

Ketamine for Suicide Prevention

Quinn M Snyder, MD

CEO, Kadelyx Health



kadelyx

Learning Objectives



1. Summarize evidence supporting ketamine's rapid and robust anti-suicidal effects



2. Compare IV ketamine vs intranasal esketamine (Spravato) in acute and outpatient settings



3. Describe clinical implementation in the ED and outpatient clinics



4. Review safety, monitoring, and regulatory requirements (REMS, documentation)

What is Ketamine?

High doses:

Most commonly used **anesthetic** in the world

Moderate doses:

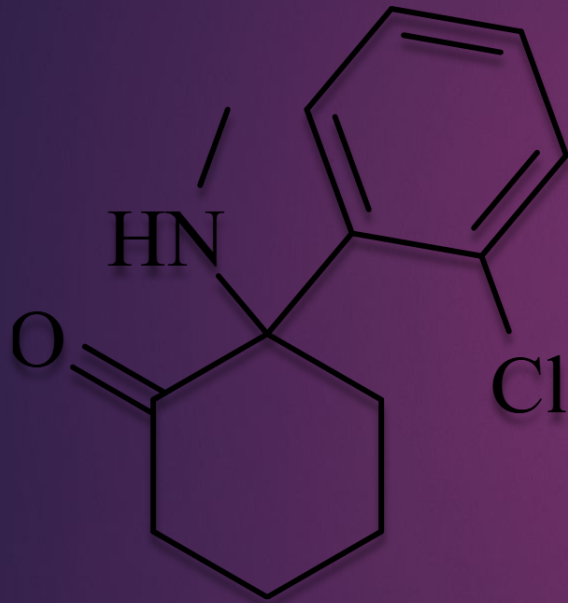
Treats a variety of **psychological conditions**

Low doses:

Effectively treats **acute and chronic pain**

Administered via injections, orally, inhaled, topically

Synthetic substance but is also found in nature



Ketamine has the
broadest
therapeutic
spectrum
of all medications

History of Ketamine



Also
Ketamine's
history...

