

# Psychedelic Medicine: Old Compounds, New Beginnings

July 14, 2021

# Housekeeping /Logistics





- This webinar will be recorded and shared with you via email.
- To post a question or a comment, please use the Q&A feature in Zoom.
- Please refer to the Bio Book in chat to read more about our panelists.

# NEHI: Network for Excellence in Health

**Innovation** 

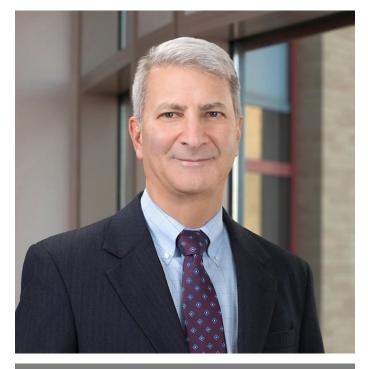
NEHI is a national nonprofit, nonpartisan organization with member organizations from diverse sectors of U.S. health care.

We are committed to developing pragmatic policy and practice recommendations that incorporate different industry perspectives to improve productivity, drive better outcomes and address unmet needs through innovation.





## Webinar Overview



Mike Apkon, MD, PhD, MBA

President,

Sand Street Advisors

Member of the Board, NEHI

(Moderator)

# MENTAL HEALTH CHALLENGES PLAGUE THE US AND THE WORLD

#### Psychiatric conditions account for 5 of the top 10 causes of disability and premature death



Stress/Anxiety

Most common mental illness 18% of population

1/3 of economic burden of mental illness



#### Depression

1.4 MM suicide attempts in 2019
8.1% of adults in any given 2-week period
80% impaired
1 in 9 adults medicated each month
18% of adult women use antidepressants
> 30% resistant to treatment



**PTSD** 

7%-8% lifetime prevalence 3.6% in past year > 1/3 seriously impaired Costs up to \$7,000/yr 1/3 resistant to treatment



Downstream Impact on Chronic Illness TME with TRD ~2x (\$17K/yr) with non-TRD-MDD (\$9.7K) and 4x those of people without depression (\$4.7K)

6x as many ED visits

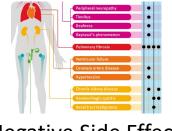


COVID-19 Pandemic is an amplifier: Mental Health Impairment estimated to cost \$1.58 trillion as result of COVID-19 crisis

# CURRENT THERAPIES ARE INEFFECTIVE [IN SOME CASES MAKING IT WORSE]



Remission/Relapse Rates



Negative Side Effects



High Treatment Variability

Remission rates ≤ 50% for depression Long term remission < 1% Small effect size for psycho-therapy High rates of relapse High rate of non-compliance b/o side effects

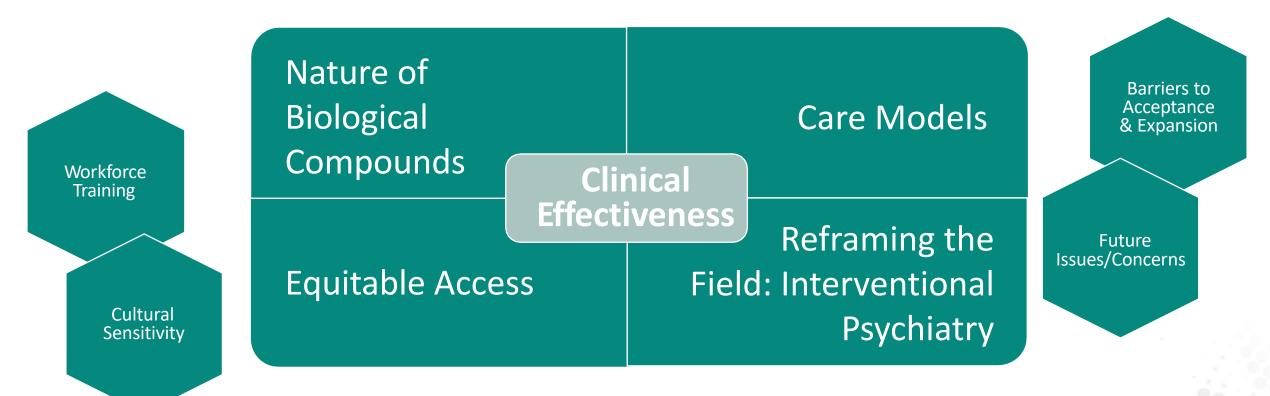
Lack of standardization in medical or nonmedical regimens Access challenging

Few novel therapeutics/drugs have progressed to Phase 3 clinical trials or regulatory approval in the last 40 years

## Webinar Goal



- Increase awareness and understanding of the issues involved in introducing psychedelic therapies in the behavioral and mental health ecosystem
- Assess implications for other innovation opportunities in this space



## Agenda Items

- Panelist Introductions & Kick-offs (30 min)
  - John Krystal, MD
  - Joseph del Moral
  - Joy Sun Cooper, MBA
  - Neil Leibowitz, MD, JD
- Panel Discussion & Q&A (20 min)
  - Mike Apkon, MD, PhD, MBA
  - Dan Grossman
- Attendee Questions (10 min)
- Panelist Closing Comments (5 min)





