methodologically framed within clinical research, particularly under the constraints of evidence-based medicine.[2] We use the clinical trial for ketamine treatment as the case study for DCP and the clinical trial for MDMA-assisted psychotherapy as the case study for DAP.

Section 3 examines evidence-based medicine (EBM) as the clinical methodology used to implement both DCP and DAP, and introduces value-based practice as a contrasting framework. While DCP and DAP differ in their epistemic commitments, both are typically operationalized through EBM—particularly via randomized controlled trials. We show how this methodological alignment creates different constraints for DCP and DAP, setting the stage for the puzzles explored in Section 4.

Section 4 identifies two puzzles that arise when DAP proponents follow EBM methodology. These two puzzles concern how they justify the causal efficacy of manualized psychotherapy in MDMA-assisted psychotherapy. We will reconstruct the causal reasoning underpinning this therapeutic model, identify two key causal assumptions, and critically examine them.

Section 5 traces DAP proponents' methodological preference for EBM methodology in part to epistemological assumptions inherent from the empirically-supported therapy tradition. We will also review proposed strategies for addressing the limitations of this framework.

Section 6 motivates another strategy using value-based practice methodology. This approach conceptualizes psychotherapy practice as an interactional, interpersonal, relational, and narrative process. We will show how value-based practice methodology can be used to collect value-related structural information that supports the analyses of recurrent patterns or long-term outcomes, offering an alternative methodological pathway for developing DAP.

2. The Crossroad between the Drug-Centered and Drug-Assisted Views

[2] Although our analysis intersects with concerns raised in the evidential pluralism literature—particularly regarding the limitations of rigid hierarchies of evidence—we do not aim to contribute to that broader debate, especially as it pertains to pharmaceutical regulation. Our focus remains on the clinical context of psychedelic-assisted psychotherapy and the epistemic and ethical tensions that arise when value-laden, relational therapeutic processes are constrained by the interventionist logic of EBM. For a regulatory-focused critique of evidential pluralism—emphasizing the risk of mechanistic evidence being misused under institutional pressures—see Sung and Holman (2023). For a pluralist philosophical critique of evidence hierarchies themselves, and a proposal to abandon them in favor of more context-sensitive, multi-dimensional evaluation tools, see Stegenga (2014).

Psychedelics refer to a diverse group of chemical compounds, including tryptamines (e.g., psilocybin), ergolines (e.g., LSD), and phenethylamines (e.g., mescaline), which are commonly associated with altered states of consciousness and often act on serotonin receptors such as 5-HT2A. While their pharmacological profiles are increasingly well-documented (Kelmendi et al. 2022), the nature and role of their subjective effects remain an active area of philosophical and clinical debate.

The therapeutic potential of psychedelics is the central focus of the recent revival of psychedelic research since the late 1990s. Kurtz et al. (2022) have examined all registered clinical trials on psychedelics from the clinicaltrials.gov database. From their selected 105 clinical trials, they showed that all of them were conducted between 2007 and 2020, and 71% of them started in 2017 or later. This indicates that the surge in psychedelic clinical trials has taken place within just the past decade. Phase 1 (53.3%) or phase 2 (25.7%) clinical trials on psychedelics are the majority of 105 clinical trials, and the most common mental health issues to address are substance addiction, post-traumatic stress disorder, and major depressive disorder.

Within this recent research boom, technical terms such as 'psychedelic therapy', 'psychedelic treatment', and 'psychedelic-assisted psychotherapy' are frequently used to label the intervention under investigation. However, these terms reflect more than semantic variation; they signal underlying differences in how researchers conceptualize what the key research target is. What, precisely, does "psychedelic-assisted" mean in psychedelic-assisted psychotherapy? Are there significant epistemic differences between psychedelic treatment and psychedelic-assisted psychotherapy?

To clarify these questions, we introduce a conceptual distinction between two contrasting views: the drug-centered view of psychedelics and the drug-assisted view of psychedelics. These views do not in themselves specify experimental methods. Rather, they reflect epistemic perspectives—background beliefs about what should be investigated as the therapeutic mechanism. These perspectives help guide how researchers formulate hypotheses, define causal variables, and design clinical studies.

Researchers who adopt the drug-centered view argue that the therapeutic potential of psychedelics is best explained by their pharmacological properties alone; the subjective or hallucinogenic experience they induce is considered incidental, or even unnecessary, for achieving clinical benefits (Olson 2020). In contrast, proponents of the drug-assisted view contend that the primary function of the drug is to facilitate a psychotherapeutic process—namely, that therapeutic efficacy arises from the interaction between the drug-induced experience and therapeutic engagement (Mithoefer et al. 2017).[3] To clarify this distinction, we offer the following characterizations:

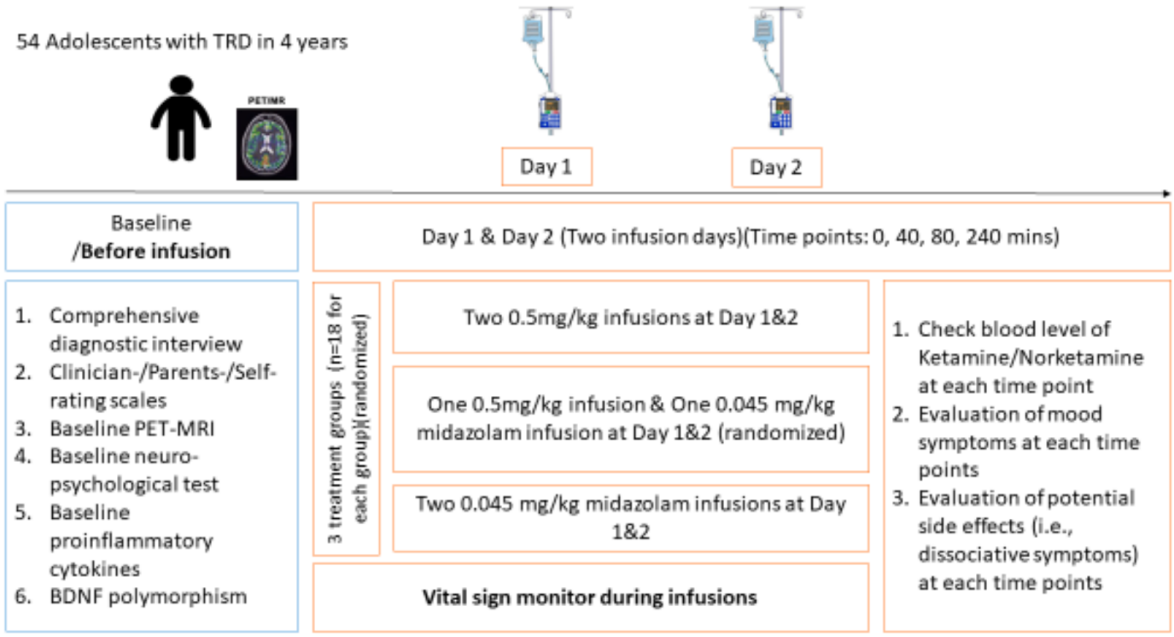
[3] It is worth noting that while some philosophers have begun exploring the role of mystical experience in therapeutic or epistemic change (Letheby 2021; Pedersen and Steglich-Petersen 2024), our distinction is methodological rather than metaphysical. We stipulate DCP and DAP based on their function in experimental design—what is being intervened upon and measured—without committing to specific theories of experience. For instance, the Esketamine nasal spray protocol aims to minimize hallucinogenic experience, reinforcing DCP. In DAP trials like MDMA-

[Drug-centered view of psychedelics, DCP] The psychedelic drug is the primary causal variable to be experimentally manipulated in order to generate evidence of therapeutic effects.

