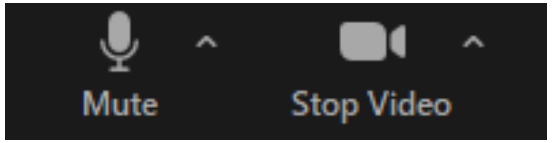
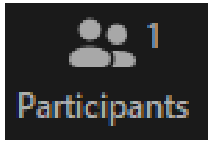
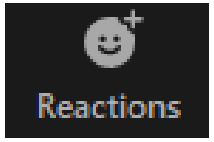
Psychedelic Medicine Task Force

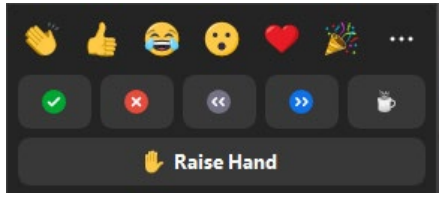
Welcome Psychedelic Medicine Task Force members!

Please use this time to test your Zoom meeting controls located at the bottom of the screen:





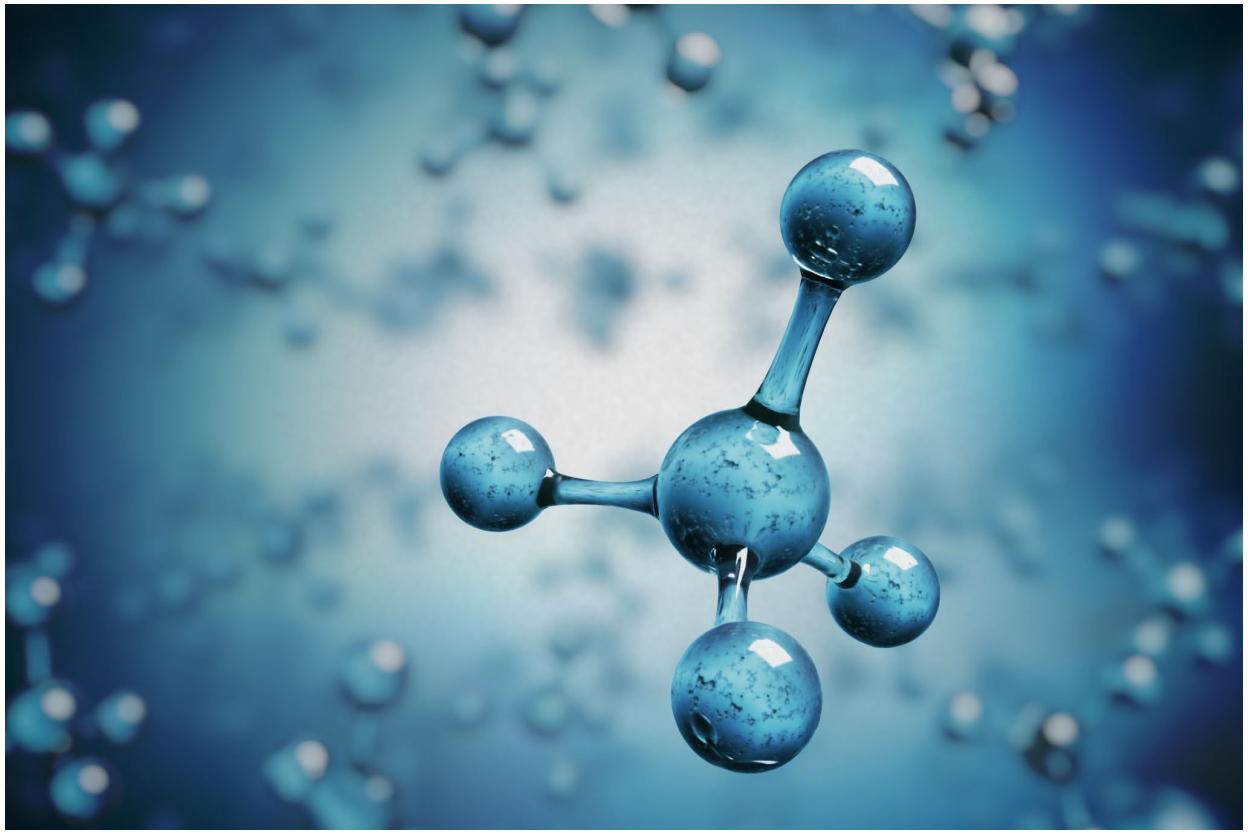




Access **Mural** via the link sent to you in your meeting invitation. Only members have access to this shared workspace. Once on the site, minimize the screen for later use during the meeting.

MDH Staff

- **Dana Farley**, Alcohol & Drug Prevention Policy Director, Drug Overdose Prevention Unit Supervisor
- **Chrissie Deutsch**, Psychedelic Medicine Program Administrator
- **Caroline Johnson**, Psychedelic Medicine Scientific Researcher



MANAGEMENT AND BUDGET
MANAGEMENT ANALYSIS AND DEVELOPMENT

Jessica Burke and Stacy Sjogren,
Senior Consultants providing planning assistance and facilitation

Dr. Jessica Nielson, Task Force Chairperson

Welcome meeting observers

- **Thank you** for your interest in the work of the Psychedelic Medicine Task Force.
- **Today's meeting is primarily organizational**. There are no plans today for taking public comment but, in accordance with Minnesota's Open Meeting Laws, you are welcome to observe this meeting.
- This meeting will not be recorded. **Minutes will be posted on the task force's website** along with other materials for this meeting:

