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

**Measure Number** (*if previously endorsed*)**:** 3205

**Measure Title**: Medication Continuation Following Inpatient Psychiatric Discharge

**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**: 11/13/2020

**Please note**: 2016 submission text in blue | 2020 submission text in red

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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: : Patient fills prescription, establishing medication continuation from the inpatient to the outpatient setting. (No change for 2020.)

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.

2020 submission: No change for 2020.

2016 submission: Effective interventions have been identified that can improve medication adherence during the transition from inpatient to outpatient care. Interventions that have been shown to increase medication compliance and prevent negative outcomes associated with nonadherence include patient education, enhanced therapeutic relationships, shared decision-making, and text-message reminders, with emphasis on multidimensional approaches (Douaihy, Kelly, & Sullivan, 2013; Haddad, Brain, & Scott, 2014; Hung, 2014; Kasckow & Zisook, 2008; Lanouette, Folsom, Sciolla, & Jeste, 2009; Mitchell, 2007; Sylvia et al., 2013). Interventions, including those described by the literature, can be implemented during steps 2 and 3 in the logic model to influence medication continuation in step 4. Because the denominator only includes patients who would require continued evidence-based pharmacotherapy and who have few barriers to access, this measure provides an indirect quality indicator of the treatment provided in steps 2 and 3.

1) Patient is admitted for inpatient psychiatric care 🡪 2) Patient receives treatment and is stabilized 🡪3) Patient is discharged with prescriptions for evidence-based medications and discharge treatment plan 🡪 4) **Patient fills initial prescription, establishing medication continuation from the inpatient to the outpatient setting** 🡪 5) Patient’s symptoms are managed by pharmacotherapy 🡪 6) Psychiatric decompensation and adverse outcomes such as emergency department visits, rehospitalization, and suicide are prevented.

\*Douaihy, A. B., Kelly, T. M., & Sullivan, C. (2013). Medications for substance use disorders. *Social Work in Public Health*, *28*(3-4), 264-278. doi: 10.1080/19371918.2013.759031

\*Haddad, P. M., Brain, C., & Scott, J. (2014). Nonadherence with antipsychotic medication in schizophrenia: Challenges and management strategies. *Patient Related Outcome Measures, 5*, 43-62. doi: 10.2147/PROM.S42735

\*Hung, C. I. (2014). Factors predicting adherence to antidepressant treatment. *Current Opinion in Psychiatry, 27*(5), 344-349. doi: 10.1097/yco.0000000000000086

\*Kasckow, J. W., & Zisook, S. (2008). Co-occurring depressive symptoms in the older patient with schizophrenia. *Drugs and Aging*, *25*(8), 631-647. doi: 10.2165/00002512-200825080-00002

\*Lanouette, N. M., Folsom, D. P., Sciolla, A., & Jeste, D. V. (2009). Psychotropic medication nonadherence among United States Latinos: A comprehensive literature review. *Psychiatric Services*, *60*(2), 157-174. doi: 10.1176/appi.ps.60.2.157

\*Mitchell, A. J. (2007). Understanding medication discontinuation in depression. *Psychiatric Times*, *24*(4).

\*Sylvia, L. G., Hay, A., Ostacher, M. J., Miklowitz, D. J., Nierenberg, A. A., Thase, M. E., . . . Perlis, R. H. (2013). Association between therapeutic alliance, care satisfaction, and pharmacological adherence in bipolar disorder. *Journal of Clinical Psychopharmacology, 33*(3), 343-350. doi: 10.1097/JCP.0b013e3182900c6f

**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

**\*\*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.**

2020 submission: Not applicable

2016 submission: Not applicable

**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)**

☒ 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

2020 submission:

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| **Source of Systematic Review:**   * **Title** * **Author** * **Date** * **Citation, including page number** * **URL** | * Practice guideline for the treatment of patients with schizophrenia: 3rd edition * American Psychiatric Association (APA) * 2019   American Psychiatric Association. (2019). Practice guideline for the treatment of patients with schizophrenia: 3rd ed. Retrieved from  <https://www.psychiatry.org/psychiatrists/practice/clinical-practice-guidelines>    Please note, the American Psychiatric Association (APA) and the U.S. Departments of Vetarns Affairs and Defence (VA/DOD) have not updated their guidelines for bipolar disorder or major depressive disorder since the initial endorsement submission in 2016. The content from these guidelines remains relevant for this measure. |
| 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. | “APA recommends (1A) that patients with schizophrenia be treated with an antipsychotic medication and monitored for effectiveness and side effects. APA recommends (grade: 1A) that patients with schizophrenia whose symptoms have improved with an antipsychotic medication continue to be treated with an antipsychotic medication. \*This guideline statement should be implemented in the context of a person-centered treatment plan that includes evidence-based nonpharmacological and pharmacological treatments for schizophrenia.” p.5 |
| Grade assigned to the **evidence** associated with the recommendation with the definition of the grade | 2019 APA practice guideline for the treatment of schizophrenia evidence grade: A (high). |
| Provide all other grades and definitions from the evidence grading system | All other evidence grades from the 2019 APA schizophrenia guideline: B (moderate), C (low). |
| Grade assigned to the **recommendation** with definition of the grade | **Schizophrenia**  The guideline from the APA (2019) to treat patients with schizophrenia with an antipsychotic medication and to continue to treat such patients whose symptoms have improved with an antipsychotic were graded I: confidence that the benefits of the intervention clearly outweigh harms. |
| Provide all other grades and definitions from the recommendation grading system | All other recommendation grades from the 2019 APA schizophrenia guideline: II, suggestion (although the benefits of the statement are still viewed as outweighing the harms, the balance of benefits and harms is more difficult to judge, or the benefits or the harms might be less clear). |
| Body of evidence:   * Quantity – how many studies? * Quality – what type of studies? | The 2019 APA schizophrenia guideline was developed in accordance with the Institute of Medicine (now known as the National Academy of Medicine) report “Clinical Practice Guidelines We Can Trust” (Institute of Medicine, 2011) and the “Principles for the Development of Specialty Society Clinical Guidelines” of the Council of Medical Specialty Societies (Institute of Medicine, 2012). The APA solicited input from subject matter experts and patient and family advocates. The guideline includes about 1,000 references. The APA identified evidence through literature searches and systematic review, and research and clinical experts provided input on topics for which there was not high quality evidence. |
| Estimates of benefit and consistency across studies | The APA found consistent benefits of evidence-based medication administration for those diagnosed with schizophrenia in terms of improved health outcomes and improved quality of life and functioning. It also found the benefits far outweighed the potential harms, which the APA notes can be mitigated.  “Use of an antipsychotic medication in the treatment of schizophrenia can improve positive and negative symptoms of psychosis (high strength of research evidence) and can also lead to reductions in depression and improvements in quality of life and functioning (moderate strength of research evidence). A meta-analysis of double-blind, randomized, placebo-controlled trials showed a medium effect size for overall efficacy (Leucht et al. 2017), with the greatest effect on positive symptoms. The rates of achieving any response or a good response were also significantly greater in patients who received an antipsychotic medication. In addition, the proportion of individuals who dropped out of treatment for any reason and for lack of efficacy was significantly less in those who were treated with an antipsychotic medication. Research evidence from head-to-head comparison studies and network meta-analysis (McDonagh et al. 2017) showed no consistent evidence that favored a specific antipsychotic medication, with the possible exception of clozapine.” p. 80  “The potential benefits of this guideline statement were viewed as far outweighing the potential harms. Although harms of antipsychotic medications can be significant, the impact of schizophrenia on patients’ lives is also substantial, and consistent benefits of antipsychotic treatment were found. Harms of treatment can be mitigated by selecting medications on the basis of individual characteristics and preferences of patients as well as by choosing a medication on the basis of its side-effect profile, pharmacological characteristics, and other factors. For clozapine, the additional benefits of treatment were viewed as outweighing the additional rare but serious harms and the need for ANC [absolute neutrophil count] monitoring to reduce the likelihood of severe neutropenia.” p. 81  Leucht, S., Leucht, C., Huhn, M., et al. (2017). Sixty years of placebo-controlled antipsychotic drug trials in acute schizophrenia: systematic review, Bayesian meta-analysis, and meta-regression of efficacy predictors. *Am J Psychiatry 174*(10):927–942.  McDonagh, M. S., Dana, T., Selph, S., et al. (2017). Treatments for adults with schizophrenia: a systematic review [Comparative Effectiveness Review No 198, AHRQ Publ No 17(18)-EHC031-EF]. Rockville, MD: Agency for Healthcare Research and Quality. Available at https://effectivehealthcare.ahrq.gov/ topics/schizophrenia-adult/research-2017. Accessed September 18, 2020. |
| What harms were identified? | From the 2019 APA schizophrenia guideline: “The harms of using an antipsychotic medication in the treatment of schizophrenia include sedation, side effects mediated through dopamine receptor blockade …, disturbances in sexual function, anticholinergic effects, weight gain, glucose abnormalities, hyperlipidemia, orthostatic hypotension, tachycardia, and QTc prolongation. Clozapine has additional harms associated with its use, including sialorrhea, seizures, neutropenia (which can be severe and life-threatening), myocarditis, and cardiomyopathy. Among the antipsychotic medications, there is variability in the rates at which each of these effects occurs, and no specific medication appears to be devoid of possible side effects.” p. 81 |
| Identify any new studies conducted since the SR. Do the new studies change the conclusions from the SR? | None. |