## Our Panel









John Krystal, MD

Chair and Chief of Psychiatry,

Yale-New Haven Hospital

Joseph del Moral
Co-Founder and Chief Executive Officer,
Field Trip

Joy Sun Cooper, MBA

Head of Commercialization and Patient

Access,

MAPS Public Benefit Corporation



# **Our Panel**





Neil Leibowitz, MD, JD Chief Medical Officer, Beacon Health Options



Dan Grossman

Managing Director & Senior Partner,

Boston Consulting Group

(Observations)





# Ketamine, Psilocybin, and MDMA: Why these drugs, now?

John Krystal, MD

Yale-New Haven Hospital



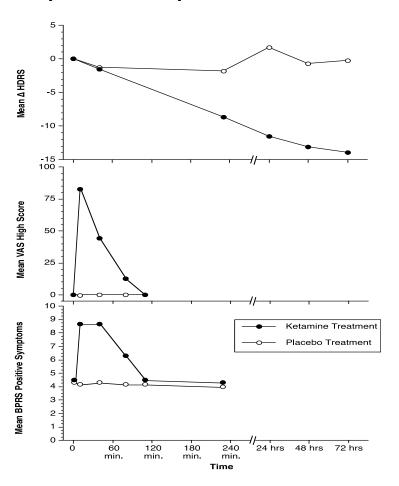
# Ketamine, Psilocybin, and MDMA: Why these drugs now?

John Krystal, M.D.

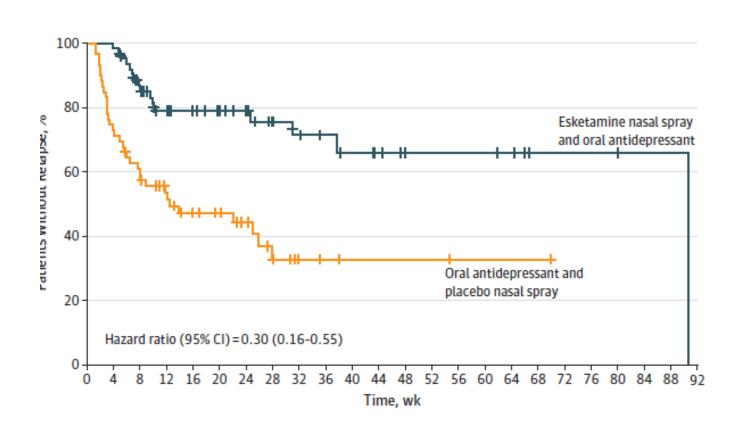
**Yale University** 

# Antidepressant effects of ketamine: FDA approved for Treatment-resistant depression, March 2019

#### Rapid initial response

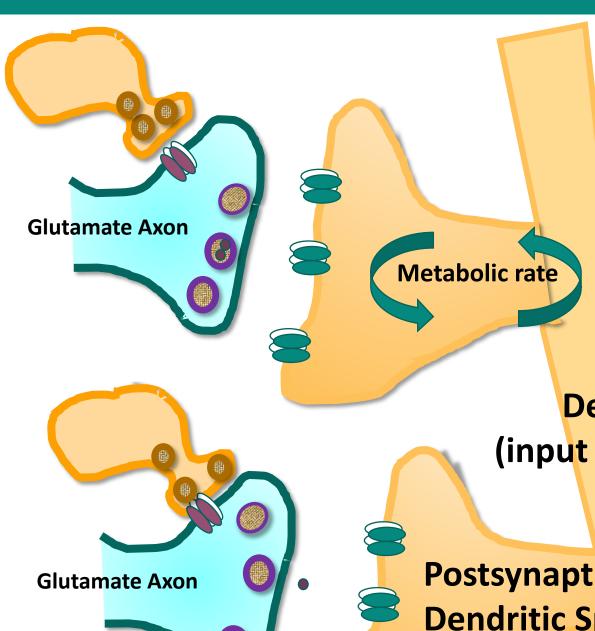


#### Maintenance of benefit and protection against relapse



# Esketamine (Spravato): Yale experience :: NEHI Network for Excellence in Health Innovation

- Opportunities:
  - High rates of efficacy, high satisfaction with treatment
  - Patient interest outstrips availability
- Barriers limit uptake:
  - REMS: Clinic-based treatment (addiction, side effects)
  - Reimbursement for Spravato more common than Ketamine
  - Inadequate public insurance reimbursement creates disincentives, disparities
- Clinic structures overcome obstacles: limited by space and staff
  - Adequate space and nursing support (3 pts/nurse)
  - 2-3 hr/treatment
  - Efficient Cohorting: IPS Clinic Ketamine (2 d/wk) and ECT (3 d/wk); some KET on ECT days
  - "Ketamine days": 4 cohorts per clinic day; up to 32 pts/day
  - Current Esketamine/Ketamine throughput: up to 50 patients/week



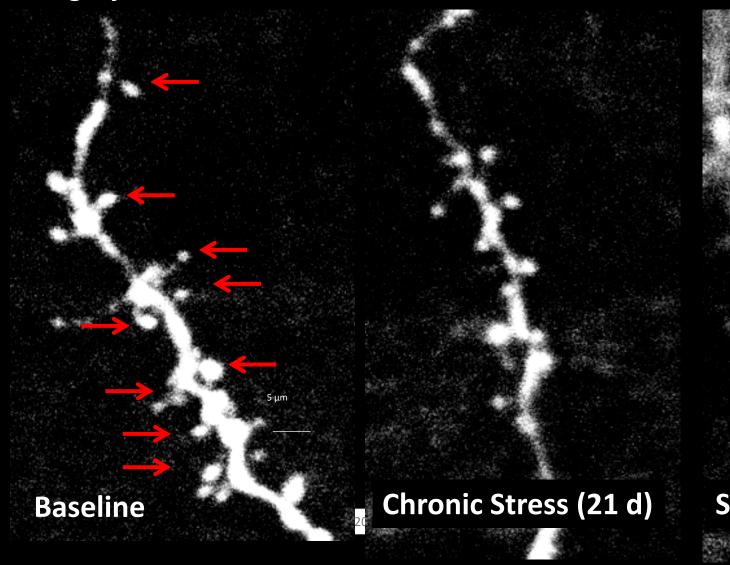
# Glutamate synapticular abnormalities in depression

