# Updates in Depression Treatment

JESSICA THACKABERRY, MD
ASSOCIATE CLINICAL PROFESSOR
DEPARTMENT OF PSYCHIATRY
CMD – OUTPATIENT PSYCHIATRIC SERVICES – HILLCREST
LEAD – INFORMATION SYSTEMS FOR PSYCHIATRY
LEAD – TELE-MENTAL HEALTH

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# Outline

- Case Example
- Measurement-Based Care
- Medication Management
- Shared decision making tools
- Interventional Psychiatry advancements
- When/where to refer

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# Case Presentation

- 35 year old woman with a history of obesity, HTN, Hypothyroidism presents to clinic to establish care for well woman visit.
- Reports 2 weeks of feeling overly sad, loss of interest in things she previously enjoyed, low appetite, poor sleep, feelings of guilt and worthlessness, low energy, denies active suicidal thoughts but has thoughts that she would be better off "not here."
- Denies auditory or visual hallucinations, denies delusions of paranoia or grandiosity, denies decreased need for sleep.
- Reports social alcohol use, slight increase in the last 2 weeks, drinking 2 glasses of wine/night.
- Current medication list: levothyroxine 50mcg daily, Lisinopril 20mg daily, atorvastatin 20mg daily.
- Past medication trials include fluoxetine 20mg daily (no effect), sertraline 50mg daily (nausea), and venlafaxine 75mg daily ("brain zaps").
- PHQ9 score = 16

# Differential Dx

- Major Depressive Episode/Disorder
- Bipolar I or II disorder
- Depressive disorder related to another medical condition
- Substance/medication induced depressive disorder
- Persistent Depressive Disorder
- Premenstrual Dysphoric Disorder
- Adjustment Disorder with Depressed Mood
- Bereavement
- Sadness

# Measurement Based Care

Depression Screen Follow-up  Manage User Versions

**PHQ9 Patient Summary Score (calculated): 16**

**Diagnosis**

**Possible Diagnosis (PHQ 15-19)**

- [ ] Major depressive disorder, single episode, moderate (CMS-HCC) [F32.1]
- [ ] Major depressive disorder, recurrent, moderate (CMS-HCC) [F33.1]
- [ ] Major depressive disorder, recurrent, severe with psychotic symptoms (CMS-HCC) [F33.3]
- [ ] Bipolar disorder, current episode depressed, moderate (CMS-HCC) [F31.32]
- [ ] Postpartum depression [O99.345, F53.0]

**Provider Note**

**Add Info to Progress Note**

- [x] Add review PHQ info to note
- [ ] Add follow up with mental health professional to note
- [ ] Depression Screening A/P Note

**Counseling/Referrals**

**Referrals (PHQ 15-19)**

- [ ] Update/Adding Medication for Patient (select from Medication section)
- [ ] Patient Currently Under Care of Mental Health Provider
- [ ] Referral to Integrated Behavioral Health (IBH)
  Routine, Internal referral, @FLOW(3035)@
- [ ] Referral to T-Care
- [ ] eConsult Psychiatry
- [ ] Patient Declines Follow-up Treatment

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# Medication Management

- SSRI's
  - Fluoxetine (Prozac)
  - Sertraline (Zoloft)
  - Escitalopram (Lexapro)
  - Citalopram (Celexa)
  - Paroxetine (Paxil)
- SNRI's/Dual agents
  - Duloxetine (Cymbalta)
  - Venlafaxine (Effexor)
  - Mirtazapine (Remeron) (SN-RAn)
- NDRI
  - Bupropion (Wellbutrin)
- TCA's
  - Amitriptyline (Elavil)
  - Nortriptyline (Pamelor)
  - Desipramine (Norpramin)
  - Imipramine (Tofranil)
- MAOI's
  - Selegiline (Ensam)
  - Phenelzine (Nardil)
  - Tranylcypromine (Parnate)

# Some Newer Antidepressants

- Desvenlafaxine (Pristiq)
  - SNRI
  - Less likely than venlafaxine to cause weight gain
- Levomilnacipram (Fetzima)
  - SNRI (norepinephrine >> serotonin)
  - Unusual to cause weight gain
- Vilazodone (Viibryd)
  - Serotonin partial agonist reuptake inhibitor
  - Usually no weight gain or sedation
- Vortioxetine (Trintellix)
  - Serotonin multi-modal antidepressant
  - Unusual to cause weight gain or sedation