2016 submission:

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| **Source of Systematic Review:**   * **Title** * **Author** * **Date** * **Citation, including page number** * **URL** | American Psychiatric Association. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. Retrieved from <http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/bipolar.pdf>  American Psychiatric Association. (2010a). Practice guideline for the treatment of patients with major depressive disorder, 3rd ed. Retrieved from <http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf>  American Psychiatric Association. (2010b). Practice guideline for the treatment of patients with schizophrenia: 2nd ed. Retrieved from <http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia.pdf>  US Department of Veterans Affairs, & US Department of Defense. (2016). Management of major depressive disorder (MDD). Retrieved from <http://www.healthquality.va.gov/guidelines/MH/mdd/VADoDMDDCPGFINAL82916.pdf>  US Department of Veterans Affairs & US Department of Defense. (2010) VA/DOD clinical practice guideline for management of bipolar disorder in adults. Retrieved from <http://www.healthquality.va.gov/guidelines/MH/bd/bd_305_full.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. | **Bipolar Disorder**  APA 2002 Guidelines  *Acute Phase*  “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 [I]. For less ill patients, monotherapy with lithium, valproate, or an antipsychotic such as olanzapine may be sufficient [I]. Short-term adjunctive treatment with a benzodiazepine may also be helpful [II]. For mixed episodes, valproate may be preferred over lithium [II]. Atypical antipsychotics are preferred over typical antipsychotics because of their more benign side effect profile [I], with most of the evidence supporting the use of olanzapine or risperidone [II]. Alternatives include carbamazepine or oxcarbazepine in lieu of lithium or valproate [II]. Antidepressants should be tapered and discontinued if possible [I]. If psychosocial therapy approaches are used, they should be combined with pharmacotherapy [I].” p.9  “Manic or mixed episodes with psychotic features usually require treatment with an antipsychotic medication [II].” p.10  *Maintenance Treatment*  “Maintenance regimens of medication are recommended following a manic episode [I]. Although few studies involving patients with bipolar II disorder have been conducted, consideration of maintenance treatment for this form of the illness is also strongly warranted [II]. The medications with the best empirical evidence to support their use in maintenance treatment include lithium [I] and valproate [I]; possible alternatives include lamotrigine [II] or carbamazepine or oxcarbazepine [II]. If one of these medications was used to achieve remission from the most recent depressive or manic episode, it generally should be continued [I].” p.11  VA/DOD 2010 Guidelines  “Patients with severe mania should be treated with a combination of antipsychotics and lithium or valproate. These antipsychotics include olanzapine, quetiapine, aripiprazole, or risperidone [B] and may include and ziprasidone [I].” p.8  “Patients with severe mixed episode should be treated with a combination of antipsychotics and lithium or valproate. These antipsychotics include aripiprazole, olanzapine, risperidone, or haloperidol [B] and may include quetiapine or ziprasidone [I].” p.9  “Clozapine, with its more serious side effect profile, may be added to existing medications for severe mania or mixed episode if it has been successful in the past or if other antipsychotics have failed [I].” p.9  “Quetiapine, [A], lamotrigine [B], or lithium [B] monotherapy should be considered as first-line treatment for adult patients with BD depression.” p.26  *Maintenance Phase*  “Patients who have had an acute manic episode should be treated for at least 6 months after the initial episode is controlled and encouraged to continue on life-long prophylactic treatment with medication. [A]” p.35  **Major Depressive Disorder**  APA 2010a Guidelines  *Acute Phase*  “An antidepressant medication is recommended as an initial treatment choice for patients with mild to moderate major depressive disorder [I] and definitely should be provided for those with severe major depressive disorder unless ECT is planned [I].” p.17  “For most patients, a selective serotonin reuptake inhibitor (SSRI), serotonin norepinephrine reuptake inhibitor (SNRI), mirtazapine, or bupropion is optimal [I].” p.17  *Maintenance Treatment*  “To reduce the risk of relapse, patients who have been treated successfully with antidepressant medications in the acute phase should continue treatment with these agents for 4–9 months [I].” p.19  VA/DOD 2016 Guidelines  “In patients with MDD who achieve remission with antidepressant medication, treatment should be continued at the same dose for at least 6 months to decrease the risk of relapse. [A]” p.106  **Schizophrenia**  APA 2010b Guidelines  *Acute Phase Treatment*  “It is recommended that pharmacological treatment be initiated promptly, provided it will not interfere with diagnostic assessment, because acute psychotic exacerbations are associated with emotional distress, disruption to the patient’s life, and a substantial risk of dangerous behaviors to self, others, or property [I]…The selection of an antipsychotic medication is frequently guided by the patient’s previous experience with antipsychotics, including the degree of symptom response, past experience of side effects, and preferred route of medication administration. In choosing among these medications, the psychiatrist may consider the patient’s past responses to treatment, the medication’s side effect profile (including subjective responses, such as a dysphoric response to a medication), the patient’s preferences for a particular medication based on past experience, the intended route of administration, the presence of co-morbid medical conditions, and potential interactions with other prescribed medications [I]. Finally, while most patients prefer oral medication, patients with recurrent relapses related to nonadherence are candidates for a long-acting injectable antipsychotic medication, as are patients who prefer this mode of administration [II].” p.11  *Stabilization Phase*  “If the patient has improved with a particular medication regimen, continuation of that regimen and monitoring are recommended for at least 6 months [I]. Premature lowering of dose or discontinuation of medication during this phase may lead to a recurrence of symptoms and possible relapse.” p.12 |
