

# Treatment Resistant Depression and Transcranial Magnetic Simulation: TRD meets TMS

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# Disclosure Statement:

Relevant financial relationships in the past 12 months

- Consultant/Speaker: none outside of OHSU CME and Horizon CME

OHSU

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## Relevant financial relationships in the past 12 months

- Financial: I am a salaried employee of Active Recovery TMS.



### TREATING DEPRESSION DIFFERENTLY

Providing TMS therapy in 6 locations across the Portland metro, Salem and SW Washington:

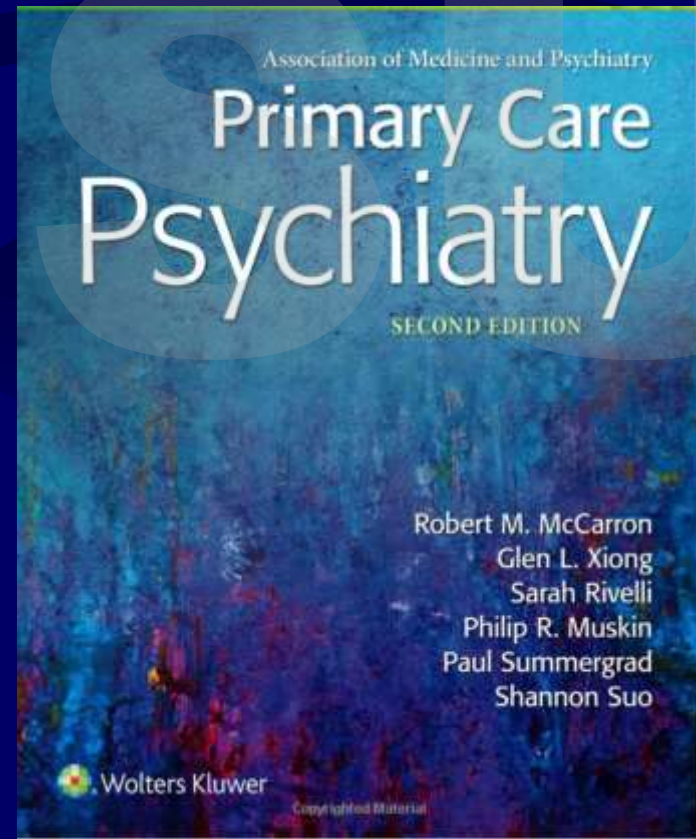
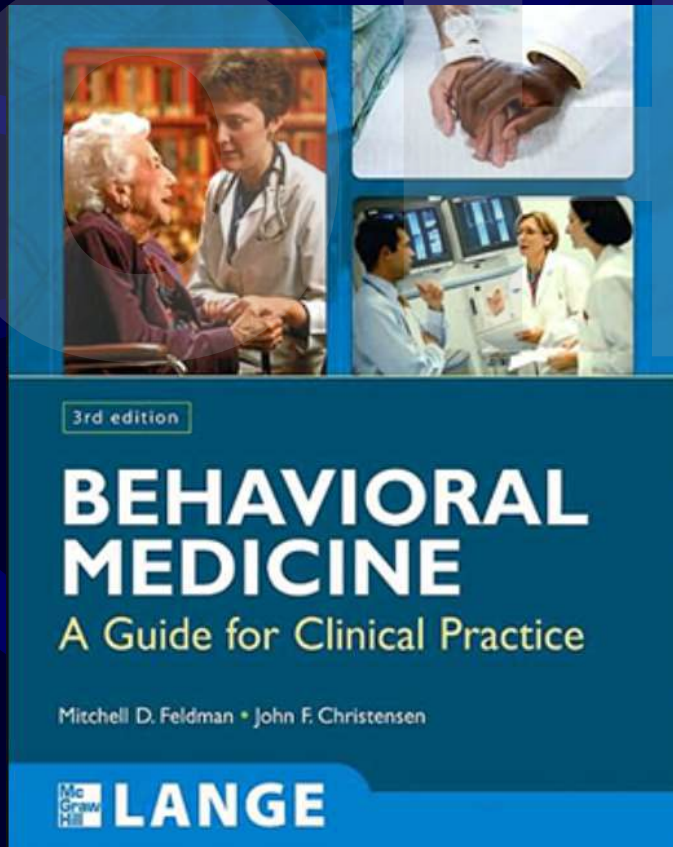
- NW Portland
- Hillsboro
- Tigard
- Salem
- Clackamas
- Vancouver, WA - now proudly open!