[Drug-assisted view of psychedelics, DAP] The relationship between the subject's drug-induced experience and the therapist's interaction is the primary causal variable to be manipulated in order to generate evidence of therapeutic effects.

These views can be further illustrated by how they guide researchers in choosing and designing experimental methodologies—most often, randomized controlled trials (RCTs). We now turn to two case studies: a ketamine RCT as a case of DCP, and a MDMA-assisted psychotherapy trial as a case of DAP.

The ketamine trial follows a standard double-blind, placebo-controlled RCT protocol with three phases: preparation (baseline), dosing (Days 1–2), and post-dosing (Days 3–28) (Figures 1 & 2). The psychedelic drug (ketamine) is the sole variable of interest; the aim is to isolate and measure its therapeutic effects. This is a clear operationalization of the DCP perspective: the drug is treated as the intervention, and there are no components of psychotherapeutic interaction.



assisted psychotherapy, by contrast, subjects' subjective reports—whether mystical or not—are interpreted within a psychotherapeutic frame, shaped through dialogue, meaning-making, and interpersonal dynamics. Therapists are not intervening on experience content per se, but rather engaging with it as it emerges in the therapeutic context.

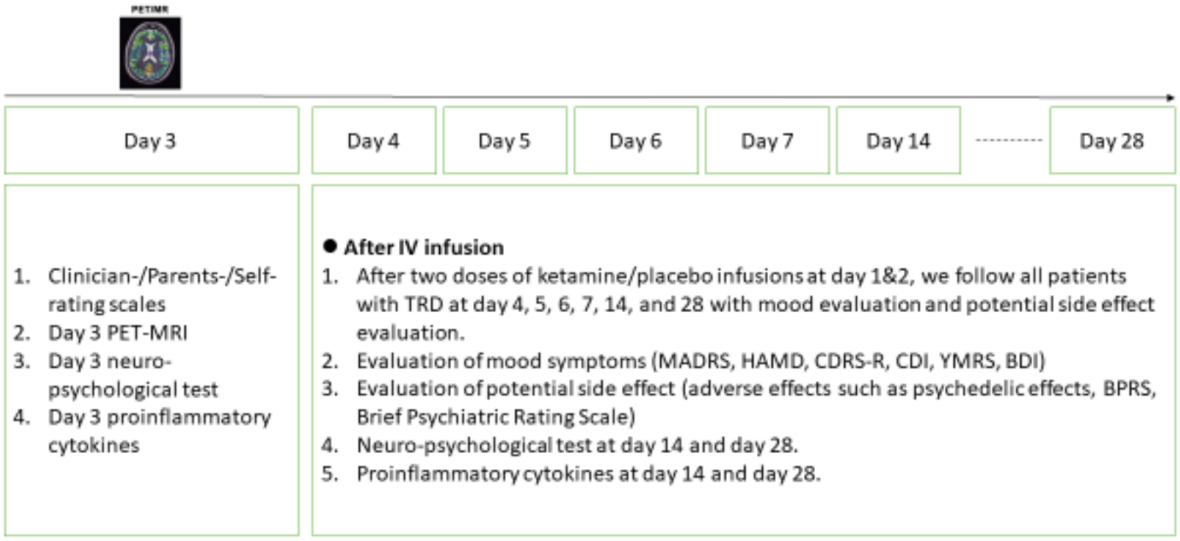


Figure 1. The Experimental Design and Protocol of Low-Dose Ketamine Infusion among Adolescents with Treatment-Resistant Depression

A structural description:

A functional description:

- Prepare patients + collect data for analysis and evaluation
- Administer psychedelics substance
- Collect data for analysis and evaluation

Figure 2. The Structural and Functional Descriptions of How the Drug-Centered View of Psychedelics is Operationalized

In contrast, the trial conducted by Mitchell et al. (2023) provides a case study for DAP. This RCT tested manualized MDMA-assisted psychotherapy for moderate to severe PTSD, following a protocol developed by the Multidisciplinary Association for Psychedelic Studies.[4][5] The intervention involved multiple psychotherapy sessions paired with MDMA administration (Figures 3 & 4).

[4] The detail of this clinical trial can be assessed here: https://clinicaltrials.gov/study/NCT04077437

[5] It is interesting to note that, in Mitchell et al.'s (2023) published article in Nature Medicine, the term 'MDMA-Assisted Psychotherapy' is never used, but only "MDMA-Assisted Therapy' and no explanation is provided as to why there is such an inconsistency in the titles between the registered clinical trial and the publication.