https://www.health.state.mn.us/people/psychmed/index.html

health.psychedelicmemedicine@state.mn.us

Today’s agenda

- Approve November 6, 2023 minutes
- Discuss overarching project workflow and key benchmarks
- **Break**
- Study of existing research
- **Break**
- Charter revisions
  - Group working agreements
  - Principles for decision making
  - Public Communications and comments
  - Task Force scope
  - Decision making tools

Legislative charge

The Psychedelic Medicine Task Force was established to advise the legislature on the legal, medical, and **policy issues** associated with the legalization of psychedelic medicine in the state. For purposes of this work, “psychedelic medicine” means MDMA, psilocybin, and LSD.

Task force duties

as outlined in legislation (Subd. 5.)

Scientific Research

1. Survey existing studies in the scientific literature on the therapeutic **efficacy** of psychedelic medicine in the treatment of mental health conditions, including depression, anxiety, post-traumatic stress disorder, bipolar disorder, and **any other mental health conditions and medical conditions** for which a psychedelic medicine may provide an **effective** treatment option.
2. Compare the efficacy of psychedelic medicine in treating the conditions described [above] with the efficacy of treatments currently used for these conditions.

Duties

Develop a comprehensive plan that covers:

1. statutory changes necessary for the legalization of psychedelic medicine.

