

Next Generation Treatments for Resistant Depression: The UMN Interventional Psychiatry Approach

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Disclosure information

- I have no financial relationships to disclose
- I will discuss off-label use of ketamine in this presentation

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Learning objectives

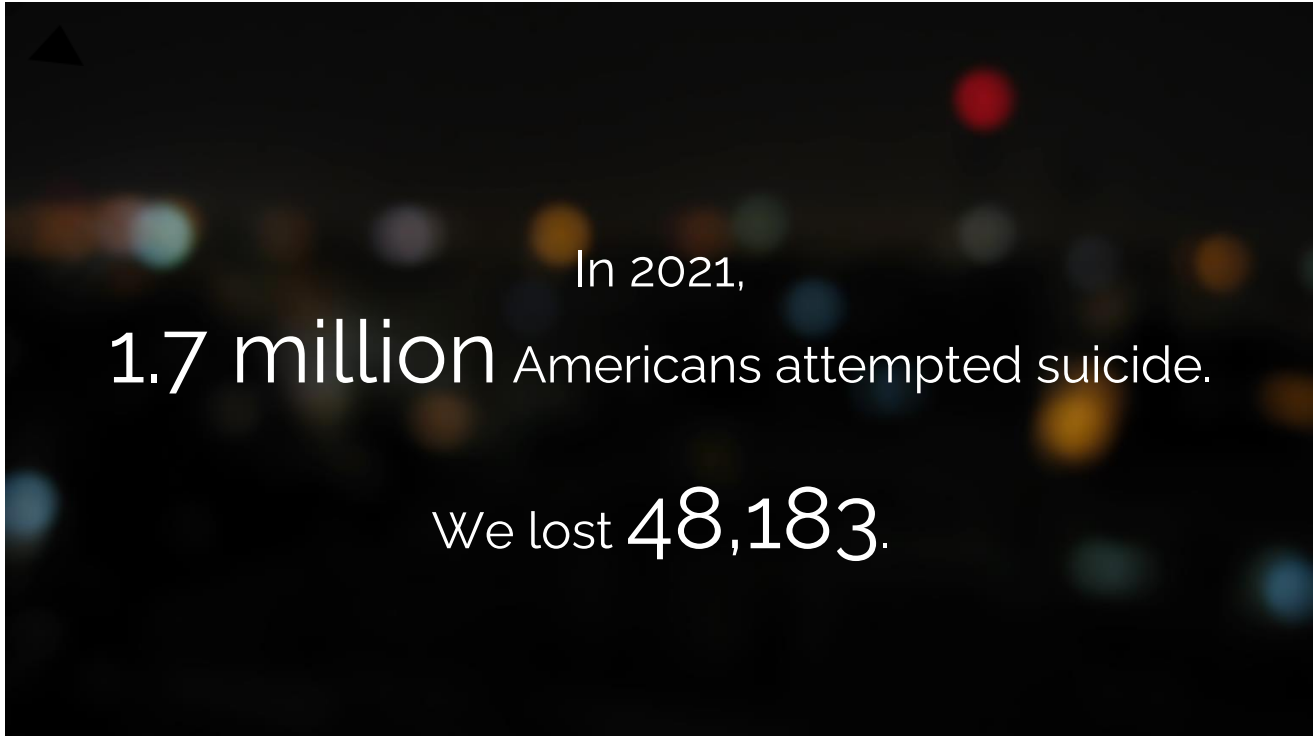
- Describe an innovative care model designed for the comprehensive management of treatment-resistant depression, integrating interventions such as ketamine, TMS, ECT, VNS, advanced pharmacotherapy, and evidence-based psychotherapy.
- Describe the optimal clinical strategies for integrating interventional psychiatric treatments into the management of treatment-resistant depression.

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An aerial photograph showing a dense network of rivers and streams winding through a lush, green forested landscape. The water bodies are dark and contrast with the surrounding greenery.

**Depression is the leading
cause of disability worldwide.**

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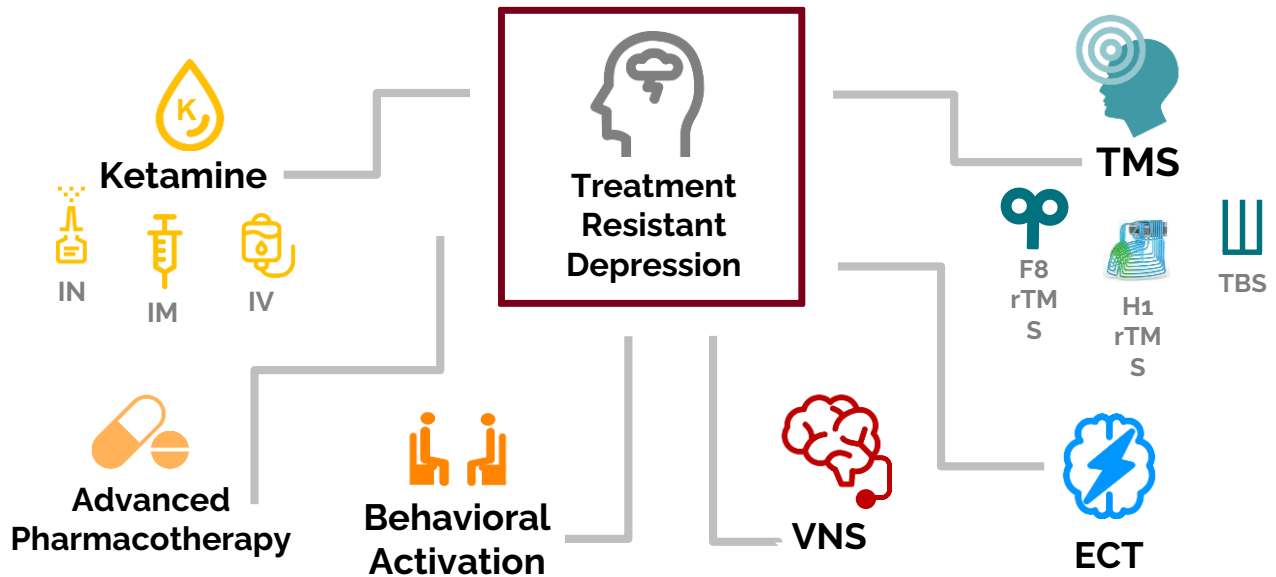
MHealth Interventional Psychiatry Program