# Shared Decision Making

- Mayo Clinic Shared Decision Making
- Patient's symptoms
- Side Effects of medications
- Interactions with other medications
- Medications which have worked for family members
- Special populations
  - Young/Old
  - Intellectually disabled
  - Severely medically ill/polypharmacy

# Clinical Presentation

- You decide to start fluoxetine, given the patient tolerated it in the past.
- Start at 20mg for 2 weeks, then increase to 40mg.
- You see the patient back in 4 weeks and she is noticing no improvement, PHQ9 is 18 today. You increase to 60mg daily.
- 4 weeks later, no improvement, PHQ9 is 17.

# What if it doesn't work?

- Make sure your diagnosis is accurate
- Try a different medication in the same class
- Try a different class
- Augmentation strategies
- Interventional Psychiatry

# Augmentation Strategies

- SSRI plus…
  - Bupropion (Wellbutrin)
  - Mirtazapine (Remeron)
  - Atypical antipsychotic
    - Aripiprazole (Abilify)
    - Quetiapine (Seroquel)
  - Buspirone (Buspar)
  - Mirtazapine PLUS venlafaxine = “California Rocket Fuel”
  - T3
  - Lithium

# Treatment Resistant Depression

- Forty to fifty percent of patients with depression do not respond (i.e., <50 % reduction in symptoms) to medication (Triverdi et al 2006)
- Remission was about 33 percent in STAR*D (Trivedi et. al 2006)
- These patients are twice as likely to be hospitalized
- Receive up to 3 times more psychiatric medications
- Six times the mean total medical costs of non-treatment-resistant depression
- For remitters up to 40 % relapse at 2 years (Bolland and Keller, 2009)

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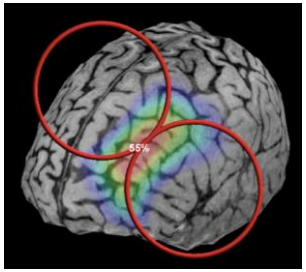
# Interventional Psychiatry

- Electro-Convulsive Therapy – Gold Standard
  - 60-80% remission rates, >80% remission in suicidality
  - Stigma/Fear limits use
- Transcranial Magnetic Stimulation
  - 50% response, 33% remission for iTMS (Three D trial 2018)
- Magnetic Seizure Therapy
  - Promising for less cognitive effects (vs ECT)
- Ketamine
  - NMDA receptor antagonist

