**National Quality Forum—Evidence (subcriterion 1a)**

**Measure Number** (*if previously endorsed*)**:** 1880

**Measure Title**: Adherence to Mood Stabilizers for Individuals with Bipolar I Disorder

**IF the measure is a component in a composite performance measure, provide the title of the Composite Measure here:** Click here to enter composite measure #/ title

**Date of Submission**: 4/2/2018

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| **Instructions**  *Complete 1a.1 and 1a.2 for all measures. If instrument-based measure, complete 1a.3.*  *Complete* ***EITHER 1a.2, 1a.3 or 1a.4*** *as applicable for the type of measure and evidence.*  *For composite performance measures:*  *A separate evidence form is required for each component measure unless several components were studied together.*  *If a component measure is submitted as an individual performance measure, attach the evidence form to the individual measure submission.*   * All information needed to demonstrate meeting the evidence subcriterion (1a) must be in this form. An appendix of *supplemental* materials may be submitted, but there is no guarantee it will be reviewed. * If you are unable to check a box, please highlight or shade the box for your response. * Contact NQF staff regarding questions. Check for resources at [Submitting Standards webpage](http://www.qualityforum.org/Measuring_Performance/Submitting_Standards.aspx). |

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| **Note: The information provided in this form is intended to aid the Standing Committee and other stakeholders in understanding to what degree the evidence for this measure meets NQF’s evaluation criteria.**   1a. Evidence to Support the Measure Focus The measure focus is evidence-based, demonstrated as follows:   * Outcome: [**3**](#Note3) Empirical data demonstrate a relationship between the outcome and at least one healthcare structure, process, intervention, or service. If not available, wide variation in performance can be used as evidence, assuming the data are from a robust number of providers and results are not subject to systematic bias. * Intermediate clinical outcome: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4)that the measured intermediate clinical outcome leads to a desired health outcome. * Process: [**5**](#Note5) a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4) that the measured process leads to a desired health outcome. * Structure: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4) that the measured structure leads to a desired health outcome. * Efficiency: [**6**](#Note6) evidence not required for the resource use component. * For measures derived from patient reports, evidence should demonstrate that the target population values the measured outcome, process, or structure and finds it meaningful. * Process measures incorporating Appropriate Use Criteria: See NQF’s guidance for evidence for measures, in general; guidance for measures specifically based on clinical practice guidelines apply as well.   **Notes**  **3.** Generally, rare event outcomes do not provide adequate information for improvement or discrimination; however, serious reportable events that are compared to zero are appropriate outcomes for public reporting and quality improvement.  **4.** The preferred systems for grading the evidence are the Grading of Recommendations, Assessment, Development and Evaluation [(GRADE) guidelines](http://www.gradeworkinggroup.org) and/or modified GRADE.  **5.** Clinical care processes typically include multiple steps: assess → identify problem/potential problem → choose/plan intervention (with patient input) → provide intervention → evaluate impact on health status. If the measure focus is one step in such a multistep process, the step with the strongest evidence for the link to the desired outcome should be selected as the focus of measurement. Note: A measure focused only on collecting PROM data is not a PRO-PM.  **6.** Measures of efficiency combine the concepts of resource use and quality (see NQF’s [Measurement Framework: Evaluating Efficiency Across Episodes of Care](http://www.qualityforum.org/Publications/2010/01/Measurement_Framework__Evaluating_Efficiency_Across_Patient-Focused_Episodes_of_Care.aspx); [AQA Principles of Efficiency Measures](http://www.aqaalliance.org/files/PrinciplesofEfficiencyMeasurementApril2006.doc)). |

**1a.1.This is a measure of**: (*should be consistent with type of measure entered in De.1*)

Outcome

Outcome: Click here to name the health outcome

Patient-reported outcome (PRO): Click here to name the PRO

*PROs include HRQoL/functional status, symptom/symptom burden, experience with care, health-related behaviors.* (*A PRO-based performance measure is not a survey instrument. Data may be collected using a survey instrument to construct a PRO measure.)*

Intermediate clinical outcome (*e.g., lab value*): Click here to name the intermediate outcome

Process: Click here to name what is being measured

Appropriate use measure: Click here to name what is being measured

Structure: Click here to name the structure

Composite: Click here to name what is being measured

**1a.2** **LOGIC MODEL** Diagram or briefly describe the steps between the healthcare structures and processes (e.g., interventions, or services) and the patient’s health outcome(s). The relationships in the diagram should be easily understood by general, non-technical audiences. Indicate the structure, process or outcome being measured.

**1a.3** **Value and Meaningfulness:**  **IF** this measure is derived from patient report, provide evidence that the target population values the measured ***outcome, process, or structure*** and finds it meaningful. (Describe how and from whom their input was obtained.)

Not Applicable. This is not a patient-reported measure.