Treatment Resistant Mood, Anxiety, & Trauma Disorders

- C. Sophia Albott, MD
- Lisa Anderson, PhD
- Lara Brown, LICSW
- Devin Hanson, PhD
- Alex Herman, MD, PhD
- Charles Lewis, MD
- Ziad Nahas, MD
- Carol Peterson, PhD
- Sabine Schmid, PhD
- Melanie Swanson, RNCC
- Alik Widge, MD, PhD
- Saydra Wilson, MD

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MHealth Interventional Psychiatry Program

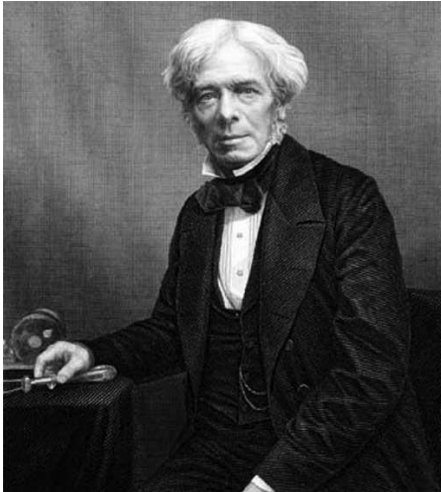


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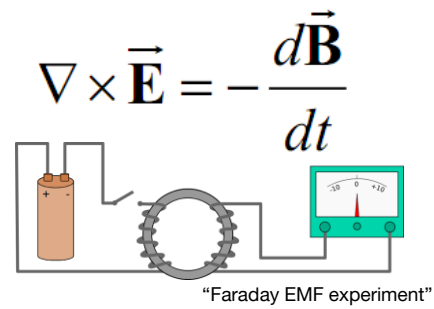
Transcranial Magnetic Stimulation

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Induction



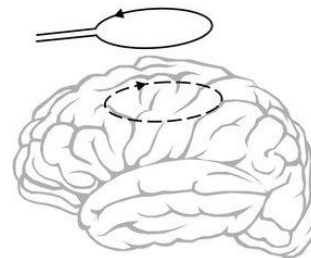
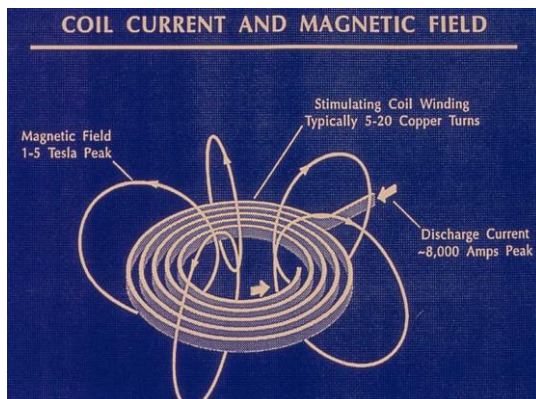
Michael Faraday (1791–1867) - Qualitative



James Clerk Maxwell (1831–1879) - Equation

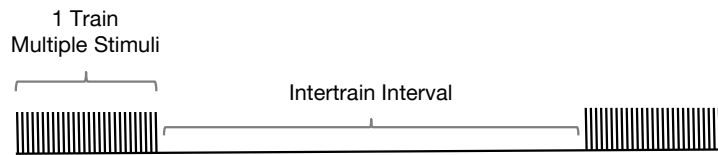
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Induction in Action



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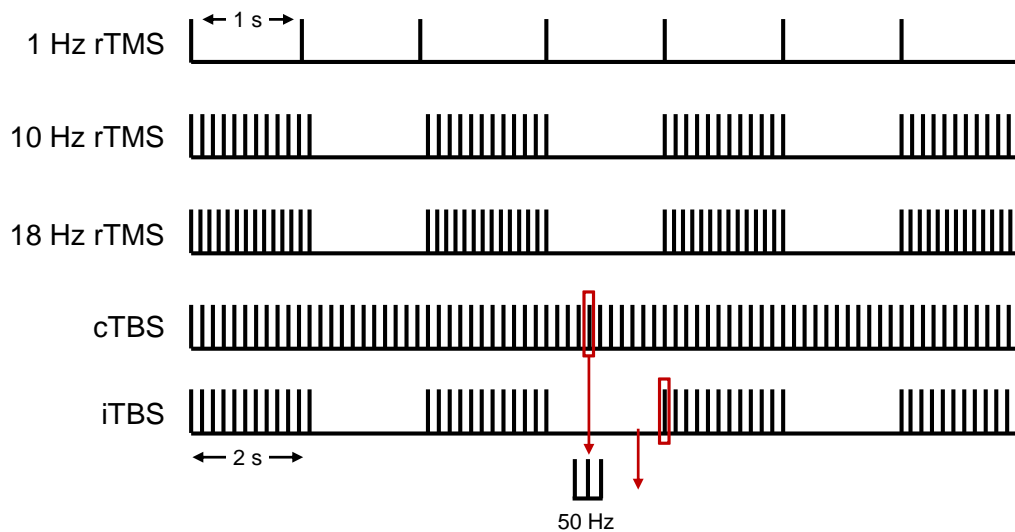
Patterned Repetitive TMS (rTMS)