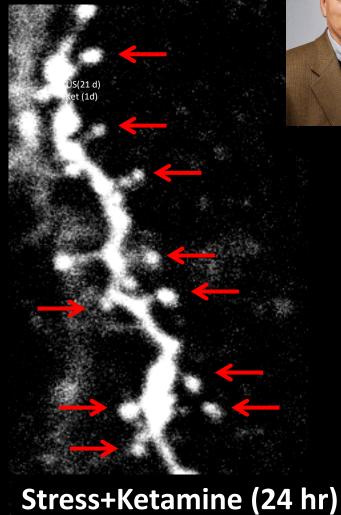
Reduced synaptic strength

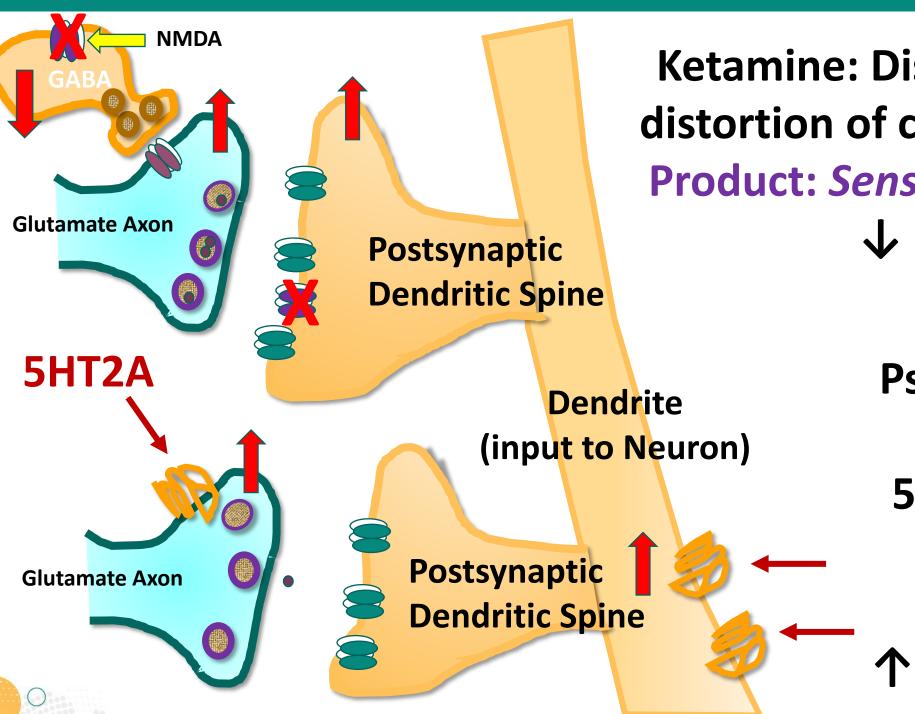
**Dendrite** (input to Neuron)

**Postsynaptic Dendritic Spine**  **Reduced synaptic density** 

Abdallah et al. MedRvix 2021 Duman et al. Neuron 2019 Holmes et al. Nat Comm 2019 Ketamine stimulates rapid regrowth of synaptic connectivity in these regions Duman and Aghajanian Science 2012







Ketamine: Disinhibition and distortion of cortical activity.

Product: Sensory Distortions

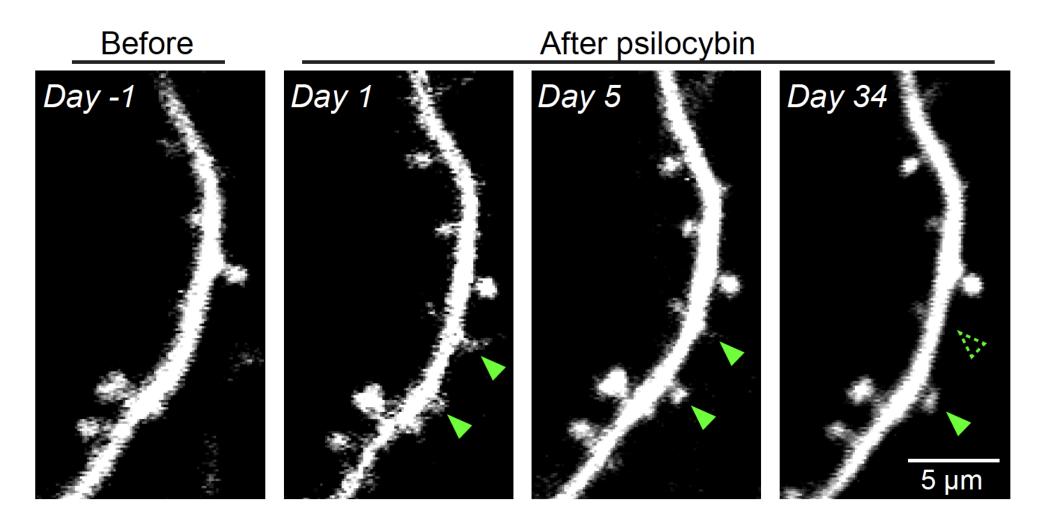
↓ neuroplasticity

Psilocybin: Direct activation via 5HT2A receptors Product:

