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**FINANCIAL/OTHER
CONFLICTS OF
INTERESTS**

DR. HALL-FLAVIN HAS NO FINANCIAL/OTHER CONFLICTS OF INTEREST OR DISCLOSURES.

2

**ETHICAL CONSIDERATIONS IN NOVEL
THERAPEUTICS IN PSYCHIATRY: THE
TRANSLATIONAL CHALLENGE**

- Why does it take on average 17 years to advance a new technology or therapeutic approach to routine clinical practice?
- What are the components of ethical decision making?
- How are ethical decisions made?
 - It takes a village.
- A Tale of Two Paradigms: DBS and Alcohol Use Disorders, and Psychedelic Use and Alcohol Use Disorders
- Self-reflection



3

THE 17 YEAR CHASM

KNOWING WHAT TO DO VS. DOING WHAT WE KNOW

- *Deimplementation vs. Implementation*
- *Personal Bias and Epistemic Humility*
- *History, Cultural change and Technological Enactment*
- Distributive Justice and Health Care Inequity
- Complexity
- Community Involvement and Resources
- Health Care Policy
- Delivery of Credible Evidence (Medical Record Systems)
- Health Disinformation
- Definition of Well-Being

Ulin R. JAMA Online. April 8, 2022. doi:10.1001/jama.2022.4387. Milnes C. A History of Evidence: The Perception and Misrepresentation of Well-Being. Abingdon, Routledge, 2019. Abu-Osta H, et al. Identifying barriers and facilitators of translating research evidence into clinical practice. Systematic Review of Reviews. Pall Soc Care. 2022. doi:10.1177/1469. WHO Innovative Care in Chronic Conditions. WHO/CCM/20.01



4

ETHICAL PRINCIPLES

- Principlism
 - Autonomy
 - Non-maleficence
 - Beneficence
 - Justice
- Care Ethics
 - More situationally based
- Consequentialism
- Virtue-based ethics
- Paternalism
- Application of harm reduction paradigms

Pilecki B, et al. Ethical and legal issues in psychedelic harm reduction and integrative therapy. Harm Reduct J. 2020;14:40



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THE FOX AND THE HEDGEHOG ARISTOTLE

- A Fox with its tail caught was a feast for Mosquitoes. A Hedgehog offered to remove them. Fox said no; those on him were full, new would take more blood.
- The moral: Consider carefully before changing your situation.

Thomas Bewick. Headpiece, p.227. The Fables of Aesop, 1818. MOMA; <https://thelibraryofalexandria.org/> The-fox-and-the-hedgehog.html



6

HOW ARE ETHICAL DECISIONS MADE: THE IDEAL

- Establish guiding principles and values.
- Collate the evidence.
- Weigh the likelihood and consequences of the outcomes supported by a societal consensus regarding rights and values.
- Decision made collectively and rationally.
- Decision applied within a moral and legal framework.
- Reassessment and change.



image.freepik.com

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HOW ARE ETHICAL DECISIONS MADE: IT TAKES A VILLAGE

- Post hoc rationalizations designed to influence others, maintain social relationships, and preserve definitional attitudes.
- The role of disgust.
- Mental health care:
 - Legal
 - Group dynamics
 - Inertia vs. Action
- *Critical factor: sharing of one another's judgments as well as reasons that the emotions and ideas of others can move*



Siva E. et al. Ethical dilemmas in psychiatry: when teams disagree. BJPsychAdvances 2017, 23: 231-238. Sell on Study shelving: A Med Clinics blog. Respecting autonomy in altered states: Navigating ethical quandries in psychedelic therapy. Mc Lane et al. Dec 22, 2021. Image: freepik.com.

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Mental Cases
 Wilfred Owen
 1894-1918

www.poets.org/poems/mental-cases

Who are these? Why at they here in twilight?
 Wherefore rock they, purgatorial shadows,
 Drooping tongues from jaws that slob their relish?
 Baring teeth that leer like skulls' tongues wicked?
 Stroke of stroke of pain,—but what slow panic,
 Goug'd these chasms round their fretted sockets?
 Ever from their hair and through their hand palms
 Misery sweaters. Surely we have perished
 Sleeping, and walk hell; but who these hellish?