- High Frequency = > 1 Hz Train – Stimulatory
- Low Frequency = < 1 Hz Train – Inhibitory

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Stimulation parameters available for rTMS to TBS



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Treatment Timeline

Step 1	Referral by Primary Provider to Psychiatrist on TMS team
Step 2	Evaluation by TMS-privileged Psychiatrist

Step 3	Monday	Tuesday	Wednesday	Thursday	Friday
Week 1	MTM + Tx	Tx	Tx	Tx	Tx
Week 2	MT + Tx	Tx	Tx	Tx	Tx
Week 3	MT + Tx	Tx	Tx	Tx	Tx
Week 4	MT + Tx	Tx	Tx	Tx	Tx
Week 5	MT + Tx	Tx	Tx	Tx	Tx
Week 6	MT + Tx	Tx	Tx	Tx	Tx
Week 7	Tx		Tx		Tx
Week 8	Tx		Tx		Tx

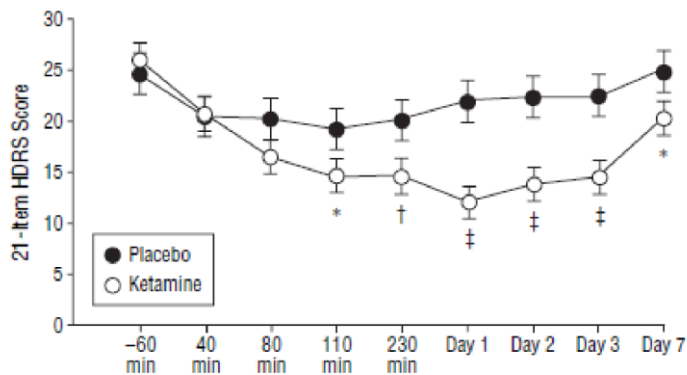
MTM = Motor Threshold Mapping (90 min appt), **MT** = Motor Threshold Determination (60 min appt), **Tx** = Treatment (10-60 min appt)

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Ketamine

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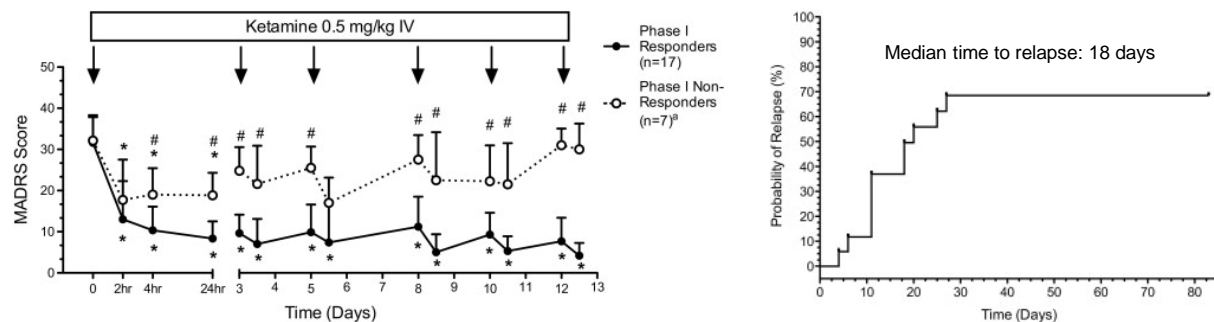
A single ketamine infusion rapidly improves symptoms of depression. (N = 18)



Zarate et al., Arch Gen Psychiatry 2006

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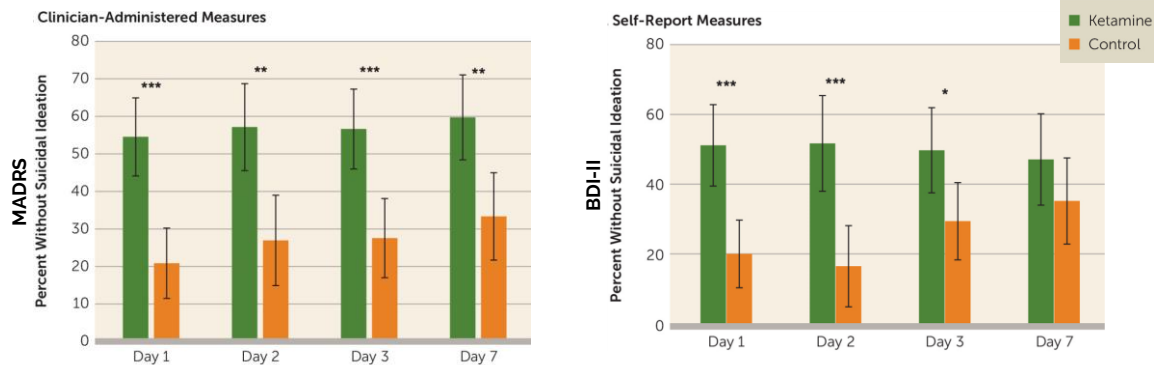
Repeated infusions increase response & durability. (N = 24)



Murrough et al., Biol Psychiatry 2013.

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A greater proportion of patients who received ketamine were without suicidal ideation compared to placebo.