**Hallucinations** 

1 neuroplasticity

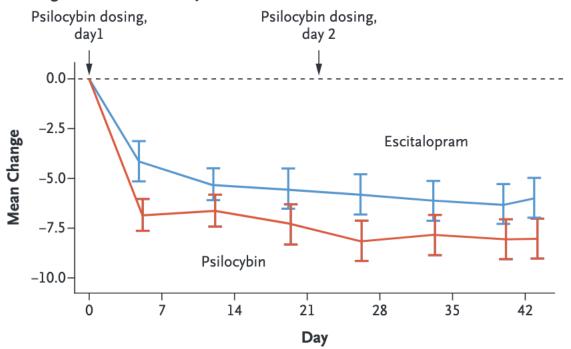
## Psychedelics also cause brain synapses to regrow



# Psilocybin (n=30) vs. Escitalopram (n=29) for MDD

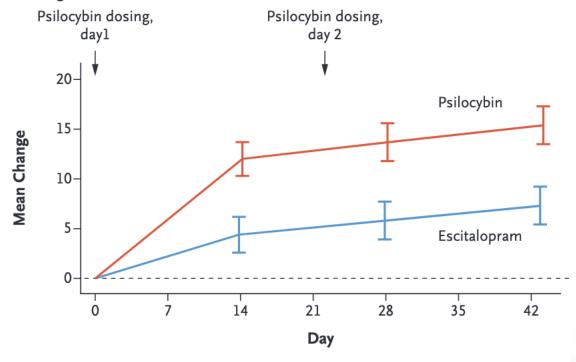
#### **Depression Scale**

#### A Change from Baseline in QIDS-SR-16 Score



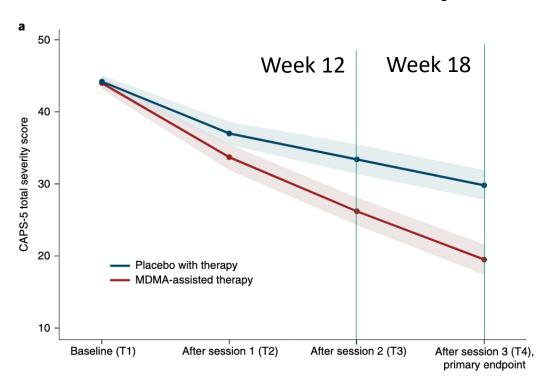
#### **Well-Being Scale**

#### **B** Change from Baseline in WEMWBS Score

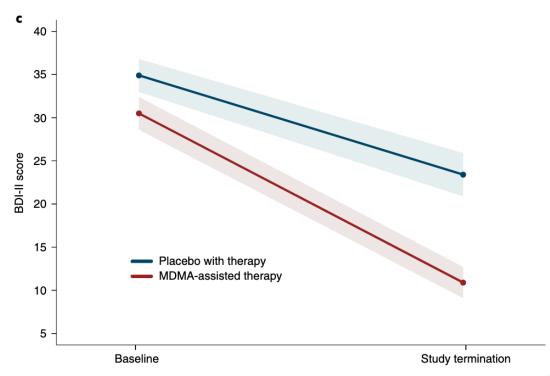


# 

### **Reduction in PTSD Severity**



### **Reduction in Depression Severity**





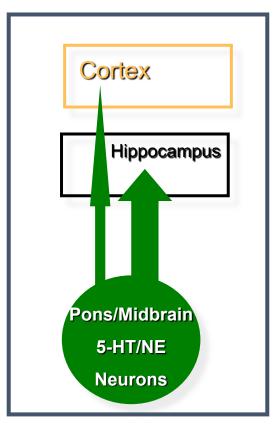
# Methylenedioxymethamphetamine (MDMA)

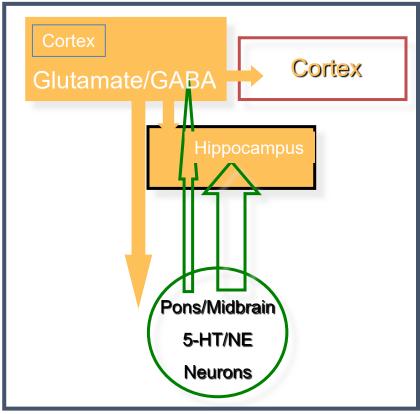


- Multiple targets (monoamine transporters, vesicular transporter, TAAR1)
- A serotonin-releasing amphetamine verses "regular" amphetamine
  - Dexamphetamine (Adderall): Norepinephrine>Dopamine>Serotonin
  - MDMA: Serotonin>Dopamine>Norepinephrine
- Alters perception, expectations, and emotions: prosocial
  - Euphorigenic/stimulating
  - Amplifies positive stimuli, suppresses negative stimuli
  - Amplifies positive responses and suppresses negative responses to social stimuli
  - Promotes positive attributions to self and others, suppresses negatives
- Mechanisms not clear, may involve 5HT2A, 5HT1A, etc. stimulation in circuits regulating mood, self-perception, and social cognition



