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The effect of providing patient-specific electronically monitored antipsychotic medication adherence results on the treatment planning of prescribers of outpatients with schizophrenia

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Abstract

To examine the impact of providing patient-specific electronic monitoring (EM) medication adherence results on the treatment planning of prescribers of outpatients with schizophrenia. Adherence to antipsychotic medication was assessed monthly over a 6-month study period using EM of medication bottle opening in 23 outpatients with schizophrenia or schizoaffective disorder. Patient-specific EM adherence results were then shared with the seven participating prescribers, who were surveyed concerning the treatment changes, if any, that they would recommend based on the EM adherence results. Prescribers indicated that they would recommend adherence-related treatment plan changes in 61% of patients, all of whom were 80% adherent. The strength of this effect was significantly stronger for psychosocial intervention treatment plan change recommendations ($r_{pb} = -0.61$) than for medication treatment plan change recommendations ($r_{pb} = -0.28$). Of the psychosocial intervention recommendations, increase case management intensity was most often recommended. Of the medication treatment plan recommendations, initiate a long-acting injectable and increase dose of current oral antipsychotic was each recommended in only one case. Prescriber recommendations of adherence interventions in this study were not necessarily consistent with major guideline recommendations. Findings suggest the need for further study and dissemination of findings regarding evidence-based adherence assessment and interventions.

Keywords

Schizophrenia; Anti-Psychotics; Adherence; Electronic Monitoring

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1. Introduction

Nonadherence to antipsychotic medication is a common problem in persons with schizophrenia and schizoaffective disorder (Byerly et al., 2007a). Compounding this problem is the challenge that nonadherence is difficult to detect by clinicians. In the only study to date, to our knowledge, that compared adherence ratings of patients' actual prescribers to that of a validated objective adherence measure (electronic monitoring), Byerly et al. (2007b) found that prescribers detected nonadherence in only 7% of schizophrenia outpatient cases. A few other previous studies (Remington et al., 2006; Yang et al., 2012), which compared EM adherence to various subjective-based adherence ratings, found that subjective clinician ratings also tend to over-estimate adherence (or under-estimate nonadherence) in outpatients with schizophrenia.

It is generally and empirically recognized that treating prescribers' (clinicians') ability to detect medication nonadherence is inadequate in schizophrenia populations (Byerly et al., 2005; Byerly et al., 2007b, Velligan et al., 2009). What is not known is whether objective adherence assessment methods such as EM can advance the detection of nonadherence, if incorporated into routine care of outpatients with schizophrenia. To our knowledge, no prior studies have evaluated the potential role of objective adherence assessment measures such as EM in real-life settings. Would, for example, informing treating prescribers of objectively-determined, previously undetected nonadherence of their own patients, impact their decisions regarding treatment and adherence-related intervention planning? If so, what would be the degree of impact and what specific treatment and intervention plan changes would prescribers recommend? We chose to address these questions in the current study by providing EM adherence results of patients with schizophrenia to their treating prescribers. Although EM adherence has its own shortcomings (Osterberg and Blaschke, 2005), it has become increasingly used as a reasonable "objective reference standard" to assess medication adherence in general medical and schizophrenia outpatient populations (Diaz et al., 2004; Osterberg and Blaschke, 2005; Remington et al., 2006; Byerly et al., 2007b; Nakonezny et al., 2008; Acosta et al., 2009; Nakonezny et al., 2010; Yang et al., 2012). Based on patient-specific EM adherence results, the current study examined what treatment plan changes, if any, practicing prescribers (treating psychiatrists) would recommend (albeit hypothetical) for improving antipsychotic medication adherence in their individual outpatients with schizophrenia.