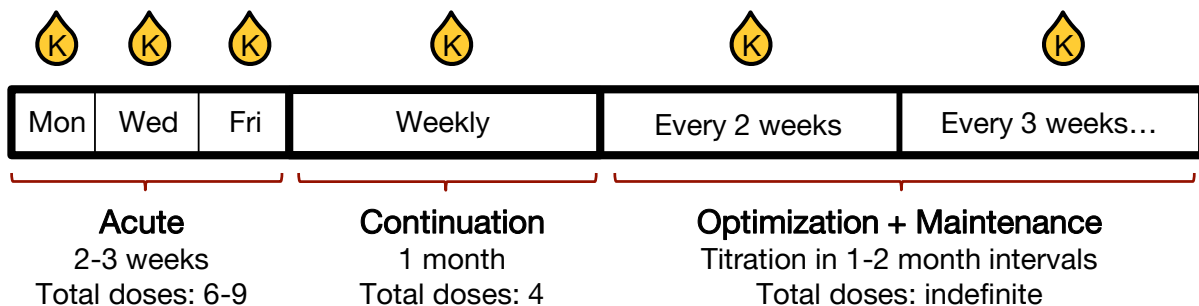
Wilkinson ST, et al. *Am Journal Psychiatry*, 2017.

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Titration to maintenance



Ketamine IV 0.5-1.25 mg/kg IBW x 40 min.



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Eligibility (MDD)

- Individuals without medical exclusions by history
 - (e.g. kidney failure, heart failure, arrhythmia, glaucoma, liver disease)
- Routine lab work-up (pre-op PE) + negative UPT (women)
- No history of substance use disorder within the past 6 months
 - (strong recommendation to exhaust alternative treatment modalities in individuals with a history of opioid use disorder or polysubstance use disorder)
- *Failure of a neuromodulation treatment modality*
- Benzodiazepine taper prior to initiation of ketamine (if taking)

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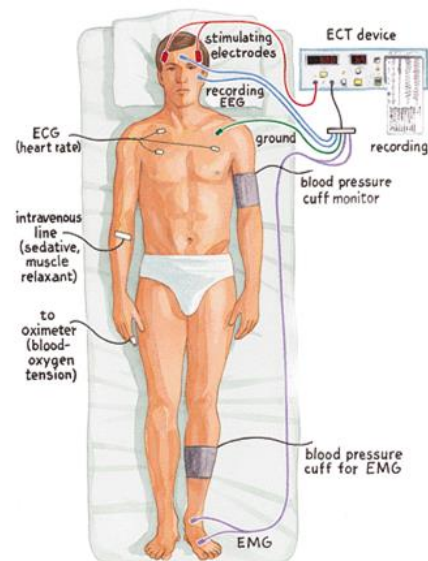
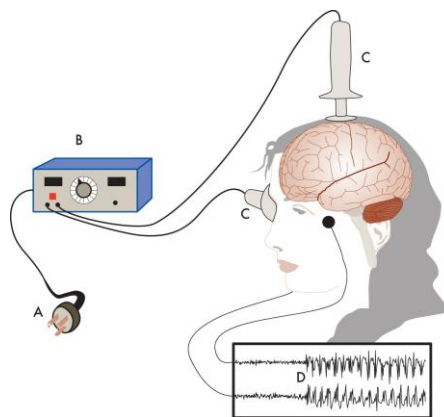
Eligibility for Maintenance

- Must meet response criteria on an outcome measure by the end of the acute period (after 6 to 9 infusions)
 - MADRS, PHQ-9, IDS-SR
- Must maintain response for a minimum of 1 week
 - Discussion of concerns for tachyphylaxis with weekly dosing
 - Encourage engagement in psychotherapy
 - Encourage use of Behavioral Activation strategies to maximize time between infusions
 - Strong recommendation for DBT if managing chronic SI

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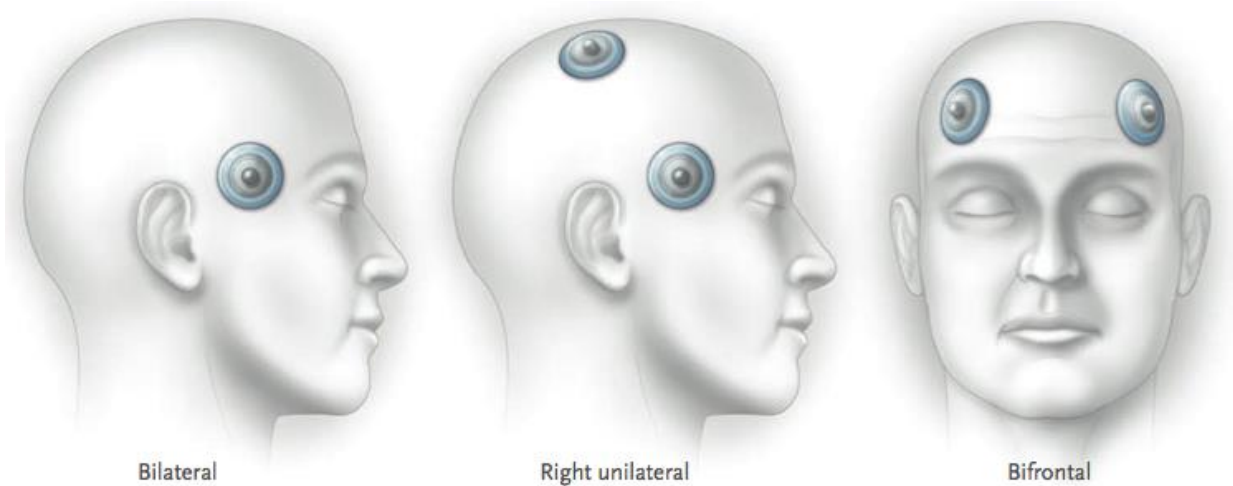
Electroconvulsive Therapy (ECT)