2. state and local regulation of psychedelic medicine

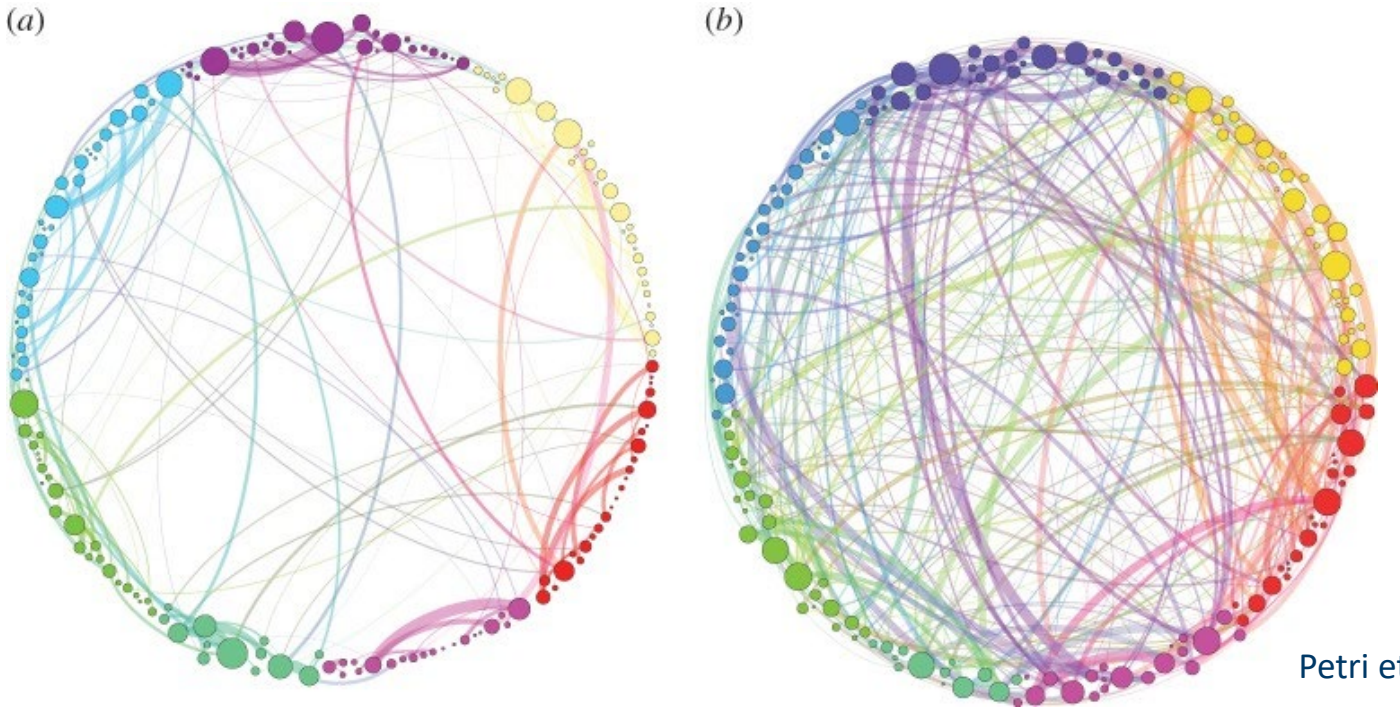
3. federal law, policy, and regulation of psychedelic medicine, with a focus on retaining state autonomy to act without conflicting with federal law, including methods to resolve conflicts.

    - Such as seeking an administrative exemption to the federal Controlled Substances Act under United States Code, title 21, section 822(d), and Code of Federal Regulations, title 21, part 1307.03; seeking a judicially created exemption to the federal Controlled Substances Act; petitioning the United States Attorney General to establish a research program under United States Code, title 21, section 872(e); using the Food and Drug Administration's expanded access program; and using authority under the federal Right to Try Act

4. Education of the public **on recommendations** made to the legislature and others about necessary and appropriate actions related to the legalization of psychedelic medicine in the state.

Work cadence

Identify benefits and challenges of legalization Identify policy areas to focus on for work groups *barriers TBD as group work and research continue*		**Plan development + recommendations** *continual review through work group updates, SME presentations, and TF collaborative decision-making*					**Information synthesis, narrowing, and prioritization of report** *research and workgroup(s) continue if needed*		**Drafting of recommendations** *continue information synthesis, narrowing, and prioritization of report as draft takes shape*			**Submit Report Jan 1, 2025**
Dec 12/4/23	**Jan** 1/8/24	**Feb** 2/5/24	**March** 3/4/24	**April** 4/1/24	**May** 5/6/24	**June** 6/3/24	**July** 7/1/24	**Aug** 8/5/24	**Sept** 9/9/24	**Oct** 10/7/24	**Nov** 11/4/24	**Dec** 12/2/24	**Jan 1 TF ends**
	Determine initial subgroups **Draft initial legislative report due Feb 1** Report will be a basic summary of task force updates, including development, workplan, initial research, etc. Written with chair support, members will be able to provide edits and notes due to quick turnaround. No recommendations will be made.							**Begin outlining** Determine potential cost of implementation, needed investments, sustainable supports, etc.					Report includes comprehensive plan, scientific research, and any other additional materials members find necessary to share.



