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

**Measure Number** (*if previously endorsed*)**:** 0560

**Measure Title**: Patients discharged on multiple antipsychotic medications with appropriate justification

**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**: 12/20/2018

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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.

The focus of the measure is to evaluate all psychiatric inpatients who are discharged on two or more antipsychotic medications to determine if appropriate justification exists for this practice. A reduction in antipsychotic polypharmacy without an appropriate justification will reduce the likelihood of developing serious side effects, thus reducing the overall cost of ongoing health care.

**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.**

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

Updated literature search did not yield any new guidelines or significant research related to antipsychotic medications that would warrant a change in the measure. An updated guideline for the Treatment of Patients with Schizophrenia is currently under development by the American Psychiatric Association.

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| **Source of Systematic Review:**   * **Title** * **Author** * **Date** * **Citation, including page number** * **URL** | **Title:** Practice Guideline for the Treatment of Patients with Schizophrenia Second Edition  **Author**: American Psychiatric Association Work Group on Schizophrenia  **Date:** February 2004  **Citation, including page number:** American Psychiatric Association (APA). Practice guideline for the treatment of patients with schizophrenia. 2nd ed. Washington (DC): American Psychiatric Association (APA); 2004 Feb. 114 p. [1391 references]  **URL:** <https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia.pdf>  **Rationale for Using this Guideline Over Others:** APA began developing practice guidelines in 1991. The development process is detailed in a document available from the APA Department of Quality Improvement and Psychiatric Services, the "APA Guideline Development Process." Key features of this process include the following:  • A comprehensive literature review  • Development of evidence tables  • Initial drafting of the guideline by a work group that included psychiatrists with clinical and research expertise in psychiatric evaluation  • Production of multiple revised drafts with widespread review  • Approval by the APA Assembly and Board of Trustees  • Planned revisions at regular intervals  This guideline represents a synthesis of current scientific knowledge and rational clinical practice on the psychiatric evaluation of adults. It strives to be as free as possible of bias toward any theoretical approach. |
| 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. | In assessing treatment resistance or partial response, it is important to carefully evaluate whether the patient has had an adequate trial of an antipsychotic medication, including whether the dose is adequate and whether the patient has been taking the medication as prescribed. An initial trial of 4–6 weeks generally is needed to determine if the patient will have any symptomatic response, and symptoms can continue to improve over 6 months or even longer periods of antipsychotic treatment [II]. Given clozapine’s superior efficacy, a clozapine trial should be considered for a patient who has had no response or partial and suboptimal response to two trials of antipsychotic medication (including at least one second-generation agent) or for a patient with persistent suicidal ideation or behavior that has not responded to other treatments [I]. |
| Grade assigned to the **evidence** associated with the recommendation with the definition of the grade | **Grading of Strength/Quality of the Body of Evidence.** Has the body of evidence been graded?  No  **System Used for Grading the Body of Evidence:** Other  **If other, identify and describe the grading scale with definitions:** Although grading of the evidence was not determined during the systematic review, it was determined that the guideline developers accounted for a balanced representation of information, looked beyond one specialty group or discipline, and provided information that was accessible and met the requirements set out in the NQF criteria. |
| Provide all other grades and definitions from the evidence grading system | Not applicable |
| Grade assigned to the **recommendation** with definition of the grade | **If guideline recommendation graded, identify the entity that graded the evidence including balance of representation and any disclosures regarding bias:** American Psychiatric Association  **Grade Assigned to the Recommendation:** I to II  For definition, see below |
| Provide all other grades and definitions from the recommendation grading system | **System Used for Grading the Strength of Guideline Recommendation:** Other  **If other, identify and describe the grading scale with definitions:**  The system for grading the strength of the guidelines recommendations is as follows:  • [I] Recommended with substantial clinical confidence.  • [II] Recommended with moderate clinical confidence.  • [III] May be recommended on the basis of individual circumstances. |
| Body of evidence:   * Quantity – how many studies? * Quality – what type of studies? | **Directness of Evidence to the Specified Measure** This measure is consistent with the guidelines recommended by the American Psychiatric Association (APA) when assessing treatment resistance or partial response in patients prescribed antipsychotic medications. It is important to carefully evaluate whether the patient has had an adequate trial of antipsychotic medications, including an adequate dose and length of time for the trial. The focus of both the performance measure and the body of evidence supports the need for monitoring antipsychotic prescribing practice, and whether there is an appropriate justification for prescribing more than one antipsychotic medication.  **Quantity:**  During a meta-analysis of studies conducted from 1966 through December 2007 the following were identified:  • Six RCTs comparing antipsychotic polypharmacy to monotherapy in samples with established treatment resistance to trials of a single antipsychotic were identified.  • Three RCTs that compared antipsychotic polypharmacy to monotherapy in samples without established treatment resistance to a single antipsychotic were identified.  • Nine noncontrolled observational trials comparing antipsychotic polypharmacy to monotherapy in samples with established treatment resistance to trials of a single antipsychotic were identified.  • Six nonrandomized controlled trials that compared antipsychotic polypharmacy to monotherapy in samples without established treatment resistance to a single antipsychotic were identified.  • Six noncontrolled observational studies that examined the relationship between antipsychotic polypharmacy and clinical outcomes in samples without documented treatment resistance to monotherapy were identified.  **Quality:**  The quality of evidence supporting the reduction in antipsychotic polypharmacy without an appropriate justification is high. RCTs have consistently reported no clear benefit in antipsychotic polypharmacy versus monotherapy for controlling symptoms without established treatment resistance to a single antipsychotic medication. As stated previously, the increased risk of sudden cardiac death has been noted with increased doses of antipsychotic medications. Pediatric exposure to multiple antipsychotic medications increased the odds of developing obesity/excessive weight gain (odds ratio [OR], 2.28), Type II diabetes (OR, 2.36) and dyslipidemia (OR, 5.26), cardiovascular conditions (OR, 2.70), digestive/urogenital problems and neurological/sensory symptoms.  As noted above, the American Psychiatric Association has had guidelines in place since 1997 addressing appropriate antipsychotic use. One antipsychotic medication should be prescribed at a time for patients with psychotic disorders. For patients who do not respond to an adequate dose and duration of different trials of monotherapy, antipsychotic combination treatment may be considered with close clinical monitoring. Future trials evaluating long term safety and tolerability trials and comparisons of specific antipsychotic medication combinations are still required.  **Summary of Controversy/Contradictory Evidence:** There is no documented evidence regarding controversy related to the three appropriate justifications for prescribing multiple antipsychotic medications: previous failed trials of monotherapy, cross-tapering to monotherapy and augmentation of clozapine. There is no empiric evidence supporting other justifications, i.e. addition of a second antipsychotic medication for sleep.  **Based on the NQF descriptions for rating the evidence, what was the developer’s assessment of the quantity, quality, and consistency of the body of evidence?**  Quantity:High  Quality:High  Consistency**:** High |
| Estimates of benefit and consistency across studies | **Benefit:**  The purpose of this measure is to evaluate the number of patients discharged on multiple antipsychotic medications to assist the clinician in determining whether there is an appropriate justification supporting the practice. The evidence shows that monitoring the justifications will lead to a change in prescribing practice leading to a reduction in the number of multiple antipsychotic medications prescribed, which will in turn decrease the chance of developing serious side effects and will ultimately result in substantial savings in health care costs.  **Consistency:**  The body of evidence consistently supports a reduction in antipsychotic polypharmacy without an appropriate justification. A minimum number of three trials of monotherapy at adequate doses and duration should be completed prior to initiation of more than one antipsychotic medication. Additionally, the evidence supports the use of a second antipsychotic medication to augment clozapine and a tapering plan to monotherapy as appropriate justifications for multiple antipsychotic medications. No position against the importance to reduce antipsychotic polypharmacy without an appropriate justification was identified in the literature. |
| What harms were identified? | No harms to the patient receiving justified multiple antipsychotic medications were found during the literature review. |
| Identify any new studies conducted since the SR. Do the new studies change the conclusions from the SR? | A review of recent studies also supports the use of quality improvement interventions to educate staff on these appropriate justifications which may further reduce antipsychotic polypharmacy. No position against reducing the number of antipsychotic medications prescribed without an appropriate justification was identified in the literature. |