2. Methods

2.1. Participants

The 23 adult outpatients included in the current study were diagnosed with schizophrenia ($n=9$) or schizoaffective disorder ($n=14$), as established by the Structured Clinical Interview for DSM-IV, and were recruited from three Dallas County public mental health outpatient clinics. Most participants were self-referred from flyers (a few being referred by their treating clinician). Participants were recruited and studied at their usual outpatient clinics. Participants were included if they were taking a single oral antipsychotic, and if they were at least 18 years of age. Participants receiving a depot antipsychotic within one treatment cycle or using a pillbox were excluded. There were no restrictions placed on the use of psychotropic or other medications other than those mentioned above for antipsychotics. The study protocol was approved by the Institutional Review Board of The University of Texas Southwestern Medical Center at Dallas and written informed consent was obtained from all participants. Participants were paid \$15 per hour of study participation.

The 23 participants of the current study were a sub-sample of outpatients from our larger parent study of 61 adult outpatients diagnosed with schizophrenia or schizoaffective

disorder, which evaluated the effect of antipsychotic medication adherence (using EM) over a 6 month period on prospectively assessed symptom severity/clinical outcomes (Nakonezny and Byerly, 2006). Because a limited number of prescribers (N=7) chose to participate in the current study, this circumscribed our current sample to the 23 outpatients who were treated by these seven participating prescribers (treating psychiatrists).

2.2. Procedures and measures

2.2.1. Antipsychotic medication—The 23 participants of the current study took either a first- ($n=5$) or second-generation ($n=18$) oral antipsychotic that was prescribed as part of routine care at study entry. No participants switched antipsychotic class during the course of the trial. Regarding dosing schedule, of the 23 participants, 16 (69.6%) received dosing once per day, 6 (26.1%) received dosing twice per day, and 1 (4.3%) received dosing three times per day.

2.2.2. Electronic monitoring and adherence—Medication adherence was assessed with the Medication Event Monitoring System (MEMS®), which is a medication vial cap that electronically recorded the date and time of bottle opening. The MEMS® caps used in our studies had no cueing mechanisms and their appearance was similar to any other medication bottle, although the cap was slightly larger than a regular pill bottle cap. The company that makes the MEMS® caps provided no support for the parent study or the current study.

The study period of the parent trial (March 2003 – April 2004) included a screening, baseline, and up to 6 consecutive monthly adherence evaluations. The content of study visits was limited to adherence and clinical assessments. No medication or adherence-related education or reminders were provided. Participants were aware of the purpose and function of the MEMS® cap, but did not have access to adherence results.

For a given patient, EM adherence was operationally defined as the proportion of medication vial caps openings in a given month relative to the prescribed doses for that month. If patients with multiple-dosing regimens opened the MEMS® cap at least the number of times prescribed each day, they received full credit for adherence for that particular day. Excessive bottle openings (i.e., openings that exceeded the number of prescribed doses for that month), however, did not count toward overall adherence. Most participants in the current study (19/23, 82.6%) completed the full 6 months of monthly adherence evaluations; 1 participant (1/23, 4.3%) completed 5 of the 6 monthly adherence evaluations (missed month 5), 1 participant (1/23, 4.3%) completed 4 of the 6 monthly adherence evaluations (missed months 5–6), and 2 participants (2/23, 8.7%) completed 3 of the 6 monthly adherence evaluations (missed months 4–6).

To further understand whether a given EM adherence level influenced prescribers' hypothetical treatment plan change recommendations, we also *a priori* operationalized EM adherence as a binary variable using three separate cutoffs: as the proportion of patients who were less than (<) and greater than or equal to (≥) the 6-month mean EM adherence of 70%, 80%, and 90%, respectively. The 70% EM adherence cutoff was selected because it was both conservative in detecting nonadherence in schizophrenia and consistent with definitions from prior published research (Byerly et al., 2005; Byerly et al., 2007b). The 80% EM adherence cutoff was selected for examination because it was endorsed by an expert consensus panel (Velligan et al., 2009) as an appropriate cutoff for adherence in schizophrenia. The 90% EM adherence cutoff, however, was selected simply for exploratory purposes in this study.

2.2.3. Prescriber evaluation and recommendation—At the completion of the parent study, both monthly-average as well as the 6-month average patient-specific EM adherence results was shared with the seven prescribers who participated in the current study. The seven prescribers, treating psychiatrists, for the current study were then surveyed (via a self-administered questionnaire) concerning the treatment plan changes, if any, that they would recommend (albeit hypothetical)--based solely on the average EM adherence results--for improving antipsychotic medication adherence in their individual outpatients with schizophrenia.