Petri et al, 2014

Research Updates

Dr. Jessica Nielson | Task Force Chair

Dr. Caroline Johnson | Psychedelic Medicine Research Scientist

DEPARTMENT OF HEALTH

Process of new drug approval

- Gold standard for approval of treatments is through clinical trials – regulated by the Food and Drug Administration (FDA)
- Clinical trials are not therapy, they are science experiments under very tightly controlled conditions (e.g. placebo controls, blinding to drug group, minimization of variability in the population, etc).
- There are 4 phases of clinical trials
  - Phase 1 – Safety, tolerability, mechanisms (typically in healthy population)
  - Phase 2 – Feasibility, preliminary efficacy (testing in people with diagnosis)
  - Phase 3 – Efficacy, final step required before FDA approval (DEA must reschedule after)
  - Phase 4 – Effectiveness of real world use post-approval

State of psychedelic clinical trials

- MDMA for PTSD has completed two separate phase 3 clinical trials – MAPS
  - Likely will be FDA approved and rescheduled before our final report is due
  - One phase 4 trial is already registered for testing with prolonged exposure therapy
  - Other phase 3 for couples therapy for PTSD that is recruiting
- Psilocybin for depression is currently enrolling for phase 3
  - Treatment resistant depression – COMPASS Pathways
    - Single dose trial
    - Repeated dose trial
- LSD has had a few successful phase 2 clinical trials
  - Mostly in Switzerland

FDA guidance on clinical trials with psychedelics

Psychedelic Drugs: Considerations for Clinical Investigations

Guidance for Industry

Additional copies are available from:

Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hamshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
https://fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs

DRAFT Guidance

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
June 2023
Clinical/Medical

FDA guidance on clinical trials with psychedelics

An AWC study uses design that permits a valid comparison with a control to provide a quantitative assessment of a drug's effect. In the context of psychedelic drug development, the use of a traditional placebo as a control can be problematic for assessing efficacy. Subjects receiving an active drug experience functional unblinding because of the intense perceptual disturbances that can develop; those who receive a placebo in the context of high expectancy may experience a *nocebo* effect (i.e., worsening symptoms as a result of knowing they did not get active treatment). However, an inactive control allows for better contextualization of any safety findings. Alternatives to an inert placebo (e.g., subperceptual doses of a psychedelic drug, other psychoactive drugs that mimic some aspects of the psychedelic experience) may be considered as well.

[Psychedelic Drugs: Considerations for Clinical Investigations | FDA]

DRAFT Guidance

FDA guidance on clinical trials with psychedelics

- Many of the psychedelic drug development programs involve administering the investigational drug and then engaging in psychological support or psychotherapy either while the subject is experiencing the acute effects of the drug or in a subsequent session. This additional variable both complicates the assessment of effectiveness and presents a challenge for any future product labeling.
    - As of the publication date of this guidance, the contribution of the psychotherapy component to any efficacy observed with psychedelic treatment has not been characterized.
    - Psychotherapeutic interventions have the potential to increase expectancy and performance biases. Sponsors should plan to justify the inclusion of a psychotherapy to quantify the contribution of psychotherapy to the overall treatment effect. A factorial design may be useful for characterizing the separate contributions of drug and psychotherapy to any observed treatment response.