# Broadening perspective: serotonin/midbrain and glutamate and cortico-limbic circuits









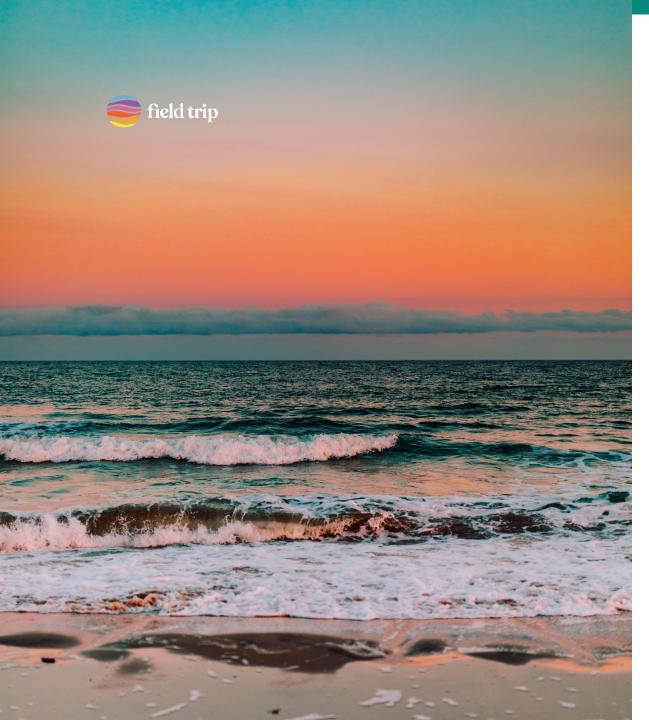


# Who we

## are

**Field Trip Health** is a new kind of mental health solution.

- Two operating divisions
  - Discovery developing novel psychedelic drugs through the FDA approval process.
  - Health largest provide of psychedelic assisted psychotherapy in the world with clinics across North America.
- Publicly traded on the TSX and have applied to list on the NASDAQ.
- Raised over \$110 million, from some of the leading biotech/healthcare investors in the country.





# The challenge Depression, Anxiety, PTSD

According to the CDC, in a 3-month period, patients with depression miss an average of 4.8 workdays and suffer 11.5 days of reduced productivity<sup>1</sup>

85% of employees say their mental health struggles at work negatively affect home life<sup>2</sup>

78% of workforce says that the pandemic has negatively affected their mental health<sup>2</sup>

76% believe their companies should do more to support their mental health<sup>2</sup>

1. CDC Workplace Health Promotion -

https://www.cdc.gov/workplacehealthpromotion/health-strategies/depression/evaluation-measures/index.html

2.Oracle Workplace Intelligence - https://www.oracle.com/a/ocom/docs/oracle-hcm-ai-at-work.pdf



### Current antidepressant approaches are failing most people.

There has not been significant innovation in depression treatments in decades

- Low responder rates
- Poor benefit/risk with chronic daily dosing
- High non-adherence and relapse rates

6-8 wks

Onset of efficacy

point improvement on **Hamilton Depression** Score (out of 52)

**75%** .....

non-adherence rate

30%

Response rates

**Side Effects** 

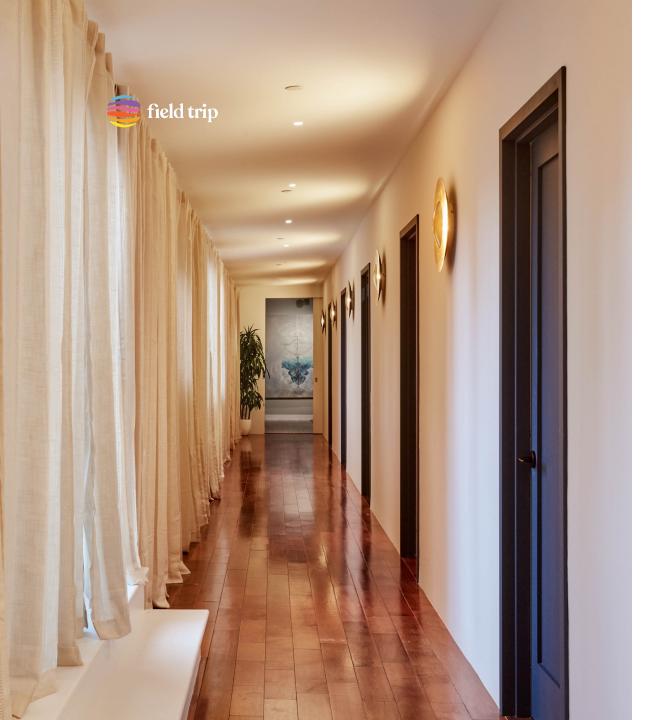
Addiction, Insomnia, Agitation, Loss of Libido, Violent Impulses, Suicidal Impulses

40-71% .....

relapse rates







## What we do

We offer FDA- approved ketamine with a tightly integrated program of psychotherapy for hard-to-treat mental health conditions.

- Depression
- Anxiety
- PTSD
- Substance-use disorders

Referral

your referral

screening appointment

· Meet with a Field Trip · We receive and review psychiatrist to Your Care Coordinator determine your eligibility for treatment will call you to set up a



#### Psychotherapy

- If eligible, we'll schedule your first psychotherapy session: Intake and Preparation session
- · You'll receive an invite to create a Field Trip Portal account where you can access your journey tools, content, appointment info, and message your Care Team.



