

# Clinical Consensus Recommendations for Urine Testing of Adherence to Antipsychotics Among People With Serious Mental Illness

Amy N. Cohen, Ph.D., Gretchen Collins, M.D., Frederick Charles Nucifora, Jr., Ph.D., D.O., Roddy Strobel, M.D., David B. Wait, M.D., Alexander S. Young, M.D., M.S.H.S.

**Objective:** This study developed clinical recommendations for the use of proven urine testing technologies to assess antipsychotic medication adherence among people with serious mental illness.

**Methods:** Guided by the RAND/UCLA Appropriateness Method, researchers conducted a literature review and semi-structured interviews and convened an expert panel to develop clinical consensus recommendations for the use of urine monitoring to assess antipsychotic medication adherence.

**Results:** The expert panel identified six circumstances in which urine monitoring was recommended at initial evaluation

and five scenarios in which monitoring was recommended after initial evaluation. Conducting monitoring at the site where psychiatric medication is prescribed and providing education prior to testing and feedback after testing were recommended.

**Conclusions:** A consensus was reached on clinical recommendations for use of urine monitoring at intake and during ongoing treatment. There was strong agreement that monitoring can be used to improve assessment and thence clinical care and outcomes.

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Antipsychotic medication is a critical evidence-based treatment for serious mental illnesses, especially schizophrenia (1). Partial adherence and nonadherence to antipsychotics are common (2). Researchers have estimated that nonadherence occurs among 50% of patients, although estimates vary widely because of differing assessment methods and definitions of adherence (2–4). Poor adherence to antipsychotic medication can have devastating clinical, social, and economic implications (5,6). Feasible strategies that improve adherence are needed. Researchers have estimated that improving antipsychotic medication adherence among patients with schizophrenia, for example, could save \$1,600 per person per year in Medicaid and criminal justice costs (7).

Assessing medication adherence presents a vexing challenge. In an examination of 161 studies of adherence measurement, Velligan and colleagues (8) found that patient self-report of adherence was very inaccurate and that clinician estimates were not much better. As a result, the authors recommended using objective measures of adherence, such as urine monitoring (8).

Urine monitoring has been used for many years to assess for illicit substances, but its use in mental health clinics has been uncommon. However, since 2013 there have been urine testing technologies that simultaneously detect illicit substances as well as ingested medications and estimate levels of

certain antipsychotic medications (aripiprazole, risperidone, and quetiapine) (9,10). These technologies include confirmatory tests that use gas chromatography-mass spectrometry to specify which drugs and metabolites are present in the urine. Reference ranges are calculated, and these are highly correlated with serum levels that indicate the degree of medication adherence. Results are available within a few days. Community mental health programs are increasingly utilizing this monitoring. However, there has been no consensus regarding effective implementation of this technology at mental health programs to improve adherence and guide treatment.

The RAND/UCLA Appropriateness Method has been used as a method for increasing consensus regarding optimal practice when there is inadequate evidence from controlled trial research (11). This report describes the use of this method to provide initial clinical consensus regarding the use of urine monitoring to assess medication adherence among individuals with serious mental illness.

## METHODS

Guided by the RAND/UCLA Appropriateness Method, this project reviewed applicable literature, interviewed clinical experts, and developed initial consensus on clinical

recommendations for the use of urine monitoring to assess medication adherence. Informed consent was obtained from participants. Institutional review board approval was obtained from the University of California, Los Angeles.

The literature review focused on the assessment of adherence to antipsychotic medications among people with serious mental illness and urine monitoring of antipsychotic adherence. This included review articles, key articles cited in those reviews, and articles published between 2014 and 2017.

The semistructured interview of clinicians focused on clinicians' experience with implementation of urine monitoring of antipsychotics, protocols developed to guide use, outcomes observed since implementing the monitoring method, and facilitators of and barriers to use. A urine testing company provided a list of 19 community mental health clinics (CMHCs) that had implemented substantial urine monitoring of antipsychotics. For each clinic, one psychiatrist in agency leadership who treated patients with serious mental illness was identified. CMHCs were targeted because the population of CMHCs includes a large number of patients who are prescribed antipsychotic medications and because implementing a new clinical test in community settings can be very challenging. The identified psychiatry leader was sent an e-mail invitation to participate. Those who responded and agreed to participate were scheduled for a phone interview. Interviews were conducted by a psychiatrist and psychologist between January and September 2016. Detailed notes were taken and reviewed by both interviewers.

On the basis of the literature review and the interviews with the CMHC psychiatrists, we developed 46 hypothetical clinical scenarios, or "indications." The purpose of the indications was to elucidate clinical variables and clinic restraints that clinicians consider when deciding whether to recommend urine monitoring. The indications were designed to be comprehensive, homogeneous, and manageable, such that each indication addressed the wide range of patients and scenarios that present at community clinics, applied to all people described in the particular indication, and could be considered and rated in a reasonable length of time. The indications were grouped into five categories: initial evaluation, urine monitoring method, education, feedback, and ongoing treatment.

