The Evidence Base for rTMS Reimbursement

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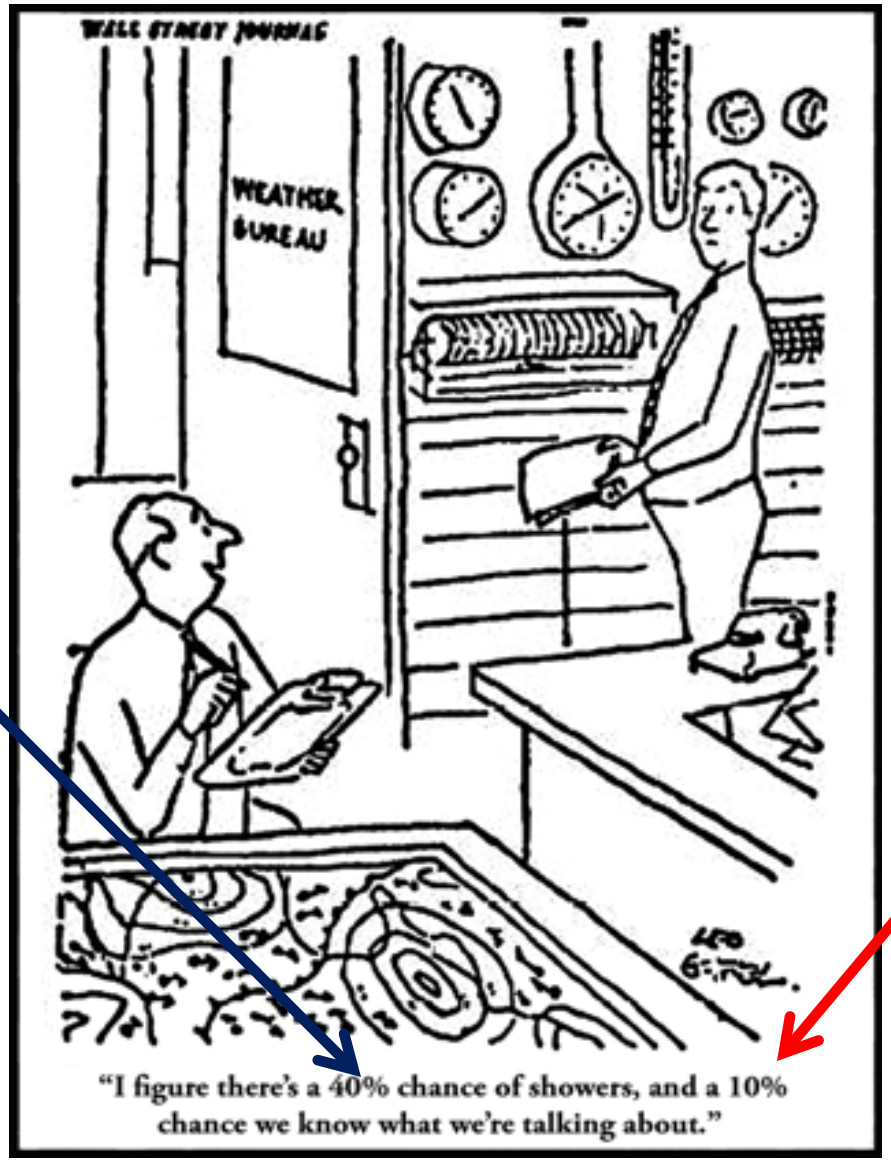
Institute of Medicine Workshop
March 3, 2015

What do we know, and what don’t we know, and how do we use that information?

Quality of evidence



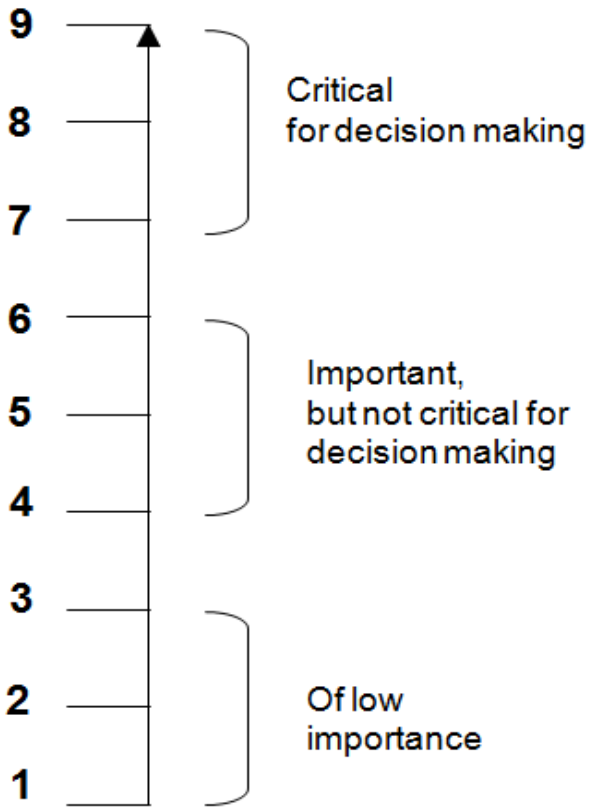
Effect estimate

Quality of evidence

Quality of Evidence

High	We are **very confident** that the true effect lies close to the estimate of the effect
Moderate	We are **moderately confident** in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our **confidence** in the effect estimate **is limited**: The true effect may be substantially different from the estimate of the effect
Very Low	We have **very little confidence** in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect

Unclear how best to rank the relative importance of outcomes



- Symptom reduction
- Remission
- Loss of MDD diagnosis
- Disability, functional impairment
- Quality of life
- Adverse events leading to withdrawals

- Prevention of comorbid conditions
- Serious adverse events

Findings of the Comparative Effectiveness Review: rTMS ± ECT Versus ECT Alone

- Benefits:
  - rTMS does not clearly differ from ECT.