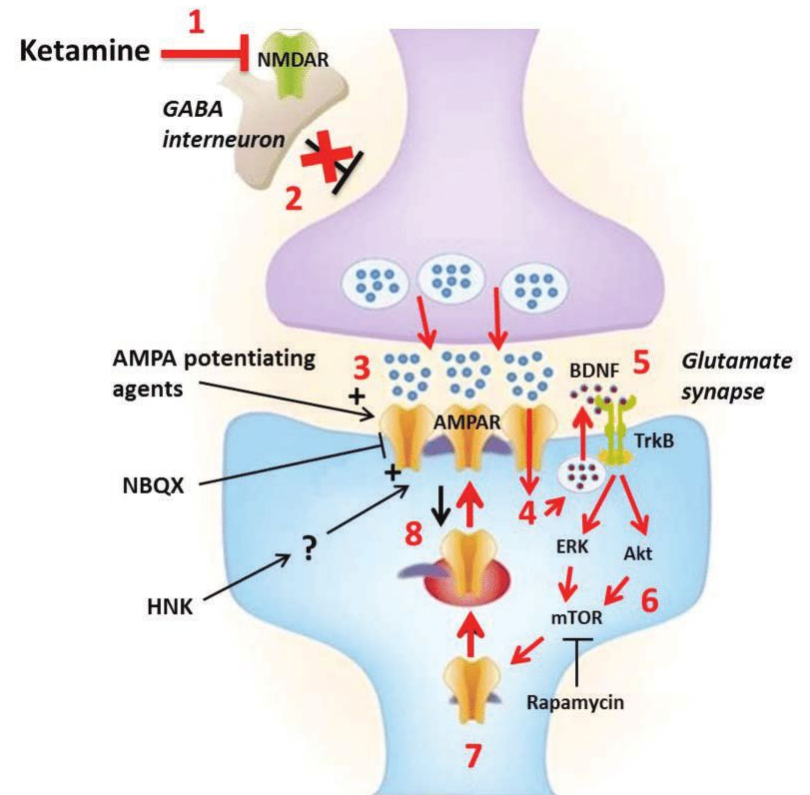




Ketamine is a medication
with *DISSOCIATIVE* and
PSYCHEDELIC properties

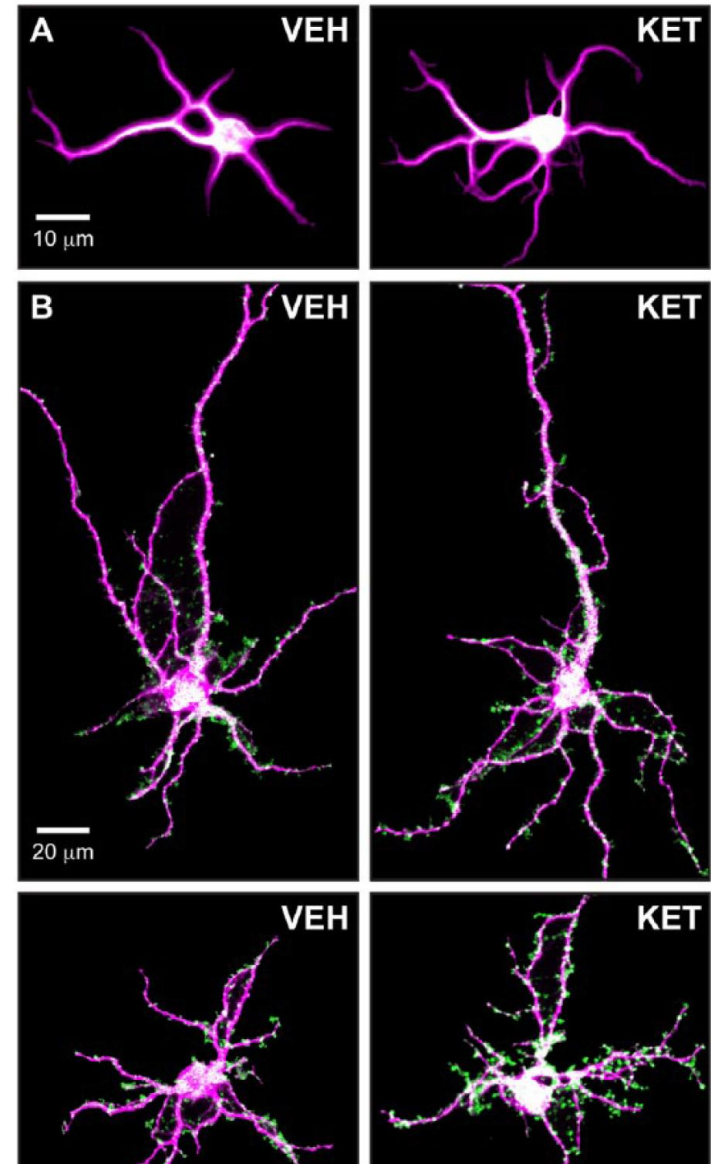
KETAMINE BIOCHEMISTRY

1. NMDA ANTAGONIST
2. GLUTAMATE REGULATION
3. BDNF REGULATION



Why Does Ketamine Work?

- ▶ **Neurogenesis, Synaptogenesis, and NEUROPLASTICITY**
- ▶ “Structural Reorganization of the Brain Itself”
- ▶ More Synapses, New Connections, New Ways of Thinking



Ketamine is the most powerful and fastest-acting medication for SUICIDE PREVENTION