DRAFT Guidance

FDA guidance on clinical trials with psychedelics

Psychedelic Medicine > Ahead of Print

A Systematic Review of Reporting Practices in Psychedelic Clinical Trials: Psychological Support, Therapy, and Psychosocial Interventions

William Brennan, Alex R. Kelman, and Alexander B. Belser

Published Online: 17 Oct 2023 – https://doi.org/10.1089/psymed.2023.0007

The paradox of forcing these drugs through the FDA

- Example of MDMA for PTSD
  - Was legal and being used in the 1970s and 1980s to treat trauma (prior to the creation of the PTSD diagnosis in DSM) and for couples' therapy
  - People started using it safely in recreational settings and the DEA decided to put it on schedule 1
  - FDA recommendations based on evidence at the time = should be schedule 3, but DEA overrode this recommendation and put it into schedule 1 anyway
  - Fast forward to now, where MDMA is about to be approved by the FDA to treat PTSD (40 years later, millions of dollars spent, and countless lives lost in the process)
  - Very little evidence is required to put a drug on schedule 1, and a mountain of evidence is required to reschedule = how is this the process we rely on for the scheduling system?

How much evidence is necessary?

Neuropharmacology 142 (2018) 143-166
Contents lists available at ScienceDirect

Neuropharmacology

Journal homepage: www.elsevier.com

Invited Review

The abuse potential of medical psilocybin according to the 8 factors of the Controlled Substance Act

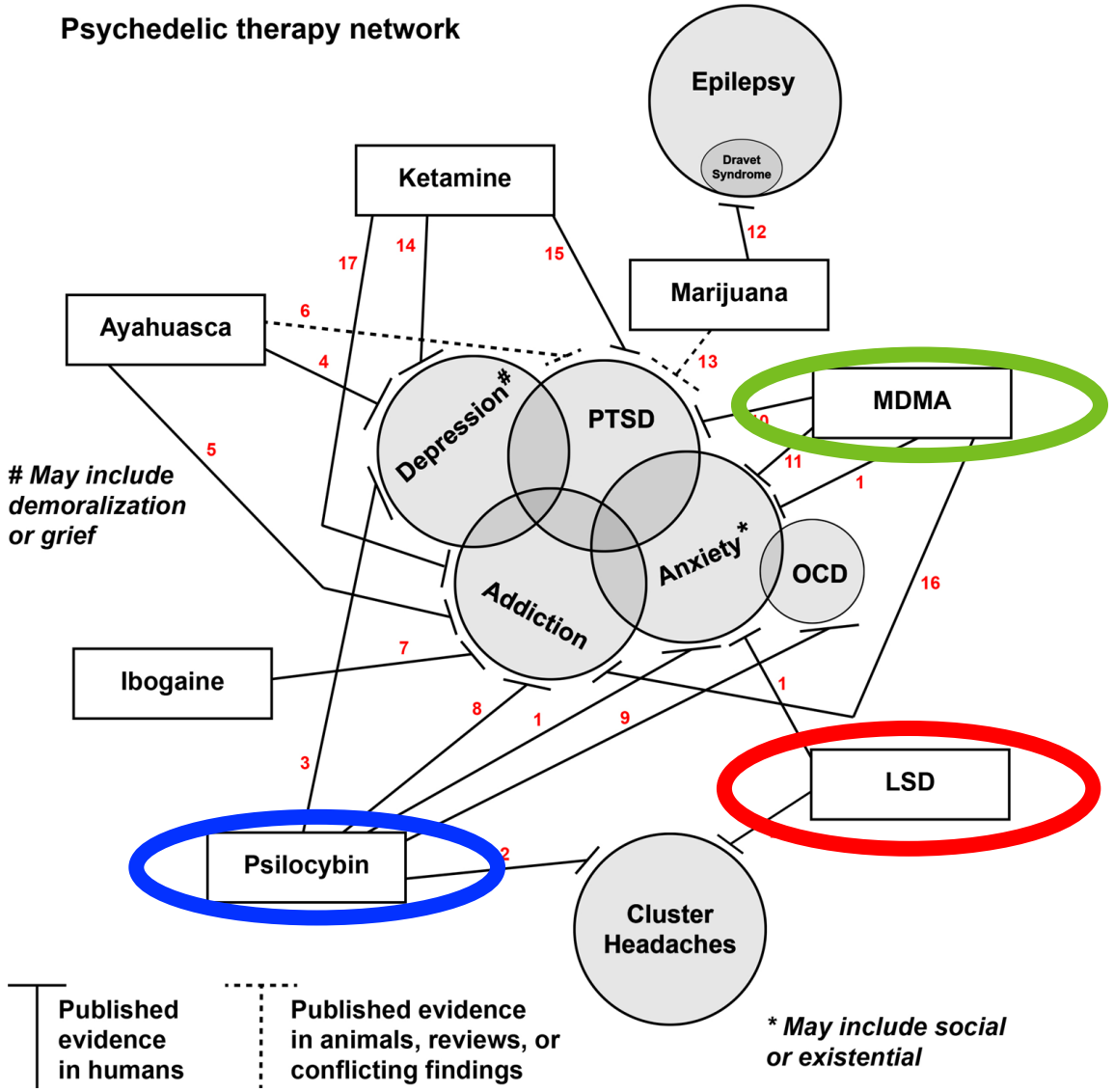
Matthew W. Johnson – Department of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine, Baltimor, MD, USA
Roland R. Griffiths – Department of Neuroscience, The Johns Hopkins University School of Medicine, Baltimore, MD, USA
Peter S. Hendricks – Department of Health Behavior, School of Public Health, University of Alabama, Birmingham, AL, USA
Jack E. Henningfield – Pinney Associates, Bethesda, MD 20814, USA