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Electrode placement



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Acute course of ECT

- Index course 6 - 8 Txs
- 2 -5 Txs per week
- Tx until improvement plateaus
- Continuation/Maintenance ECT
- Prophylactic medication

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Indications for ECT

- Treatment-refractory conditions
- Severe or life-threatening psychiatric illness
- Most often used for the treatment of medication-resistant depression (MDD)

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Vagus Nerve Stimulation (VNS)

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Brain Stimulation Tools

- Electroconvulsive therapy (ECT)
- Magnetic seizure therapy (MST)
- Focal electrically-administered seizure therapy (FEAST)

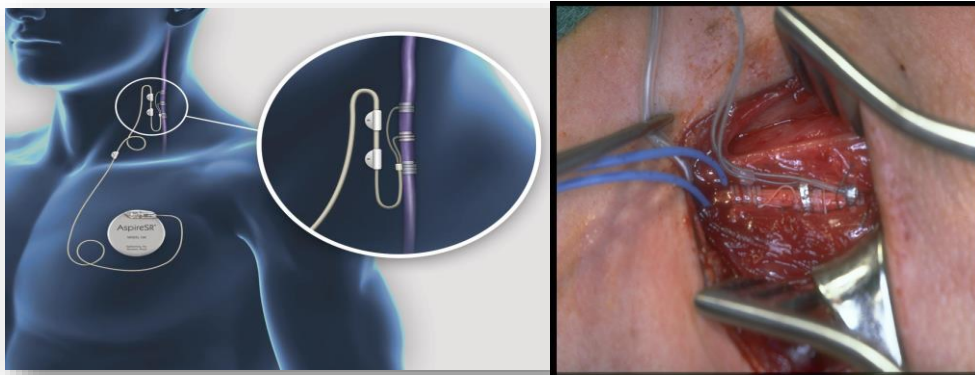
Convulsive

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- Auricular Vagus Nerve Stimulation (taVNS)
 - Trigeminal Nerve Stimulation
 - Transcranial Direct Current Stimulation (tDCS)
 - Transcranial magnetic stimulation (TMS)
 - Focus ultrasound (FUS)
 - Focal electrically-administered therapy (FEAT)
 - **Cervical Vagus Nerve Stimulation (VNS)**
 - Deep brain stimulation (DBS)
 - Responsive Neurostimulation (RNS)
 - Prefrontal cortical stimulation (PCS)

Sub-Convulsive

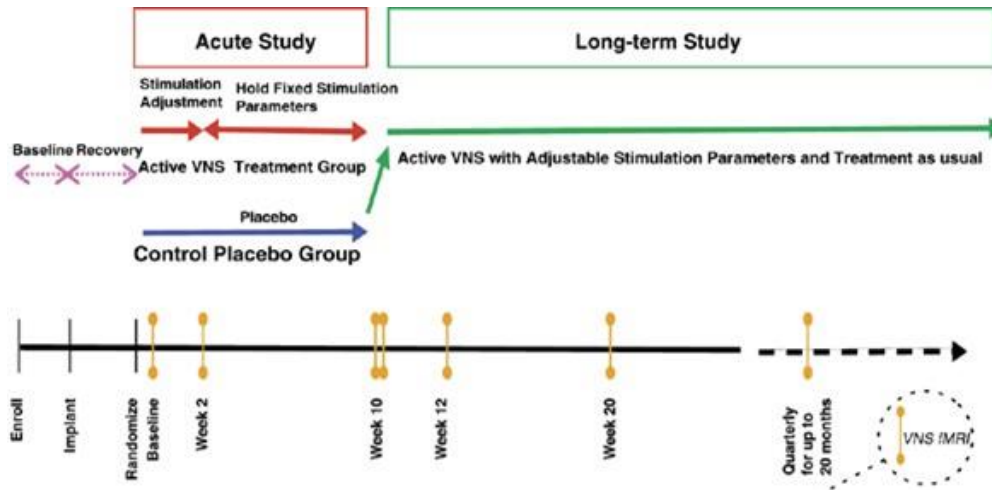
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(invasive) Cervical VNS



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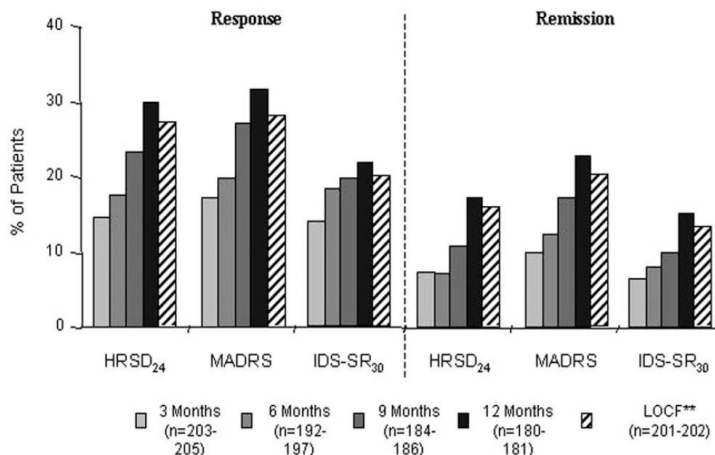
RCT Design (D-02; 2001)



Rush AJ et al., *Biol Psychiatry* 2005;58:347-354.