| Grade assigned to the **evidence** associated with the recommendation with the definition of the grade | The guideline authors did not grade the evidence or separate the grade for the evidence from the grade from the recommendation. |
| Provide all other grades and definitions from the evidence grading system | Not applicable |
| Grade assigned to the **recommendation** with definition of the grade | **Bipolar Disorder**  Guidelines from the APA (2002) on the various treatment approaches related to initiating and continuing the medications in the numerator of this measure following an acute episode of bipolar disorder were graded as either I (recommended with substantial clinical confidence) or II (recommended with moderate clinical confidence). The recommendations for pharmacotherapy in the acute phase and maintenance regimens of medication after a manic episode were both graded as I.  Guidelines from the VA/DoD (2010) on the various treatment approaches following an acute episode of bipolar disorder were graded as:  B: At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm. I: Evidence that the intervention is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.  Guidelines from the VA/DoD (2010) on the continuation of medications in the numerator of this measure were graded as:  A: Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.  **Major Depressive Disorder**  Guidelines from the American Psychiatric Association (APA; 2010a) to initiate and continue the medications in the numerator of this measure following an acute episode of MDD were graded as:  I: Recommended with substantial clinical confidence  Guidelines from the Department of Veterans Affairs/Department of Defense (VA/DoD; 2016) to continue the medications in the numerator of this measure for at least six months following an acute episode of MDD were graded as:  A: Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.  **Schizophrenia**  Guidelines from the APA (2010b) to initiate and continue the medications in the numerator of this measure following an acute episode of schizophrenia were graded as:  I: Recommended with substantial clinical confidence  The guideline from the APA (2010b) to use long-acting injectables for patients hospitalized for schizophrenia was graded as follows:  II: Recommended with moderate clinical confidence |
| Provide all other grades and definitions from the recommendation grading system | APA grade I: Recommended with substantial clinical confidence APA grade II: Recommended with moderate clinical confidence APA grade III: May be recommended on the basis of individual circumstances  VA/DoD grade A: Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.  VA/DoD grade B: At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm.  VA/DoD grade I: Evidence that the intervention is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined. |
| Body of evidence:   * Quantity – how many studies? * Quality – what type of studies? | The guidelines are evidence-based rather than expert opinion. Information regarding the quantity, quality, and consistency of the information on the treatment of MDD, bipolar disorder, and schizophrenia is based on extensive literature searches reviewed by expert workgroups and panels, which included practicing clinicians and research experts.  The current APA clinical guidelines for the treatment of bipolar disorder were built upon a literature search of articles from 1992 to 2001. A total of 472 citations are included in the current guideline (APA, 2002). The VA/DoD clinical guidelines relied heavily on the APA guidelines and include 276 citations (VA/DoD, 2010).  For the treatment of MDD, the current APA guidelines were built upon literature reviews from pervious guidelines with the objective of emphasizing newer treatments. The literature search was conducted on studies published from January 1999 to December 2006. A total of 1,170 citations are reported in the current guideline (APA, 2010a). In a similar manner, the VA/DoD searched literature published from July 2000 to the end of 2006. A total of 253 citations are included in the current guideline (VA/DoD, 2010).  The APA clinical guidelines for the treatment of schizophrenia were developed from a literature search conducted for the years 1994 to 2002. A total of 1,391 citations were included in the current guideline (APA, 2010b). |
| Estimates of benefit and consistency across studies | **Bipolar Disorder**  Overall, the literature cited by the guidelines consistently found that pharmacotherapy is effective for the treatment of bipolar disorder. Many studies have demonstrated the efficacy of mood stabilizers (including lithium, anticonvulsants, and typical and atypical antipsychotics) as a treatment for reducing the depressive symptoms and manic episodes associated with bipolar disorder. Five studies found lithium to be a superior treatment for bipolar disorder compared to placebo (Bowden, et al., 1994; Goodwin, Murphy, & Bunney, 1969; Schou, Juel-Nielson, Stroomgreen, & Voldky, 1954; Maggs, 1963; Strokes, Shamoian, Stoll, & Patton, 1971). It should be noted the interpretation of these results is limited due to the use of a cross-over design in four of the trials (Goodwin et al., 1969; Schou et al., 1954; Maggs, 1963; Strokes et al., 1971), non-random assignment (Goodwin et al., 1969; Strokes et al., 1971), and variability in diagnostic criteria.  