Hypothetical treatment plan changes (from which to select on the structured questionnaire) comprised a general recommendation, “I would not recommend any treatment changes at this time,” and seven specific recommendations that encompassed *Medication Treatments* and eight specific recommendations that encompassed *Psychosocial Treatments*. Sample recommendations of the *Medication Treatments* include “increase dose of current antipsychotic,” “if patient is on a newer [second-generation] antipsychotic, switch to a different newer oral antipsychotic agent,” and “initiate second-generation long-acting injectable.” Sample recommendations of the *Psychosocial Treatments* include “increase case management intensity,” “initiate use of pill box,” and “initiate psychoeducational program.” The prescriber responses to the general and specific recommendations were operationalized as binary variables coded as “yes” (dummy-coded as 1) or “no” (dummy-coded as 0). Prescribers were permitted to select all treatment plan changes from among the hypothetical response choices on the structured questionnaire that were applicable, in their clinical judgment, to a given patient. Prescribers were also permitted to write-in “other” treatment plan changes for a given patient that was not part of the response choices on the structured questionnaire.

Although there were seven treating psychiatrists for the current study, prescriber 1 rated 10 of the 23 patients (43.48%), prescriber 2 rated 4 of the 23 patients (17.39%), prescribers 3 and 4 each rated 3 of the 23 patients (13.04% each), and prescribers 5 thru 7 each rated 1 of the 23 patients (4.35% each). We note that a Likelihood Ratio Chi-Square test of independence found no statistical association (contingency) between the prescriber and the general treatment plan change recommendation ($\chi^2 = 5.19$, $p = 0.52$). This means that any general treatment plan change recommendation was not associated with the prescriber (which, in general, mitigates a rater or prescriber effect).

2.3. Statistical analysis

Demographic and clinical characteristics for the sample of 23 patients were described using the sample mean and standard deviation for continuous variables and the frequency and percentage for categorical variables. A descriptive frequency analysis was carried out to examine the frequency of general and specific medication-based and psychosocial-based treatment plan change recommendations. For analytic purposes, we used (operationalized) adherence as an aggregate based on the 6-month mean EM adherence. Next, the Pearson point-biserial correlation coefficient (r_{pb}) was used to examine the relationship between the continuously-measured 6-month mean EM adherence and the prescriber responses to the general and specific medication-based and psychosocial-based treatment plan change recommendations. Finally, Fisher's exact test was used to test for an association (contingency) between the proportion of prescribers who recommended a treatment plan change (general, psychosocial, and medication, respectively) and the proportion of patients who had a 6-month mean EM adherence of at least 70%, 80%, and 90%, respectively. We also reported the Phi correlation coefficient (ϕ) here.

We performed all of the statistical analyses using SAS, version 9.2 (SAS Institute, Inc.). The level of significance for all tests was set at $\alpha = 0.05$ (two-tailed) and p -values were left unadjusted for multiple testing.

3. Results

3.1. Participant characteristics

The study sample included 12 females (52.2%) and 11 males (47.8%), with an average age of 46.0 years, $SD=6.9$ (age range = 34 to 59 years). The average age at illness onset was 21.2 years ($SD=8.7$). Participants included 12 (52.2 %) Caucasians and 11 (47.8 %) African Americans. Four (17.4%) participants had less than a high school education, while 19 (82.6%) had at least a high school education. Eighteen (78.3%) participants did not have a caregiver. The average baseline PANSS total score was 68.8 ($SD=11.1$) and the average PANSS total score at study end (month 6) was 71.8 ($SD=10.4$). The 6-month mean EM adherence was 78.2% ($SD=18.6$). We note that we found no significant relationship between antipsychotic dosing schedule and 6-month mean EM adherence ($p = 0.73$).