Treating Depression with TMS

# Disclosure Statement:

Most recent book chapters authored

- Depression
- Somatic Symptom Disorder
- Bipolar Disorder



# A Med-Psych Physician's Journey



2001 Chief Resident at Duke  
Clinical Research in AD/MCI, Obesity, and TMS rating (2005)

2006 OHSU Started GIM Med-Psych Teaching Clinic (winner of OPA Access to Care Award)

2015 Stepped down as GIM Med Dir and named Chair of Psychiatry at Adventist Medical Center

2017 Opened the Emotional Wellness Center at AHP - 2018 TMS (2019 AABH Program of the Year Finalist)

2021 Named CMO of Active Recovery TMS



# Burnout Prevention

## My Advice:

- Protect 0.1 FTE (10% of your work life) to do something you are **PASSIONATE** about!
- If you notice signs of burnout, consider the **Three Good Things** exercise



# Clinical Case



- Dee Prest is a 65 yo WW with a h/o single vessel CAD, stage I HTN, and recurrent major depressive disorder who presents complaining of increased “stress”, poor sleep, and worsening mood during the pandemic. Her vital signs are normal but she has been gaining weight (7 lbs in the past 6 months).

# Clinical Case



- Current medications: sertraline 200mg, bupropion XL 300mg, metoprolol XL 150mg, HCTZ 25mg, atorvastatin 10mg, and potassium supplement daily
- Past psychotropic medications: fluoxetine (stopped working), venlafaxine (worsened blood pressure), escitalopram (didn't work), selegiline patch (too expensive).
- **What is your next move?**



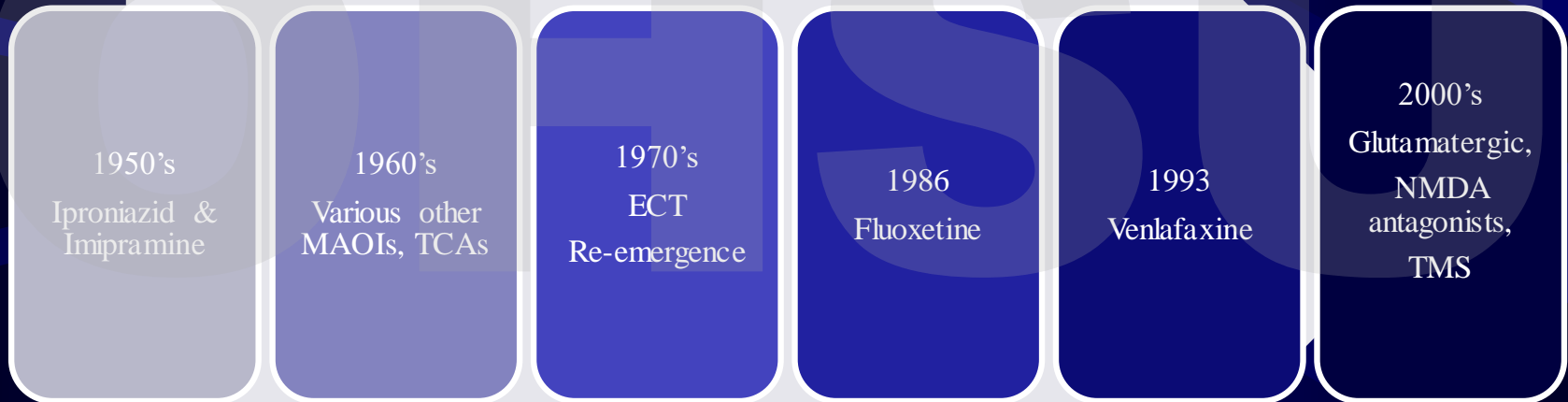
# Answer Choices

1. psychotherapy (because you know a board answer when you see it)
2. physical activity (because you like natural options)
3. transcranial magnetic stimulation (because you saw me on TV advertising it during Jeopardy)
4. electroconvulsive therapy (because this usually works when other options fail)
5. esketamine (because you heard it works quickly)

# Current Options for Treating MDD

- **Physical Activity (Physical Neuromodulation):**  
SMILE study by Blumenthal JA et al.
- **Medications (Chemical Neuromodulation):**  
STAR\*D trial
- **Psychotherapy (Behavioral Neuromodulation):**  
Numerous individual and group modalities
- **Neurostimulation (“Electrical Neuromodulation”):**  
Such as ECT, VNS or TMS

# A Brief History of Antidepressants



What is Treatment Resistant  
Depression (TRD)?