In trials comparing lithium to other active pharmacological agents, lithium displayed similar efficacy to carbamazepine (Lerer, Moore, Meyendorff, Cho, & Gershon, 1987; Small et al., 1991), risperidone (Segal, Berk, & Brook, 1998), olanzapine (Berk, Ichim, & Brook, 1999), chlorpromazine, and other typical antipsychotics (Johnson, Gershon, Burdock, Floyd, & Hekimian, 1971; Platman, 1970; Prien, Caffey, & Klett, 1972; Shopsin, Gershon, Thompson, & Collins, 1975; Spring, Schweid, Gray, Steinberg, & Horwitz, 1970; Takahashi, Sakuma, Itoh, K., Itoh, H., & Kurihara, 1975 ). Open studies (Himmelhoch & Garfinkel, 1986; Kramlinger & Post, 1989; Prien, Himmelhoch, & Kuper, 1988) and randomized active comparator-controlled studies (Bowden, 1995; Freeman, Clothier, Pazzaglia, Lesem, & Swann, 1992; Swann et al., 1997) demonstrate that lithium is an effective treatment for manic states but is less effective in the treatment of mixed states.  The efficacy of anticonvulsants (e.g., divalproex, valproate, valproic acid) compared to placebo has been demonstrated in four randomized controlled trials (Bowden, et al., 1994; Brennan, Sandyk, & Borsook, 1984; Emrich, Zerssen, Kissling, Miller, & Windorder, 1981; Pope, McElroy, Keck, & Hudson, 1991) with response rates ranging from 48% to 58%.  One randomized, placebo-controlled study has evaluated antipsychotics for the treatment of bipolar disorder. The results indicated that chlorpromazine was superior to placebo in the overall improvement of manic symptoms (Klein, 1967). Typical antipsychotics are comparable to lithium in effectiveness (Platman, 1970; Prien, et al., 1972; Shopsin, et al., 1975; Spring et al., 1970; Takahashi, 1975). Atypical antipsychotics (i.e., risperidone and ziprasidone) have been shown to be superior to placebo and similar to haloperidol in effectiveness (Sachs, 2001).  All of the pharmacotherapies evaluated in these studies are included in the numerator definition of this measure to allow for flexibility in prescribing an evidence-based treatment for bipolar disorder.  **Major Depressive Disorder**  Overall, the literature cited by the guidelines consistently found that pharmacotherapy is effective for the treatment of MDD. Several pharmacotherapies were reviewed through multiple meta-analyses (Anderson, 2000; Cipriani et al., 2005; Cipriani et al., 2009; Edwards & Anderson, 1999; Gartlehner, 2008), systematic reviews (Murdoch & Keam, 2005; Panzer, 2005), and numerous randomized trials that evaluated the efficacy and tolerability of pharmacological treatments for depression. Overall, the results of these studies indicate that SSRIs and SNRIs have relatively similar efficacies and tolerability. There is some evidence that tricyclic antidepressants (TCAs) may be more efficient for inpatient populations. SNRIs have been shown to be superior to placebo in multiple placebo-controlled studies (DeMartinis, Yeung, Entsuah, & Manley, 2007; Nemeroff, Entsuah, Benattia, Demitrack, Sloan, & Thase, 2008; Papakostas, Thase, Fava, Nelson, & Shelton, 2007; Papakostas, Homberger, & Fava, 2008; Septien-Velez, Pitrosky, Padmanabhan, Germain, & Tourian, 2007; Thase, Prtichette, Ossanna, Swindle, Xu, & Detke, 2007; Papakostas, Thase, Fava, Nelson, & Shelt, 2007). Several meta-analyses of controlled trials have documented small (4% – 10%) differences in treatment response for SNRIs compared to SSRIs (Cipriani, Barbui, Brambilla, Furukawa, Hotoph, & Geddes, 2006; Nemeroff et al., 2008; Papakostas et al., 2008; Smith, 2002; Thase, 2001; Thase et al., 2007).  Alternative depression medications have been efficacious in reducing depressive symptoms compared to placebo, including bupropion (Fava, Rush, Thase, Clayton, Stahl, Pradko, & Johnston, 2005) and mirtazapine (Claghorn & Lesem, 1995; Holm & Markham, 1999). Monoamine oxidase inhibitors (MAOIs) have similar efficacy to TCAs (Clayton, McGarvey, Abouesh, & Pinkerton, 2001; Himmelhock, Thase, Mallinger, & Houck, 1991; Masand, Ashton, Gupta, & Frank, 2001; McGrath, Stewart, Harrison, Wager, & Quitkin, 1986; White, Razani, Cadow, Gelfand, Palmer, Simpson, & Sloan, 1984), particularly for patients who have not responded to other antidepressant medication (Himmelhoch, Fuchs, & Symons, 1982; Himmelhoch et al., 1991; White et al., 1984). All of the classes of pharmacotherapies evaluated in these studies are included in the numerator definition of this measure to allow for flexibility in prescribing an evidence-based treatment for MDD.  **Schizophrenia**  Overall, the literature cited by the guidelines consistently found that pharmacotherapy is effective for the treatment of schizophrenia. According to the APA guidelines for the treatment of schizophrenia (APA, 2010b), evidence supporting the use of typical (i.e., first-generation) antipsychotics was first established in the 1960s (Laskey, Klett, Caffey, Bennett, Rosenblum, & Hollister, 1962) and repeatedly confirmed by subsequent clinical trials (Davis, Barter, & Kane, 1989). These studies compared the efficacy of one or more antipsychotic medications to that of a sedative or a placebo, and nearly all confirmed the antipsychotic medication to be a superior treatment (APA, 2010b). Research on typical antipsychotics has decreased substantially since the development of atypical (i.e., second-generation) antipsychotics.  There are a number of atypical antipsychotics that are effective in the treatment of schizophrenia. At the time of the development of the clinical guidelines, clozapine was considered a superior treatment compared to typical antipsychotics in six of eight published double-blind randomized trials (Buchanan, Brier, Kirkpatrick, Ball, & Carpenter, 1998; Essock, Hargreaves, Covell, & Goethe, 1996; Hong, Chen, Chiu, & Sim, 1997; Kane, Honigfeld, Singer, & Meltzer, 1988; Kane et al., 2001; Kumra et al., 1996; Rosenheck et al., 1997; Volavka et al., 2002). A subsequent meta-analysis of five of these studies confirmed that clozapine-treated patients were 2.5 times more likely to improve compared to those treated with a typical antipsychotic. Clinical trials that informed the clinical guidelines demonstrated other atypical antipsychotics to be superior to placebo and to typical antipsychotics, including risperdone (Borison, Pathiraja, Diamond & Meibach, 1992; Chouinard et al., 1993; Marder & Meibach, 1994) and olanzapine (Beasley, Sanger, Satterless, Tollefson, Tran, & Hamilton, 