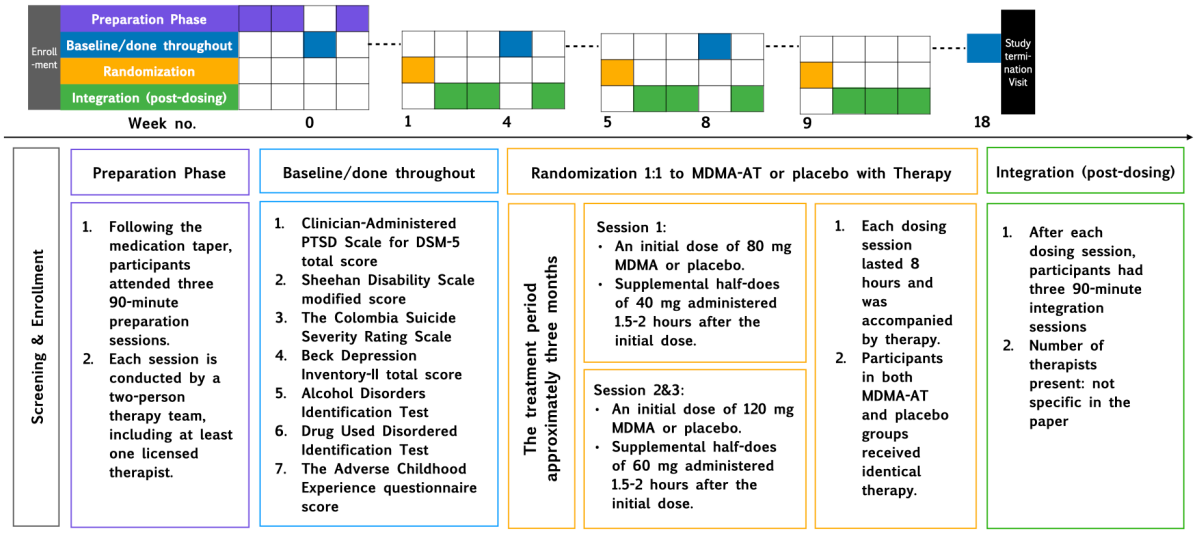
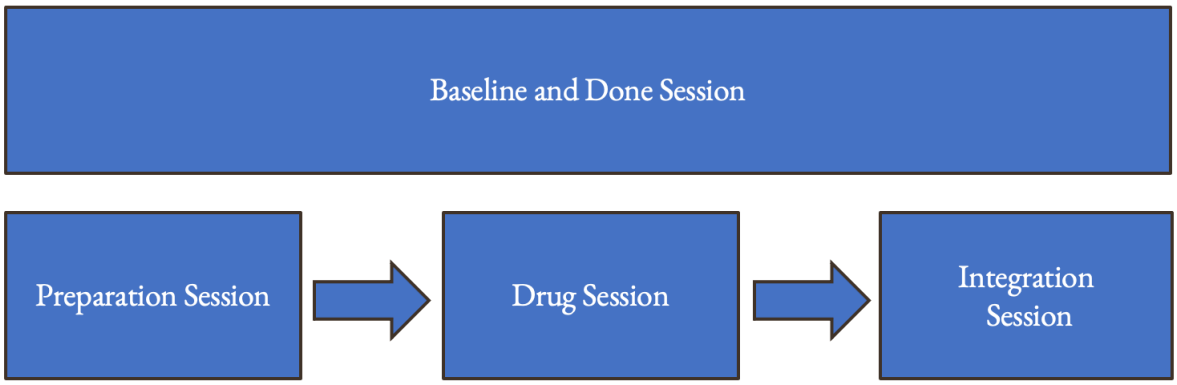


Figure 3. The Experimental Design and Protocol of Mitchell et al. (2023)

A structural description:



A functional description:

- Prepare patients
- Administer psychedelics substance + Applying *Manual for MDMA-Assisted Psychotherapy in the Treatment of Posttraumatic Stress Disorder*
- Applying *Manual for MDMA-Assisted Psychotherapy in the Treatment of Posttraumatic Stress Disorder*
- Collecting data for analysis and evaluation

Figure 4. The Structural and Functional Descriptions of How the Drug-Assisted View of Psychedelics is Operationalized

Structurally, this trial consists of four phases: preparation (informed consent, screening), dosing (3 MDMA sessions), integration/post-dosing (9 psychotherapy sessions), and final assessment. The therapeutic mechanism is not attributed to the drug alone, but to how MDMA catalyzes a

therapeutic process involving trust, emotional openness, and trauma processing in a structured psychotherapeutic context. This aligns with the DAP perspective: the causal target is a relational process enabled—but not exhausted—by pharmacological effects.

Notably, in both instances, the selected RCT design functions as a methodological expression of the epistemic commitments underlying DCP and DAP. That is, researchers use RCTs to investigate what they take to be the relevant therapeutic mechanism—whether a discrete drug effect (DCP) or a relational drug-assisted interaction (DAP). In Section 4, we will show how this alignment becomes problematic: although DAP conceptualizes the therapeutic target as an interaction, the trial design often fails to treat that interaction as a manipulable or testable variable.

To further clarify the structure of our analysis, it is important to distinguish between epistemic perspectives and methodological frameworks. DCP and DAP represent epistemic perspectives—that is, assumptions about what should be investigated and what counts as causally relevant. In contrast, evidence-based medicine and value-based practice serve as methodological frameworks that determine how such investigations are carried out.

In the next section, we explore how both DCP and DAP are operationalized within the methodological framework of evidence-based medicine, and examine the consequences of this alignment—especially for the relational assumptions embedded in DAP. We also briefly introduce value-based practice as a complementary framework to be discussed in more depth later.

3. Evidence-Based Medicine and the Epistemic Commitments of DCP and DAP

In the previous section, we introduced DCP and DAP as two distinct epistemic perspectives: background assumptions about what should be considered the therapeutic target in psychedelic research. In this section, we examine the clinical methodology most commonly used to operationalize both perspectives—evidence-based medicine (EBM). Although these epistemic perspectives differ in how they conceptualize therapeutic change, both DCP and DAP are typically implemented within the evidentiary and evaluative framework of EBM. We also briefly introduce value-based practice as a contrasting methodology, which we return to in Section 6 as a possible complement to the limitations of EBM in modeling the relational structure of DAP.

EBM is often described as a paradigm shift in clinical medicine, emphasizing the use of systematically gathered evidence to guide healthcare decisions. It operates according to a formal hierarchy of evidence, with systematic reviews and meta-analyses of randomized controlled trials (RCTs) at the top, followed by RCTs themselves, observational studies, and finally expert opinion (Reiss and Ankeny 2016; Chao and Kao 2023). While EBM acknowledges the relevance of practitioner expertise and patient preferences, in practice, its institutional emphasis falls heavily on the production of RCT-based evidence. This emphasis reflects an interventionist logic: to identify causal effects, the methodology privileges trials that isolate variables, randomize assignment, and control for potential confounders.

This structure aligns naturally with DCP, which conceptualizes the psychedelic drug as a discrete intervention to be isolated and tested. RCTs are well-suited to this approach because they aim to quantify the direct causal effects of a pharmacological agent on clinical outcomes. By contrast, DAP defines the therapeutic mechanism not as a drug effect per se, but as a dynamic interaction between the drug-induced experience and psychotherapeutic engagement. This relational ontology presents significant methodological challenges: it is difficult to isolate, manipulate, or test interactions within the framework of an RCT that treats psychotherapy as a background constant. Nevertheless, DAP studies often rely on EBM conventions in order to establish clinical legitimacy, leading to a potential misalignment between epistemic commitments and methodological tools.