# Early TRD Definition

- Treatment-resistant depression (TRD) typically refers to inadequate response to at least one antidepressant trial of adequate doses and duration.
- TRD is a relatively common occurrence in clinical practice, with up to 50% to 60% of the patients not achieving adequate response following antidepressant treatment.

» Fava M. Diagnosis and definition of treatment-resistant depression.  
*Biological Psychiatry* 2003, 53(8):649-659.

# STAR\*D

4041 Patients

## Citalopram

30% Remission

Higher dose – 41.8mg

Longer duration – 47 days

727 Non-Remitters Randomized for 14 weeks to:

### Bupropion SR

Out of class

Max: 400mg

25.5% Remission

### Sertraline

In-class

Max: 200mg

26.6% Remission

### Venlafaxine XR

Dual-action

Max: 375mg

25.0% Remission

# STAR\*D

4041 Patients

## Citalopram

30% Remission

Higher dose – 41.8mg

Longer duration – 47 days

565 Non-Remitters Augmented for 12 weeks with:

### Bupropion SR

DA + NE reuptake inh.

Max: 400mg

39% Remission

### Buspirone

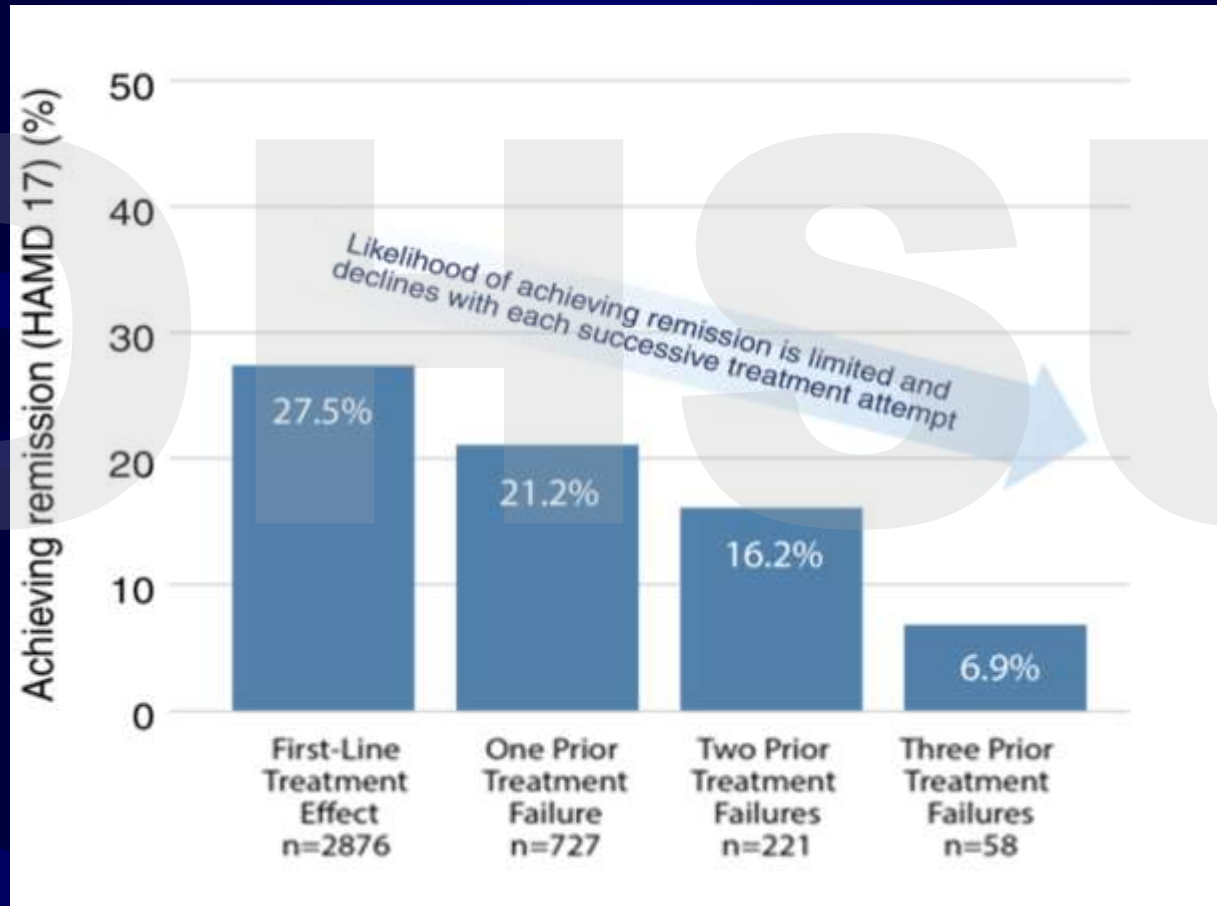
5HT-1A partial agonist

Max: 60mg

32.9% Remission

### Cognitive Therapy

# STAR\*D Trial







1 in 3

### In the STAR\*D trial<sup>1</sup>

About one-third of patients with major depressive disorder did not respond to two or more oral antidepressants and may be considered to have treatment-resistant depression.