1996; Beasley et al., 1997; Hamilton, Revicki, Genduso, & Beasley, 1998; Lieberman et al., 2003; Tollefson et al., 1997). Quetiapine and aripiprazole were demonstrated to be superior to placebo and typical antipsychotics (Borison, Arvanitis, & Milier, 1996; Fabre, Arvanitis, Pultz, Jones, Malick & Slotnick, 1995; Marder et al., 2003; Small, Kirsch, Arvanitis, Miller, & Link, 1997), although their effectiveness at reducing negative symptoms of schizophrenia is variable (Borison et al., 1996; Fabre et al., 1995; Small et al., 1997; Marder et al., 2003). Meta-analyses of these studies suggest that the efficacy of quetiapine is similar to that of typical antipsychotics (Geddes, Freemantle, Harrison, & Bebbington, 2000; Leucht, Pitschel-Walz, Abraham, & Kissling, 1999; Leucht, Wahlbeck, Hamann, & Kissling, 2003). Studies of ziprasidone found that it is superior compared to placebo and typical antipsychotics (Daniel, Zimbroff, Potkin, Reeves, Harrigan, & Lakshminarayanan, 1999; Keck, Buffenstein, Ferguson, Feighner, Jaffe, Harrigan, & Morrissey, 1998), including significantly reducing the risk of relapse (Goff et al., 1998). All of the pharmacotherapies evaluated in these studies are included in the numerator definition of this measure to allow for flexibility in prescribing an evidence-based treatment for schizophrenia.  \*American Psychiatric Association. (2002). Practice guideline for the treatment of patients with bipolar disorder, second edition. Retrieved from <http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/bipolar.pdf>  \*American Psychiatric Association. (2010a). Practice guideline for the treatment of patients with major depressive disorder, 3rd ed. Retrieved from <http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf>  \*American Psychiatric Association. (2010b). Practice guideline for the treatment of patients with schizophrenia: 2nd ed. Retrieved from <http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia.pdf>  \*Anderson, I. M. (2000). Selective serotonin reuptake inhibitors versus tricyclic antidepressants: A meta-analysis of efficacy and tolerability. *Journal of Affective Disorders*, *58(*1), 19–36. doi:10.1016/s0165-0327(99)00092-0  \*Beasley, C. M., Sanger, T., Satterlee, W., Tollefson, G., Tran, P., & Hamilton, S. (1996). Olanzapine versus placebo: Results of a double-blind, fixed-dose olanzapine trial. *Psychopharmacology, 124*(1-2), 159-167. doi:10.1007/bf02245617  \*Beasley, C. M., Hamilton, S. H., Crawford, A. M., Dellva, M. A., Tollefson, G. D., Tran, P. V., … Beuzen, J.-N. (1997). Olanzapine versus haloperidol: Acute phase results of the international double-blind olanzapine trial. *European Neuropsychopharmacology, 7*(2), 125-137. doi:10.1016/s0924-977x(96)00392-6  \*Berk, M., Ichim, L., & Brook, S. (1999). Olanzapine compared to lithium in mania: A double-blind randomized controlled trial. *International Clinical Psychopharmacology, 14*(6), 339-343. doi:10.1097/00004850-199911000-00003  \*Bowden, C. L., Brugger, A. M., Swann, A. C., Calabrese, J. R., Janicak, P. G., Petty, F….Small, J. G. (1994). Efficacy of divalproex vs lithium and placebo in the treatment of mania: The Depakote Mania Study Group. *JAMA: The Journal of the American Medical Association, 271*(12), 918-924. doi:10.1001/jama.271.12.918  \*Bowden, C. L. (1995). Predictors of response to divalproex and lithium. *Journal of Clinical Psychiatry, 56*(3), 25-30.  \*Borison, R. L., Pathiraja, A. P., Diamond, B. I., & Meibach, R. C. (1992). Risperidone: Clinical safety and efficacy in schizophrenia. *Psychopharmacological Bulletin, 28*, 213-218.  \*Borison, R. L., Arvanitis, L. A., & Milier, B. G. (1996). ICI 204,636, an atypical antipsychotic. *Journal of Clinical Psychopharmacology, 16*(2), 158-169. doi:10.1097/00004714-199604000-00008  \*Bowden, C. L., Brugger, A. M., Swann, A. C., Calabrese, J. R., Janicak, P. G., Petty, F., Dilsaver, S. C….Small, J. G. (1994). Efficacy of divalproex vs lithium and placebo in the treatment of mania. The Depakote Mania Study Group. *JAMA: The Journal of the American Medical Association, 271*(12), 918-924. doi:10.1001/jama.271.12.918  \*Brennan, M. J. W., Sandyk, R., & Borsook, D. (1984). Use of sodium valproate in the management of affective disorders: Basic and clinical aspects. In Emrich, H. M., Okuma, T., & Muller, A. A. (Eds.), *Anticonvulsants in Affective Disorders* (pp. 56-65). Amsterdam: Excerpta Medica.  \*Buchanan, R. W., Breier, A., Kirkpatrick, B., Ball, P., & Carpenter Jr., W. T. (1998). Positive and negative symptom response to clozapine in schizophrenic patients with and without the deficit syndrome. *American Journal of Psychiatry, 155*, 751-760.  \*Cipriani, A., Brambilla, P., Furukawa, T. A., Geddes, J., Gregis, M., Hotopf, M., … Barbui, C. (2005). Fluoxetine versus other types of pharmacotherapy for depression. *Reviews.* doi:10.1002/14651858.cd004185.pub2  \*Cipriani, A., Barbui, C., Brambilla, P., Furukawa, T. A., Hotopf, M., & Geddes, J. R. (2006). Are all antidepressants really the same? The case of Fluoxetine. *The Journal of Clinical Psychiatry, 67*(06), 850–864. doi:10.4088/jcp.v67n0601  \*Cipriani, A., Furukawa, T. A., Salanti, G., Geddes, J. R., Higgins, J. P., Churchill, R., … Barbui, C. (2009). Comparative efficacy and acceptability of 12 new-generation antidepressants: A multiple-treatments meta-analysis. *The Lancet, 373*(9665), 746–758. doi:10.1016/s0140-6736(09)60046-5  \*Chouinard, G., Jones, B., Remington, G., Bloom, D., Addington, D., MacEwan, G. W., … Arnott, W. (1993). A Canadian multicenter placebo-controlled study of fixed doses of risperidone and haloperidol in the treatment of chronic schizophrenic patients. *Journal of Clinical Psychopharmacology, 13*(1), 25???40. doi:10.1097/00004714-199302000-00004  \*Claghorn, J. L., & Lesem, M. D. (1995). A double-blind placebo-controlled study of Org 3770 in depressed outpatients. *Journal of Affective Disorders, 34*(3), 165-171. doi:10.1016/0165-0327(95)00014-e  \*Clayton, A. H., McGarvey, E. L., Abouesh, A. I., & Pinkerton, R. C. (2001). Substitution of an SSRI with bupropion sustained release following SSRI-induced sexual dysfunction. *The Journal of Clinical Psychiatry, 62*(3), 185-190. doi:10.4088/jcp.v62n0309  \*Daniel, D. G., Zimbroff, D. L., Potkin, S. G., Reeves, K. R., Harrigan, E. P., Lakshminarayanan, M. (1999). Ziprasidone 80 mg/day and 160 mg/day in the acute exacerbation of schizophrenia and schizoaffective disorder: A 6-week placebo-controlled trial. *Neuropsychopharmacology, 20(*5), 491-505. doi:10.1016/s0893-133x(98)00090-6  \*Davis, J. M., Barter, J. T., Kane, J. M. (1989). Antipsychotic drugs. In H. I. Kaplan & B. J. Sadock (Eds.), *Comprehensive Textbook of Psychiatry, 5th ed* (pp. 1591-1626). Baltimore, MD. Williams & Wilkins.  \*DeMartinis, N. A., Yeung, P. P., Entsuah, R., & Manley, A. L. (2007). A double-blind, placebo-controlled study of the efficacy and safety of desvenlafaxine succinate in the treatment of major depressive disorder*. The Journal of Clinical Psychiatry, 68*(05), 677-688. doi:10.4088/jcp.v68n0504  \*Edwards, J. G., & Anderson, I. (1999). Systematic review and guide to selection of selective serotonin reuptake inhibitors. *Drugs, 57*(4), 507-533. doi:10.2165/00003495-199957040-00005  \*Emrich, H. M., Zerssen, D., Kissling, W., Miller, H.-J., & Windorfer, A. (1980). Effect of sodium valproate on mania. *Archive for Psychiatrie and Nervenkrankheiten, 229*(1), 1-16. doi:10.1007/bf00343800  \*Emrich, H. M., Zihl, J., Raptis, C., & Wendl, A. (1990). Reduced dark-adaptation: An indication of lithium’s neuronal action in humans. *American Journal of Psychiatry, 147*(5), 629-631. doi: 10.1176/ajp.147.5.629  \*Essock, S. M., Hargreaves, W. A. Covell, N. H., & Goethe, J. (1996). Clozapine’s effectiveness for patients in state hospitals: Results from a randomized trial. *Psychopharmacological Bulletin, 32*, 683-697.  \*Fabre, L. F., Arvanitis, L., Pultz, J., Jones, V. M., Malick, J. B., & Slotnick, V. B. (1995). ICI 204,636, a novel, atypical antipsychotic: Early indication of safety and efficacy in patients with chronic and subchronic schizophrenia. *Clinical Therapeutics, 17*(3), 366-378. doi:10.1016/0149-2918(95)80102-2  \*Fava, M., Rush, A. J., Thase, M. E., Clayton, A., Stahl, S. M., Pradko, J. F., & Johnston, J. A. (2005). 15 years of clinical experience with bupropion HCl. *The Primary Care Companion to The Journal of Clinical Psychiatry, 07*(03), 106-113. doi:10.4088/pcc.v07n0305  \*Freeman, T. W., Clothier, J. L., Pazzaglia, P., Lesem, M. D., & Swann, A. C. (1992). A double-blind comparison of valproate and lithium in the treatment of acute mania. *American Journal of Psychiatry, 149*(1), 108–111. doi:10.1176/ajp.149.1.108  \*Gartlehner, G. (2008). Comparative benefits and harms of second-generation antidepressants: Background paper for the American College of Physicians. *Ann Intern Med, 149*(10), 734. doi:10.7326/0003-4819-149-10-200811180-00008  \*Geddes, J., Freemantle, N., Harrison, P., & Bebbington, P. (2000). Atypical antipsychotics in the treatment of schizophrenia: Systematic overview and meta-regression analysis. *British Medical Journal*, *321*(7273), 1371-1376. doi:10.1136/bmj.321.7273.1371  \*Goff, D. C., Posever, T., Herz, L., Simmons, J., Kletti, N., Lapierre, K., … Ko, G. N. (1998). An exploratory haloperidol-controlled dose-finding study of ziprasidone in hospitalized patients with schizophrenia or schizoaffective disorder. *Journal of Clinical Psychopharmacology, 18*(4), 296-304. doi:10.1097/00004714-199808000-00009  \*Goodwin, F. K. (1969). Lithium-carbonate treatment in depression and mania. *Archives of General Psychiatry, 21*(4), 486. doi:10.1001/archpsyc.1969.01740220102012  \*Hamilton, S. H., Revicki, D. A., Genduso, L. A., Beasley, C. M. (1998). Olanzapine versus placebo and haloperidol: Quality of life and efficacy results of the North American Double-blind Trial. *Neuropsychopharmacology, 18*(1), 41-49. doi:10.1016/s0893-133x(97)00111-5  \*Himmelhoch, J. M., Fuchs, C. Z., & Symons, B. J. (1982). A double-blind study of tranylcypromine treatment of major anergic depression. *The Journal of Nervous and Mental Disease, 170*(10), 628-634. doi:10.1097/00005053-198210000-00007  \*Himmelhoch, J. M. & Garfinkel, M. E. (1986). Sources of lithium resistance in mixed mania. *Psychopharmacological Bulletin, 22*, 613-620.  \*Himmelhoch, J. M., Thase, M. E., Mallinger, A. G., & Houck, P. (1991). Tranylcypromine versus imipramine in anergic bipolar depression. *American Journal of Psychiatry, 148*(7), 910-916. doi:10.1176/ajp.148.7.910  \*Holm, K. J., & Markham, A. (1999). Mirtazapine. *Drugs, 57*(4), 607–631. doi:10.2165/00003495-199957040-00010  \*Hong, C. J., Chen, J. Y., Chiu, H. J., & Sim, C. B. (1997). A double-blind comparative study of clozapine versus chlorpromazine on Chinese patients with treatment-refractory schizophrenia. *International Clinical Psychopharmacology, 12*(3), 123-130. doi:10.1097/00004850-199705000-00001  \*Johnson, G., Gershon, S., Burdock, E. I., Floyd, A., & Hekimian, L. (1971). Comparative effects of lithium and chlorpromazine in the treatment of acute manic states. *The British Journal of Psychiatry, 119*(550), 267–276. doi:10.1192/bjp.119.550.267  \*Kane, J., Honigfeld, G., Singer, J., & Meltzer, H. (1988). Clozapine for the treatment-resistant schizophrenic. *Archives of General Psychiatry, 45*(9), 789. doi:10.1001/archpsyc.1988.01800330013001  \*Kane, J. M., Marder, S. R., Schooler, N. R., Wirshing, W. C., Umbricht, D., Baker, R. W., … Borenstein, M. (2001). Clozapine and haloperidol in moderately refractory schizophrenia. *Archives of General Psychiatry, 58*(10), 965. doi:10.1001/archpsyc.58.10.965  \*Keck Jr, P., Buffenstein, A., Ferguson, J., Feighner, J., Jaffe, W., Harrigan, E. P., & Morrissey, M. R. (1998). Ziprasidone 40 and 120 mg/day in the acute exacerbation of schizophrenia and schizoaffective disorder: A 4-week placebo-controlled trial. *Psychopharmacology, 140*(2), 173–184. doi:10.1007/s002130050755  \*Klein, D. F. (1967). Importance of psychiatric diagnosis in prediction of clinical drug effects. *Archives of General Psychiatry, 16*(1), 118. doi:10.1001/archpsyc.1967.01730190120016  \*Kramlinger, K. G., & Post, R. M. (1989). Adding lithium carbonate to carbamazepine: Antimanic efficacy in treatment-resistant mania. *Acta Psychiatrica Scandinavica, 79*(4), 378–385. doi:10.1111/j.1600-0447.1989.tb10273.x  \*Kumra, S., Frazier, J. A., Jacobsen, L. K., McKenna, K., Gordon, C. T., Lenane, M. C.,…Rapoport, J. L. (1996). Childhood-onset schizophrenia. *Archives of General Psychiatry, 53*(12), 1090. doi:10.1001/archpsyc.1996.01830120020005  \*Laskey, J. J., Klett, C. J., Caffey, E. M. Jr., Bennett, J. L., Rosenblum, M. P., and Hollister, L. E. (1962). Drug treatment of schizophrenic patients: A comprehensive evaluation of chlorpromazine, chlorprothixene, fluphenazine, reserpine, thioridazine, and triflupromazine. *Diseases of the Nervous System,* 23. 