To better understand this tension, it is helpful to examine broader philosophical critiques of EBM. Worrall (2007) questioned the privileged status of RCTs, arguing that while randomization effectively controls for selection bias, it does not eliminate all forms of confounding or guarantee epistemic superiority. Larroulet Philippi (2022) defends randomization's value but cautions against rigid hierarchies, emphasizing that high-quality observational studies can also yield reliable causal claims. Jukola (2015) adds that EBM's formal hierarchy often overlooks how institutional factors—such as publication bias and commercial influence—distort the evidence base. Similarly, Ghomi and Stegenga (2025) demonstrate, through modeling and simulations, that clinical experience can sometimes offer reliable causal insight, especially when placebo effects are minimal. These critiques suggest that the epistemic foundations of EBM are more context-sensitive and contingent than often acknowledged.

While our project does not aim to contribute directly to ongoing philosophical debates about the structure of evidence across all domains of medicine, we acknowledge that alternative frameworks—such as the Russo–Williamson thesis, which advocates combining mechanistic and probabilistic evidence—offer promising avenues for evidential pluralism (Russo and Williamson 2007; Parkkinen et al. 2018). Our focus is more domain-specific: we aim to show how standard EBM frameworks may be ill-suited to capturing the relational and value-laden dynamics central to psychedelic-assisted psychotherapy, and to motivate complementary methodologies tailored to this context.

This body of work highlights the importance of attending not only to the internal mechanics of trial design, but also to the fit between methodology and epistemic target. In the context of psychedelic-assisted psychotherapy, where therapeutic efficacy may be shaped by subjective, interpersonal, and value-laden processes, the limitations of EBM become particularly pronounced. RCTs may struggle to capture the complexity of these relational interactions—despite being used in DAP research precisely to evaluate them.

These considerations motivate the need for methodological alternatives that can better accommodate the relational and dynamic nature of DAP. One such alternative is value-based practice (VBP), a clinical framework that emphasizes stakeholder values, contextual meaning, and narrative structure in guiding care. In Section 6, we return to VBP as a complementary methodology—one that offers tools for empirically modeling value-laden dimensions of psychotherapy that are often invisible within the EBM framework.

4. Puzzles regarding MDMA-Assisted Psychotherapy

This section examines two methodological puzzles that emerge when DAP researchers adopt RCTs with manualized psychotherapy—an approach that may be poorly suited to capturing the relational dynamics they aim to validate.

To clarify the conceptual structure: the drug-centered view (DCP) and the drug-assisted view (DAP) are epistemic perspectives—that is, background beliefs about what the therapeutic target is and what mechanisms ought to be investigated. These perspectives shape how researchers define the object of inquiry: what variable or relationship is treated as causally central in psychedelic therapy. In contrast, RCTs—especially those using manualized psychotherapy—constitute a methodological framework typically aligned with the DCP perspective, and they create important tensions when used to operationalize the relational assumptions of DAP.

This distinction sets the stage for the first puzzle. DAP posits that therapeutic benefits arise from the interaction between a subject's drug-induced experience and therapeutic engagement. However, the clinical trial conducted by Mitchell et al. (2023)—the most prominent RCT supporting MDMA-assisted psychotherapy—does not treat this interaction as a manipulable variable. Instead, the psychotherapy component is held fixed across conditions, treated as a controlled background element.

The first puzzle is this: if DAP implies that clinical trials should intervene on the relationship between drug effects and therapist engagement, why does Mitchell et al.'s trial design hold this component constant? The manualized psychotherapy protocol is applied identically in both the experimental and control groups, and the published report provides no account of how this therapeutic element is experimentally manipulated. The result is that a study framed around DAP ends up operationalizing assumptions consistent with DCP.

Since Mitchell et al. (2023) treat the manualized psychotherapy component as a controlled variable, their reasoning appears to follow this structure:

(1) The experimental group receives: MDMA + manualized psychotherapy
(2) The control group receives: Placebo + manualized psychotherapy
(3) The outcome comparison assesses whether MDMA-assisted psychotherapy significantly outperforms manualized psychotherapy alone

This reasoning presupposes that manualized psychotherapy is essential, but it is not itself subject to experimental manipulation. As a result, the contribution of psychotherapy can only be inferred indirectly and is never directly tested.

This leads to the second puzzle: what assumptions are necessary to infer a causal role for manualized psychotherapy, and how might those assumptions be justified? Let us start with the perspective of the Multidisciplinary Association for Psychedelic Studies (MAPS), the organization that developed the manualized psychotherapy used in Mitchell et al.'s (2023) trial. In their treatment manual, MAPS states:

> [T]he MDMA-assisted psychotherapy being studied in these clinical trials, involves developing drugs that will *catalyze the therapeutic process* when used in conjunction with psychotherapy…(Mithoefer et al. 2017, Section 1.1, emphases added)

They continue:

> The foundation for this therapeutic approach was laid by Stan and Christina Grof, Leo Zeff, George Greer and Requa Tolbert, Ralph Metzner, and many others...*The basic premise of this treatment approach is that the therapeutic effect is not due simply to the physiological effects of the medicine; rather, it is the result of an interaction between the effects of the medicine, the therapeutic setting and the mindsets of the participant and the therapists*. MDMA produces an experience that appears to temporarily reduce fear…, increase the range of positive emotions toward self and others, and increase interpersonal trust without clouding the sensorium or inhibiting access to emotions. *MDMA may catalyze therapeutic processing by allowing participants to stay emotionally engaged while revisiting traumatic experiences without being overwhelmed by anxiety or other painful emotions.* Frequently, participants are able to experience and express fear, anger, and grief as part of the therapeutic process with less likelihood of either feeling overwhelmed by these emotions or of avoiding them by dissociation or emotional numbing. In addition, *MDMA can enable a heightened state of empathic rapport that facilitates the therapeutic process… and allows for a corrective experience of secure attachment and collaboration with the therapists*. At some point during the MDMA experience, feelings of empathy, love, and deep appreciation often emerge in conjunction with a clearer perspective of the trauma as a past event and a heightened awareness of the support and safety that exist in the present. (Mithoefer et al. 2017, Section 1.2, emphases added)

From these descriptions, we can extract two implicit causal assumptions:

> (C1) Therapeutic effects of MDMA-assisted psychotherapy arise not from MDMA alone, but from an interaction involving the drug's effects, the therapeutic setting, and the mindsets of both the participant and the therapists.

> (C2) There is a causal relationship between MDMA's drug effect and how the therapeutic process unfolds in a specific way, i.e., MDMA catalyzes the therapeutic process by putting subjects in suitable emotional states to revisit traumatic experiences, being collaborative and attached to therapists, and so on.

Given these two causal assumptions, it seems that the causal role of MAPS's manualized psychotherapy is indirectly inferred by the following reasoning:

(1) MDMA-assisted psychotherapy significantly outperforms MAPS's manualized psychotherapy alone, established by the results from Mitchell et al. (2023)
(2) The therapeutic effect does not stem from MDMA alone (per C1)
(3) Therefore, the observed outcome must be explained by C2
(4) Hence, MAPS's manualized psychotherapy plays a necessary and primary causal role in producing the observed outcomes.