1. Rush AJ et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR\*D report *Am J Psychiatry* 2006 Nov;163(11):1905-17.

# Medicare 2018 TRD Definition Study

- TRD is commonly defined as a failure of treatment to produce response or remission for patients after **two or more** treatment attempts of adequate dose and duration, but **no clear consensus** exists about this definition.
- TRD definitions in treatment studies do not closely match the definition above; only 17 percent of studies do so.
- To improve TRD treatment research, experts should standardize the number of prior treatment failures and specify the adequacy of both dose and duration. In addition, they should identify the core outcome measures to be used in such research.

# TMS: Indicated for Treatment Resistant Depression (TRD)

- FDA Guidelines: At least one failed trial of an antidepressant and one failed trial of psychotherapy.
- “Failure” can be either lack of effectiveness or intolerable side effects.
- Most commercial insurance plans require 2-4 antidepressant trials. Medicare sticks to FDA guidelines.



# How Does TMS Work?



A pulsing magnetic coil induces electrical activity in conductive tissue

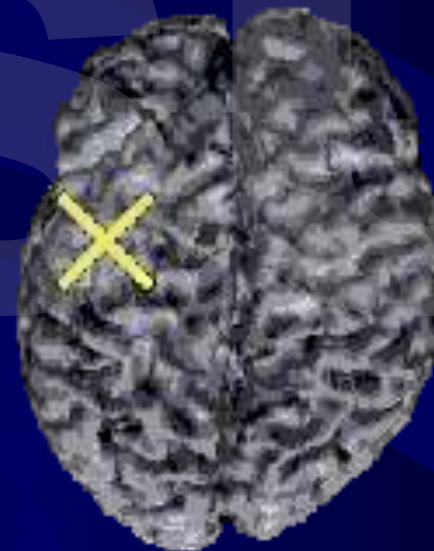
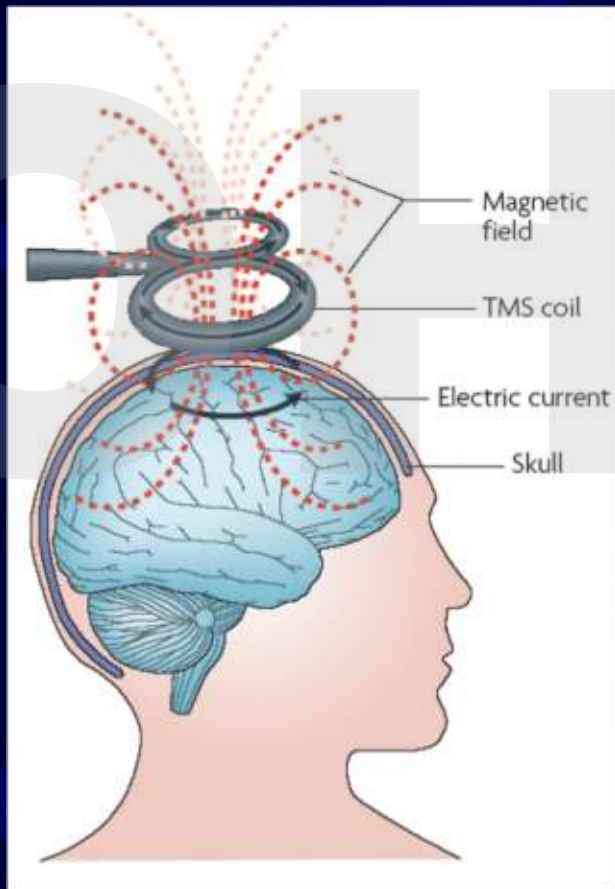
The magnet itself is similar to an MRI and the coil induces a magnetic field.