*These are men whose minds the Dead have ravished.
 Memory fingers in their hair of murders,
 Multitudinous murders they once witnessed.
 Wodding sloughs of flesh these helpless wond'ring
 Treading blood from lungs that had loved laughter,
 Always they must see these things and hear them,
 Batter of guns and shatter of flying muscles,
 Carnage inconceivable and human squander
 Rucked too thick for these men's extrication.*

Therefore still their eyeballs shrink tormented
 Back into their brains, because on their sense
 Sunlight seems a bloodmeat; night comes blood-black;
 Dawn breaks open like a wound that bleeds afresh —
 Thus their heads wear this hilarious, hideous,
 Awful likeness of set-smiling corpses. —
 Thus their hands are plucking at each other;
 Picking at the rope-knots of their scourging;
 Snatching after us who smote them, brother,
 Pawing us who dealt them war and madness.

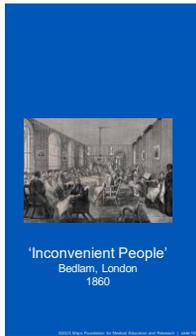
Illustration by Michael Godwin and Pauline J. 2004

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HEROIC THERAPIES

- Insulin Coma Therapy (Manfred Sakel, declined after WWII)
- Chemical Shock Therapy (Laszlo Medina)
- Psychosurgery/Leucotomy (Egas Moniz)
- Lobotomy (Walter Freeman 228 patients in 12 days)
- ECT (Ugo Cerletti and Lucio Bini)
 - Informed consent.

www.sciencemuseum.org.uk/objects-and-stories/medicine/heroic-therapies-psychiatry



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A TALE OF TWO PARADIGMS

DBT AND ALCOHOL USE DISORDER
HALLUCINOGEN PHARMACOTHERAPY IN ALCOHOL USE DISORDER



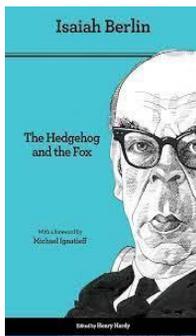
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THE HEDGEHOG AND THE FOX

ISAIAH BERLIN

- "It is not merely that the fox knows many things. The fox accepts that he can only know many things and that the unity of reality must escape his grasp. The critical feature of foxes is that they are reconciled to the limits of what they know. We are part of a larger scheme of things than we can understand...wise only to the measure of what we can understand."
- "A hedgehog will not make peace with the world. He is not reconciled. He cannot accept that he knows many things. He seeks to know one big thing, and strives without ceasing to give reality a shape." Foxes settle for what they know, and may live happy lives. Hedgehogs will not settle and their lives may not be happy."

Berlin I: The Hedgehog and the Fox: An Essay on Tolstoy's View of History, Second Edition, Princeton, Princeton University Press, 2013.

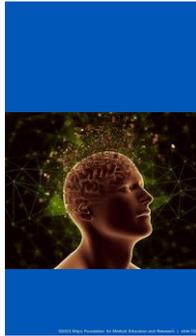


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DBS AND SEVERE ALCOHOL USE DISORDER

- Harm reduction measures including alcohol consumption, craving, alcohol-related compulsivity and anxiety, n=6. Reduced Nac activity at 6 months, reduced Nac and visual association cortex, decreased activation of the dorsal striatum. (Davidson et al, Molecular Psychiatry 27, 3992-4000, 2022.)
- n=12 inpatients, DBS vs. sham, effects primarily higher proportion of abstinent days, lower alcohol craving and anhedonia. High alcohol craving, depression, and anhedonia responded to DBS. (Bach et al, Trans Psychiatry 13: 49, 2023.)

Image: freepik.com

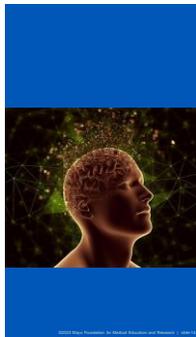


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DBS IN SEVERE ALCOHOL USE DISORDER

- 14 studies 2007-2019, longer term abstinence in 43% -61% of patients (Hassan et al: Outcomes of DBS for SUD: A Systemic Review. Neurosurg Review, 44, 1967-1976, 2021.)
- DBS NAc 5 pts 8 years, 2 abstinent, 3 substantially decreased consumption, all reported no craving (Muller et al: Nac DBS for Alcohol Addiction – Safety and Clinical Results of a LT trial Pharmacopsych 2016;49(04)L 170-173.)

