# Prioritizing Comparative Effectiveness Research Questions for the Treatment of Major Depressive Disorder: A Stakeholder Workshop Meeting Summary

## Overview

On June 9, 2015, PCORI brought together stakeholder groups to identify, refine, and prioritize comparative effectiveness research (CER) questions regarding the treatment of major depressive disorder whose findings could improve patient-centered outcomes. Major depressive disorder (MDD) is a serious mood disorder that causes significant distress and interferes with a person's basic functioning. As many as one-third of people diagnosed with MDD have severe symptoms or fail to respond to at least two successive trials of an antidepressant medication and are classified as having treatment-resistant depression (MDD: Topic Brief). Workgroup participants were tasked with identifying research questions that addressed current gaps in knowledge and were most relevant to patients with treatment-resistant depression. Philip Wang, MD, DrPh, chaired the meeting. A wide range of stakeholders attended, and the meeting was audio recorded and open to the public via teleconference and webinar.

## Key Questions

Questions for discussion were submitted by workshop participants prior to the meeting and refined by PCORI staff to yield a total of 30 distinct questions within the scope of PCORI. After further refinement and distillation by PCORI staff, eight questions were shared via survey and ranked by workshop attendees prior to the meeting.

Morning Session

During the workshop's morning session, attendees were asked to prioritize and discuss the top five ranked questions using PCORI research prioritization criteria. Thirty-six of the attendees voted. Conversation revolved around each question's relation with each of the following criteria:

- **Patient-Centeredness**: Is the comparison relevant to patients, their caregivers, clinicians, or other key stakeholders, and are the outcomes relevant to patients?
- **Impact of the Condition on the Health of Individuals and Populations**: Is the condition or disease associated with a significant burden in the U.S. population, in terms of disease prevalence, costs to society, loss of productivity, or individual suffering?
- **Assessment of Current Options**: Does the topic reflect an important evidence gap related to current options that is not being addressed by ongoing research?
- **Likelihood of Implementation in Practice**: Would new information generated by research be likely to have an impact in practice?
- **Durability of Information**: Would new information on this topic remain current for several years, or

would it be rendered obsolete quickly by new technologies or subsequent studies?

The top five ranked questions that were discussed were:

*Question 1. What is the comparative effectiveness of different available interventions to engage and enable patients in following effective treatments for their severe depression, such as interventions that promote adherence to medications or regular attendance at individual/group therapy sessions? What is their comparative effectiveness in promoting adherence to treatment and thereby improvement of wellness, symptoms, and functioning?*

*Two different processes:*

a. *Engage patients in treatment*
b. *Maintain/adhere to treatment*

Comments included:

o Should peer support be addressed in the question as an opportunity for adherence?
o A need to address adherence in the presence of multiple co-occurring treatments; avoid silos of care; use interventions across the spectrum.
o One participant noted the need for coordination with some decision support to provide tools, and the group agreed.

*Question 2. What is the comparative effectiveness of cognitive behavioral therapy (or other evidence-based psychosocial treatment traditionally delivered face-to-face) for severe depression when delivered by alternatives to individual face-to-face therapy? Examples include remote delivery (e.g., phone, online, patient use of self-guided online programs), expertise in computer-based testing (CBT) delivery, use of healthcare professionals with varying levels of postgraduate training, and individual versus group settings.*

Comments included:

o Remove "use of healthcare professionals with varying levels of postgraduate training" from question wording.
o Unclear what is effective in CBT and, given the scarcity of mental health professionals, CBT may be difficult to deliver.
o This may be an issue more for mild to moderate depression as opposed to severe depression.
o This could result in numerous head-to-head comparisons. It may be better to focus instead on care optimization and individual preferences.

*Question 3. For patients who are likely to lack access to comprehensive assessment or are at high risk of under-treatment or inappropriate treatment for severe depression due to socio-demographics (e.g., racial minorities, cultural and linguistic differences in expressing/seeking help for depression, living in areas with few service providers), what is the comparative effectiveness of interventions designed to increase access and appropriate treatment?*

Comments included:

o Logistical and cultural barriers to engaging in depression treatment need to be considered. There are unique challenges for different subpopulations of need.
o This question may need to be refined and refocused to special subpopulations of need.

*Question 4. What is the comparative effectiveness of switching and/or augmenting therapies in improving symptoms and functioning in treatment-resistant depression? For example, transcranial magnetic stimulation (TMS) versus second-generation antipsychotics (SGAs) versus psychosocial therapy versus electroconvulsive therapy (ECT) versus algorithm-guided care. Does this vary with age (e.g., in adolescents or the elderly) and medical comorbidities (e.g., patients with cancer or myocardial infarction) or special circumstances (e.g., post-partum)?*

Comments included:
- Series of questions regarding treatment steps and how to formulate questions into testable hypotheses.
- The group agreed that this question resonates with providers' struggles.
- The group discussed the importance of considering wellness as the outcome goal.
- Remove "versus algorithm-guided care" from question wording.