    Strength of Evidence = Low
- Harms:
  - ECT and rTMS may not differ in withdrawals due to adverse events, but overall withdrawal rates were lower with rTMS.

    Strength of Evidence = Low
  - Evidence is insufficient to evaluate ECT versus rTMS with respect to adverse events and effects on cognitive/daily functioning.
  - Treatment interventions combining ECT with rTMS do not clearly differ from treatment with ECT alone.

    Strength of Evidence = Low

Gaynes BN, Lux L, Lloyd S, et al. AHRQ Comparative Effectiveness Review No. 33. September 2011, updated 2014. Available at: http://www.effectivehealthcare.ahrq.gov/trd.cfm.

Findings of the Comparative Effectiveness Review: rTMS (1 of 3)

- Benefits: When compared to sham treatment, rTMS:
  - Produced a greater decrease in depression severity.

    Strength of Evidence = High
  - Was three times as likely to produce a response.

    Strength of Evidence = High
  - Was six times as likely to achieve remission.

    Strength of Evidence = Moderate
  - Produced a greater improvement in health status and daily functioning.

    Strength of Evidence = Low
  - Evidence i insufficient to evaluate the ability of rTMS to maintain response or remission.

Gaynes BN, Lux L, Lloyd S, et al. AHRQ Comparative Effectiveness Review No. 33. September 2011, updated 2014. Available at: http://www.effectivehealthcare.ahrq.gov/trd.cfm

Findings of the Comparative Effectiveness Review: rTMS (2 of 3)

- Benefits: When compared to sham treatment, rTMS:
  - Produced better outcomes for depression severity and response rates for young adults.

    Strength of Evidence = Low
  - Produced better outcomes for depression severity in older adults with poststroke depression.

    Strength of Evidence = Low

Gaynes BN, Lux L, Lloyd S, et al. AHRQ Comparative Effectiveness Review No. 33. September 2011, updated 2014
Available at: http://www.effectivehealthcare.ahrq.gov/trd.cfm.

Findings of the Comparative Effectiveness Review: rTMS (3 of 3)

- Harms:
  - rTMS produces more scalp pain at the stimulation site than sham treatment.

    Strength of Evidence = Low
  - Evidence is insufficient to permit conclusions about withdrawals because of adverse events or because of patient nonadherence to rTMS versus sham treatment.

Gaynes BN, Lux L, Lloyd S, et al. AHRQ Comparative Effectiveness Review No. 33. September 2011, updated 2014. Available at: http://www.effectivehealthcare.ahrq.gov/trd.cfm.

Findings of the Comparative Effectiveness Review: Insufficient Evidence

- Evidence is insufficient to evaluate the comparative effectiveness or adverse effects between the following comparators:
  - ECT versus sham treatment
  - rTMS + pharmacotherapy versus pharmacotherapy alone or sham treatment
  - Psychotherapy versus control treatment or pharmacotherapy

Gaynes BN, Lux L, Lloyd S, et al. AHRQ Comparative Effectiveness Review No. 33. September 2011, updated 2014. Available at: http://www.effectivehealthcare.ahrq.gov/trd.cfm.

Mean average outcomes for pharmacologic treatments

- For switching strategies
  - mean pharmacologic response rates averaged 39.8 percent (95% CI, 30.7% to 48.9%)
  - mean remission rates averaged 22.3 percent (95% CI, 16.2% to 28.4%).
- For augmentation
  - mean response rates averaged 38.1 percent (31.0% to 45.3%)
  - mean remission rates averaged 27.2 percent (20.4% to 34.0%).
- For maintenance strategies
  - mean response rates averaged 27.3 percent (19.8% to 34.8%)
  - mean remission rates averaged 16.8 percent (13.5% to 20.2%).

What are the challenges to the quantitative synthesis of evidence?

- Varying definitions of treatment resistant depression
- Unclear number of prior treatment episodes (trail of tiers)
- Evolving intervention—a field, not a specific treatment
  - Varying stimulation parameters for “adequate” treatment
    - Coil location
    - Motor threshold
    - Stimulus pulse
    - Number of pulses (HF; LF)
  - Differing lengths of time
  - Is it a switch treatment or an augmentation treatment?
- Direct comparisons of rTMS vs. other interventions remain limited

- Subgroup analyses very limited
  - Have access to group level responses, but not having individual level data prevents meaningful synthesis
  - Example: depressive severity
- Data available from publications are more limited (restrictions on what you can publish)
- Adverse events measures few and not standardized

Moving from a Systematic Review to Recommendations

- Information from systematic review (the evidence) is only one part to consider.

- Equally important are:

1. Balance between benefits and harms
2. Patient preferences and values (little known about rTMS here)
3. Equity and acceptability
4. Sometimes costs

Knowledge Gaps and Future Research Needs

- Information about health-related outcomes that concern quality of life or levels of functional impairment is sparse.
- Few studies directly compare nonpharmacologic interventions with each other or with pharmacologic interventions.
  - Augment?
  - Switch?
- Evidence is lacking about efficacy in subgroups defined by
  - sociodemographic characteristics
  - symptom severity
  - psychiatric comorbidity
  - coexisting medical conditions

so, need individual patient level data

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- Study shortcomings:
  - Inconsistent definitions of TRD
  - Inconsistent reporting of measured outcomes
  - Short followup periods
  - Number of treatment failures not well documented
  - Limited, short-term, variable, and inconsistent adverse event reporting
  - Application of consistent, accepted, adequately dose protocols

Next Steps?