



CEPAC Voting and Policy Implications Summary
Nonpharmacologic Interventions for Treatment-Resistant Depression
December 9, 2011

The New England Comparative Effectiveness Public Advisory Council (CEPAC) is an independent forum in which clinical and public policy experts publicly deliberate on evidence reviews of the clinical effectiveness and value of health care services. Through these deliberations, and summary votes held on key evidence questions, CEPAC provides guidance on how the existing evidence can best be applied to improve the quality and value of health care services across New England. CEPAC is comprised of 17 members, a mix of clinicians and public representatives from each New England state. Representatives of state Medicaid programs and of regional private payers are included as ex-officio members of CEPAC. CEPAC members are recruited through an open public nomination process, and are selected on the basis of their experience and training in the interpretation and application of medical evidence in health care delivery.

The second public meeting of CEPAC discussed nonpharmacologic interventions for treatment-resistant depression. Staff from the Institute for Clinical and Economic Review (ICER) provided CEPAC with an adapted evidence report that included the evidence review developed by the Agency for Healthcare Quality and Research (AHRQ), supplemented with new material and analyses. This supplementary material included 1) updated information on the patient management options for treatment-resistant depression published since the AHRQ review; 2) regional and national data on prevalence, utilization, and existing clinical guidelines as well as payer coverage policies; 3) the results of budgetary impact and cost-effectiveness analyses developed to support discussion of the comparative value of different management options. Two psychiatrists expert in the treatment of patients with resistant-depression, Dr. Linda Carpenter of Brown University and Butler Hospital, and Dr. Erik Plakun of the Austen Riggs Center in Stockbridge, MA were selected to participate in a clinical expert conference call held before the in-person meeting to present the various treatment options available for TRD. Following the votes and deliberation, CEPAC participated in a roundtable discussion with a panel comprised of representatives from the clinical expert community and from regional private health plans that explored the implications of CEPAC votes for clinical practice and payer policies. The meeting was held on Friday, December 9, 2011 in Providence, Rhode Island. All but two CEPAC members were in attendance, with one ex-officio member sending a replacement to serve in his place. The meeting agenda and full attendance list, including roundtable panelists, are shown in Appendix A.

Summary of Votes and Recommendations

CEPAC members voted on questions concerning the comparative clinical effectiveness of the four treatment options discussed: 1) repetitive transcranial magnetic stimulation (rTMS); 2) electroconvulsive therapy (ECT); 3) vagus nerve stimulation; and 4) cognitive behavioral therapy/interpersonal therapy (CBT/IPT).

- **Comparative clinical effectiveness: rTMS vs. usual care**

For patients who have TRD, is the evidence adequate to demonstrate that rTMS provides a net health benefit *equivalent* or *superior* to usual care (i.e., general supportive psychotherapy with or without continued use of antidepressant medication)?

CEPAC Vote: 10 Yes 5 No

a. If yes:

- Is rTMS *equivalent* or *superior* to usual care?

5 Equivalent 5 Superior

b. If no, is this due to:

- Inadequate evidence with which to judge comparative net health benefit

5 Yes

- Adequate evidence of an *inferior* net health benefit

0 Yes

Comments:

- CEPAC desired greater clarity on the ideal number of treatment failures required before rTMS is used, since standard practice differs from the FDA label (one failed trial of antidepressants).
- Although the majority of CEPAC voted that the evidence is adequate to suggest that rTMS is more effective than usual care, comments from some CEPAC members noted the need for more data on which patients are ideal candidates for rTMS.
- Some members expressed concern about the potential for overutilization of rTMS without a standard definition of the ideal patient population.
- Many CEPAC members who voted that the evidence was inadequate to determine if rTMS is as effective or better than usual care cited the dearth of evidence on the benefits of rTMS beyond the initial 4-6 week treatment phase.

- **Comparative clinical effectiveness: rTMS vs. ECT**

For patients who have TRD, is the evidence adequate to demonstrate that rTMS provides a net health benefit *equivalent* or *superior* to ECT?

CEPAC Vote: 9 Yes 6 No

a. If yes:

- Is rTMS *equivalent* or *superior* to ECT?

9 Equivalent 0 Superior

b. If no, is this due to:

- Inadequate evidence with which to judge comparative net health benefit

6 Yes

- Adequate evidence of an *inferior* net health benefit

0 Yes

Comments:

- CEPAC emphasized the need to identify the subpopulations that would benefit more from each therapy. Some CEPAC members suggested the need to establish target subpopulations for each treatment, with more severe patients receiving ECT and less severe patients receiving rTMS.

- **Comparative clinical effectiveness: ECT vs. usual care**

For patients who have TRD, is the evidence adequate to demonstrate that ECT provides a net health benefit *equivalent* or *superior* to usual care (i.e., general supportive psychotherapy with or without continued use of antidepressant medication)?