The abuse potential of medical psilocybin according to the 8 factors of the Controlled Substances Act - ScienceDirect

State of psychedelic clinical research

1. LSD, psilocybin or MDMA for end of life anxiety
2. LSD and psilocybin for migraine and cluster headaches
3. Psilocybin for depression
4. Ayahuasca for depression
5. Ayahuasca for addiction
6. Ayahuasca for PTSD
7. Ibogaine for addiction
8. Psilocybin for addiction
9. Psilocybin for OCD
10. MDMA for PTSD
11. MDMA for social anxiety in autistic adults
12. Cannabidiol for Dravet's syndrome
13. Marijuana for PTSD
14. Ketamine for depression (*in progress, many trials on this)*
15. Ketamine for PTSD
16. MDMA for addiction
17. Ketamine for addiction

Full reference list at:
nielsonlab.umn.edu



Proposed Scientific Research Methods

DEPARTMENT OF HEALTH

Scope of presentation

- The scientific research is just one piece of the pie.
  - Cultural, anthropological, sociopolitical, legislative, policy considerations
  - This presentation is only focusing on the methods by which the scientific research portion will be conducted

Methodology: Overview

- Overview
  - Consider scientific review type
  - Define the boundaries of research
  - Define the research question(s)
  - Identify databases
  - Develop a search strategy
  - Develop comprehensive inclusion/exclusion criteria
  - Levels of Evidence
  - Perform search
  - Appraise the quality of data
  - Analyze results
  - Write & present report on scientific literature

Scientific Review Type

- Type of review:
  - Meta-analysis
    - Is an objective scientific method of combining and analyzing results from multiple scientific studies, typically randomized controlled trials (which generally have the highest level of evidence). Meta-analyses use statistical methods on estimates from two or more studies to form a pooled estimate.
  - Systematic Review
    - An objective, reproducible method to find answers to specific research questions by collecting all available studies and analyzing their results.
  - Rapid review
    - Similar to a systemic review, though the questions are typically narrower and the search strategies are more limited in the interest of saving time

Subdivision 5, Duties

The task force shall:

1) survey existing studies in the scientific literature on the therapeutic **efficacy** of psychedelic medicine in the treatment of mental health conditions, including depression, anxiety, post-traumatic stress disorder, bipolar disorder, and any other mental health conditions and medical conditions for which a psychedelic medicine may provide an **effective** treatment option;

2) compare the efficacy of psychedelic medicine in treating the conditions described in clause (1) with the efficacy of treatments currently used for these conditions

Define the boundaries of scientific research

- Efficacy: The performance of the treatment only under ideal and controlled circumstances, such as those in a clinical trial
- Effectiveness: How the drug performs in "real world conditions."