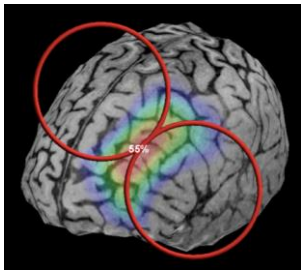
# The THREE-D Trial

414 Patients with Major Depressive Disorder



FDA Standard Protocol

3000 pulses at 10 Hz
37.5 minutes
20-30 sessions

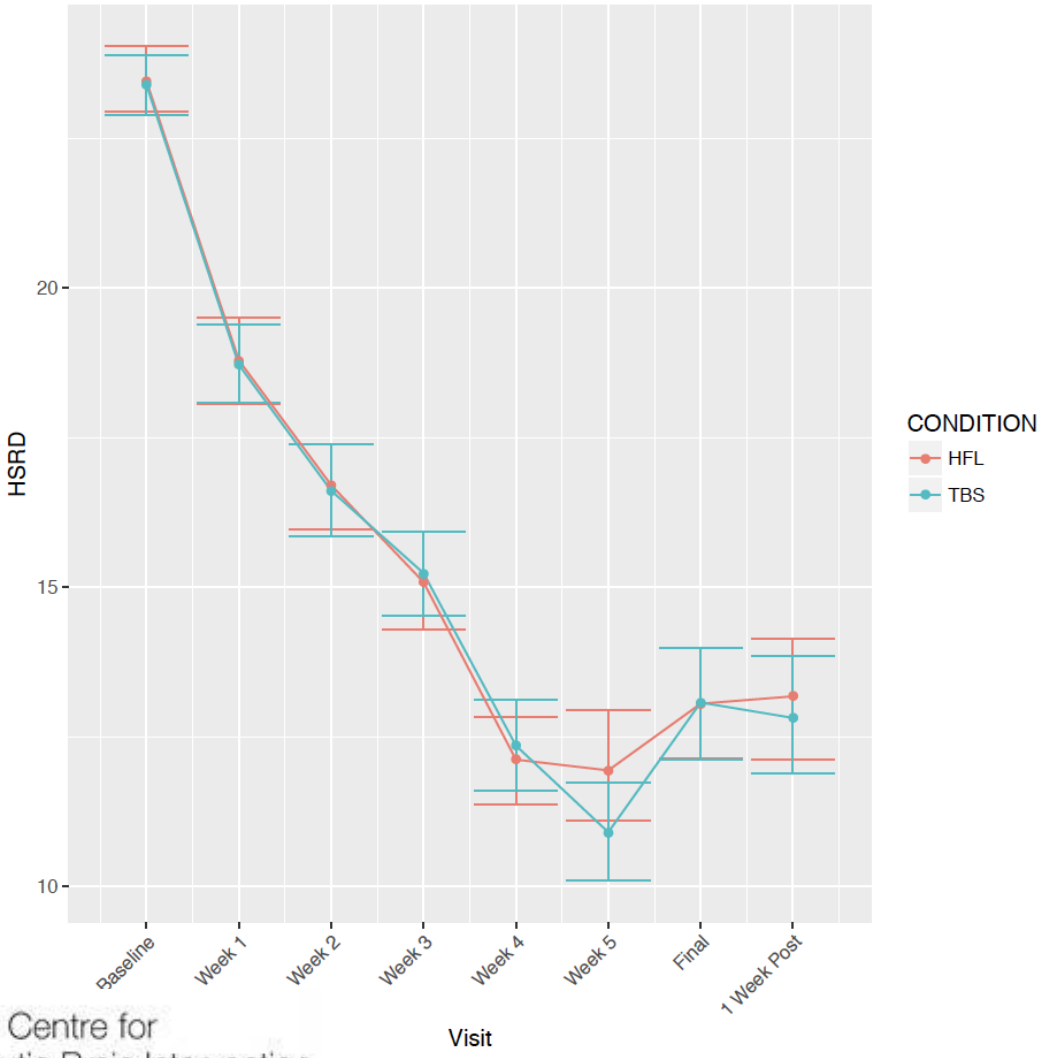


Theta-Burst Protocol



600 pulses of iTBS
3 minutes 9 seconds
20-30 sessions

# iTBS in Depression: Treating Depression in 3 min



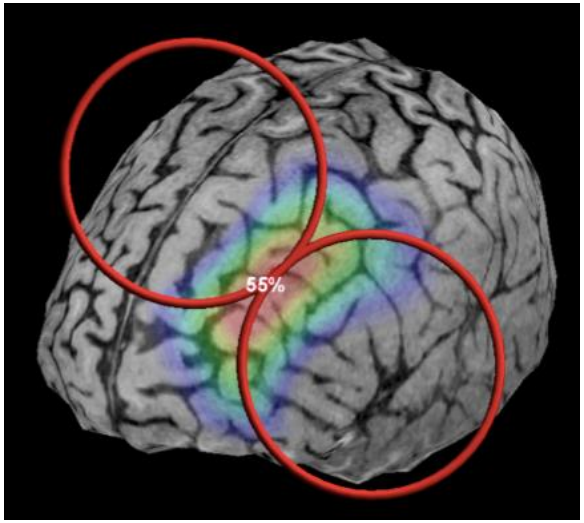

camh Temerty Centre for Therapeutic Brain Intervention
mental health is health

Blumberger et al. 2018, Lancet

# 2018: THREE-D Clinical Outcomes for L Dorsolateral Prefrontal rTMS:

iTBS: 50% Response, 33% Remission

10 Hz: 49% Response, 28% Remission



# Ketamine

## Synthesizing the Evidence for Ketamine and Esketamine in Treatment-Resistant Depression: An International Expert Opinion on the Available Evidence and Implementation