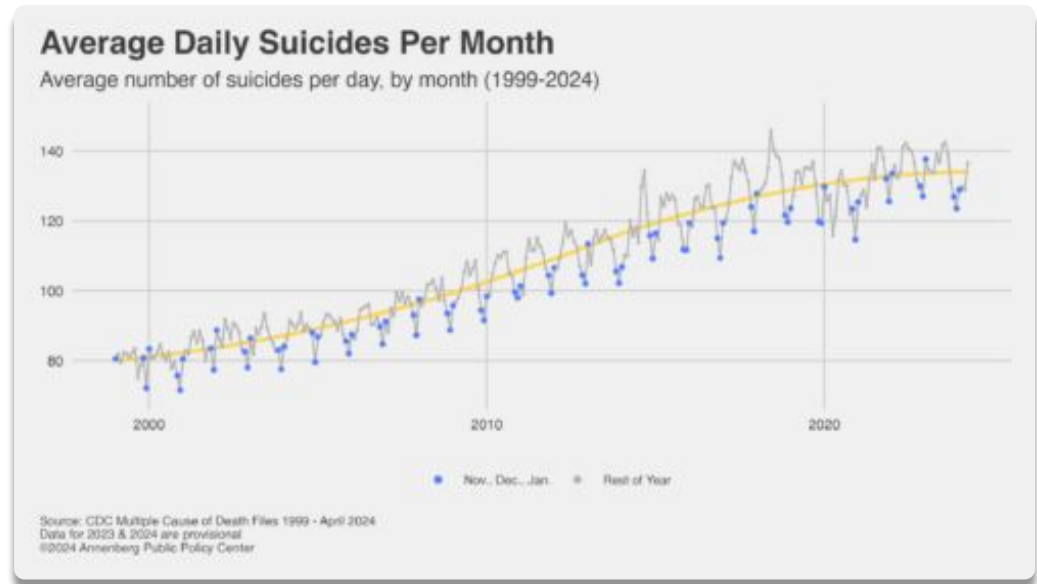
ChatGPT ▾

What is the most powerful and fastest acting drug for suicide prevention?

The most powerful and fastest-acting drug for suicide prevention currently known is **ketamine**, including both its intravenous form (**racemic ketamine**) and its FDA-approved intranasal formulation (**esketamine**, brand name *Spravato*).

Suicide Crisis & Treatment Gap

- ▶ Suicide is a leading cause of death in the U.S. (CDC, 2023)
- ▶ Conventional antidepressants take weeks to work, if at all
- ▶ Ketamine offers rapid mood and suicidality reduction within hours



DEPRESSION is a time sensitive disease with a significant mortality rate

Review of Current Evidence

- ▶ Randomized controlled trials
- ▶ Meta-analyses of suicidal ideation outcomes
- ▶ ED pilot trials
- ▶ Real-world observational data

Ketamine RCTs: Rapid Reduction in Suicidal Ideation

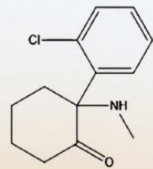
- ▶ Ketamine v Midazolam (Grunebaum 2018)
 - ▶ 1x 0.5 mg/kg IV dose → rapid reduction in SI within 24 hrs (n=80)
 - ▶ Sustained effects for at least 6 weeks beyond treatment
- ▶ Ketamine vs Placebo (Abbar 2022)
 - ▶ 2x 0.5 mg/kg IV dose → rapid reduction in SI
 - ▶ 63% vs 31.6% achieved full remission at the 3 day mark

Ketamine Meta-Analyses & Systematic Reviews

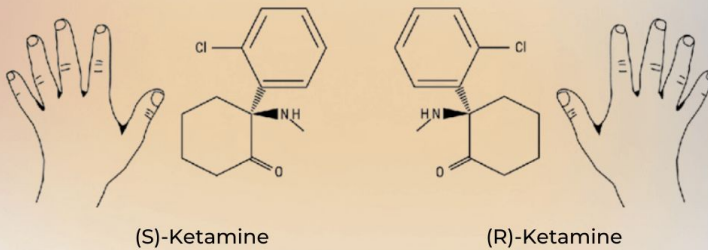
- ▶ Best Recent Meta-analysis (Shen et al., 2024)
 - ▶ 14 studies with 1,380 participants
 - ▶ Overall SMD -0.45 to -0.65 for SI reduction
 - ▶ Significant reduction in suicidal ideation within the first day after treatment
 - ▶ In repeated treatment, the degree of recovery of suicidal ideation after the last dose was significantly greater than that after the first dose
 - ▶ Effect strongest at 24–72 hrs