- **Does the task force want to focus on efficacy or effectiveness?**

- Phase 1 – Safety, tolerability, mechanisms (typically in healthy population)
- Phase 2 – Feasibility, preliminary efficacy (testing in people with diagnosis)
- Phase 3 – Efficacy, final step required before FDA approval (DEA must reschedule after)
- Phase 4 – Effectiveness of real world use post-approval

Define the Research Question(s)

- Task 1: Identify the conditions that each of the drugs may treat.
  - What are the health conditions that each drug shows efficacy/effectiveness in treating?
- Task 2: Compare the psychedelic treatments against current gold-standard treatments for the identified conditions.
  - What is the efficacy/effectiveness of each drug in treating the above-named conditions as compared to the current gold-standard treatment?
- **Refinement of question(s).**

Identify the Databases

- Academic Literature
  - PubMed
  - Indigenous research sources
- Grey Literature
  - National Clinical Trial registry
  - Cochrane Library
  - bioArXiv/medArXiv

- **Any other recommended sources?**

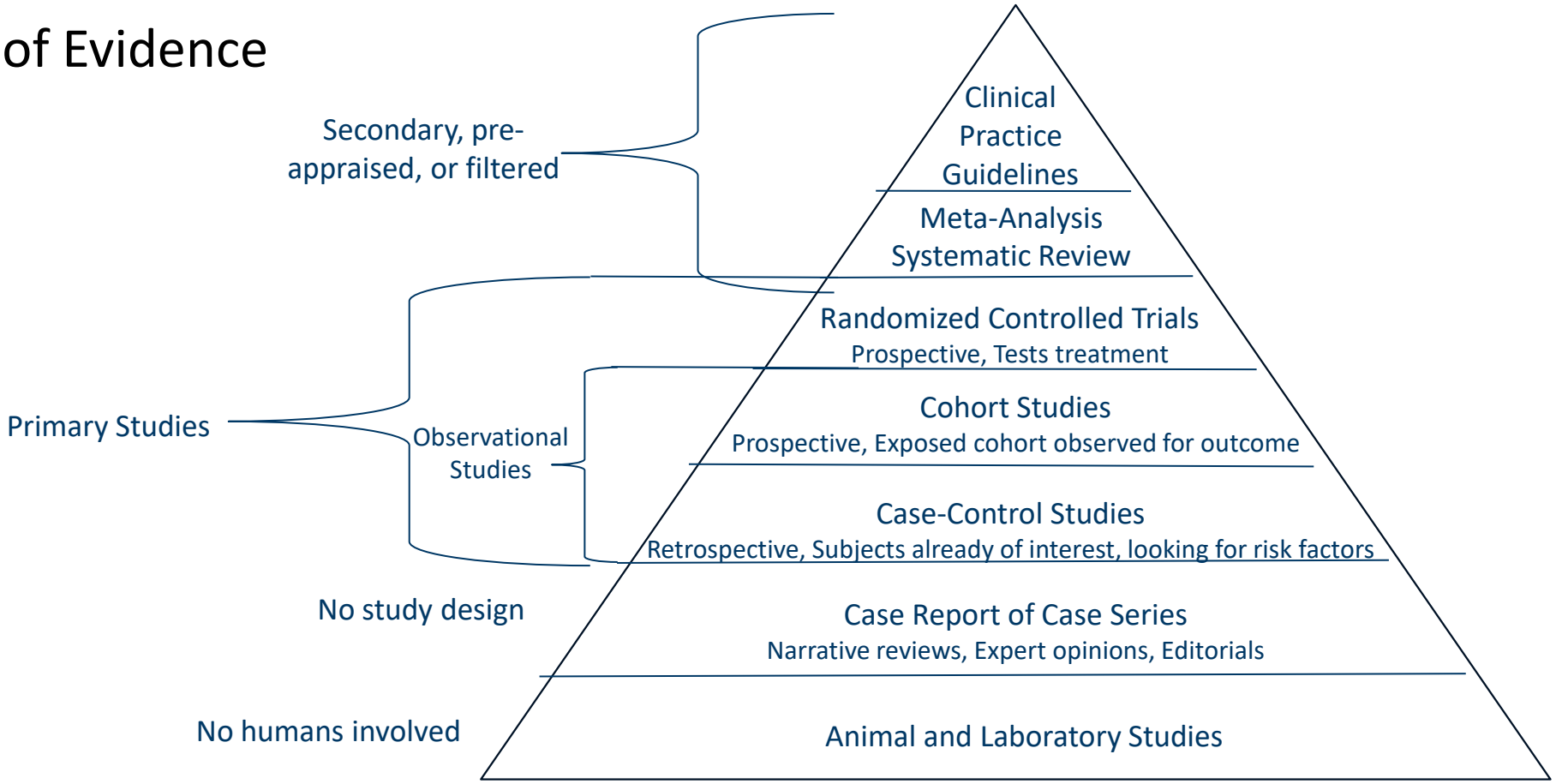
Develop Search Strategies

- Boolean logic queries and specific language used to run the searches, based on research questions.
- Define specific terms for each database, search only those terms, and log them.
- Example, PubMed search for MDMA:

((MDMA) OR (3,4-methylenedioxymethamphetamine) OR (ecstasy)) AND ((mental*) OR (therap*) OR (treat*))

Level of Evidence

- Levels of Evidence



Develop Inclusion/Exclusion Criteria

- Date ranges
- Exposure of interest
- Geographic location
- Language of publication
- Population
- Peer-review status
- Types of reports
- Therapeutic setting
- Study design(s)
- Types of publication
- Any other criteria considerations

Perform Search and Analyze Results

- Search and results will be logged and made public.
- Inclusion/exclusion criteria applied to search results.

Assess the quality of studies