**\*\*RESPOND TO ONLY ONE SECTION BELOW -EITHER 1a.2, 1a.3 or 1a.4) \*\***

**1a.2** **FOR OUTCOME MEASURES including PATIENT REPORTED OUTCOMES - Provide empirical data demonstrating the relationship between the outcome (or PRO) to at least one healthcare structure, process, intervention, or service.**

**1a.3.****SYSTEMATIC REVIEW(SR) OF THE EVIDENCE (for intermediate outcome, PROCESS, or STRUCTURE PERFORMANCE measures, including those that are instrument-based) If the evidence is not based on a systematic review go to section 1a.4) If you wish to include more than one systematic review, add additional tables.**

**What is the source of the systematic review of the body of evidence that supports the performance measure? A systematic review is a scientific investigation that focuses on a specific question and uses explicit, prespecified scientific methods to identify, select, assess, and summarize the findings of similar but separate studies. It may include a quantitative synthesis (meta-analysis), depending on the available data. (IOM)**

X Clinical Practice Guideline recommendation (with evidence review)

☐ US Preventive Services Task Force Recommendation

☐ Other systematic review and grading of the body of evidence (*e.g., Cochrane Collaboration, AHRQ Evidence Practice Center*)

☐ Other

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| **Source of Systematic Review:**   * **Title** * **Author** * **Date** * **Citation, including page number** * **URL** | National Institute for Clinical Excellence (NICE)- Bipolar Disorder: Assessment and Management  National Institute for Clinical Excellence  National Collaborating Centre for Mental Health  2014  The National Institute for Clinical Excellence and the National Collaborating Centre for Mental health. Bipolar Disorder: Assessment and Management. Retrieved from https://www.nice.org.uk/guidance/cg185/evidence/full-guideline-pdf-193212829 |
| Quote the guideline or recommendation verbatim about the process, structure or intermediate outcome being measured. If not a guideline, summarize the conclusions from the SR. | If the person is already taking valproate or another mood stabilizers as prophylactic treatment, consider increasing the dose, up to the maximum level in the British National Formulary (BNF) if necessary, depending on clinical response. If there is no improvement, consider adding haloperidol, olanzapine, quetiapine or risperidone, depending on the person’s preference and previous response to treatment.  If a person develops mania or hypomania and is taking an antidepressant (as defined by the BNF) in combination with a mood stabilizer, consider stopping the antidepressant. |
| Grade assigned to the **evidence** associated with the recommendation with the definition of the grade | The guideline developers used the GRADE system but did not provide independent grades for each recommendation’s evidence. All studies identified evaluating the efficacy of mood stabilizers, lithium and valproate, were rated as having a low quality of evidence. |
| Provide all other grades and definitions from the evidence grading system | Randomized control trials (RCT) without important limitations provide high quality evidence.  Observational studies without special strengths or important limitations provide low quality evidence.  For each outcome, quality may be reduced depending on five factors: methodological limitations, inconsistency, indirectness, imprecision and publication bias. |
| Grade assigned to the **recommendation** with definition of the grade | The Guidelines did not provide independent grades to each recommendation. |
| Provide all other grades and definitions from the recommendation grading system | The Guidelines did not provide independent grades to each recommendation. |
| Body of evidence:   * Quantity – how many studies? * Quality – what type of studies? | Thirty-six RCTs were included in the body of evidence. The Guideline Development Group found very limited evidence for lithium and valproate monotherapy for acute episodes, but many participants in clinical trials were taking these medications in addition to investigational treatments, and the expert consensus was that mood stabilizers should normally be continued during acute episodes, with doses and plasma levels checked to optimize treatment. |
| Estimates of benefit and consistency across studies | Most of the studies suffered from very serious limitations, owing to the inappropriate methods that were used for evidence synthesis. According to the remaining studies, valproate semi sodium and lithium (mood stabilizers) were similar in terms of costs and outcomes in an analysis conducted in the US. Olanzapine was found to dominate lithium in a UK study. Quetiapine in addition to mood stabilizer (including quetiapine in XR formulation) was found to be more cost-effective than a mood stabilizer alone in a number of US and UK studies. The existing economic literature review reports conflicting results and is characterized by serious limitations. The guideline cost analysis indicates that lithium may be a cost-effective and potentially cost-saving treatment option for the long-term management of adults with bipolar disorder. |
| What harms were identified? | Lithium has adverse effects on the kidneys, thyroid and parathyroid. Lithium is a known human teratogen, that is, it is potentially harmful to an unborn child.  Valproate is associated with a number of side effects including tremor, weight gain and, rarely, liver damage. It can interact with a number of commonly prescribed medicines and notably is known to decrease plasma levels of olanzapine.  Carbamazepine is associated with dizziness, drowsiness, nausea and headaches, and it can cause a low white blood cell count, hyponatremia (low level of sodium in the blood) and rarely, liver damage.  Lamotrigine is associated with a rash, drowsiness, dizziness and blurred vision, and it can depress the bone marrow. |
| Identify any new studies conducted since the SR. Do the new studies change the conclusions from the SR? | Not Applicable |