However, this inference structure is vulnerable to several challenges:

First, one might question whether C2 is the only or best explanation for the empirical findings. It is possible that MDMA itself accounts for the observed outcomes, independent of any psychotherapeutic interaction. MDMA's known effects on serotonin, dopamine, and oxytocin might directly alleviate PTSD symptoms such as hyperarousal and emotional numbing. If so, the results might reflect pharmacological action alone, not a drug-assisted interaction.

Second, even if MAPS is correct that psychotherapy is necessary (C1), this claim remains untested. To substantiate it, one would need trials comparing MDMA alone to MDMA with psychotherapy. Yet MAPS has not conducted such studies. Without this comparison, the necessity of psychotherapy remains an assumption, not an established empirical result.

Third, one might question whether MDMA plays a unique causal role in shaping how therapy unfolds (C2). To evaluate this, MAPS would need to compare MDMA-assisted psychotherapy to the same psychotherapy combined with other substances (e.g., ketamine or psilocybin). If similar therapeutic dynamics emerge, then MDMA's role might not be unique, weakening the case for its specific causal contribution.

Finally, MAPS's manualized psychotherapy should also be tested on its own—without MDMA—to determine whether it has independent therapeutic effects. This would clarify whether MDMA merely enhances an already effective therapy, or whether the therapy itself is ineffective without pharmacological support.

In short, the core puzzles stem from a disconnect between DAP's epistemic commitments and the methodological design of the trials meant to operationalize it. Proponents of MDMA-assisted psychotherapy claim that its therapeutic effects result from an interaction between drug and psychotherapy, but the design used to validate this claim does not test that interaction directly. Instead, the RCT treats psychotherapy as a background constant, leaving a crucial component of the hypothesis unexamined.

These puzzles lead to a deeper question: why has the field adhered so closely to the RCT method, despite their apparent misalignment with DAP's relational ontology? Part of the answer lies in the broader institutional and epistemological influence of EBM, which has prioritized RCTs as the default standard for clinical evaluation. While this framework has clear strengths—particularly in contexts where discrete interventions and outcome measures are well defined—it also tends to favor methodologies that align with pharmacological models of causation. As a result, even when researchers endorse DAP, their investigations are often structured according to evidentiary norms that may be better suited to drug-centered interventions. This is not to suggest

that RCTs are inappropriate in all cases, but rather that their dominance may limit the methodological tools available to study therapies grounded in relational, experiential, or context-sensitive processes.

This raises a pressing philosophical and practical question: must EBM remain the exclusive standard for evaluating psychedelic-assisted psychotherapy, or should alternative methodologies be considered? In the next section, we examine whether the assumptions inherited from EBM—and, more specifically, from the empirically supported treatment (EST) tradition—are well-suited to the distinctive challenges posed by psychedelic therapies. We also explore whether methodologies like value-based practice might complement existing approaches by offering tools better suited to capturing relational and value-sensitive dimensions of care.

5. Rethinking Psychotherapy's Evidence Standards: From EST Assumptions to Methodological Alternatives

One may wonder, if, as we have shown, the RCTs for MDMA-assisted psychotherapy are difficult to design, conduct, and justify, why do researchers continue to invest so much effort and resources into such trials? We suggest that this is partly due to the influence of the EBM framework that has come to dominate psychotherapy research over the past several decades. While a range of historical and institutional forces likely contributed to this development—including shifts in healthcare regulation, pressures for standardization, and the appeal of biomedical legitimacy—we focus here on one particularly visible milestone: the 1995 publication of the Task Force on Psychological Intervention Guidelines (Westen, Novotny, and Thompson-Brenner 2004, 632). This report helped formalize the concept of "empirically-supported therapy" (EST) (Kendall 1998), which was framed around the RCT methodology. Though not the sole driver of change, the report played a significant role in institutionalizing the assumption that RCTs are the gold standard for psychotherapy research. This move was widely seen as a way to elevate the empirical credibility of psychotherapy, bringing it into epistemic alignment with pharmacological research.

More precisely, this framework rests on an institutionalized assumption—reinforced by influential initiatives such as the 1995 APA Task Force Report—that RCTs are the default route for establishing empirical credibility in psychotherapy. This assumption not only privileges one form of evidence but also encourages a conflation between what is empirically unvalidated and what is empirically invalid. In other words, if a therapy has not yet been tested—or cannot easily be tested—via RCT methodology, it is often treated as if it has already failed an empirical test. This conflation collapses the distinction between absence of evidence and evidence of absence, thereby distorting how epistemic status is assigned within the field. As a result, other potentially valid forms of evidence—particularly those suited to relational, value-laden, or context-sensitive interventions—are systematically marginalized. As Stegenga (2014) argues, hierarchical approaches to evidence can distort epistemic reasoning by overgeneralizing the legitimacy of a single methodology across diverse clinical domains. His critique highlights the need for more

context-sensitive frameworks that avoid the methodological rigidity embedded in dominant paradigms such as EST.

Westen, Novotny, and Thompson-Brenner (2004) have critically examined the empirical status of ESTs and advocated for more nuanced epistemic standards for interpreting and evaluating the RCT data for ESTs. They also propose an alternative methodology to generate empirically tested interventions to help clinicians develop "empirically informed treatments" that respect more individual, contextual, and cultural variations clinicians must deal with daily (Westen et al. 2004, 658). In the following, we elaborate on these two claims to lay the groundwork for proposing additional experimental strategies to collect evidence of therapeutic effects, and for introducing value-based practice as a complementary clinical methodology for developing more context-sensitive, empirically informed interventions in psychedelic-assisted psychotherapy.

5.1. Four Problematic Assumptions in the EST Methodology

The RCT methodology can serve various purposes in psychotherapy research. Not all uses of RCTs are subject to the criticisms raised by Westen et al. (2004). Their critique targets a specific configuration they call the "EST methodology" (633), which combines RCT methods with four core assumptions. They argue these assumptions are "neither well-validated nor broadly applicable to most disorders and treatments" (632).

This section briefly outlines the first three assumptions and focuses in more detail on the fourth, which concerns the use of manualized treatment protocols.

First, EST methodology presumes that psychological symptoms can be treated in isolation from underlying personality traits. Yet studies using factor analysis, latent class analysis, and structural equation modeling suggest otherwise: symptoms are often deeply interconnected with personality variables such as high negative affect or low positive affect (Brown et al. 1998; Krueger 2002; Mineka, Watson, & Clark 1998; Watson & Clark 1992; Watson et al. 1995; Zinbarg & Barlow 1996).