3.2. Frequency of treatment plan change recommendations

The descriptive frequency analysis revealed that prescribers (hypothetically) recommended (based on the 6-month average EM adherence results) a general treatment plan change for 14 of 23 (60.8%) patients, a psychosocial treatment plan change for 13 of 23 (56.5%) patients, and a medication treatment plan change for 8 of 23 (34.7%) patients. The 6-month average EM adherence associated with the general treatment plan change, psychosocial treatment plan change, and medication treatment plan change was 68.7% ($SD=17.4\%$), 68.4% ($SD=18.1\%$), and 71.1% ($SD=12.2\%$), respectively.

Of the psychosocial treatment plan change recommendations, increase case management intensity was most often recommended (11/23 patients, 47.8%), followed by initiate psychoeducational program (4/23 patients, 17.4%) and initiate use of pill box (4/23 patients, 17.4%). A one-time nurse visit (2/23, 8.7%) and contacting the family/caregiver (2/23, 8.7%), however, were least recommended. Initiate ACT team and initiate social skills program were not recommended for any patients by the prescribers.

Medication treatment plan changes were rarely recommended by prescribers. Initiate a long-acting injectable (1/23 patients, 4.3%) and increase dose of current oral antipsychotic (1/23 patients, 4.3%) was each recommended in only one case. The other potential medication changes for which the prescribers could have suggested—initiate the use of a second-generation oral antipsychotic, switch to a different second-generation oral antipsychotic, add an additional oral antipsychotic, and initiate adjunctive psychotropic medications—were not recommended for any patients by the prescribers. Medication treatment plan changes that were recommended (via written-in) the open-ended space by prescribers that was not part of the (hypothetical) response choices on the structured questionnaire included “discuss medication regimen, adherence issues, and side effects with patients” (7/23 patients, 30.4%). The results of the frequency analysis of treatment plan change recommendations are reported in Table 1.

3.3. EM adherence and treatment plan change recommendations

The Pearson point-biserial correlation coefficient (r_{pb}) revealed a significant negative relationship between continuously measured 6-month mean EM adherence and the *General Treatment plan change recommendation* ($r_{pb} = -0.65$, $p = 0.0008$) and the *Psychosocial Treatment plan change recommendation* ($r_{pb} = -0.61$, $p = 0.002$), but a non-significant negative relationship with *Medication Treatment plan change recommendation* ($r_{pb} = -0.28$,

$p = 0.18$). The general interpretation of the negative relationship here is that as EM adherence decreased prescribers tend to (hypothetically) recommend a *Treatment Plan* change. The results of the correlation analysis are shown in Table 1.

Fisher's Exact test and the Phi correlation coefficient (ϕ) revealed a significant association between the prescribers' psychosocial treatment plan change recommendation and patient's EM adherence of at least 70%, 80%, and 90%, respectively. That is, for patients who had an EM adherence of at least 70%, 80%, and 90%, prescribers recommended a *psychosocial treatment plan* change in 8 of 18 cases (44.4%, $\phi=|0.46|$, $p=0.04$), 3 of 11 cases (27.2%, $\phi=|0.56|$, $p=0.01$), and 0 of 8 cases (0.0%, $\phi=|0.83|$, $p=0.0004$), respectively. Also, for patients who had an EM adherence of at least 70%, 80%, and 90%, prescribers recommended a *medication treatment plan* change in only 5 of 18 cases (27.7%, $\phi=|0.28|$, $p=0.29$), 1 of 11 cases (9.1%, $\phi=|0.51|$, $p=0.02$), and 0 of 8 cases (0.0%, $\phi=|0.53|$, $p=0.02$), respectively. Finally, for patients who had an EM adherence of at least 70%, 80%, and 90%, prescribers recommended a *general treatment plan* change in 9 of 18 cases (50.0%, $\phi=|0.42|$, $p=0.11$), 3 of 11 cases (27.2%, $\phi=|0.66|$, $p=0.003$), and 0 of 8 cases (0.0%, $\phi=|0.91|$, $p=0.0001$), respectively. These results are reported in Table 1.