**TABLE 1. Appropriateness, impact, and feasibility of 15 clinical recommendations for urine monitoring of antipsychotic medications<sup>a</sup>**

Recommendation	Appropriateness		Impact		Feasibility	
	M	SD	M	SD	M	SD
Initial evaluation						
Conduct urine monitoring for patients who present for evaluation of symptoms of a serious mental illness with no previously established diagnosis	9.0	.0	8.8	.4	8.3	.4
Conduct urine monitoring for patients with a serious mental illness	8.5	.9	8.5	.5	7.8	.4
Conduct urine monitoring for patients with a serious mental illness who have a risk factor for poor treatment adherence	8.8	.4	8.8	.4	8.0	.7
Conduct urine monitoring for patients with a serious mental illness who are homeless	8.8	.4	8.8	.4	7.5	.5
Conduct urine monitoring for patients with serious mental illness and a co-occurring substance use disorder	9.0	.0	8.8	.4	8.5	.5
Conduct urine monitoring for patients who are elderly and who have a serious mental illness	9.0	.0	9.0	.0	8.8	.4
Urine monitoring method						
Urine collection should be conducted at the site where the medication is prescribed	8.3	.4	8.3	.4	8.3	.4
Education						
Patients should receive education (written or verbal) prior to urine monitoring testing on the importance of psychotropic medication adherence, the role of urine monitoring, and cost	9.0	.0	8.8	.4	8.8	.4
Feedback						
Provide patients with access to urine monitoring results when they become available	8.5	.5	8.5	.5	8.3	.8
A provider engaged with the patient should discuss any issues of concern pertaining to the urine monitoring with the patient within a clinically appropriate timeframe	9.0	.0	9.0	.0	7.5	.9
Ongoing treatment						
Repeat urine monitoring at a subsequent visit to address any issues of concern from the results of previous urine monitoring	8.5	.5	8.5	.5	8.3	.4
Repeat urine monitoring if clinicians identify clinical deterioration or inadequate therapeutic response by the patient	8.5	.5	8.3	.8	8.8	.4
Repeat urine monitoring when there has been a substantial change in the patient's situation (for example, a change in level of care, living environment, health care providers, or pharmacy) that may require medication reconciliation	8.0	.7	7.8	.4	7.8	.4

*continued*

TABLE 1, *continued*

Recommendation	Appropriateness		Impact		Feasibility	
	M	SD	M	SD	M	SD
Repeat urine monitoring periodically (at set or random intervals), with additional testing tailored to clinical need	8.5	.9	8.3	.8	7.8	.4
Repeat urine monitoring at least annually among patients with a prior normal test and no indications of deterioration or risk	7.3	1.5	8.0	1.0	9.0	.0

<sup>a</sup> The recommendations are based on ratings by a panel of experts of 46 indications for the use of urine monitoring to assess antipsychotic medication adherence. Indications were rated on appropriateness to the population, impact on patient treatment and outcomes (including symptoms or functioning), and feasibility of implementation in typical community mental health care settings, and indications with a mean score between 7.0 and 9.0 for each category were included as clinical recommendations. Appropriateness was rated from 1, extremely inappropriate, to 9, extremely appropriate; impact from 1, highly unlikely, to 9, highly likely; and feasibility from 1, extremely difficult, to 9, very easy.

A panel was convened to discuss and rate these indications during a one-day, in-person meeting in September 2016. Panel members came from the pool of interviewees and, specifically, from those whose interview responses revealed considerable experience with urine monitoring for patients with serious mental illness. Panel members independently and confidentially rated three aspects of each indication: appropriateness to the population (from 1, extremely inappropriate, to 9, extremely appropriate); impact on patient treatment, symptoms, and functioning (1, highly unlikely, to 9, highly likely); and feasibility in typical community mental health care (1, extremely difficult, to 9, very easy). Immediately after each indication was scored, the psychiatrist and psychologist looked for discrepancies among the panelists' ratings. Discrepancies of one-third or more (a rating of 1–3 versus 4–6 or 7–9 or a rating of 4–6 versus 7–9) warranted discussion. Panel members who made a discrepant rating were not identified. Although the goal was to increase consensus, complete consensus was not required as an outcome. Panelists were encouraged to negotiate areas of disagreement in an effort to increase support of the final indication that would be voted on. Based on the discussion, discrepant indications were edited and rerated or discarded.

## RESULTS

Following the literature search, 13 articles and four unpublished reports were read by two investigators. The review confirmed known problems with existing measures of adherence; specifically, patient self-report and clinician assessment of antipsychotic adherence have a weak correlation or no correlation with objective measures of adherence, including blood plasma and electronic monitoring (3,8). The review also identified a lack of published data on implementation of urine monitoring of antipsychotics.

All 19 community mental health programs that were identified as substantial users of the technology were invited for a semistructured interview. Nine did not respond, one declined,

and nine consented. Some clinics requested that more than one person be interviewed. In total, 13 individuals, seven men and six women, were interviewed. These included 11 physicians, one nurse, and one professional counselor. The nine clinics represent community clinics in six different states that serve a population with serious mental illness and that use urine monitoring to assess antipsychotic adherence.