Roger S. McIntyre, M.D., Joshua D. Rosenblat, M.D., M.Sc., Charles B. Nemeroff, M.D., Ph.D., Gerard Sanacora, M.D., Ph.D., James W. Murrough, M.D., Ph.D., Michael Berk, Ph.D., M.B.B.Ch., Elisa Brietzke, M.D., Ph.D., Seetal Dodd, Ph.D., Philip Gorwood, M.D., Ph.D., Roger Ho, M.D., M.B.B.S., Dan V. Iosifescu, M.D., Carlos Lopez Jaramillo, M.D., Ph.D., Siegfried Kasper, M.D., Kevin Kratiuk, B.Pharm., Jung Goo Lee, M.D., Ph.D., Yena Lee, H.B.Sc., Leanna M.W. Lui, Rodrigo B. Mansur, M.D., Ph.D., George I. Papakostas, M.D., Mehala Subramaniapillai, M.Sc., Michael Thase, M.D., Eduard Vieta, M.D., Ph.D., Allan H. Young, M.Phil., M.B.Ch.B., Carlos A. Zarate, Jr., M.D., Stephen Stahl, M.D., Ph.D.

**TABLE 2. Comparison of routes of administration of ketamine and esketamine**

| Route | Bioavailability | Dose Range (Acute) |
|---|---|---|
| Intravenous | 100% | 0.5–1.0 mg/kg infused over 40–60 minutes twice weekly for 2 weeks |
| Intramuscular | 90%–95% | Not established, likely similar to intravenous |
| Subcutaneous | 90%–95% | Not established, likely similar to intravenous |
| Intranasal | 30%–50% (significant differences between devices and solution) | Esketamine: 56–84 mg intranasally twice weekly for 4 weeks<br>Racemic ketamine: 50–150 mg intranasally twice weekly |
| Oral | 10%–20% (potential variability between capsules and liquid forms) | Highly variable (0.5–7.0 mg/kg daily to once weekly), with 100–250 mg 2–3 times per week most accepted |
| Sublingual | 20%–30% | Not established, likely similar to oral |
| Transdermal | 10%–50% (highly variable by vehicle used) | Not established |

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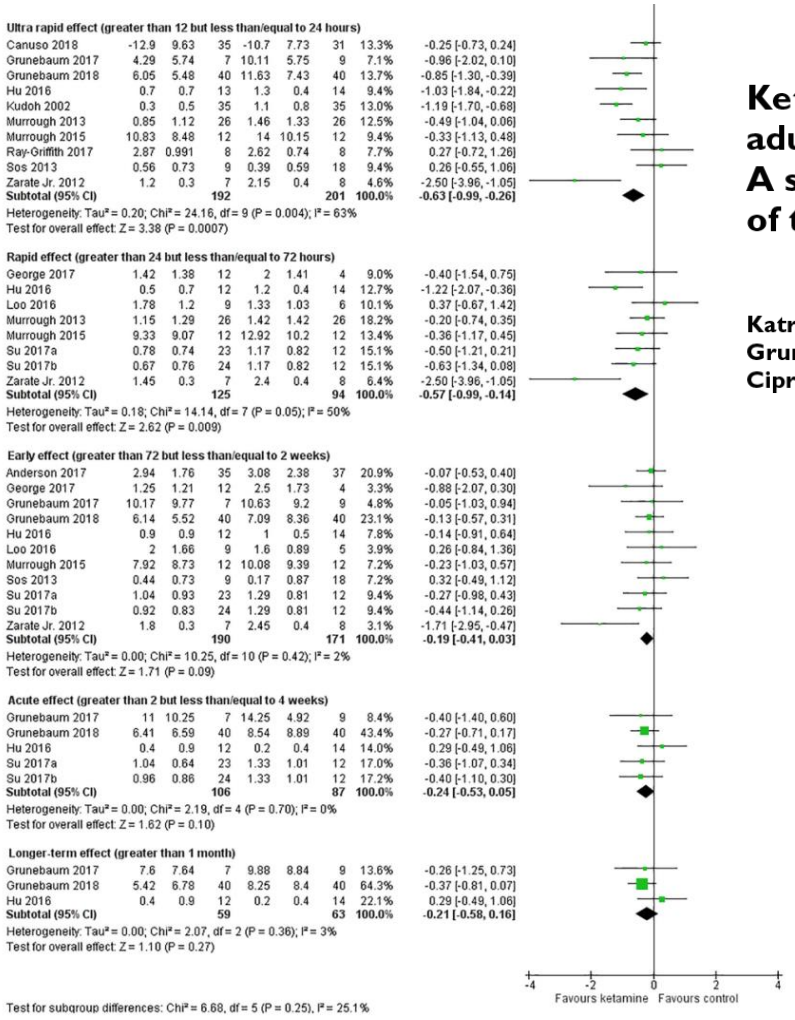
# Ketamine