Emergency Department Evidence

- ▶ RCT in ED (Domany et al., 2019)
 - ▶ Ketamine 0.2mg/kg IV x 1 dose in ED (n=18)
 - ▶ At 90 minutes...
 - ▶ 88% of ketamine group achieved full remission of SI
 - ▶ 33% of placebo group achieved remission
 - ▶ Effect seemed to be durable to 2 weeks beyond infusion



(R,S)-Ketamine
Conventional, racemic ketamine



PSYCHEDELIC ALPHA

Adapted from Jelen et al. (2021), *Ketamine: A tale of two enantiomers*

SPRAVATO
(esketamine)

O-Chem
Timeout

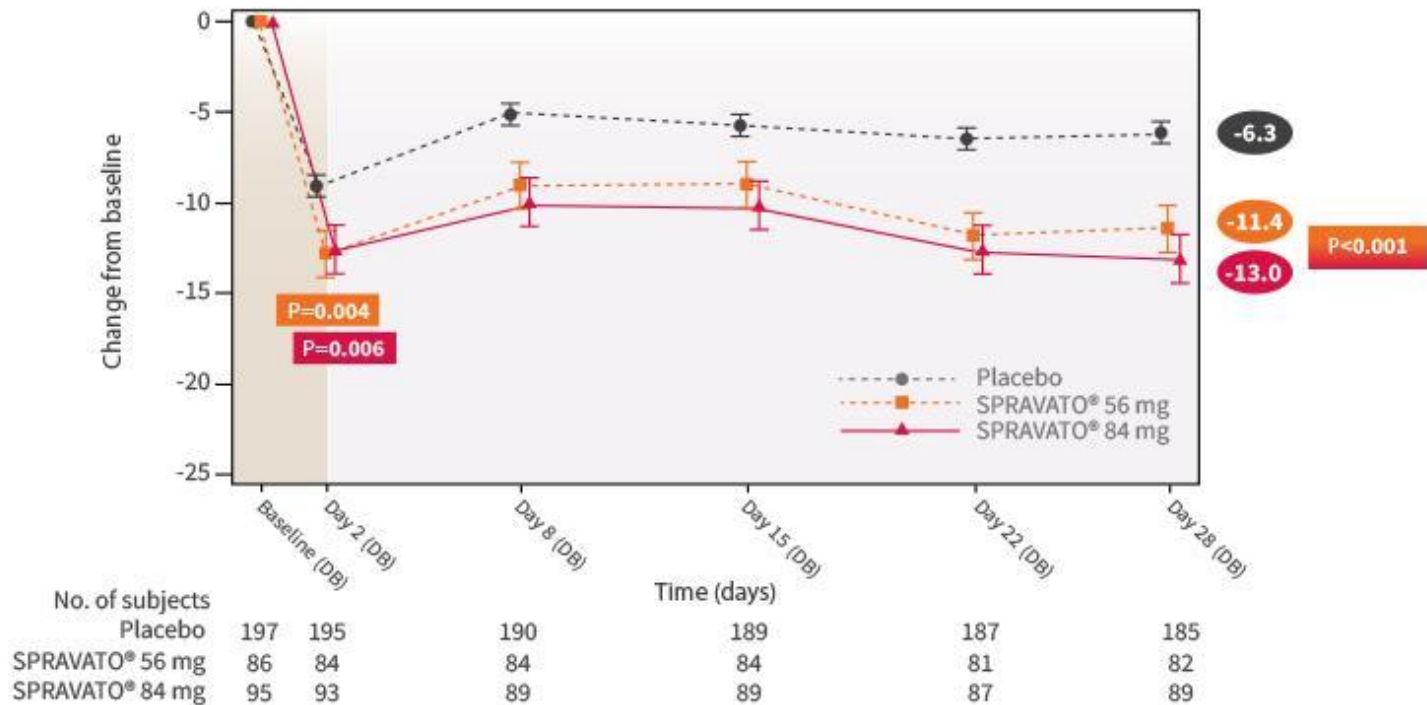
More on Spravato

- ▶ Patented in 2019 by J&J
- ▶ Inhaled Version of Ketamine
- ▶ “Ketamine-Lite”
- ▶ 41% of people dissociate (less per clinical experience)



Esketamine (Spravato) for TRD

Least-squares Mean Change from Baseline in MADRS Total Score Over Time in Patients with TRD in Study 3 (Full Analysis Set)²



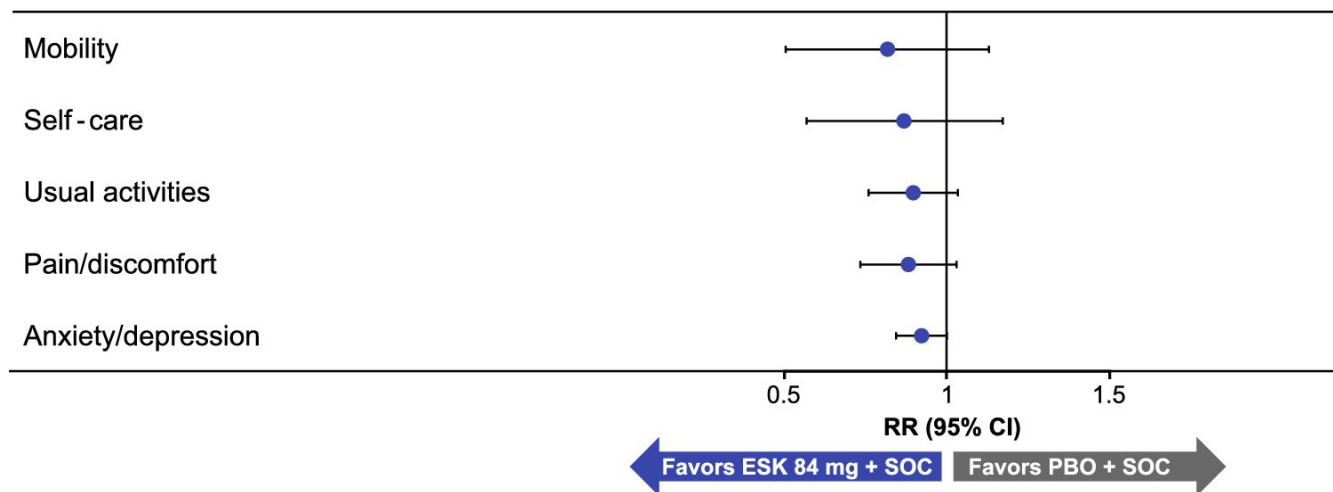
Spravato Trial Results

Trial Name	Sample Size	Population	Primary Outcome	Key Findings	Reference
TRANSFORM-2	N = 223	Adults with TRD	Change in MADRS at Day 28	Significant reduction in MADRS (mean diff = -4.0; $p = 0.020$)	Popova et al., 2019 ¹⁴
SUSTAIN-I	N = 297	TRD patients in remission	Time to relapse	Esketamine significantly delayed relapse (HR = 0.49; $p = 0.003$)	Daly et al., 2019 ³⁶
ASPIRE I	N = 226	MDD with suicidal ideation	MADRS score reduction at 24 hrs	Significant reduction in MADRS (difference = -3.8; $p < 0.05$)	Fu et al., 2020 ⁴⁵
ASPIRE II	N = 240	MDD with suicidal ideation	MADRS score reduction at 24 hrs	Significant MADRS improvement (difference = -3.9; $p < 0.05$)	Ionescu et al., 2021 ⁴⁶
Pooled Data	-	Pooled phase 3 trials	Remission, time to response	Remission rates 27–50%, onset within 24 hours	Wajs et al, 2020 ⁴⁸

Abbreviations: MDD, Major Depressive Disorder; MADRS, Montgomery-Åsberg Depression Rating Scale; TRD, Treatment-Resistant Depression.