CEPAC Vote: 3 Yes 11 No 1 Abstain

a. If yes:

- Is ECT *equivalent* or *superior* to usual care?

0 Equivalent 3 Superior

b. If no, is this due to:

- Inadequate evidence with which to judge comparative net health benefit

11 Yes

- Adequate evidence of an *inferior* net health benefit

0 Inferior

Comments:

- Several CEPAC members qualified their “no” vote on the evidence for ECT with recognition that ECT is an older treatment adopted in an era with far lower standards for evidence on clinical effectiveness. CEPAC members acknowledged that ECT is accepted broadly as standard of care for patients with severe depression who need immediate treatment due to features including catatonia, psychosis, active suicidal ideation, and serial failure to respond to drug treatment.
- The one abstention vote was predicated on the lack of data regarding the appropriate patient population to receive ECT.

- **Comparative clinical effectiveness: VNS vs. usual care**

For patients who have TRD, is the evidence adequate to demonstrate that VNS provides a net health benefit *equivalent* or *superior* to usual care (i.e., general supportive psychotherapy with or without continued use of antidepressant medication)?

CEPAC Vote: 0 Yes 15 No

a. If yes:
N/A

b. If no, is this due to:

- Inadequate evidence with which to judge comparative net health benefit
15 Yes
- Adequate evidence of an *inferior* net health benefit
0 Yes

- **Comparative clinical effectiveness: CBT/IPT vs. usual care**

For patients who have TRD, is the evidence adequate to demonstrate that CBT/IPT provides a net health benefit *equivalent* or *superior* to usual care (i.e., general supportive psychotherapy with or without continued use of antidepressant medication)?

CEPAC Vote: 6 Yes 9 No

a. If yes:

- Is CBT/IPT *equivalent* or *superior* to usual care?
6 Equivalent 0 Superior

b. If no, is this due to:

- Inadequate evidence with which to judge comparative net health benefit
9 Yes
- Adequate evidence of an *inferior* net health benefit
0 Yes

Comparative Value

When a majority of CEPAC votes that the evidence is adequate to demonstrate that an intervention produces patient outcomes equivalent or superior to a reference option, the Council members are also asked to vote on whether the intervention represents a “high,” “reasonable,” or “low” value. The value “perspective” that members of CEPAC are asked to assume is that of a state Medicaid program that must make resource decisions within a fixed budget for care. While information about hypothetical budget tradeoffs are provided, CEPAC is not given prescribed boundaries or thresholds for budget impact, PMPM changes, or incremental cost-effectiveness ratios to guide its judgment of high, reasonable, or low value. For each vote on comparative value Council members are asked to complete a multi-criteria decision analysis scoring sheet to make more transparent how they weighed different criteria in their ultimate judgment of comparative value. Only those CEPAC members who vote that the evidence is adequate to demonstrate equivalent or superior clinical effectiveness are asked to vote on comparative value.

Votes on Comparative Value

In response to public comment provided in advance of the December 9 meeting, an additional analysis was conducted prior to voting. The comment suggested that a more relevant comparison might be the use of rTMS as an *adjunct* to usual care vs. usual care with another adjunctive therapy (e.g., CBT, adding an antipsychotic drug). A simple calculation was made to address this by adding the median cost of antipsychotic therapy observed in a TRD cohort study (Ivanova, 2010) and applying it to the cost-effectiveness model; no change in effectiveness was assumed. Over 5 years, this change would be estimated to increase the direct cost of usual care to approximately \$3,370 per patient, thereby decreasing the incremental cost of rTMS to approximately \$1,900, and the resulting cost per QALY gained to \$98,000.

1. rTMS vs. usual care

Based on reimbursement levels provided with this report, would you judge the comparative value of rTMS to be of 1) high value; 2) reasonable value; or 3) low value compared to usual care?

CEPAC Vote: 4 Low 6 Reasonable

Multi-criteria decision analysis voting was done by all voting CEPAC members in order to describe their judgment and weighting of several criteria potentially relevant to an overall rating of comparative value. The results for the vote on rTMS vs. usual care is shown in the table below on the following page:

Table of Multi-criteria decision analysis votes.