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Long-Term Analyses Demonstrate Response Rates Increase Over Time During Adjunctive VNS Therapy



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FDA Approval 1998-2005

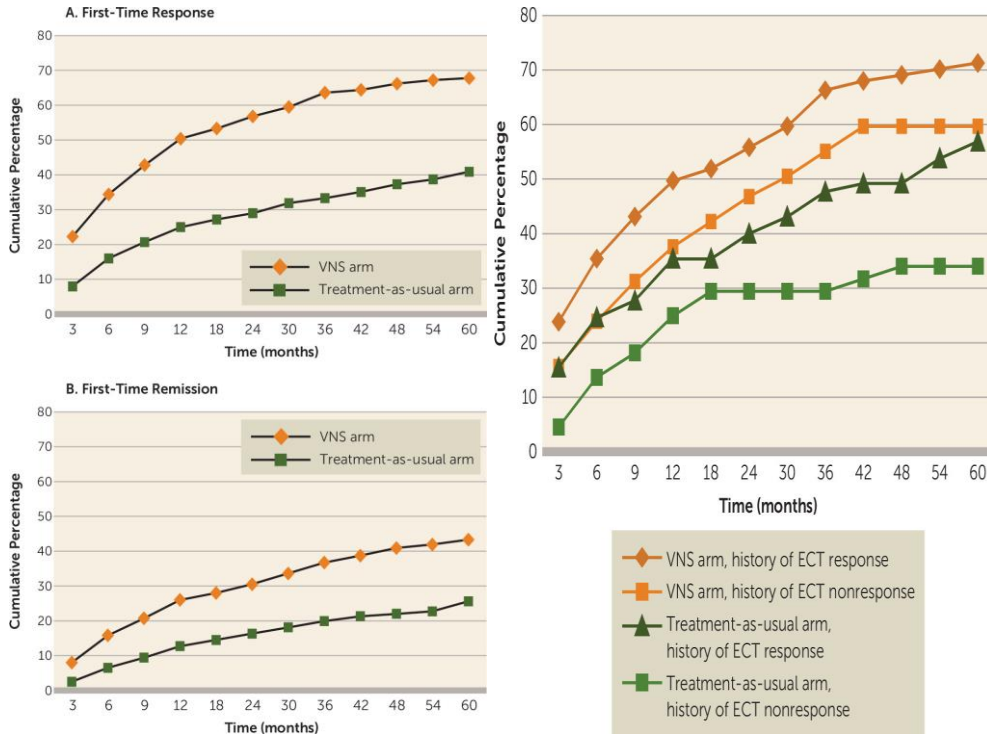
Controversy and CMS 2007 – 2018 (CMS determined VNS for TRD non-covered)

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A 5-Year Observational Study of Patients With Treatment-Resistant Depression Treated With Vagus Nerve Stimulation or Treatment as Usual: Comparison of Response, Remission, and Suicidality

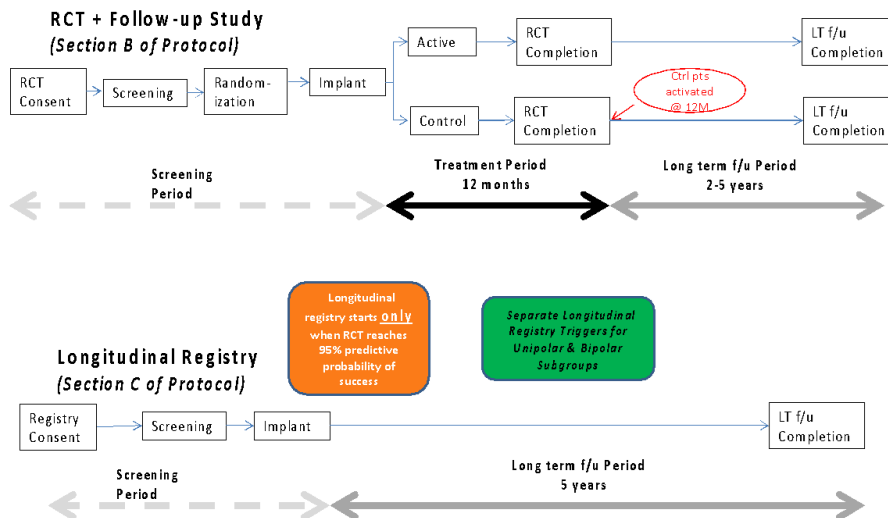
Scott T. Aaronson, M.D., Peter Sears, C.C.R.P., Francis Ruvuna, Ph.D., Mark Bunker, Pharm.D., Charles R. Conway, M.D.,
Darin D. Dougherty, M.D., Frederick W. Reimherr, M.D., Thomas L. Schwartz, M.D., John M. Zajecka, M.D.