Image freepik.com



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DBS IN SEVERE ALCOHOL USE DISORDER- INFORMED CONSENT

- Patient
 - Research v. treatment
 - Voluntarism
 - Realistic expectations
- Disease
 - Reason about trial
 - Demonstrated severity, chronicity, failure prior treatment
 - Risk vs. Benefit
 - Reality testing
 - Ego-dystonic vs. ego-syntonic
- Technology
 - Known and unknown risks
 - Clinical equipoise
 - Full disclosure

Lipman et al: J Med Ethics 2021; 38:107-111 Image freepik.com.



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PSYCHEDELICS AND AUD

- 20 year systematic review to December 2021. 27 of 639 selected. 20 human studies, preclinical studies 7. Low numbers, lack of control group, difficulty in determining effect of classic psychedelics in isolation. 7 pre-clinical studies scarce and conflicting data. Psilocybin most consistent data potential candidate. **No study worsened alcohol consumption.** (Calleja-Conde, et al: Addiction Biology 2022;27:e13229)

MDLinx, March 21, 2023, image freepik.com



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PSYCHEDELICS AND AUD

- QUANTUM TRIP TRIAL PLAN Psilocybin-assisted therapy randomized, DBPC12 week clinical trial in patients with AUD. PeTH and fMRI corroboration self-report, serum psilocybin may help establish range, blinding difficult. **90 patients aged 20-70 years, primary outcome reduction in heavy drinking days. Secondary total alcohol, PeTh, plasma psilocybin, subjective drug experience as predictor of treatment outcome, fMRI corticostriatal pathways** (Jensen ME et al, BMJ Open 2022;12:e066019)

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PSYCHEDELICS AND AUD

- 2 doses high dose psilocybin vs. diphenhydramine with manualized psychotherapy MET or CBT weeks 4 and 8 with outcomes assessed over 32 week double blind period after first dose. **Percentage of heavy drinking days TLFB, no adverse effects, with substantial decrease in heavy drinking days and mean daily alcohol consumption.** (Bogenschutz et al; Percentage of HDD following Psilocybin-Assisted Psychotherapy vs. Placebo. JAMA Psychiatry 2022;79(10):953-962.)

MDLinx, March 21, 2023, image freepik.com



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NOVEL ETHICAL AND REGULATORY CHALLENGES

- Informed Consent
 - Novel changes in mental states
 - Difficulty of changing course once begun
 - Unrealistic expectations from media
 - Consequences not known for high -risk groups
 - Subjective vs. Non-subjective use
 - Concept of self
- Underground Use
 - Heterogeneity of Practice
 - Therapeutic Touch, Boundary Violations
 - Curating the emerging underground

Smith W, Appelbaum P: Novel ethical and policy issues in psychiatric uses of psychedelic substances. *Neuropsychopharmacology*, 21(6)(2022): 1091-65
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NOVEL ETHICAL AND REGULATORY CHALLENGES

- Commercialization
 - Regulation of commercial interests and patenting
 - Respect for fair treatment of indigenous cultures
- Regulation and Means and Speed of Legislation
 - Timing or rescheduling
 - Regulation
 - Decriminalization vs. Accumulation of data bases

Smith W, Appelbaum P: Novel ethical and policy issues in psychiatric uses of psychedelic substances. *Neuropsychopharmacology*, 21(6)(2022): 1091-65
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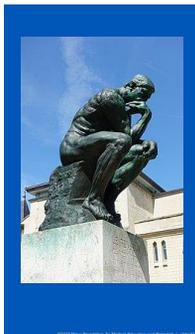


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SELF-REFLECTION-HARMS REDUCTION

- What are my reasons for doing work that relates to psychedelics?
- Am I comfortable with psychedelic content?
- What is my level of competency in working with psychedelics and with harm reduction? What might I do to develop competency?
- What level of risk am I comfortable taking on?
- What is my personal level of experience?
- What is my privilege and how safe it is for me to practice Harms Reduction Integration Therapy?
- What is my level of support?

Pilecki et al: *Harm Reduction Journal* (2021)18:40 image Wikipedia



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**QUESTIONS
& ANSWERS**



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