4. Discussion

In the current study, providing prescribers with EM adherence results of their own patients had an impact on hypothetical treatment planning, with EM adherence-related treatment changes recommended for the majority (61%) of patients of whom had a 6-month mean EM adherence of about 69%. These findings perhaps suggest that treating psychiatrists were unaware of the degree of non-adherence in their own patients. This interpretation is supported by results of the parent study of this project, in which non-adherence (defined as 70% adherence) was found in just 7% of patients based on prescriber ratings but 57% based on EM ratings (Byerly et al., 2007b). Providing objective adherence results to prescribers appear to offer valuable clinical information that is not available in routine approaches to clinical care and suggests that, when they are made aware of such adherence results, the treating psychiatrists in the current study have the intent to recommend treatment plan changes.

Not surprising, results suggest that as EM antipsychotic medication adherence decreases, treating psychiatrists tend to recommend a treatment plan change for their outpatients with schizophrenia. We found that the strength of this effect was stronger for psychosocial intervention treatment plan change recommendations ($r_{pb} = -0.61$) than for medication treatment plan change recommendations ($r_{pb} = -0.28$). Although the pattern here of prescriber recommendations is not necessarily in line with major guideline recommendations, perhaps this basic finding here is in line with the supposition that treatment should combine optimal pharmacotherapy with targeted psychosocial interventions, as recommended by the Schizophrenia Patient Outcomes Research Team (PORT) (Lehman et al., 2004a).

When we examine whether a given EM adherence level (EM adherence cutoffs of 70%, 80%, and 90%) influences prescribers' (hypothetical) treatment plan change recommendations, we find that prescribers do not recommend a treatment plan change for schizophrenia outpatients who are at least 90% adherent to their antipsychotic medication adherence. Specifically, when patients are at least 90% adherent, prescribers recommend neither a psychosocial intervention nor a medication treatment plan change. However, for patients who are 70% to 80% adherent to their antipsychotic medication, prescribers tend to recommend a psychosocial intervention (44% and 27%, respectively) more than a medication treatment plan change (28% and 9%, respectively). This finding here falls in line

with the 80% adherence definition that is endorsed by an expert consensus panel in the Velligan et al article (Velligan et al., 2009) as an appropriate cutoff for adherence in schizophrenia. Further, the 70% EM adherence definition is consistent with that used in previous research (Lacro et al., 2002; Byerly et al., 2005; Byerly et al., 2007b). And previous research suggests that schizophrenia patients who are < 70% adherent to their antipsychotic medication are at greater risk of hospitalization than those who are 70% adherent (Weiden et al., 2004).

We also examine the frequency of prescribers' specific treatment/intervention recommendations for improving antipsychotic medication adherence in their individual outpatients with schizophrenia. Of the psychosocial intervention recommendations, increase case management intensity is most often recommended (47.8%), followed by initiate psychoeducational program and initiate use of pill box (each at 17.4%). Of the medication treatment plan changes, initiate a long-acting injectable and increase dose of current oral antipsychotic is each recommended in only one case (4.3%). The other potential medication changes for which the prescribers could have suggested—initiate the use of a second-generation oral antipsychotic, switch to a different second-generation oral antipsychotic, add an additional oral antipsychotic, and initiate adjunctive psychotropic medications—were not recommended for any patients by the prescribers. However, “discuss medication regimen, adherence issues, and side effects” were suggested by prescribers for 30% of their outpatients with schizophrenia. This pattern of adherence-related treatment/intervention recommendations is not necessarily consistent with major guideline recommendations. For example, the second most commonly recommended psychosocial intervention in the current study, psychoeducation, has been widely studied with less than positive effects (Byerly et al., 2007a). Most striking, the top recommended adherence intervention in major treatment guidelines (Lehman et al., 2004b; Moore et al., 2007), long-acting injectable antipsychotics, was recommended for only one patient in the current study. Although the pattern of prescriber recommendations is not necessarily in line with major guideline recommendations, perhaps the prescriber recommendations here reflect what treating psychiatrists would “ideally” like to do (since they were indeed hypothetical suggestions) as opposed to what they know they could “realistically” do in practice.