ASPIRE Trials in Detail

- ▶ MDD + acute suicidality (n = 466)
- ▶ MADRS and C-SSRS improved rapidly
- ▶ Effects within 4 hours, persisting up to 25 days



Real-World Outcomes

- ▶ Observational data: Fewer ED revisits and admissions (J Clin Psychiatry, 2025).
- ▶ Mayo Rochester Depression Center (n=97)
- ▶ After the acute treatment phase for both ketamine and Spravato:
 - ▶ ED visits for suicidal ideation decreased by 84% (IRR=0.16, 95% CI, 0.06–0.46, $P=.001$)
 - ▶ Total ED visits for suicidality decreased by 63% (IRR=0.37, 95% CI, 0.18–0.77, $P=.007$)

Ideation vs Behavior

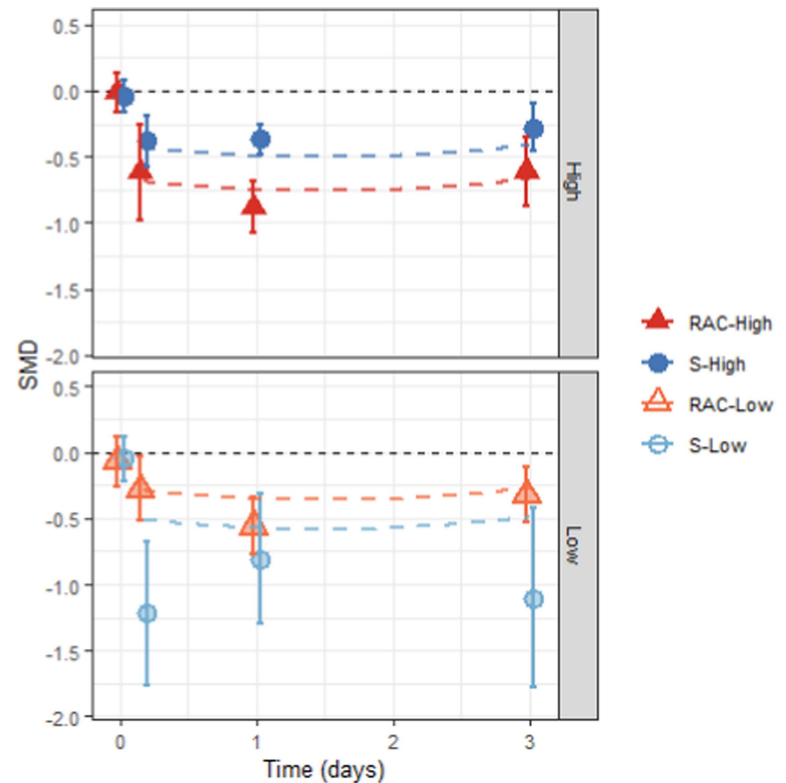
- ▶ Robust evidence for suicidal ideation reduction
- ▶ No definitive RCT showing reduction in suicide attempts or mortality for ketamine or Spravato

MY PERSONAL
EXPERIENCE

THIS STUFF
ACTUALLY
WORKS

Ketamine vs Esketamine

- ▶ Meta-analysis in Lancet (Nikolin et al, 2023)
- ▶ Ketamine outperformed esketamine in single and repeated dosing
- ▶ Higher doses were more effective than lower doses
- ▶ “Differences were evident in initial effects, ongoing treatment, and lasting effects after the final dose.”