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| **Source of Systematic Review:**   * **Title** * **Author** * **Date** * **Citation, including page number** * **URL** | Practice Guidelines for the Treatment for Patients with Bipolar Disorder  American Psychiatric Association  2004  Pyles, R., Cross, C.D., Peele, R., Anzia, D.J., Shemo, J.P., Lurie, L., Walker, R. D., Barnovitz, M.A., Gray, S.H., Saxena, S., and Tonnu, T. (2010). Practice Guidelines for the Treatment of Patients with Bipolar Disorder. American Psychiatric Association. Retrieved from https://psychiatryonline.org/pb/assets/raw/sitewide/practice\_guidelines/guidelines/bipolar.pdf |
| Quote the guideline or recommendation verbatim about the process, structure or intermediate outcome being measured. If not a guideline, summarize the conclusions from the SR. | The first-line pharmacological treatment for more severe manic or mixed episodes is the initiation of either lithium plus an antipsychotic or valproate plus an antipsychotic [Recommendation Grade - I].  For less ill patients, monotherapy with lithium, valproate, or an antipsychotic such as olanzapine may be sufficient [Recommendation Grade - I].  For mixed episodes, valproate may be preferred over lithium [Recommendation Grade - II]. |
| Grade assigned to the **evidence** associated with the recommendation with the definition of the grade | The attributing evidence is not clearly linked to each recommendation, but evidence is linked to specific medications. Each rating of clinical confidence considers the strength of the available evidence and is based on the best available data. When evidence is limited, the level of confidence also incorporates clinical consensus with regard to a particular clinical decision. |
| Provide all other grades and definitions from the evidence grading system | The following coding system is used to indicate the nature of the supporting evidence in the summary recommendations and references:  [A] Double-blind, randomized clinical trial. A study of an intervention in which subjects are prospectively followed over time; there are treatment and control groups; subjects are randomly assigned to the two groups; both the subjects and the investigators are blind to the assignments.  [A–] Randomized clinical trial. Same as above but not double-blind.  [B] Clinical trial. A prospective study in which an intervention is made and the results of that intervention are tracked longitudinally; study does not meet standards for a randomized clinical trial.  [C] Cohort or longitudinal study. A study in which subjects are prospectively followed over time without any specific intervention.  [D] Case-control study. A study in which a group of patients is identified in the present and information about them is pursued retrospectively or backward in time. |
| Grade assigned to the **recommendation** with definition of the grade | See brackets after each recommendation above for specific recommendation grades. Overall the grades were:  [I] Recommended with substantial clinical confidence.  [II] Recommended with moderate clinical confidence. |
| Provide all other grades and definitions from the recommendation grading system | The other grade in the recommendation grading system is:  [III] May be recommended on the basis of individual circumstances |
| Body of evidence:   * Quantity – how many studies? * Quality – what type of studies? | Lithium: Five studies have demonstrated lithium is superior to placebo (evidence grade A or B). Three of these studies had randomized assignments, four used crossover designs, and one was a placebo-controlled, parallel design trial. Lithium showed similar efficacy to other mood stabilizers and antipsychotics in 10 other trials (evidence grade A)  Valproate: Four randomized placebo-controlled trials (evidence grades A or B) have demonstrated the efficacy of Divalproex/valproate/valproic acid compared to placebo (response rates ranged 48-53%). Valproate was shown to have similar efficacy to other mood stabilizers in four other studies (evidence grades A or B).  Olanzapine: Two, large, randomized controlled trials demonstrated that Olanzapine is superior to placebo. Three other randomized controlled trials found similar efficacy to other mood stabilizers (evidence grade A). |
| Estimates of benefit and consistency across studies | Nearly all studies found that the mood stabilizer was superior for treating bipolar disorder compared to placebo. These studies demonstrated the efficacy of mood stabilizers for every subtype and subgroup of patients with bipolar disorder. Effectiveness of specific medications will vary by patient symptoms and history, see evidence summarized above. |
| What harms were identified? | Lithium: More common side effects include polyuria, polydipsia, weight gain, cognitive problems, tremor, sedation or lethargy, impaired coordination, gastrointestinal distress, hair loss, benign leukocytosis, acne, and edema.  Valproate: More common side effects include sedation, gastrointestinal distress, benign hepatic transaminase elevations, osteoporosis, and tremor.  Olanzapine: More common side effects include somnolence, constipation, dry mouth, increased appetite, weight gain, and during titration- orthostatic hypotension. |
| Identify any new studies conducted since the SR. Do the new studies change the conclusions from the SR? | Not Applicable |

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**1a.4 OTHER SOURCE OF EVIDENCE**

*If source of evidence is NOT from a clinical practice guideline, USPSTF, or systematic review, please describe the evidence on which you are basing the performance measure.*

**1a.4.1** **Briefly SYNTHESIZE the evidence that supports the measure.** A list of references without a summary is not acceptable.

**1a.4.2 What process was used to identify the evidence?**

**1a.4.3.** **Provide the citation(s) for the evidence.**