Changing magnetic field induces electrical field in the brain.

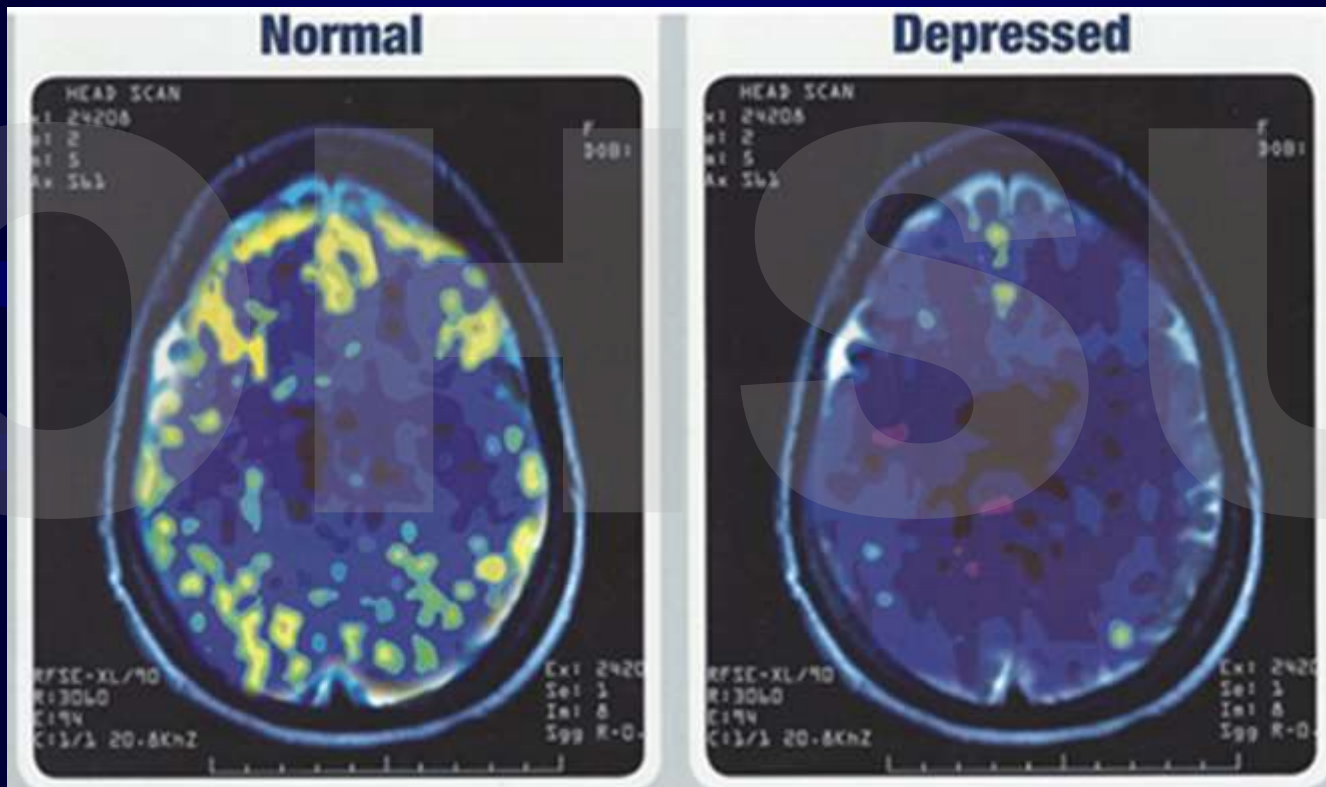
Electric field stimulates localized neurons in the brain.

Neuronal stimulation modulates neuronal<sup>20</sup> “firing”, resulting in behavioral effects.