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RECOVER Overview

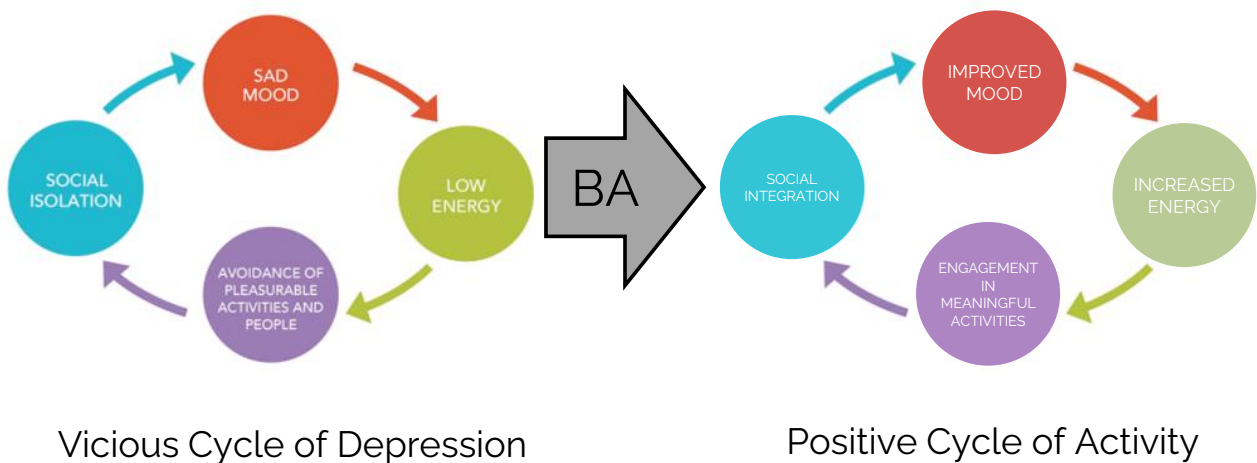


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Behavioral Activation

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Behavioral Activation

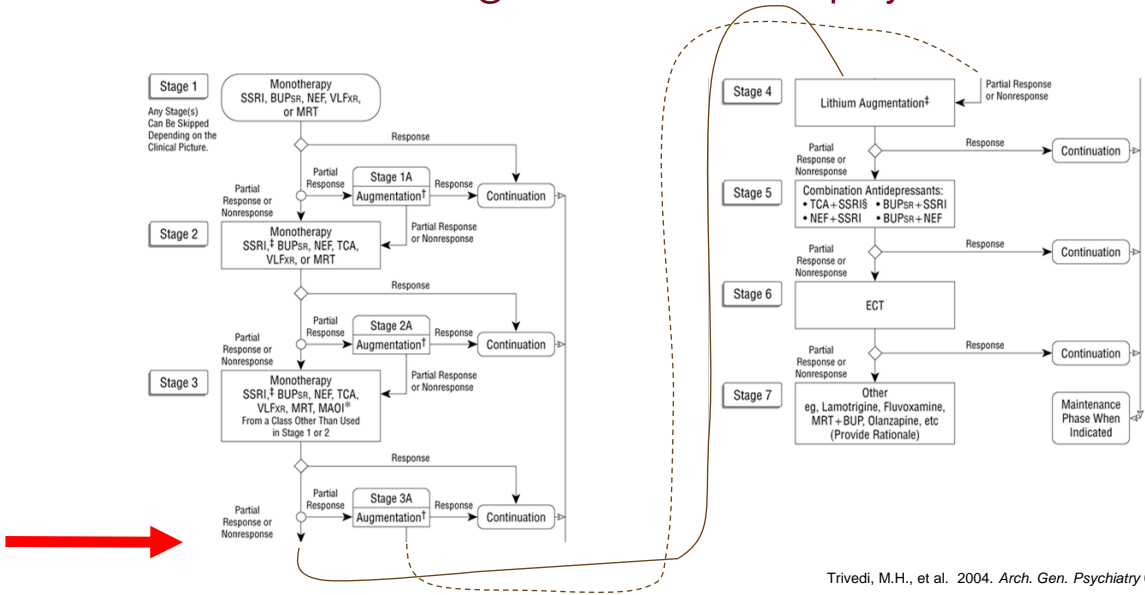


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Treatment Algorithm

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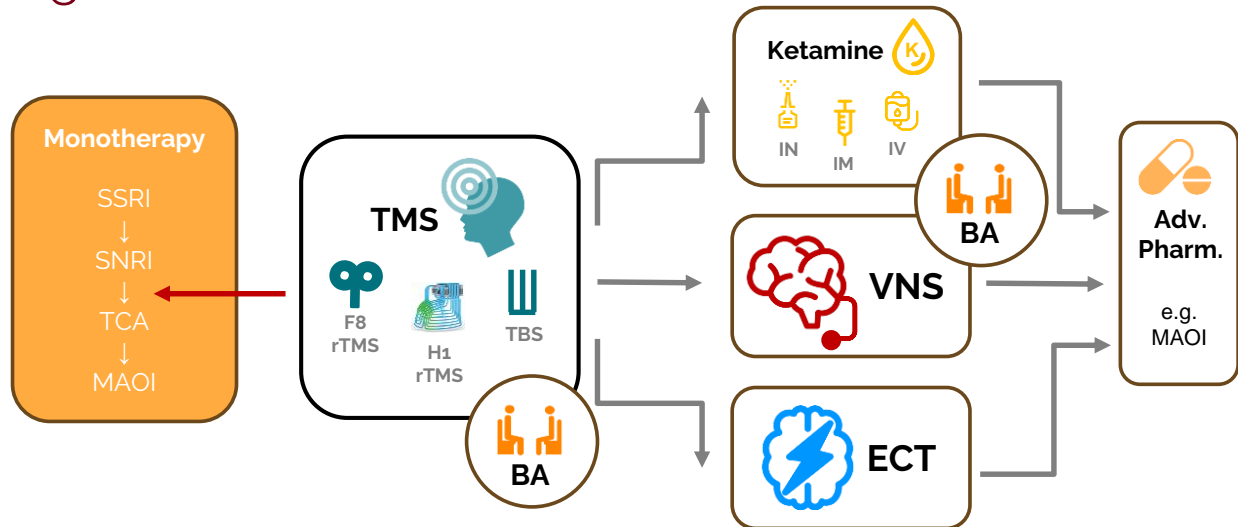
Texas Medication Algorithm for nonpsychotic MDD



Trivedi, M.H., et al. 2004. *Arch. Gen. Psychiatry* 61, 669–680.