#### Ketamine

· Visit your Field Trip Health Center for your first Ketamine **Exploratory Session** 



( 2 hours



· Fourth Ketamine **Exploratory Session** 





2 hours



Third Ketamine

**Exploratory Session** 

#### Ketamine

Integration · First integration session with your Field Trip psychiatrist or

psychotherapist

90 min



1 hour

#### Ketamine

• Second Ketamine **Exploratory Session** (usually 1-2 days after first Ketamine dose)



2 hours

Integration



#### Ketamine

 Second integration session with your Field Trip psychiatrist or psychotherapist



field trip



• Fifth Ketamine **Exploratory Session** 



#### Ketamine

· Sixth Ketamine

#### **Exploratory Session**

· Final integration session with your Field Trip psychiatrist or psychotherapist

Integration



1 hour



#### Follow Up

 We will continue to support you along your journey by providing mindfulness tools, content, and support through our Patient Portal



#### Evaluation

· You and your Care Team will discuss additional treatments if recommended or desired



## The program

Field Trip Health's personalized approach to ketamine-assisted psychotherapy

We recognize the value of combining the fast-acting, acute antidepressant effects of ketamine with an evidence-based psychotherapeutic approach for sustained improvements in mental health and patient self-efficacy.

To achieve these sustainable outcomes, we augment ketamine administration with client-centered talk therapy techniques (e.g. cognitive behavioral therapy, motivational interviewing, behavioral activation), as well as digitally-delivered educational and interactive content, including mood-monitoring and mindfulness exercises.

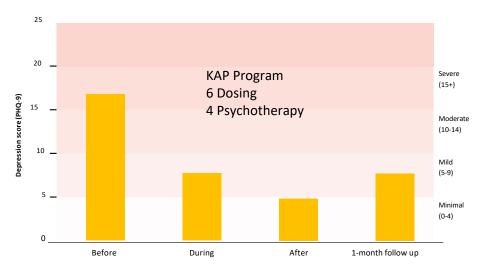
A typical patient journey is illustrated by the infographic on the left.



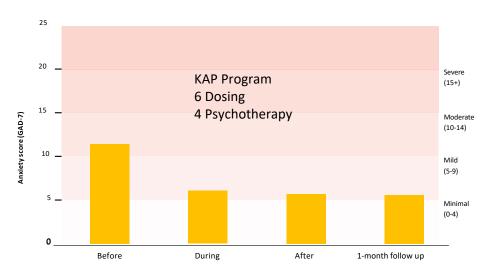


# Delivering significant quality of life improvements for our patients.

Patient depression scores after ketamine-assisted psychotherapy for hard-to-treat mental health disorders (n=26)



Patient anxiety scores after ketamine-assisted psychotherapy for hardto-treat mental health disorders (n=26)



Results not peer-reviewed. The typical KAP program duration is 3-4 weeks. "Before" data are based on surveys taken at psychiatric consultation; where data are missing, surveys from psychologist intake session are supplemented.





### Cost and productivity gains

#### **Treatment Programs**

- Cost: Approx. \$5000 for the Core program, some insurance coverage
- Structure of Core Program: 1 preparatory session; 6 ketamine dosing + therapy sessions; 3 integration therapy sessions

#### **Productivity gains**

- Studies<sup>1</sup> show that for every 1 point increase in PHQ-9 there is a productivity loss of 1.65%
- Patients who undergo Field Trip's ketamine assisted psychotherapy have an average reduction of 8.6 points on the PHQ-9 scale.
- Many of our patients have been able to return to work after being on disability leave.



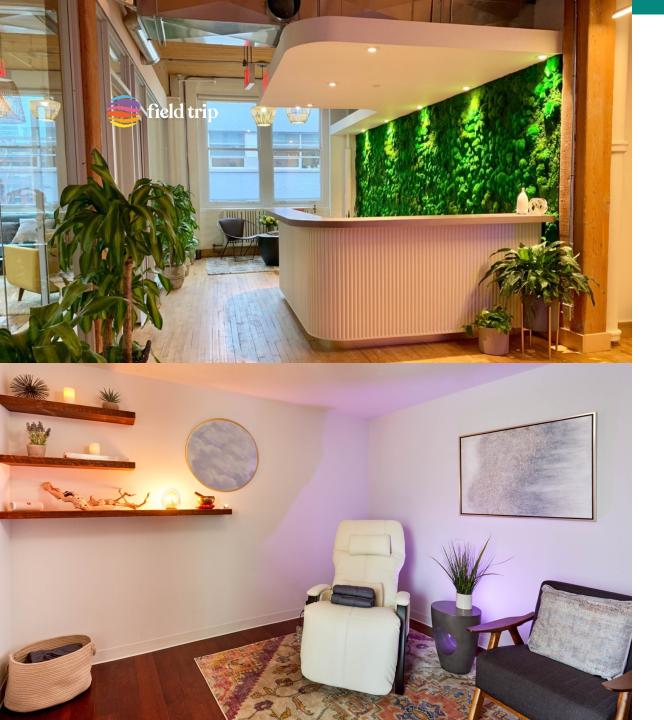
## Testimonials

'For the first time I was going about my life without that pit in my stomach, without the waves of fear roiling in my chest, without feeling my throat constrict at the simple thought of having to go to the grocery store. That, in itself, was amazing.'

'FT was one of the few places that I felt truly and consistently viewed me holistically, as a full person with passions, hobbies, and dreams outside of simply getting better.'