Second, EST assumes that symptoms can be hierarchically organized into primary and secondary problems, which can be treated sequentially using different manuals (Wilson 1998). For example, a patient with PTSD as a primary and depression as a secondary diagnosis might first receive a PTSD manual, followed by a depression manual. Westen et al. challenge the validity and clinical effectiveness of this sequential model.

Third, EST assumes that brief and focal treatment packages—typically 6 to 16 sessions—can yield enduring therapeutic effects for a given set of symptoms. Yet empirical data suggest that outside a few narrowly defined conditions (e.g., specific anxiety disorders), most patients relapse or require further treatment within 12 to 24 months (Westen et al. 2004, 633). If these three assumptions lack general empirical support, the epistemic value of validating therapies via brief, manualized RCTs becomes questionable.

The fourth assumption, central to psychedelic psychotherapy, concerns how manualization is used within the EST framework. Originally, manualization aimed to

operationalize therapeutic procedures for research purposes—analogous to how experimental manipulations operationalize psychological constructs like "positive affect." Under this view, different techniques (e.g., recalling pleasant memories, receiving compliments) can serve as operational proxies for the same target construct, and measurement validity is triangulated through diverse methods.

However, the EST methodology transforms manuals from operational tools into constitutive definitions of treatment. Rather than serving as one of many possible ways to model a therapeutic process, a manual becomes the treatment itself. This shift from exemplarization to constitution introduces significant epistemological, ethical, and clinical consequences.

Epistemologically, manuals under EST are no longer viewed as approximate tools for investigating treatment principles. They become prescriptive packages, validated wholesale through RCTs. This discourages experimentation with alternative formats and shifts the goal from studying mechanisms of change to validating standardized interventions.

Clinically, this has far-reaching implications. Therapists and patients are expected to adhere to fixed treatment protocols. Any deviation from the manual is treated as a threat to internal validity—and by extension, to scientific legitimacy. Therapists risk becoming robotic implementers of pre-defined scripts, while patients are rendered passive recipients, with diminished agency over the therapeutic process.

When EST logic carries over into everyday clinical practice, it pathologizes clinical discretion. Customizing care based on a patient's evolving needs becomes an epistemic liability. Since only entire treatment packages are validated, clinicians are discouraged from mixing or modifying components. As Truijens, Zühlke-van Hulzen, and Vanheule (2019) show, there is no clear empirical evidence that manualized therapies outperform non-manualized ones, undermining the rationale for rigid standardization.

The EST model thus redefines the therapeutic relationship. Instead of a collaborative, relational process shaped by mutual interpretation and evolving goals, therapy becomes a top-down application of a preapproved intervention. This is fundamentally misaligned with how many relational and narrative psychotherapies—including DAP—conceptualize change: not as a linear effect of protocol adherence, but as an emergent property of interaction.

Given these distortions, we think that EST methodology is ill-suited for evaluating psychedelic-assisted psychotherapy. DAP rests on the assumption that therapeutic change emerges from the interaction between drug effects and psychotherapeutic engagement—not from standardized delivery of fixed packages. The EST model erases this dynamic by reducing therapy to a background constant, subordinated to the pharmacological intervention.

5.2. Alternative Methodology for Empirically-Informed Psychotherapy

Although Westen et al. (2004) are critical of how RCTs are used in the EST framework, they do not reject RCTs altogether. Their methodological stance is nuanced: they emphasize that not all patient conditions lend themselves to standard RCT-based validation, and they propose context-sensitive alternatives.

Based on meta-analyses of the RCTs using the EST methodology (644-650), Westen et al. identify conditions well-suited to brief, manualized treatment protocols:

> [A] link between a specific stimulus or representation and a specific cognitive, affective, or behavioral response that is not densely interconnected with (or can be readily disrupted despite) other symptoms or personality characteristics. (655)

Examples include simple phobias, social phobia, panic symptoms, obsessive-compulsive symptoms, and PTSD following a single traumatic event. For these conditions, the EST methodology may be appropriate—provided that reporting standards are improved to increase external validity and clinical applicability (650–654).

However, for more complex psychological profiles—particularly those involving generalized affective disorders, high comorbidity, and entrenched personality traits—the EST framework is less effective. These patients are often resistant to change and require tailored, long-term interventions. In response, Westen et al. propose two alternative methodologies to guide the development of empirically-informed psychotherapy.

First, they recommend shifting from a manual-based to an intervention-based RCT design. Here, researchers test individual strategies, principles, or mechanisms of change (e.g., cognitive restructuring, emotional regulation), rather than full treatment packages. This approach avoids the burden of proving the superiority of one comprehensive protocol. Instead, researchers can ask more modest and informative questions: for whom, under what conditions, and over what time frame does a particular intervention yield clinically significant improvement?

Second, Westen et al. advocate treating clinical practice as a natural laboratory. Instead of relying solely on controlled experimental conditions, researchers can use real-world clinical settings to observe how therapists adapt and integrate interventions. These observations can generate correlational data on which interventions are associated with positive outcomes—both initially and over multi-year follow-ups (657). The insights gained can then inform future RCTs, structured around empirically grounded hypotheses.

This proposal addresses a crucial epistemic gap in the EST model: the lack of transparency in how treatment packages are assembled. Westen et al. argue that selection bias often shapes the content of manualized treatments, as developers prioritize certain techniques based on their theoretical orientation or training. Without systematic comparisons of how different combinations of interventions perform, we lack a clear basis for treating any package as epistemically superior.

In this sense, clinical practice offers an underutilized empirical resource: a heterogeneous environment in which therapists already adapt and blend interventions in response to patient needs. Studying these variations can complement RCT evidence by revealing what works in ecologically valid conditions. This reflects a broader shift in the philosophy of science—from abstract debates about methods to close analysis of scientific practices in context, whether experimental, clinical, or social (Longino 2019; Anderson 2024; Ludwig and Ruphy 2024).

6. Value-Based Practice as a Complementary Clinical Methodology for DAP

Westen et al.'s proposed refinements to RCT-based designs—including their call to treat clinical practice as a natural laboratory—offer valuable strategies for generating ecologically valid evidence. Building on this insight, we propose that value-based practice (VBP) can serve as a complementary methodology that helps systematically model the relational, narrative, and value-laden dynamics of psychedelic-assisted psychotherapy. Whereas Westen et al. emphasize real-world adaptation and observation, VBP provides structured tools for capturing how value configurations shape therapeutic processes and outcomes.

As discussed in Section 3, philosophical critiques have challenged the rigidity of EBM's evidence hierarchies and interventionist assumptions. These concerns are heightened in psychedelic-assisted psychotherapy, where therapeutic change may emerge through dynamic interactions shaped by trust, meaning-making, and value alignment—dimensions not easily accommodated by standard RCTs.