The participants reported that prior to implementation of urine monitoring, the clinics relied on patient self-report or clinician estimates of medication adherence, admitting that these were inaccurate. Three sites had established protocols that dictated when to administer urine monitoring. Of the six clinics without protocols, four used monitoring at the initial visit, and all six used monitoring

during ongoing treatment. Monitoring during treatment was triggered by several clinical scenarios: increase in level of care (for example, from care in an outpatient clinic to hospitalization), increase in symptoms (for example, an increase in paranoia), decrease in level of functioning (for example, not eating well), nonadherence to psychosocial treatments (for example, missed appointments), and unexpected results from previous urine monitoring (for example, detecting medications that were not prescribed, detecting illicit substances, and not finding medications that were prescribed). Only two clinics reported annual urine monitoring for all patients. Four clinics had developed either written handouts or verbal scripts for educating patients about urine monitoring. Interviewees from eight clinics emphasized the use of urine monitoring to enhance treatment, using evidence of nonadherence or illicit substances as opportunities to discuss treatment options but not to exclude the patient from services. Seven clinics reported few refusals to monitoring. Barriers to implementing urine monitoring included problems integrating the monitoring results with the clinic's electronic medical record, challenges integrating the monitoring into clinic workflow, and not having sufficient staff. Every interviewee stated that monitoring was extremely useful in improving medication adherence and understanding causes of clinical deterioration.

A total of nine individuals were sent invitations to participate in the expert panel, and four—all physicians—agreed (two men and two women). Of the five who declined, three declined because of the necessity of travel, one declined because she was not available, and one declined because of a potential conflict of interest caused by having accepted a new position at the Center for Mental Health Services. The participants represented four community clinics serving a population with serious mental illness in four different states.

Of the 46 indications discussed, many were combined during the panel discussion. Table 1 lists the panel's clinical consensus recommendations, which comprise the 15 indications with an average rating of 7.0 or higher on appropriateness, impact, and feasibility. Indications that had an average rating below 7.0 in

appropriateness, impact, or feasibility were dropped. A rating of 7 corresponds to indications that are “usually appropriate,” have a “probable impact on treatment and outcomes,” and are “generally easy to implement.”

Urine monitoring at initial intake was recommended for patients presenting with new symptoms of serious mental illness, patients with an established diagnosis of serious mental illness, patients with serious mental illness who have a risk factor for poor adherence or who are homeless, patients with serious mental illness and a co-occurring substance use disorder, and geriatric patients with serious mental illness. Conducting urine monitoring where the medication is prescribed was recommended. Written or verbal education prior to testing was deemed critical and should include information on the importance of adherence, the role of urine monitoring in treatment planning, and any costs that the patient might incur. Transparency of the results was considered important. It was recommended that results be shared with the patient as soon as they were available and that a clinician be available to discuss patient concerns. Repeated urine monitoring was recommended if there were concerns regarding a previous result, if the patient experienced clinical deterioration or inadequate therapeutic response, or if there was substantial change in the patient's situation that may require medication reconciliation. In addition, the panel recommended periodic testing, either at set intervals or on random occasions, as well as annual testing, at a minimum, among stable patients.

## DISCUSSION AND CONCLUSIONS

Medication adherence is important in treatment planning, affects patient outcomes, and is very challenging to accurately assess. Urine monitoring is an objective tool for assessing medication adherence, although it has not been widely implemented, and use of this strategy by community mental health programs is feasible. Prior to this project, there was no detectable research or consensus development to inform implementation and use of urine monitoring of antipsychotics in the treatment of people with serious mental illness. In this study, a process involving a literature review, semistructured interviews, and an expert panel produced consensus clinical recommendations pertaining to the use of urine monitoring at initial evaluation and during ongoing treatment.

The experts who participated in consensus development were clinicians working at CMHCs who had considerable experience in using urine monitoring for antipsychotic adherence. There was strong agreement that monitoring can be used to improve assessment and thence clinical care and outcomes in these settings. Implementation challenges included integration with an electronic medical record, use within clinic workflow, and limited staff resources. Future directions should include research studying the comparative effectiveness of urine monitoring and alternative strategies for assessing medication adherence among people with serious mental illness. Research is also needed regarding the costs and benefits of urine monitoring, including the effect on

hospitalizations, incarcerations, and improvements in quality-adjusted life years. Special practice groups and institutions, such as the American Psychiatric Association and the National Institutes of Health, may be interested in this method as a tool to help improve adherence and outcomes, and they may wish to consider exploration and study of this method.

## AUTHOR AND ARTICLE INFORMATION

Dr. Cohen and Dr. Young are with the Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles (UCLA). Dr. Collins is with View Point Health, Lawrenceville, Georgia, and the Department of Psychiatry, Emory University, Atlanta. Dr. Nucifora is with the Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore. Dr. Strobel is with the Permian Basin Community Center, Midland, Texas. Dr. Wait is with Heritage Health, Coeur d'Alene, Idaho. Send correspondence to Dr. Cohen (e-mail: ancohen@ucla.edu).

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