'I simply don't have enough good things to say about the incredible team of professionals at Field Trip. They are kind, compassionate, incredibly wise and intelligent.'

'Before this work I was trying to keep walls up and people out, now I feel safe to let the walls down and people in.'



# Our clinics



State-of-the-art mental health centers across the USA and Canada

Current Locations: Locations Under Construction:

New York

Chicago

Los Angeles

Atlanta

Houston

Toronto

Seattle

San Diego

San Carlos

Austin

Washington, DC

Fredericton, NB

Many more...



## Questions & Challenges

How do you scale access to these types of treatments? Cost and lack of insurance coverage are the main barriers to access.

How will psychedelic assisted psychotherapy integrate into the existing ecosystem? Need for specialized centers?

What are the implications for clinicians, drug developers, payers, and patients?

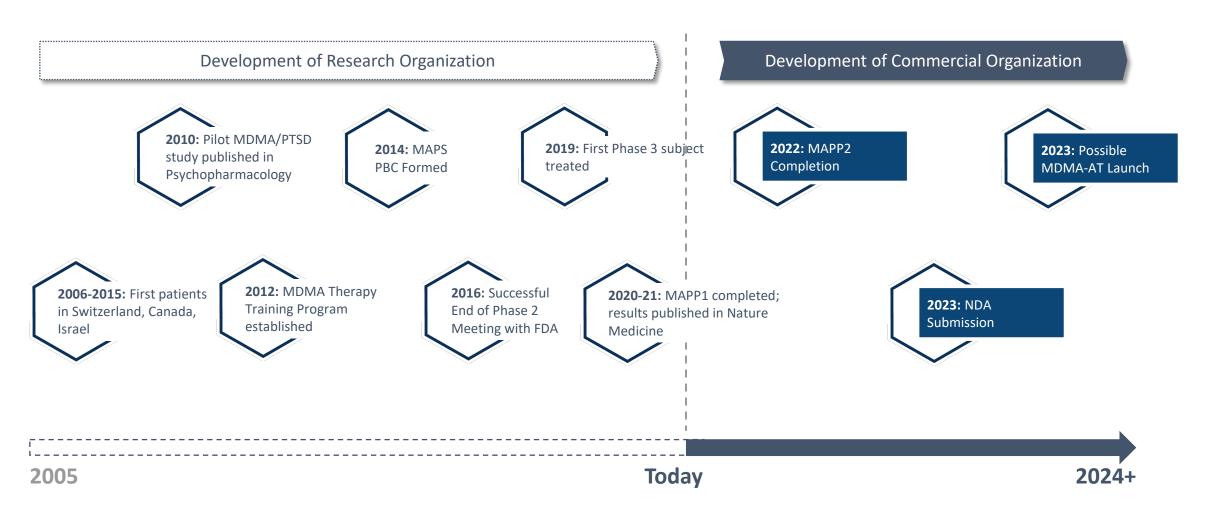




# We are rapidly approaching the possible launch of MDMA-assisted therapy as an approved treatment for PTSD



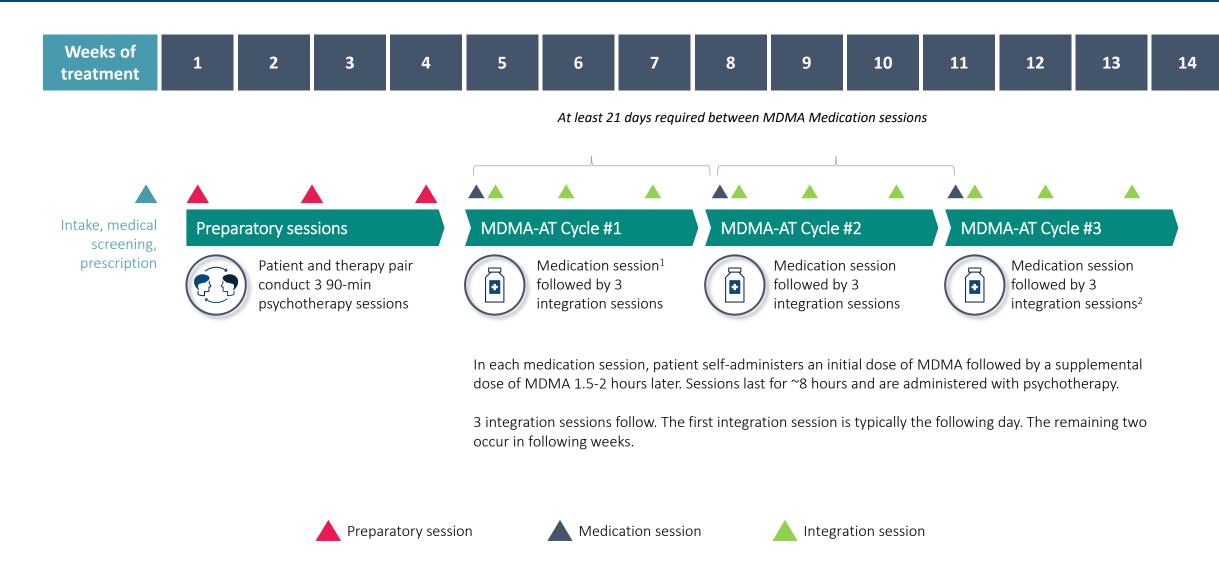
#### **Evolution of MAPS Public Benefit Corporation**