Possible Factors in Your Judgment of "Comparative Value"	Rating from lowest to highest (0 – 5) of each factor for this intervention		Rating of how important this factor was in overall judgment of comparative value	
	Vote Average	Vote Range	Vote Average	Vote Range
Magnitude of the net clinical benefit compared with other available options	2.8	0 – 5	4	3 – 5
Confidence in the evidence on comparative clinical benefit	2.2	0 - 5	4.1	3 -5
Magnitude of improvement in safety and tolerability	2.7	0-5	3.4	0-5
Confidence in the evidence on improvement of safety and tolerability	2.9	1 - 5	2.9	0 – 4
Magnitude of the incremental cost-effectiveness ratio (ICER)	2.4	0-4	3.1	1 – 5
Confidence in the accuracy of the ICER	2.6	1 – 5	2.6	1 – 5
Budget impact/opportunity cost (other potential uses for \$\$)	3.2	1 – 5	3.4	1 – 5
Other reasonable treatment options are available	2.1	0 – 5	3.6	0 – 5
Severity of the condition	3.8	1 – 5	3.4	0 - 5
Ability of the intervention to address healthcare disparities	1.5	0 – 5	1.6	0 – 5
Support for the intervention from clinicians	2.3	0 – 5	2.0	0 – 5
Special (vulnerable) population	3.5	1 – 5	3.4	1 – 5
Risk of overuse or misuse	3.2	1 – 5	2.8	1 – 5

2. rTMS vs. ECT

Based on reimbursement levels provided with this report, would you judge the comparative value of rTMS to be of 1) high value; 2) reasonable value; or 3) low value compared to ECT?

CEPAC Vote: 5 Low 3 Reasonable 1 High

Multi-criteria decision analysis results for the comparative value votes on rTMS vs. ECT are shown in the table on the following page:

Table of multi-criteria decision analysis votes.

Possible Factors in Your Judgment of “Comparative Value”	Rating from lowest to highest (0 – 5) of each factor for this intervention		Rating of how important this factor was in overall judgment of comparative value	
	Vote Average	Vote Range	Vote Average	Vote Range
Magnitude of the net clinical benefit compared with other available options	2.5	0 – 5	3.875	1 – 5
Confidence in the evidence on comparative clinical benefit	1.6	1 – 4	3.5	1 – 5
Magnitude of improvement in safety and tolerability	3.1	0 – 5	3.25	0 – 5
Confidence in the evidence on improvement of safety and tolerability	2.5	0 – 4	3.125	0 – 5
Magnitude of the incremental cost-effectiveness ratio (ICER)	2.0	0 – 5	2.5	1 – 5
Confidence in the accuracy of the ICER	2.4	1 – 5	3.125	1 – 5
Budget impact/opportunity cost (other potential uses for \$\$)	2.4	0 – 5	2.75	0 – 5
Other reasonable treatment options are available	3.1	0 – 5	3.5	0 – 5
Severity of the condition	3.6	0 – 5	4.25	3 – 5
Ability of the intervention to address healthcare disparities	2.3	0 – 5	2.286	0 – 4
Support for the intervention from clinicians	2.8	0 – 5	2.75	0 – 5
Special (vulnerable) population	2.8	0 – 5	2.75	0 – 5
Risk of overuse or misuse	2.7	0 – 5	3.286	0 – 5

Social value considerations for policymakers

The final question of the meeting explored broader considerations of public health, equity, and access:

- Are there any considerations related to public health, equity, disparities in access or outcomes for specific patient populations, or other social values that should be considered in medical policies related to the use of rTMS, ECT, VNS, or CBT/IPT?

CEPAC voiced concern that with no third party reimbursement for rTMS, only patients who can afford to pay out-of-pocket can obtain treatment. Therefore, there may be concerns over equity in access to rTMS for certain populations.

Roundtable Discussion

Following the CEPAC votes and deliberation of the evidence, CEPAC engaged in a roundtable discussion with a panel composed of two representatives from the clinical expert community and two representatives of regional private health plans. The goal of the roundtable was to explore the implications of CEPAC votes for clinical practice and payer policies. The topics discussed included:

Future Research

Panelists outlined the gaps in current evidence and outlined future research needs to support future coverage decisions, including evidence of the long-term health benefit and duration of effect for rTMS. Panelists also indicated their concern for the shortage of funding for these types of clinical trials.

Coverage considerations

Payer representatives and CEPAC discussed the prospect of using specific medical policies for rTMS such as coverage with evidence development, patient registries, and limited networks with centers of excellence, but voiced concern for the practicalities of each. Payers at the table cautioned that with such a significant population in need of interventions to treat resistant-depression, that centers of excellence and limited networks may not be able to accommodate the demand for these services, and that payers will have to be able to prioritize which patients receive treatment if coverage becomes available.

Payers also stressed their concerns for indication creep if rTMS became available for everyone to use, highlighting that without further evidence on the specifics of treatment duration, maintenance therapy, and selection in the appropriate patient population, that rTMS could be used inappropriately.

Policy Implications:

Physician Specialty Societies

- Professional societies should lead the effort in establishing training and practice standards and promote the development of registries to monitor outcomes of patients receiving treatment for TRD that can be used to guide quality improvement.
- Professional societies should develop clinical guidelines for TRD that include recommendations for : 1) the appropriate subpopulations to receive treatment with rTMS and ECT; 2) treatment duration and frequency for rTMS; 3) maintenance therapy requirements; and 4) the threshold for previously failed treatments required before considering rTMS.