# The Physics of TMS



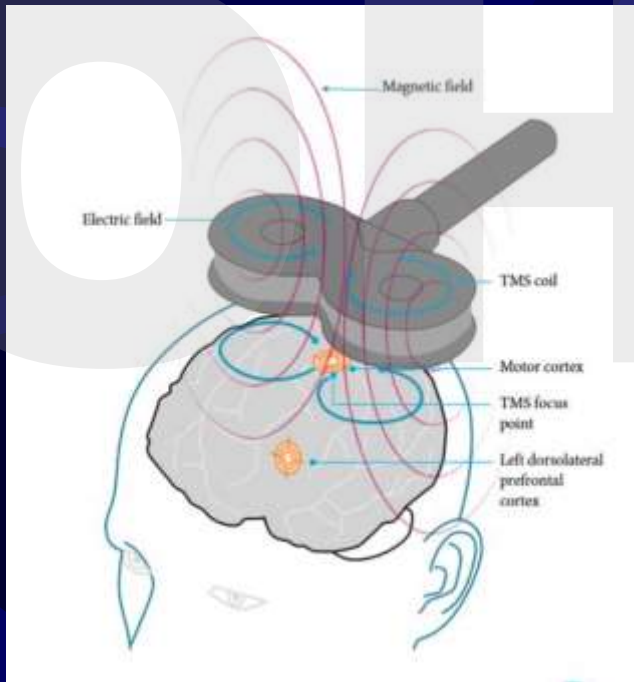
# Depressed Brains Look Different



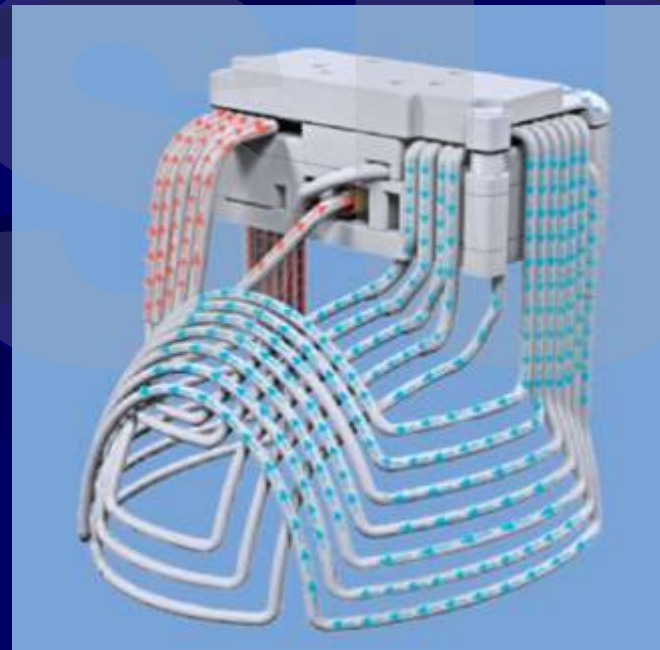
Mark S. George, MD. Fluorodeoxyglucose positron emission tomography (PET) images acquired at the National Institute of Mental Health (NIMH, Bethesda, MD), 1994.

# Two Types of TMS Coils

**rTMS Figure 8 Coil  
(Neurostar 2008)**



**dTMS H-1 Coil  
(BrainsWay 2013)**



# What is the Evidence for TMS in Depression?

## O'Reardon et al Biological Psychiatry 2007

- 301 patients, unipolar depression, s/p med washout
- Randomized, double blind, sham controlled
- Significant differences in HAM-D for responders and remitters at 4 and 6 weeks.

2007

2015

## Levkowitz, et al World Psychiatry 2015

- 212 patients, unipolar depression, s/p med washout
- Randomized, double blind, sham controlled
- Response rates 37% vs. 27.8% ( $p < .03$ )
- Remission rates 30.4% vs. 15.8% ( $p < .016$ )