- Critical appraisal tools (CATs) will be utilized to evaluate the results of the search and determine which studies will be included for review, and to provide justification for why studies might not be included.
  - JBI (Joanna Briggs Institute) CATs for academic literature
  - Developing CATs for gray literature

Analyze Results

- Each study will be read, logged, and relevant data will be extracted.

Write the scientific report

- A narrative review of all studies will be written for presentation to and review by the task force.

Tasks

- What we need from the task force (on Mural):
  - Agreement on scientific research report
  - Agreement on boundaries of included research
  - Agreement on research questions
  - Any other databases to include
  - What level of evidence would you be comfortable with?
  - Agreement on inclusion/exclusion criteria
- By December 8th, 2023

Proposed timeline

Week of:	Research Task
December 4, 2023	Task force provides inputs to methods by December 8, 2023
December 11, 2023	Task force inputs are incorporated, methods refined & finalized by December 15, 2023
December 18, 2023	Formal literature search of academic databases
December 25, 2023	Formal literature search of gray databases
January 1, 2024	Formal literature search of gray databases
January 8, 2024	Presentation of search results to task force

Proposed timeline

Month	Research Task
January – March 2024	In-depth analysis of literature on MDMA
April – June 2024	In-depth analysis of literature on psilocybin
July – September 2024	In-depth analysis of literature on LSD
October 2024	Preparation of final research report
November 2024	Task Force review of research report
December 2024	Task Force finalizes research report

Use of outside sources

- Dr. Ruth Lynfield—State Epidemiologist & MDH Medical Director
- Dr. Tyler Oesterle—Addiction Psychiatry at Mayo Clinic

Next steps and adjournment

- **Opportunity for member feedback:** please leave your feedback in Mural.
- **Questions between meetings:** contact Jess Burke (jessica.burke@state.mn.us)
- Next meeting: Monday, January 8, 2024, 9:30 am – 12:30 pm