Bottom Line:

KETAMINE is

MORE EFFECTIVE than

esketamine

Regulatory Environment

- ▶ Ketamine is only FDA-approved for anesthesia and procedural sedation (IV/IM only)
- ▶ All current ketamine use outside of this designation is off-label
- ▶ 1/5 of all prescribed medications are off-label
- ▶ Results in very confusing regulatory environment
- ▶ Esketamine is FDA-approved for:
 - ▶ Treatment-Resistant Depression (TRD) – failed 2x antidepressants
 - ▶ MDD with “Suicidal Thoughts or Actions”

Ketamine or Spravato?

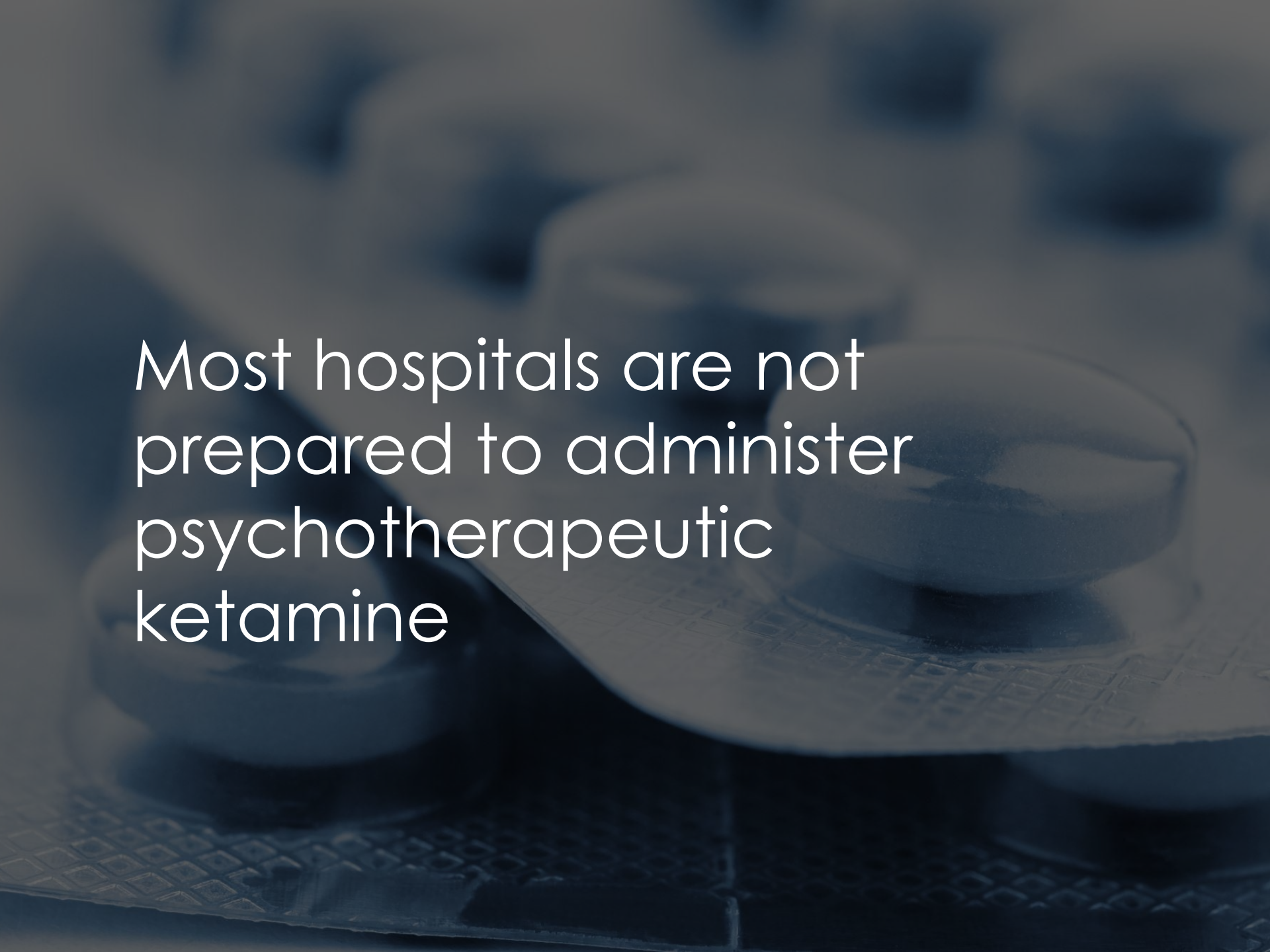
	Ketamine	Spravato
Better Outcomes	X	
Faster Effects	X	
Safer for Patient	---	---
Ease of Access	X	
Actual Drug Cost	X	
Cost to Patient		X