The current study may be tempered by a few limitations. The study had a small, non-random sample of 23 patients. Also, although there were seven prescribers (treating psychiatrists) for the current pilot study, one prescriber rated almost half of the 23 patients (10/23, 43.48%). Further, EM may overestimate adherence because the events captured by EM (date/time of bottle opening) do not ensure medication ingestion (Farmer, 1999; Osterberg and Blaschke, 2005). A period documenting a lack of medication bottle opening, however, most likely represents non-adherence (Osterberg and Blaschke, 2005).

Despite these few limitations, the current study has strengths, including the use of an objective method, electronic monitoring, to measure medication adherence. Further, the participants in the current study are typical outpatients with schizophrenia who reside in the community (public mental health setting). And the prescribers in the current study are typical practicing psychiatrists from the public mental health setting. The use of both outpatients and practicing psychiatrists from the public health care system, thus, provides a greater degree of generalizability of our findings.

4.1. Conclusions

To our knowledge, this is the first study to share patient-specific EM medication adherence results with treating psychiatrists and then examine what treatment plan changes, if any, they would recommend (albeit hypothetical) for improving antipsychotic medication adherence in their individual outpatients with schizophrenia. Sharing patient-specific EM adherence

results with treating psychiatrists, vis-à-vis their own patients, led to general treatment plan change recommendations for the majority (61%) of outpatients with schizophrenia (all of whom were 80% adherent). These findings perhaps suggest that treating psychiatrists were unaware of the degree of non-adherence in their own patients and if made aware of such adherence results, they would recommend treatment plan changes. The adherence-related treatment/intervention recommendations were not necessarily consistent with prior evidence about the efficacy of psychosocial interventions, and in only one patient case led to a choice of the guideline recommendation for long-acting injectable antipsychotics. These findings emphasize shortcomings in treating psychiatrists' ability to detect non-adherence and highlight the need for further study and dissemination of findings regarding evidence-based adherence assessments (such as EM) and interventions in community settings.

Finally, based on the findings of the current study and that from previous adherence research, we offer the following recommendations for future studies in schizophrenia outpatient research as well as recommendations/implications for clinicians who treat schizophrenia outpatients in community practice settings.

4.2. Recommendations for future studies in schizophrenia outpatient research

Because our findings only report on the hypothetical decisions prescribers said they would make regarding treatment plan changes for improving antipsychotic medication adherence in their individual outpatients with schizophrenia, future research with a larger sample size is needed so as to determine: (a) the feasibility of using objective adherence assessment methods such as EM in usual care of outpatients with schizophrenia, including the receptiveness/acceptance of patients in a community setting to EM; (b) the effect of objectively-determined medication adherence results on the actual (not hypothetical) treatment and intervention planning/decisions of prescribers for their individual outpatients with schizophrenia and the receptivity of patients to such treatment plan changes; (c) the impact of such treatment plan changes on the actual clinical outcomes of outpatients with schizophrenia; and (d) the cost-effectiveness of objective adherence assessment methods such as EM in the treatment of schizophrenia outpatients in “real-world” community practice settings.

4.3. Recommendations/implications of our findings for practicing clinicians

The clinician should undertake formal monitoring efforts or assessment to ascertain if the patient is taking the prescribed medication, because adherence problems make it very difficult, if not impossible, for the prescribing clinician to fully evaluate treatment response and determine if dosing is appropriate or if concomitant medication is needed or if a medication switch is warranted (Byerly et al., 2007a; Velligan et al., 2009; Nakonezny et al., 2010). The unanswered questions outlined in the abovementioned recommendations for future studies/research suggest that much is yet to be learned about the feasibility and impact of objective adherence assessment methods in routine clinical care of outpatients with schizophrenia. However, electronic monitoring devices (such as MEMS®) are now readily available, EM (MEMS®) caps cost just about \$100 per cap, they can capture continuous data for up to 36 months, and they have already demonstrated that they can detect nonadherent outpatients that would otherwise remain undetected (i.e., “adherent”) in the community setting. Thus, it is quite possible that EM-based adherence results could lead to improvements in clinical care of schizophrenia outpatients in the community setting—especially to help to mitigate improper decisions that result from the false assumption of patient adherence, such as declaration of treatment resistance, when indeed nonadherence is really the culprit. If nonadherence is suspected during the course of treatment, then the clinician should try to identify the core barrier(s) or reason(s) behind the nonadherence so as to mitigate relapse and insufficient response (Glazer and Byerly, 2008; Velligan et al., 2009;