### MDMA-assisted therapy protocol

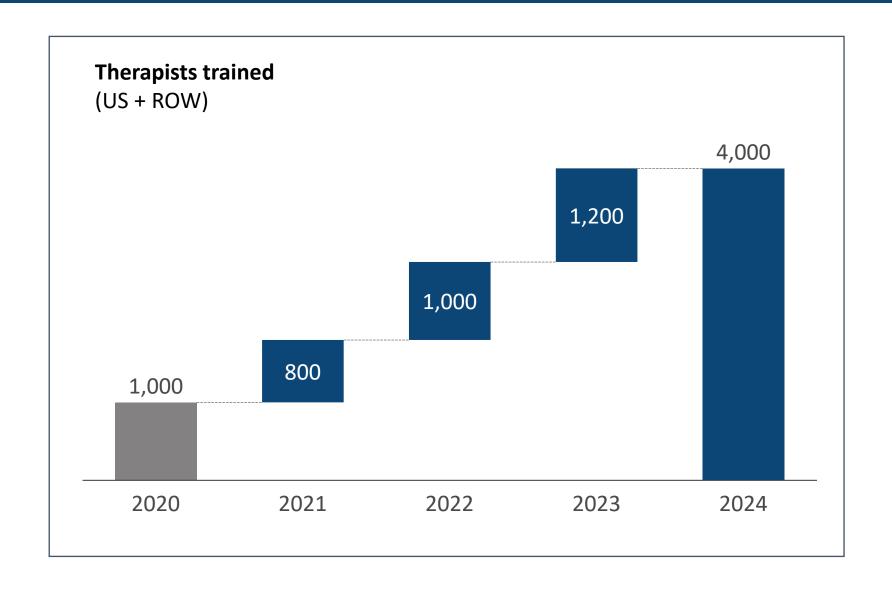






# MAPS' MDMA Therapy Training Program is scaling aggressively in preparation for launch





### Equitable access is a central priority for our commercialization efforts





It's not this hierarchical model, it's more like 'Can we meet somebody at this level together and collaborate and create trust and empower them to be able to understand and to know where their path is? And to really respect that path.'

-Marcela Ot'alora, Therapist, Co-Investigator, Trainer

### We are studying both the clinical effectiveness and cost-effectiveness of MDMA-assisted therapy

#### **PLOS ONE**

The cost-effectiveness of MDMA-assisted psychotherapy for the treatment of chronic, treatment-resistant PTSD

Elliot Marseille 12, James G. Kahn2, Berra Yazar-Klosinski3, Rick Doblin3

1 Health Strategies International, Oakland, California, United States of America, 2 University of California, San Francisco, California, United States of America, 3 Multidisciplinary Association for Psychedelic Studies (MAPS), Santa Cruz, California, United States of America

\* emarseille @ comcast.net



OPEN ACCESS Citation: Marseille E. Kahn JG. Yazar-Klosinski B. Doblin R (2020) The cost-effectiveness of MDMAassisted osychotherapy for the treatment of chronic, treatment-resistant PTSD. PLoS ONE 15(10): e0239997. https://doi.org/10.1371/journal.

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Data Availability Statement: Interested researchers may submit a data use proposal to

Abstract

Chronic posttraumatic stress disorder (PTSD) is a disabling condition that generates consid erable morbidity, mortality, and both medical and indirect social costs. Treatment options are limited. A novel therapy using 3.4-methylenedioxymethamphetamine (MDMA) has shown efficacy in six phase 2 trials. Its cost-effectiveness is unknown.

#### Methods and findings

To assess the cost-effectiveness of MDMA-assisted psychotherapy (MAP) from the health care payer's perspective, we constructed a decision-analytic Markov model to portray the costs and health benefits of treating patients with chronic, severe, or extreme, treatmentresistant PTSD with MAP. In six double-blind phase 2 trials, MAP consisted of a mean of 2.5 90-minute trauma-focused psychotherapy sessions before two 8-hour sessions with MDMA (mean dose of 125 mg), followed by a mean of 3.5 integration sessions for each active session. The control group received an inactive placebo or 25-40 mg. of MDMA, and otherwise followed the same regimen. Our model calculates net medical costs, mortality, qualityadjusted life-years (QALYs), and incremental cost-effectiveness ratios. Efficacy was based responses alongside final, published articles. The on the pooled results of six randomized controlled phase 2 trials with 105 subjects; and a four-year follow-up of 19 subjects. Other inputs were based on published literature and on assumptions when data were unavailable. We modeled results over a 30-year analytic horiaccess article distributed under the terms of the zon and conducted extensive sensitivity analyses. Our model calculates expected medical Creative Commons Attribution License, which costs, mortality, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratio. Future costs and QALYs were discounted at 3% per year. For 1,000 individuals, MAP generates discounted net savings of \$103.2 million over 30 years while accruing 5.553 discounted QALYs, compared to continued standard of care, MAP breaks even on cost at 3.1 years while delivering 918 QALYs. Making the conservative assumption that benefits cease MAPS (askmaps@maps.org) to gain access to the after one year, MAP would accrue net costs of \$7.6 million while generating 288 QALYS, or underlying de-identified data. Following internal \$26,427 per QALY gained.

PLOS ONE | https://doi.org/10.1371/journal.pone.0239997 October 14, 2020

Third-party payers are likely to save money within three years by covering this form of therapy.

Covering 1,000 PTSD patients would generate \$103M in savings over 30year time frame.



# Thank you for joining us. Please provide your feedback by completing our survey.