Outpatient Spravato Workflow

- ▶ 1. Confirm REMS certification and Insurance Benefits
- ▶ 2. Baseline Psychiatric Screen: BP, PHQ-9, C-SSRS
- ▶ 3. Must obtain PRIOR AUTHORIZATION
 - ▶ Minutes to Weeks for approval
 - ▶ Can request “urgent review”
- ▶ 4. Induction: 2x/week × 4 weeks then 1x/week x 4 weeks
- ▶ 5. Track outcomes

ED Workflow Example

- ▶ 1. Screen & clear patient.
- ▶ 2. ED Psychiatric Eval (CRSS, etc)
- ▶ 3. Consent for off-label use
- ▶ 4. Administer Ketamine 0.5 mg/kg IV over 40 mins
- ▶ 5. Observe 2–4 hrs
- ▶ 6. Transfer to facility or to home?

A close-up photograph of a hand wearing a white nitrile glove, holding a single white, oval-shaped pill. The hand is positioned over a white paper napkin with a subtle grid pattern. The background is dark and out of focus, showing more of the same napkins. The overall lighting is soft, highlighting the texture of the glove and the pill.

Most hospitals are not
prepared to administer
psychotherapeutic
ketamine

Safety Profile

- ▶ Ketamine/esketamine should be only used in a controlled and monitored medical setting
- ▶ Biggest Danger: Respiratory Depression at high levels
- ▶ Common side effects: dizziness, transient BP elevation, nausea.
- ▶ Dissociation (therapeutic effect or adverse reaction?)
- ▶ Long-term: monitor cognition, urinary function (ketamine-induced cystitis)

Contraindications

H/o Psychosis

Bipolar Disorder with uncontrolled mania

Current Pregnancy

Uncontrolled HTN

H/o Intracerebral hemorrhage

Aneurysmal Vascular Disease

Allergy to ketamine or Spravato ingredients

REMS & Regulatory Points

- ▶ Required for all outpatient clinics and hospitals administering Spravato
- ▶ Spravato: Document vitals, adverse events, and 2-hour observation
- ▶ Ketamine: Should be administered by Providers with licensed to provide DEA Schedule III drugs (NO REMS)
- ▶ Monitoring protocols for ketamine are far less regulated than for Spravato

SPRAVATO[®] REMS

(Risk Evaluation and Mitigation Strategy)

Key Takeaways

- ▶ Fastest-acting and most powerful anti-suicidal medications known
- ▶ Reliable reduction in suicidal ideation within hours
- ▶ Ketamine works better than Spravato but is NOT covered by insurance
- ▶ Integration into ED and outpatient workflows can save lives
- ▶ Research gap: More studies needed on long-term prevention of suicide attempts

THANK
YOU

Quinn M Snyder MD
quinn@kadelyx.com
602-206-4980



kadelyx

References

1. Shen ZY et al., 2024.
2. Abbar M et al., BMJ, 2022.
3. Kashani P et al., J Emerg Med, 2014.
4. Grunebaum MF et al., Am J Psychiatry, 2018.
5. FDA Spravato Clinical Review, 2020.
6. Patarroy L et al., J Clin Psychiatry 2025.