Nakonezny et al, 2010). Finally, the identification of nonadherence could also provide opportunities to bolster the patient-physician relationship, as barriers and reasons behind such nonadherence can be addressed and discussed between the patient and physician/clinician.

In summary, the reader is referred to Galzer and Byerly (2008) and Velligan et al. (2009) for a detailed presentation and discussion of medication adherence in patients with mental illness, including adherence assessment, barriers, guidelines, recommendations, and strategies/interventions for addressing medication adherence problems.

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Table 1

EM adherence and treatment plan change recommendations

Treatment Plan Change Recommendation ^a	Total Sample ^b n (%), N=23	EM Adherence					
		70% EM ^c n (%), N=18	80% EM ^c n (%), N=11	90% EM ^c n (%), N=8	Continuous EM ^d <i>M</i> <i>SD</i> <i>r_{pb}</i>		
General Treatment, n (%)	14 (60.8%)	9 (50.0%) [†]	3 (27.2%) ^{**}	0 (0.0%) ^{***}	68.7%	17.4%	−0.65 ^e
Psychosocial Treatment, n (%)	13 (56.5%)	8 (44.4%) [*]	3 (27.2%) ^{**}	0 (0.0%) ^{***}	68.4%	18.1%	−0.61 ^f
Case Management	11 (47.8%)						
Pill Box	4 (17.4%)						
Educational Program	4 (17.4%)						
Behavioral Program	3 (13.0%)						
Contact Family/Caregiver	2 (8.7%)						
One-time Nurse visit	2 (8.7%)						
Social Skills Program	0 (0.0%)						
ACT team	0 (0.0%)						
Medication Treatment, n (%)	8 (34.7%)	5 (27.7%) ^{††}	1 (9.1%) [*]	0 (0.0%) ^{**}	71.1%	12.2%	−0.28 ^g
Long-Acting Injectable, n (%)	1 (4.3%)						
2nd-Generation	1 (4.3%)						
1st-Generation	0 (0.0%)						
Oral Antipsychotic, n (%)	1 (4.3%)						
Increase Dose of Current Agent	1 (4.3%)						
Switch to different Newer Agent	0 (0.0%)						
Initiate 2nd-Generation (newer) Agent	0 (0.0%)						
Add additional Oral Agent	0 (0.0%)						
Adjunctive Psychotropic, n (%)	0 (0.0%)						
Other (discuss medication regimen/side effects with patients), n (%)	7 (30.4%)						

Note. The means (*M*) presented in this table are the sample means; *SD* = Standard Deviation; EM = Electronic Monitoring; *r_{pb}* = Pearson point-biserial correlation coefficient between the continuously-measured 6-month mean EM adherence and the general/medication/psychosocial-based treatment plan recommendations (coded as yes/no).

^aPrescribers were permitted to select all treatment plan recommendations that were applicable, in their clinical judgment, to a given patient.

^bNumber (and %) of patients for whom a treatment plan change was recommended out of the total sample size (N=23).

^cNumber (and %) of patients who met the EM adherence cutoff (threshold) and for whom a treatment plan change was recommended.

^d6-month mean EM adherence.

^e*p* < 0.001, two-tailed.

^f*p* < 0.01, two-tailed.

^g*p* < 0.18, two-tailed.

^{*}*p* < 0.05, two-tailed, Fisher's Exact Test.

^{**}*p* < 0.01, two-tailed, Fisher's Exact Test.

 $p < 0.001$, two-tailed, Fisher's Exact Test.

[†]
 $p < 0.11$, two-tailed, Fisher's Exact Test.

^{††}
 $p < 0.29$, two-tailed, Fisher's Exact Test.