Psychotherapy is a multifaceted process that generates various types of information—not just causal, but also relational, structural, and narrative. Depending on a study's epistemic aims, non-interventionist information (e.g., patterns of engagement, evolving goals) may offer better insight into therapeutic transformation. Yet when DAP trials adopt RCT protocols, they often hold the therapeutic relationship constant, undermining their own stated causal commitments.

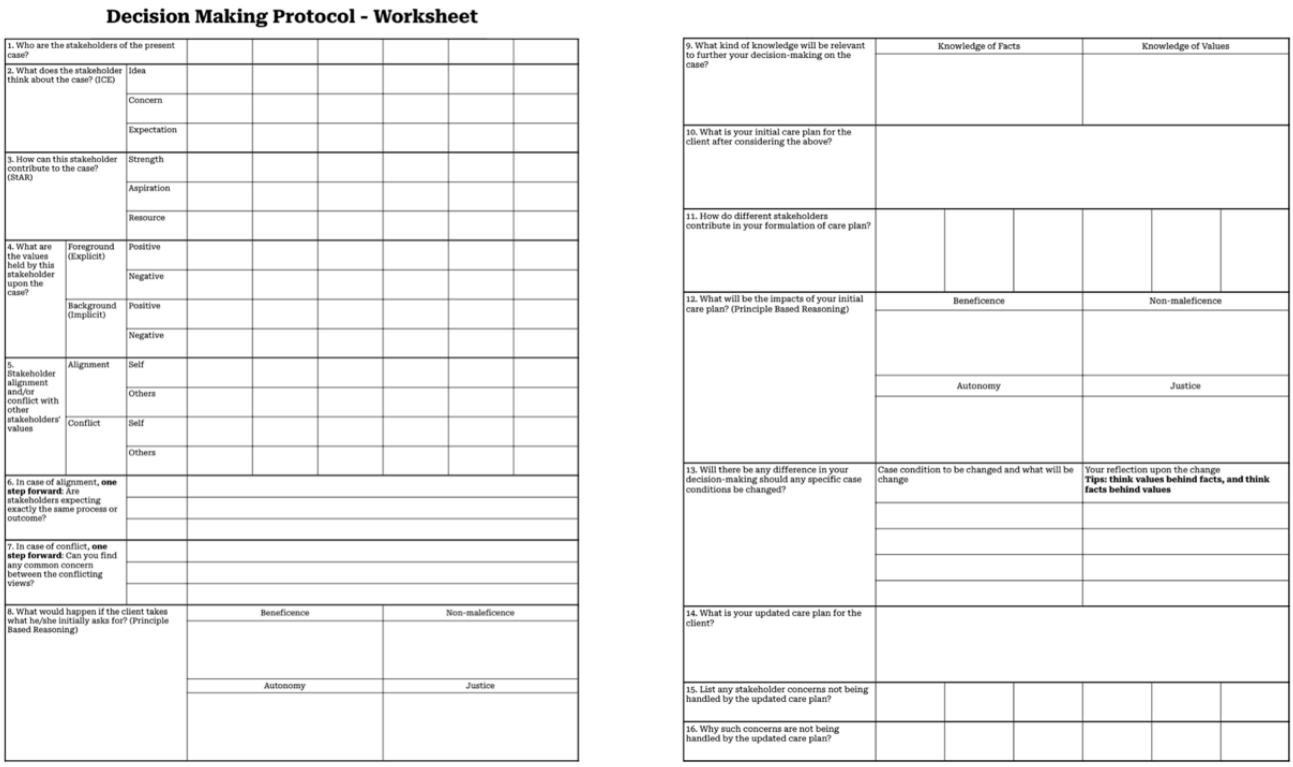
To address this, we propose incorporating VBP—a methodology developed by Fulford (2003, 2004, 2008)—as a complementary tool for modeling how value dynamics shape care. VBP enables researchers to map stakeholders' preferences, alignments, and conflicts, making relational and ethical dimensions empirically visible. This is especially pertinent for proponents of DAP, who hold that therapeutic outcomes depend not only on the pharmacological effects of psychedelics but also on how those effects unfold within a relational and psychotherapeutic context. While the causal impact of such dynamics remains an open empirical question, their epistemic relevance warrants methodological attention.

VBP typically involves structured data collection (e.g., interviews, diagrams) to chart the values of therapists, patients, and caregivers. These representations can inform care decisions and help identify how value alignment or conflict correlates with therapeutic outcomes. For example, tensions between therapist and client value systems—such as differing views on autonomy or family roles—can be explicitly mapped and reflected upon, rather than implicitly imposed or ignored.

In the following, we will employ some details from VBP to illustrate how it helps model the value-related structural information inherent in the psychotherapy processes and how proponents of DAP can utilize this value-related structural information to design some relevant measurement tools for evaluating the epistemic quality of the therapeutical care they provide to their subjects. Moreover, we will show how this can complement Westen et al.'s suggested improvement, leading to better experimental designs for investigations under the EBM methodology.

It is important to emphasize that we are not proposing a general call to include all types of evidence or perspectives in clinical research. Rather, we present VBP as a context-sensitive methodological supplement—one that responds to the distinctive challenges of psychedelic-assisted psychotherapy. In such settings, elements like trust, meaning-making, and value alignment often play an important role in shaping therapeutic outcomes. VBP is motivated by the need to make these elements empirically visible and analytically tractable, particularly in cases where traditional models may overlook or marginalize them.

The core idea of VBP is to use some tools to model the relevant stakeholders' values and preferences in a specific clinical context. The goal is to systematically describe the relevant stakeholders' shared and diverged values and preferences. The resultant description can then inform the clinical decision-making process and evaluate the planned care practice. It typically involves some process of communication and data collection to map each relevant stakeholder's values and preferences with visual models, such as a table diagram. Figure 5 illustrates how the value-related information is modeled by a table diagram (Woo 2014, 4-5[6]).



Decision Making Protocol - Worksheet

1. Who are the stakeholders of the present case?								
2. What does the stakeholder think about the case? (ICE)		Idea						
		Concern						
		Expectation						
3. How can this stakeholder contribute to the case? (SRAR)		Strength						
		Aspiration						
		Resource						
4. What are the values held by this stakeholder upon the case?	Foreground (Explicit)	Positive						
		Negative						
	Background (Implicit)	Positive						
		Negative						
5. Stakeholder alignment and/or conflict with other stakeholders' values	Alignment	Self						
		Others						
	Conflict	Self						
		Others						
6. In case of alignment, **one step forward**: Are stakeholders expecting exactly the same process or outcome?								
7. In case of conflict, **one step forward**: Can you find any common concern between the conflicting views?								
8. What would happen if the client takes what he/she initially asks for? (Principle Based Reasoning)			Beneficence			Non-maleficence		
			Autonomy			Justice		

9. What kind of knowledge will be relevant to further your decision-making on the case?	Knowledge of Facts			Knowledge of Values		
10. What is your initial care plan for the client after considering the above?						
11. How do different stakeholders contribute in your formulation of care plan?						
12. What will be the impacts of your initial care plan? (Principle Based Reasoning)	Beneficence			Non-maleficence		
	Autonomy			Justice		
13. Will there be any difference in your decision-making should any specific case conditions be changed?	Case condition to be changed and what will be change			Your reflection upon the change **Tips: think values behind facts, and think facts behind values**		
14. What is your updated care plan for the client?						
15. List any stakeholder concerns not being handled by the updated care plan?						
16. Why such concerns are not being handled by the updated care plan?						