*Question 5. What is the comparative effectiveness of manualized therapies as "add-on" treatment to severely depressed patients who are incompletely treated with first-line or any other therapies? Examples include Wellness Recovery Action Plan (WRAP), Whole Health Action Management (WHAM), and others.*

Comments included:
- WRAP and WHAM can be used by peers.
- Does this question overlap with the previous question?
- Do these have less risk than some of the add-ons in the questions above?
- Two phases of treating depression: acute setting and community setting.

Stakeholders were encouraged to comment on the feasibility and implications of each research question, and the research question language evolved accordingly. The possibility of grouping questions 2 and 3 regarding delivery and questions 4 and 5 regarding treatment options was discussed but later voted against.

Afternoon Session

During the workshop's afternoon session, results from the morning prioritization session were shared. Participants were asked to refine the research questions and identify the (1) patient population, (2) intervention, (3) comparators, (4) outcomes of interest, (5) time frame, (6) setting, and (7) study design for each priority question. Only the top three ranked questions were discussed:

**Priority Question 1.** What is the comparative effectiveness of switching and/or augmenting therapies in improving symptoms and functioning in treatment-resistant major depression? For example, transcranial magnetic stimulation (TMS) versus second-generation antipsychotics (SGAs) versus psychosocial therapy versus electroconvulsive therapy (ECT). Does this vary with age (e.g., in adolescents or the elderly) and medical co-morbidities (e.g., patients with cancer or myocardial infarction) or special circumstances (e.g., post-partum)?

**Patient population**: The question allows for broad consideration of priority populations, but two such populations that were identified by stakeholders were women in the pregnancy and post-partum periods, and adolescents with treatment-resistant depression.

**Intervention**: Transitional care for the broader treatment-resistant depression population,

as well as inpatient and outpatient care, could be considered.

**Comparators**: Comparators are described in the question.

**Outcomes of interest**: Patient burden of participating in the treatment; long-term side effects; global measure of satisfaction; least intensity of effective care

**Time frame**: Should consider both short-term and long-term (e.g., one year) treatment outcomes

**Setting**: In addition to traditional mental health treatment settings, should consider less traditional settings such as peer-run crisis respite, hospitalization, and online therapies

**Other comments**: Patient registry as possible major outcome of a project

**Priority Question 2.** What is the comparative effectiveness of different available interventions to engage and enable patients in following effective treatments for their severe depression, such as interventions that promote adherence to medications or regular attendance of individual/group therapy sessions? What is their comparative effectiveness in promoting adherence to treatment and therapy, and improvement of wellness, symptoms, and functioning?

**Patient population**: Populations of interest can be delineated based on specific systems of care, or patients with co-occurring disorders.

**Intervention**: Some interventions identified by stakeholders that hold promise for improving adherence include person-centered planning and collaborative documentation, and programs such as peer respite for individuals in crisis so as to avoid the additional stresses of emergency room and inpatient treatments.

**Comparators**: Individual and setting of treatment; different support-related interventions

**Outcomes of interest**: Number of treatment changes needed to get to a wellness state

**Time frame**: Should consider both short-term and long-term (e.g., one year) treatment outcomes

**Setting**: Different clinical settings and types of clinicians; emergency rooms

**Other comments**: Keeping a patient in treatment is not always a success; the same evidence-based treatment is not effective for every patient, so studies should consider outcomes beyond adherence to a specific treatment.

**Priority Question 3.** For patients who are likely to lack access to comprehensive assessment or at high risk of under-treatment or inappropriate treatment for severe depression due to socio-demographics, what is the comparative effectiveness of interventions designed to increase access to appropriate treatment?

**Patient population**: Focus could be on many priority populations, including ethnic/racial minorities; cultural and linguistic differences in expressing/seeking help for depression; living in areas with few service providers; immigrant groups; pregnancy and post-partum; trauma/abuse; veterans; foster care youth; elders; cognitively impaired; homeless; patients with multiple chronic conditions; LGBT community; caregivers

**Intervention**: Specific interventions that could improve health disparities: screening; community health workers; telemedicine and online resources; outreach teams; legal services; peer support; family involvement; clinical decision support

**Comparators**: Same as above in terms of types of treatments

**Outcomes of interest**: Detection and engagement; functioning and social determinants of health; reduction of untreated mental illness

**Time frame**: Should consider both short-term and long-term (e.g., one year) treatment outcomes

**Setting**: Meet patients where they are

**Other comments**: Stigma is important to measure and an important focus for outcomes.

## Moving Forward

The workshop provided an opportunity for key questions to be discussed and refined by a diverse range of stakeholders. There was a significant amount of deliberation and conversation surrounding each research question presented. PCORI will present the highest-priority question derived from this workshop at the August 18, 2015, Board of Governor's meeting to pursue the development of research funding opportunities.