698-706.  \*Lerer, B., Moore, N., Meyendorff, E., Cho, S. R., & Gershon, S. (1987). Carbamazepine versus lithium in mania: A double-blind study. *Journal of Clinical Psychiatry, 48,* 89-93.  \*Leucht, S., Pitschel-Walz, G., Abraham, D., & Kissling, W. (1999). Efficacy and extrapyramidal side-effects of the new antipsychotics olanzapine, quetiapine, risperidone, and sertindole compared to conventional antipsychotics and placebo. A meta-analysis of randomized controlled trials. *Schizophrenia Research, 35*(1), 51-68. doi:10.1016/s0920-9964(98)00105-4  \*Leucht, S., Wahlbeck, K., Hamann, J., & Kissling, W. (2003). New generation antipsychotics versus low-potency conventional antipsychotics: A systematic review and meta-analysis. *The Lancet, 361*(9369), 1581–1589. doi:10.1016/s0140-6736(03)13306-5  \*Maggs, R. (1963). Treatment of manic illness with lithium carbonate. *The British Journal of Psychiatry, 109*(458), 56–65. doi:10.1192/bjp.109.458.56  \*Marder, S. R. & Meibach, R. C. (1994). Risperidone in the treatment of schizophrenia. *American Journal of Psychiatry, 151*, 825-835.  \*Marder, S. R., McQuade, R. D., Stock, E., Kaplita, S., Marcus, R., Safferman, A. Z., … Iwamoto, T. (2003). Aripiprazole in the treatment of schizophrenia: Safety and tolerability in short-term, placebo-controlled trials. *Schizophrenia Research, 61*(2-3), 123–136. doi:10.1016/s0920-9964(03)00050-1  \*Masand, P. S., Ashton, A. K., Gupta, S., & Frank, B. (2001). Sustained-release bupropion for selective serotonin reuptake inhibitor-induced sexual dysfunction: A randomized, double-blind, placebo-controlled, parallel-group study. *American Journal of Psychiatry, 158*(5), 805–807. doi:10.1176/appi.ajp.158.5.805  \*McGrath, P. J., Stewart, J. W., Harrison, W., Wager, S., & Quitkin, F. M. (1986). Phenelzine treatment of melancholia. *Journal of Clinical Psychiatry, 47*, 420-422.  \*Muller, A. A. & Stoll, K. D. (1984). Anticonvulsants in affective disorders. In Emrich, H. M., Okuma, T., & Muller, A. A. (Eds.) *Carbamazepine and Oxcarbazepine in the treatment of manic syndromes: Studies in Germany* (pp. 134-147). Amsterdam, The Netherlands: Exerpta Medica.  \*Murdoch, D. & Keam, S. J. (2005). Escitalopram: A review of its use in the management of major depressive disorder. *Drugs, 65*,2379-2404. doi: [10.2165/00003495-200565160-00013](http://dx.doi.org/10.2165/00003495-200565160-00013)  \*Nemeroff, C. B., Entsuah, R., Benattia, I., Demitrack, M., Sloan, D. M., & Thase, M. E. (2008). Comprehensive analysis of remission (COMPARE) with Venlafaxine versus SSRIs. *Biological Psychiatry, 63*(4), 424-434. doi:10.1016/j.biopsych.2007.06.027  \*Panzer, M. J. (2005). Are SSRIs really more effective for anxious depression? *Annals of Clinical Psychiatry, 17*(1), 23-29. doi:10.1080/10401230590905317  \*Papakostas, G. I., Thase, M. E., Fava, M., Nelson, J. C., & Shelton, R. C. (2007). Are antidepressant drugs that combine serotonergic and noradrenergic mechanisms of action more effective than the selective serotonin reuptake inhibitors in treating major depressive disorder? A meta-analysis of studies of newer agents. *Biological Psychiatry, 62*(11), 1217-1227. doi:10.1016/j.biopsych.2007.03.027  \*Papakostas, G., Homberger, C., & Fava, M. (2008). A meta-analysis of clinical trials comparing mirtazapine with selective serotonin reuptake inhibitors for the treatment of major depressive disorder. *Journal of Psychopharmacology, 22*(8), 843–848. doi:10.1177/0269881107083808  \*Platman, S. R. (1970). A comparison of lithium carbonate and chlorpromazine in mania. *American Journal of Psychiatry, 127*(3), 351–353. doi:10.1176/ajp.127.3.351  \*Pope, Jr., H. G., McElroy, S. L., Keck, Jr., P. E., & Hudson, J. I. (1991). Valproate in the treatment of acute mania: A placebo-controlled study. *Archives of General Psychiatry, 48*, 62-68.  \*Prien, R. F., Caffey Jr., E. M., Klett, C. J. (1972). Comparison of lithium carbonate and chlorpromazine in the treatment of mania: Report of the Veterans Administration and National Institute of Mental Health Collaborative Study Group. *Archives of General Psychiatry, 26*(2), 146. doi:10.1001/archpsyc.1972.01750200050011  \*Prien, R. F., Himmelhoch, J. M., & Kupfer, D. J. (1988). Treatment of mixed mania. *Journal of Affective Disorders, 15*(1), 9–15. doi:10.1016/0165-0327(88)90003-1  \*Rosenheck, R., Cramer, J., Xu, W., Thomas, J., Henderson, W., Frisman, L., … Charney, D. (1997). A comparison of clozapine and haloperidol in hospitalized patients with refractory schizophrenia. *New England Journal of Medicine, 337*(12), 809–815. doi:10.1056/nejm199709183371202  \*Sachs, G. S. (2001). Emerging data: Atypical antipsychotics in bipolar disorder.In *Program and Abstracts of the 52nd Institute on Psychiatric Services*. Washington, D. C.: American Psychiatric Association.  \*Schou, M., Juel-Nielsen, N., Stromgren, E., & Voldby, H. (1954). The treatment of manic psychoses by the administration of lithium salts*. Journal of Neurology, Neurosurgery & Psychiatry, 17*(4), 250–260. doi:10.1136/jnnp.17.4.250  \*Shopsin, B., Gershon S., Thompson, H., & Collins, P. (1975). Psychoactive drugs in mania. *Archives of General Psychiatry, 32*(1), 34. doi:10.1001/archpsyc.1975.01760190036004  \*Segal, J., Berk, M., & Brook, S. (1998). Risperidone compared with both lithium and haloperidol in mania: A double-blind randomized controlled trial. *Clinical Neuropharmacology, 21*, 176-180.  \*Septien-Velez, L., Pitrosky, B., Padmanabhan, S. K., Germain, J.-M., & Tourian, K. A. (2007). A randomized, double-blind, placebo-controlled trial of desvenlafaxine succinate in the treatment of major depressive disorder. *International Clinical Psychopharmacology, 22*(6), 338–347. doi:10.1097/yic.0b013e3281e2c84b  \*Small, J. G. (1991). Carbamazepine compared with lithium in the treatment of mania. *Archives of General Psychiatry, 48*(10), 915. doi:10.1001/archpsyc.1991.01810340047006  \*Small, J. G., Hirsch, S. R., Arvanitis, L. A., Miller, B. G., & Link, C. G. (1997). Quetiapine in patients with schizophrenia. *Archives of General Psychiatry, 54*(6), 549. doi:10.1001/archpsyc.1997.01830180067009  \*Smith, D. (2002). Efficacy and tolerability of venlafaxine compared with selective serotonin reuptake inhibitors and other antidepressants: A meta-analysis. *The British Journal of Psychiatry, 180*(5), 396–404. doi:10.1192/bjp.180.5.396  \*Spring, G., Schweid, D., Gray, C., Steinberg, J., & Horwitz, M. (1970). A double-blind comparison of lithium and chlorpromazine in the treatment of manic states. *American Journal of Psychiatry, 126*(9), 1306–1310. doi:10.1176/ajp.126.9.1306  \*Stokes, P., Shamoian, C., Stoll, P., & Patton, M. (1971). Efficacy of lithium as acute treatment of manic-depressive illness. *The Lancet, 297*(7713), 1319–1325. doi:10.1016/s0140-6736(71)91886-1  \*Swann, A. C., Bowden, C. L., Morris, D., Calabrese, J. R., Petty, F.,…Davis, J. M. (1997). Depression during mania: Treatment response to lithium or divalproex. *Archives of General Psychiatry, 54*(1), 37. doi:10.1001/archpsyc.1997.01830130041008  \*Takahashi, R. (1975). Comparison of efficacy of lithium carbonate and chlorpromazine in mania. *Archives of General Psychiatry, 32*(10), 1310. doi:10.1001/archpsyc.1975.01760280108010  \*Thase, M. E., Pritchett, Y. L., Ossanna, M. J., Swindle, R. W., Xu, J., & Detke, M. J. (2007). Efficacy of Duloxetine and selective serotonin reuptake inhibitors. *Journal of Clinical Psychopharmacology, 27*(6), 672–676. doi:10.1097/jcp.0b013e31815a4412  \*Thase, M. E. (2001). Remission rates during treatment with venlafaxine or selective serotonin reuptake inhibitors. *The British Journal of Psychiatry, 178*(3), 234–241. doi:10.1192/bjp.178.3.234  \*Tollefson, G. D., Beasley Jr., C. M., Tran, P. V., Street, J. S., Krueger, J. A., Tamura, R. N.,… Thieme, M. E. (1997). Olanzapine versus haloperidol in the treatment of schizophrenia and schizoaffective and schizophreniform disorders: Results of an international collaborative trial. *American Journal of Psychiatry*, *154*(4), 457–465. doi:10.1176/ajp.154.4.457  \*Volavka, J., Czobor, P., Sheitman, B., Lindenmayer, J.-P., Citrome, L., McEvoy, J. P., … Lieberman, J. A. (2002). Clozapine, olanzapine, risperidone, and haloperidol in the treatment of patients with chronic schizophrenia and schizoaffective disorder. *American Journal of Psychiatry, 159*(2), 255–262. doi:10.1176/appi.ajp.159.2.255  \*White, K., Razani, J., Cadow, B., Gelfand, R., Palmer, R., Simpson, G., & Sloane, R. B. (1984). Tranylcypromine vs nortriptyline vs placebo in depressed outpatients: A controlled trial. *Psychopharmacology, 82*(3), 258–262. doi:10.1007/bf00427786  \*US Department of Veterans Affairs, & US Department of Defense. (2009). management of major depressive disorder (MDD). Retrieved from <http://www.healthquality.va.gov/mdd/mdd_full09_c.pdf> |
| What harms were identified? | Medications associated with the treatment of MDD, schizophrenia, and bipolar disorder have been shown to reduce negative symptoms, and the clinical guidelines indicate that the benefits outweigh harms for patients with severe mental illness. However, many of the medications require careful monitoring to avoid harmful side effects. Clinicians prescribing medications for the treatment of these disorders must consider the specific medication and the side effects that might occur. These considerations may vary given a patient's clinical and personal characteristics, as well as the expected improvement in the patient's outcomes.  The implementation of this measure will provide the important benefit of quality improvement by helping to identify patients who do not continue their pharmacotherapy post-discharge. Improved medication continuation would help reduce the risk of symptom relapse, prevent future depressive/manic/psychotic episodes, decrease re-hospitalization and suicide rates, and improve the quality of care for individuals with major depressive disorder, schizophrenia, and bipolar disorder. |
| Identify any new studies conducted since the SR. Do the new studies change the conclusions from the SR? | Since the development of the clinical guidelines for schizophrenia, the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Project compared the longer-term effects and usefulness of typical (perphenazine, fluphenazine decanoate) and atypical (olanzapine, quetiapine, risperidone, ziprasidone, clozapine) antipsychotics. A study based on data from that project found that perphenazine, a typical antipsychotic, was equally as effective as the atypical antipsychotics quetiapine, risperidone, and ziprasidone (Lieberman, et al., 2010). This finding further supports the inclusion of both types of antipsychotics in the numerator definition for schizophrenia in this measure.  \*Lieberman, J. A., Tollefson, G., Tohen, M., Green, A. I., Gur, R. E., Kahn, R., … Hamer, R. M. (2003). Comparative efficacy and safety of atypical and conventional antipsychotic drugs in first-episode psychosis: A randomized, double-blind trial of olanzapine versus haloperidol. *American Journal of Psychiatry*, *160*(8), 1396–1404. doi:10.1176/appi.ajp.160.8.1396 |

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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.

2020 submission: Not applicable

2016 submission: Not applicable

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

2020 submission: Not applicable

2016 submission: Not applicable

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

2020 submission: Not applicable

2016 submission: Not applicable