## Ketamine for suicidal ideation in adults with psychiatric disorders: A systematic review and meta-analysis of treatment trials

*Australian & New Zealand Journal of Psychiatry*
2020, Vol. 54(1) 29–45
DOI: 10.1177/0004867419883341



Katrina Witt[1], Jennifer Potts[2,3], Anna Hubers[1,4], Michael F Grunebaum[5], James W Murrough[6], Colleen Loo[7], Andrea Cipriani[2,3] and Keith Hawton[1,2]

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# When to refer

- Medication questions = Econsult
  - Dosage
  - How to change from one med to another
  - Augmentation strategies
  - How to safely taper
  - Etc.
- Diagnostic Clarity = Refer
- Nothing is working? End of your rope? = Refer
- Can also refer to specialty services
  - Addiction
  - College Mental Health
  - Interventional
  - Women's Mental Health

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# How to Refer to Interventional Psychiatry

- Direct referral through EPIC:

***CON90471 (Consult/Referral to Interventional Psychiatry) to DVC PSYCH***

- Email: TMS@HEALTH.UCSD.EDU
- Call: 858-207-0938

For more information please visit: https://health.ucsd.edu/tms

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# Insurances covered for TMS

- Aetna
- Anthem
- Cigna
- Kaiser *(pre-approved)*
- Medicare *(1 failed antidepressant)*
- MHN (HealthNet carve out)
- Optum (United Health Care carve out)
- Tricare

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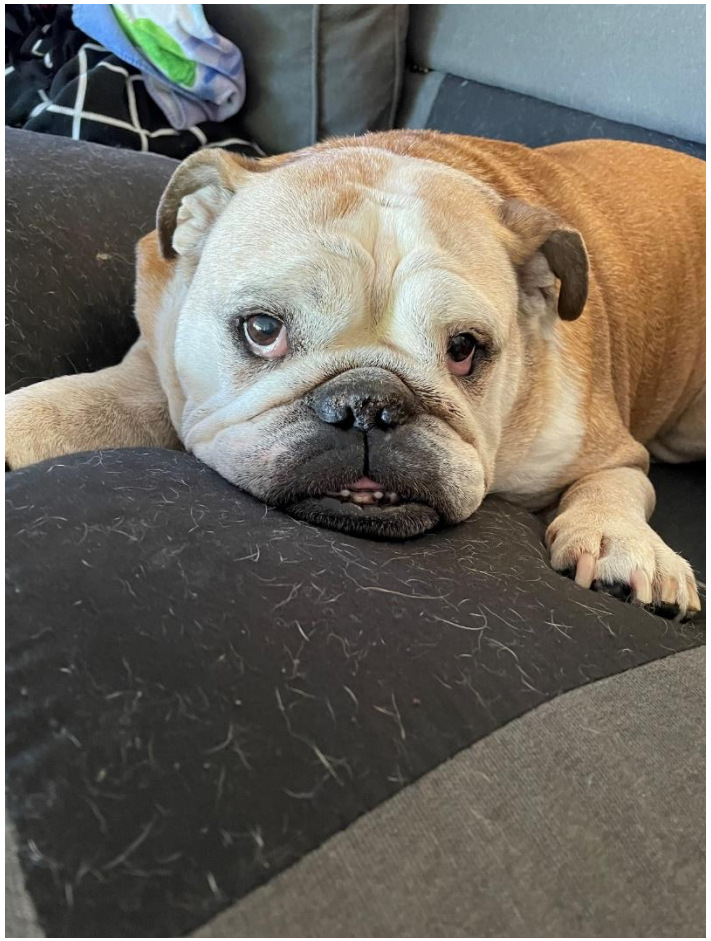
# Questions?



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