Figure 5. Redraw from Woo, 2014, 4-5.

Figure 5 models the relevant stakeholders' ideas, concerns, expectations, strengths, aspirations, resources, explicit and implicit positive values, explicit and implicit negative values, self-value alignments and conflicts, others value alignments and conflicts, and so on. It is worth noting that this is not the only way to implement VBP. Depending on the nature of the case and the context

[6] https://valuesbasedpractice.org/wp-content/uploads/2015/04/Values-Based-Practice-Decision-Making-Protocol.pdf

of clinical practice, VBP might be implemented differently. However, the core idea remains: Using some tools to model value-related structural information (such as alignment and disagreement) in each clinical context concerning a set of possible clinical and non-clinical actions.

This turn toward modeling value-related structural information invites reflection on how our VBP proposal engages with broader philosophical debates about the role of values in science. Some philosophers, such as Menon and Stegenga (2023), offer a renewed defense of the value-free ideal in medical research. While acknowledging that complete value-neutrality is unattainable, they warn that allowing non-epistemic values to guide evidential reasoning can distort scientific inference and undermine epistemic objectivity. Others, such as Holman and Wilholt (2022), have reframed this challenge as the "New Demarcation Problem": if values are inevitable in scientific practice, how can we distinguish their legitimate from illegitimate influence? They argue that resolving this question is essential for maintaining the core goals of science—veracity, universality, and epistemic authority.

We share these concerns about epistemic integrity, and we believe that psychedelic-assisted psychotherapy presents a distinctive case in which value-ladenness is not a methodological risk to be minimized, but an epistemic feature to be understood and tracked. The therapeutic process in this domain is constituted through value-sensitive dynamics—narratives of personal meaning, cultural identity, ethical agency, and relational alignment—which shape not only how healing is experienced but also how it unfolds causally. Our use of VBP is not intended as a normative endorsement of particular values, nor as a general call for pluralism. Rather, it is a domain-specific methodological response that aims to make these value dynamics empirically visible and open to structured analysis.

Psychotherapy is arguably one of the most value-saturated domains in clinical care, involving judgments about well-being, identity, and ethical norms. These value dimensions manifest in four key ways: (1) therapists' own values influence interpretation and intervention; (2) treatment goals reflect cultural assumptions; (3) therapeutic methods encode philosophical commitments; and (4) clients bring their own value systems, which may conflict with the above. Ethical challenges—e.g., confidentiality, boundary setting, directive guidance—further intensify this complexity.

Given this, it is hard to justify a clinical methodology that entirely filters out value-related information. EBM's strength lies in modeling treatment-outcome relationships under controlled conditions. But this is only part of the epistemic picture. VBP offers a means to study how therapeutic efficacy may depend on how values are navigated and negotiated in practice.

VBP also provides a way to build richer datasets that can feed back into EBM-compatible designs. For example, if researchers systematically track value conflicts and alignments during therapy, they can later test whether specific configurations predict better outcomes. Such findings could inform more nuanced RCT designs or identify promising intervention strategies to be tested under standard protocols.

In psychedelic contexts, these possibilities are particularly ripe. With ketamine and esketamine already in clinical use, researchers could begin applying VBP tools to real-world

practice. This could serve as a testbed for developing richer methodological frameworks for DAP, broadening the evidentiary approaches currently used to establish therapeutic credibility.

In short, our proposal does not reject EBM but urges developing a complementary methodology for making relational and ethical dimensions empirically visible. When therapeutic change involves value-sensitive interactions—whether or not they turn out to be causally primary—they deserve to be studied on their own terms. VBP offers one promising pathway for doing so, enriching both our understanding of psychedelic care and our methodological repertoire.

7. Conclusion

To understand the therapeutic potential of psychedelics, proponents of DAP aim to collect data related to the relationship between the subjects' drug-induced experience and the therapists' interactions with them. Since the mid-1990s, however, psychotherapy research has been shaped by methodological frameworks that prioritize a narrow form of RCT-based evidence, culminating in the dominance of the EST approach. This institutional dominance has influenced not only research design but also clinical norms, effectively reconfiguring psychotherapy into a standardized, protocol-driven model. As a result, clinical ethics have increasingly been tied to conformity with these treatment packages, rendering deviation from them both professionally and ethically suspect.

It is important to avoid conflating empirical unvalidation with empirical invalidation. A therapy that has not been tested—or cannot easily be tested—under the EST framework is not thereby disconfirmed; alternative clinical or research methodologies may still provide meaningful empirical validation. In this spirit, we have proposed a promising role for the VBP methodology in capturing normative and narrative dimensions embedded in psychotherapy processes. This information can support the identification of statistically significant patterns and guide the design of new, context-sensitive intervention studies. Rather than treating the relationship between drug-induced experiences and therapist interactions as a discrete causal variable, VBP treats it as a source of structured, value-laden information that can inform both outcome modeling and future experimental designs.

Our analysis of how EST methodology is applied to psychedelic-assisted psychotherapy highlights not merely a local methodological issue, but a broader insight for the philosophy of medicine. Psychedelic-assisted psychotherapy—precisely because it involves dynamic, relational, and value-laden processes—reveals deep tensions between standard interventionist epistemologies and the nature of the therapeutic change under investigation. Our analysis suggests that the epistemic structure of psychotherapy is not merely underserved by dominant evidence hierarchies, but may be distorted by them.

Rather than simply calling for the inclusion of more forms of evidence, our proposal emphasizes the need for evidentiary approaches that are responsive to the ontological and relational characteristics of therapeutic practice. VBP serves as one such model, illuminating how normative and narrative dimensions of therapeutic processes can be rendered epistemically

visible. While we do not aim to contribute directly to general debates about evidential pluralism, the case of psychedelic psychotherapy offers a concrete instance where pluralistic strategies may be necessary for epistemic adequacy. In this sense, it supports ongoing calls for evidential flexibility in medicine, particularly in domains where therapeutic efficacy is shaped by interaction, context, and meaning rather than discrete interventions.

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