Hospitals and other clinical providers

- Each hospital providing treatment for TRD should participate in registries to gather data on the short and long-term outcomes of patients undergoing ECT or rTMS. The data derived from these registries should be used to guide internal quality improvement and inform the

appropriateness of each therapy for various subpopulations as well as an evaluation of the long-term outcomes for patients receiving treatment for TRD.

Payers

- If payers elect to cover rTMS, they should consider limiting coverage to patients with ≥ 2 failed drug treatments during the most recent episode of depression, a higher threshold than that included in the FDA license. In addition, payers should consider options for limiting coverage to designated centers of excellence, perhaps with an additional requirement for continued evidence generation through a national registry to be organized by professional societies. These limitations would be useful to assure the following: 1) consistent, rigorous training standards are established for providers; and 2) coverage will support rather than hinder efforts to gather further evidence to help guide future patient, provider, and payer decisions regarding appropriate patient selection for both rTMS and ECT. Payers on the roundtable voiced concerns for the feasibility and practicality of a centers of excellence approach for coverage of rTMS due to the large number of patients potentially eligible for this service and the consequent difficulty of assuring equitable access. All participants on the roundtable agreed that it is difficult to find funding to support large, effective registries.

Appendix A: Meeting Agenda and Attendee List

Public Meeting – Providence, RI

December 9, 2011

10:00 AM – 3:30 PM

10:00 – 10:15 AM: Meeting Convened and Introductions

10:15 – 10:45 AM: Adaptation Presentation

10:45 AM – 12:00 PM: Q&A with ICER Staff and CEPAC Deliberation

12:00 PM – 12:30 PM: Public Comment

12:30 – 1:00 PM: Lunch

1:00 – 2:00 PM: Votes on Questions

2:00 – 3:20 PM: Roundtable Discussion on Implications of CEPAC Votes

3:20 – 3:30 PM: Close

MEETING PARTICIPANTS

CEPAC Members

Name	State	Organization	Disclosures
Ellen Andrews, PhD	CT	CT Health Policy Project	
Robert Aseltine, PhD	CT	University of Connecticut Health Center	
R. William Corwin, MD	RI	Miriam Hospital	
Michael Deren, MD	CT	Private Practice	
Chuck Eaton, MD	RI	Memorial Hospital of Rhode Island, Center for Primary Care and Prevention	
Teresa Fama, MD	VT	Central Vermont Rheumatology	
Michael Farber, MD (ex-officio)	VT	State of Vermont	
Sandra Fritsch, MD	ME	Maine Medical Center	
Deidre Gifford, MD	RI	Rhode Island Chronic Care Sustainability Initiative	Salary funded by multi-stakeholder collaboration included Blue Cross Blue Shield Rhode Island, United Health Care, Neighborhood Health Plan of Rhode Island, and Tuft's Health Plan
Claudia Gruss, MD (Vice Chair)	CT	Arbor Medical Group, LLC	Wellpoint shares held jointly with spouse in excess of \$10,000
William Cyrus Jordan, MD	VT	Vermont Program for Quality in Health Care	
Jekkie Kim, MD, JD	MA	Ropes and Gray LLP	
Richard Lopez, MD (Chair)	MA	Atrius Health	
Lori Nerbonne, RN	NH	New Hampshire Patient Voices	
Jeffrey Simmons, MD* (ex-officio)	MA	Blue Cross Blue Shield of Massachusetts	
Keith Stahl, MD	NH	Family Health and Wellness Center	
William Taylor, MD	MA	Harvard Medical School	Also employed by Harvard Pilgrim Health Care Institute (HPHCI) which received funding from Harvard Pilgrim Health Care; Payments also received as medical consultant to malpractice insurers.
Members not in attendance:			
Felix Hernandez, MD	ME	Eastern Maine Medical Center	
John Fallon, MD	MA	Blue Cross Blue Shield of Massachusetts	
Thomas Lee, MD	MA	Partners Community Healthcare, Inc.	

* Dr. Simmons is filling in for Dr. Fallon as the private payer ex-officio members for this meeting

Roundtable Panelists

Linda Carpenter, MD, Brown University, Butler Hospital
 Jeffrey Fetter, MD, NH Psychiatric Society, Concord Hospital
 Joseph Kozachek, MD, Aetna
 Carolyn Langer, MD, Harvard Pilgrim Health Care

ICER

Steve Pearson, MD, President
 Dan Ollendorf, MPH, Chief Review Officer
 Sarah Emond, MPP, Chief Operating Officer
 Kristen Migliaccio-Walle, BS, Sr. Decision Scientist
 Jennifer Colby, PharmD, Research Associate
 Sarah Jane Reed, MSc, Program Coordinator