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UMN Interventional Psychiatry Treatment Algorithm

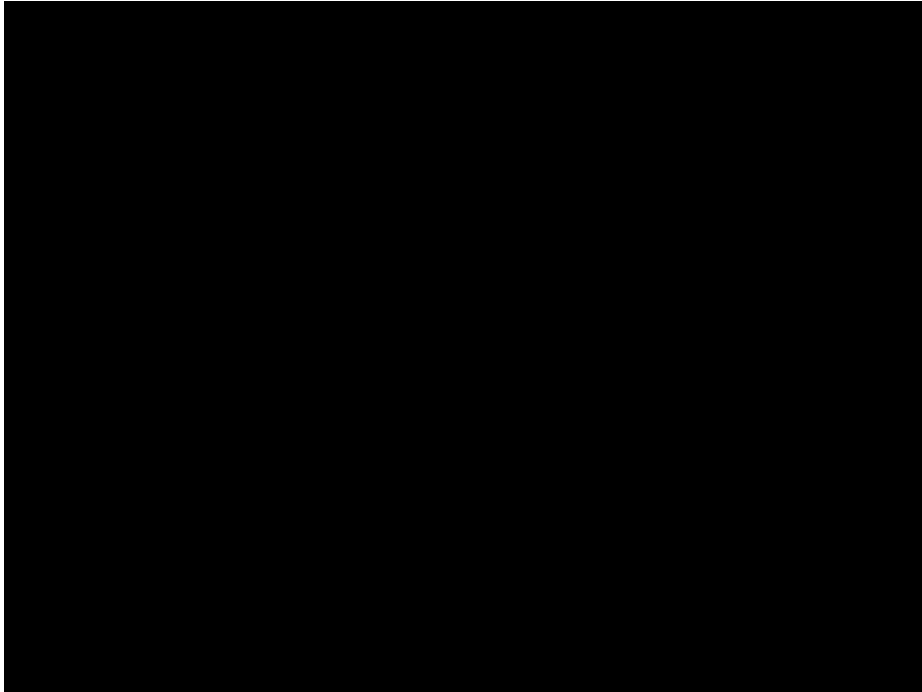


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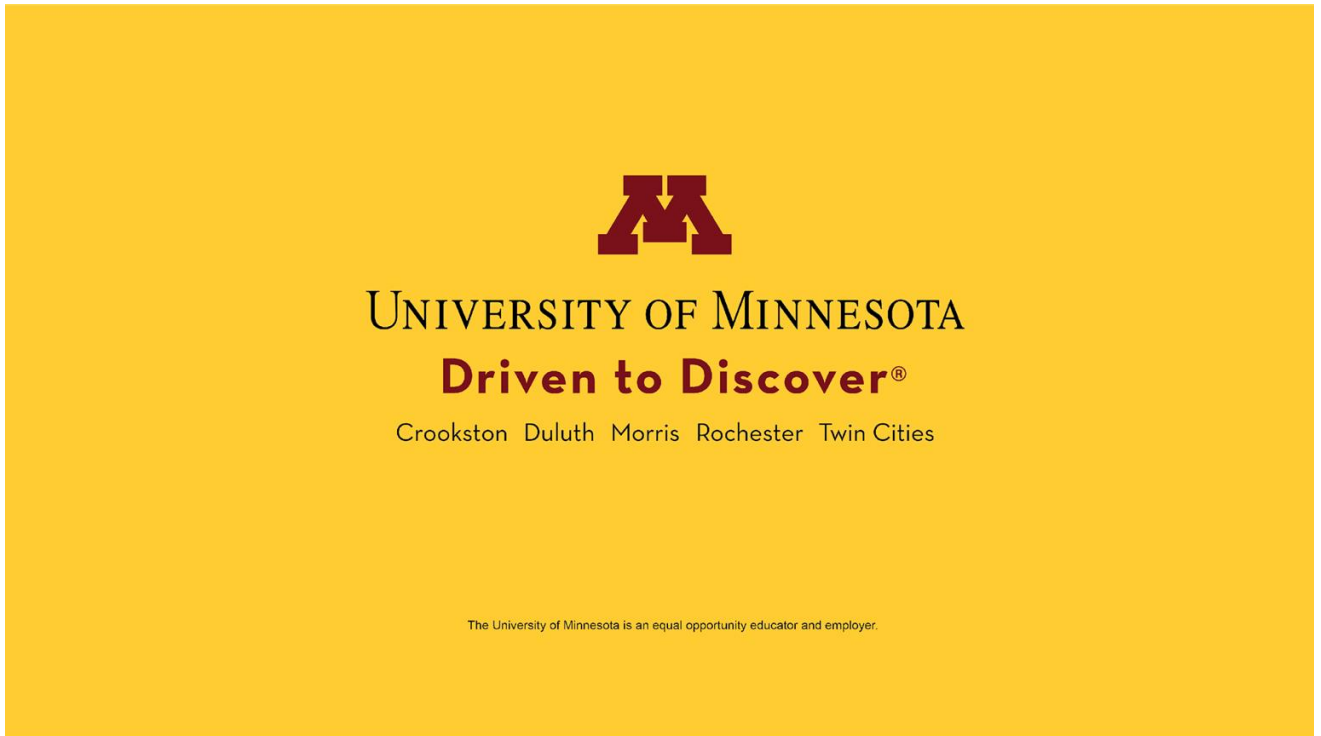
Clinic Renovation 2022-2023

- 17 patient exam rooms
- 3 team workspaces
- 18 touchdown spaces
- 7 individual work alcoves
- 2 two-person shared work spaces
- 3 TMS treatment rooms
- Infusion space with 3 infusion bays
- Phlebotomy space
- 2 acupuncture treatment rooms
- Lactation room
- 2 CMA stations with adjacent vitals stations

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