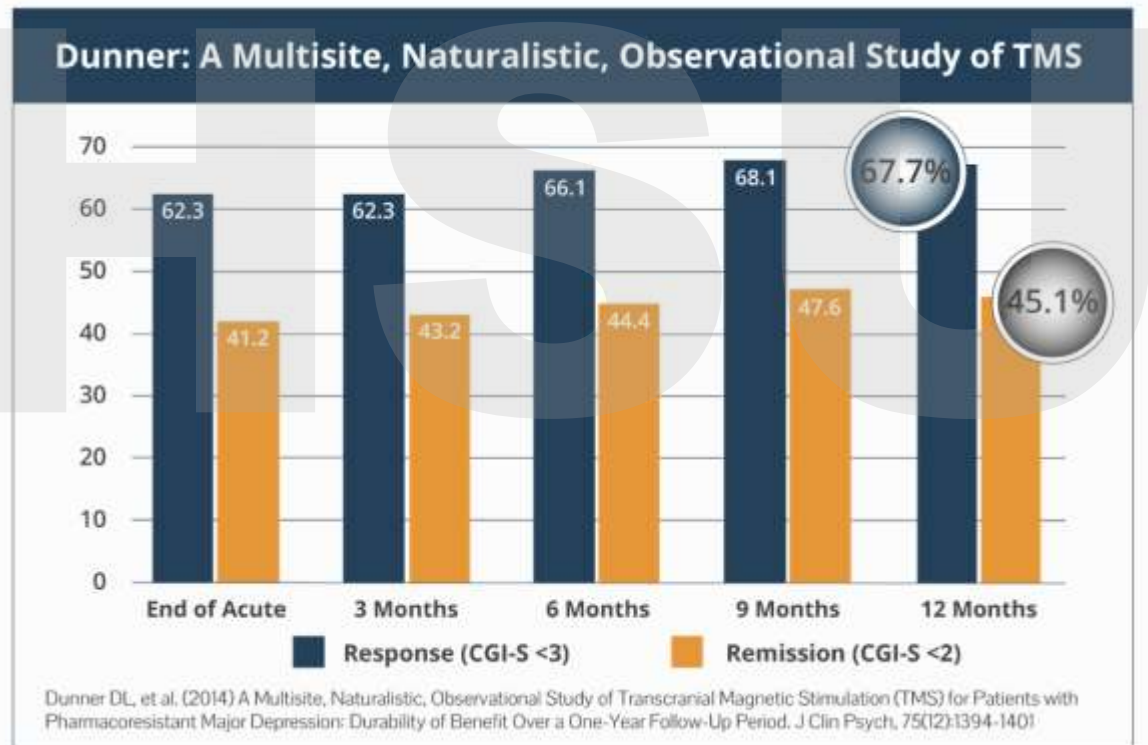
# What is the Evidence for TMS in Depression?

Dunner, et al 2014:

67.7% of acute remitters sustained response at one year.

- Responders tended to maintain their gains over the year.

2014



# Side Effects of TMS



## RARE

- Seizure: less than 1 in 30,000 treatment sessions (<.003%), less than 6 in 5,000 patient exposures (<0.12%).
- Risk of hearing damage (earplugs are used which minimizes risk)
- Syncope (initial session)
- Less than 5% of patients in TMS trials discontinue b/c of side effects.

## LESS RARE

- Scalp discomfort → usually responds to reassurance and a slower titration.
- Headache—Usually limited to a few minutes after session. Can pre-treat with NSAIDS.
- Lightheadedness, esp. in initial sessions.
- No effect on memory.

# Contraindications to TMS

- Only absolute contraindication is non-removable metallic objects in and around the head.
- Relative Contraindications:
  - Seizure Disorders
  - Significant TBIs/stroke (depends on location)
  - Active substance use disorder (MJ usually ok)
  - Certain Medications (usually dose can be adjusted)
  - Other Psychiatric Disorders (can be used off-label for some of these)

# What is an Acute Course of TMS?



First treatment is “mapping session” and takes about an hour.



Subsequent treatments are 20 minutes.



Treatment is 5 days/week (M-F) for six weeks, then six “tapering” sessions over the last three weeks for a total of 36 sessions.



Most patients see improvement between 3-5 weeks of treatment.



Treatment may be extended based on clinical situation.



## Does Insurance Cover TMS?

- For Major Depressive Disorder: **YES**
  - Medicare, Medicaid (in many states, including Oregon, Washington).
  - Almost all commercial insurance plans.
- For Obsessive Compulsive Disorder: Not Yet . . .
- Other potential indications: Migraine, Anxiety Disorders, Addiction, Pain Disorders, etc.

Thank You

*Fortune Favors the Prepared Mind*

- Louis Pasteur