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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.

Not applicable for this submission

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

Not applicable for this submission

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

Not applicable for this submission

**From previous submission - Citations for Evidence other than Guidelines:**

* American Psychiatric Association (APA). (2004). Steering Committee on Practice Guidelines. Practice guideline for the treatment of patients with schizophrenia, second edition. Am J Psychiatry. 161(2 Suppl):1-56
* Ananth, J., Parameswaran, S., & Gunatilake, S. (2004). Antipsychotic polypharmacy comparing monotherapy with polypharmacy and augmentation. Curr Med Chem. 11(3):313-327 Curr Pharm Des. 10(18):2231-2238.
* Baandrup, L., Sorensen, J., Lublin, H., Nordentoft, M. & Glenthoj, B. (2011). Association of antipsychotic polypharmacy with health service cost: a register-based cost analysis. Eur J Health Econ. Retrieved March 27, 2012 at: http://www.ncbi.nlm.nih.gov/pubmed.

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• Jerrell, J.M. & McIntyre, R.S. (2008). Metabolic and cardiovascular adverse events associated with antipsychotic treatment in children and adolescents. Pediatr Adolesc Med. 162(10):929-35.

• Joukamaa, M., Heliovaara, M., Knekt, P., Aromaa, A., Raitasalo, R. & Lehtinen, V. (2006). Schizophrenia, neuroleptic medication and mortality. Br J Psychiatry. 188:122-7.

• Kreyenbuhl, J., Valenstein, M., McCarthy, J.F., Ganocyz, D., & Blow, F.C. (2006). Long-term combination antipsychotic treatment in VA patients with schizophrenia. Schiz Res.84:90-99.

• National Association of State Mental Health Program Directors (NASMHPD). (2001).Technical report on psychiatric polypharmacy. Alexandria, VA.

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