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## *A review of behavioral tailoring strategies for improving medication adherence in serious mental illness*

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### Introduction

**A**dherence has been defined as “the extent to which a person’s behavior—taking medication, following a diet, and/or executing lifestyle changes—corresponds with agreed recommendations from a health care provider”<sup>1</sup> and is critical for achieving optimal therapeutic outcomes. Nonadherence to psychiatric

*Nonadherence to psychopharmacological treatments poses a significant challenge to treatment success in individuals with serious mental illness, with upwards of 60% of people not taking their psychiatric medications as prescribed. Nonadherence is associated with adverse outcomes, including exacerbation of psychiatric symptoms, impaired functioning, increased hospitalizations and emergency room use, and increased health care costs. Whereas interventions using psychoeducation or cognitive approaches, such as motivational interviewing, have largely proven ineffective in improving adherence, approaches employing behavioral tailoring that incorporate medication taking into the daily routine and/or use environmental supports have shown promise. Recently, adherence-enhancing behavioral tailoring interventions that utilize novel technologies, such as electronic monitors and mobile phones, have been developed. Although interventions utilizing these platforms have the potential for widespread dissemination to a broad range of individuals, most require further empirical testing. This paper reviews selected behavioral tailoring strategies that aim to improve medication adherence and other functional outcomes among individuals with serious mental illness.*

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## Selected abbreviations and acronyms

<b>AEI</b>	<i>adherence-enhancing intervention</i>
<b>CAT</b>	<i>cognitive adaptation training</i>
<b>CBT</b>	<i>cognitive behavioral therapy</i>
<b>CI</b>	<i>confidence interval</i>
<b>EMA</b>	<i>ecological momentary assessment</i>
<b>Full-CAT</b>	<i>cognitive adaptation training focused on many aspects of functioning</i>
<b>MATS</b>	<i>Mobile Assessment and Treatment for Schizophrenia</i>
<b>MM</b>	<i>Med-eMonitor</i>
<b>MMAS</b>	<i>Morisky Medication Adherence Scale</i>
<b>MPR</b>	<i>medication possession ratio</i>
<b>PANSS</b>	<i>Positive and Negative Syndrome Scale</i>
<b>Pharm-CAT</b>	<i>cognitive adaptation training focused only on medication and appointment adherence</i>
<b>RCT</b>	<i>randomized controlled trial</i>
<b>TIPS</b>	<i>Telephone Intervention Problem Solving</i>

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medications among individuals with serious mental illness poses a significant challenge to treatment success, with 20% to 60% of people not taking their medications as prescribed.<sup>2-6</sup> Much research has sought to explain the causes of poor adherence in individuals with serious mental illness in order to develop effective adherence-enhancing interventions (AEIs). These risk factors include younger age, minority race, homelessness, poor illness insight, substance abuse, cognitive deficits, lack of social support, poor therapeutic alliance, persistent side effects, and practical problems (eg, financial, environmental, lack of routine).<sup>2,5,7-9</sup> Partial or complete nonadherence to psychiatric medications is associated with numerous adverse outcomes, including exacerbation and relapse of symptoms, impaired functioning, suicidal behavior, increased hospitalizations and emergency room use, and increased health care costs.<sup>2,5-8,10-11</sup>

Studies and reviews addressing the effectiveness of psychosocial AEIs have concluded that providing psychoeducation alone is ineffective for improving medication adherence in individuals with serious mental illness,<sup>12-15</sup> and interventions involving cognitive approaches, such as motivational interviewing (eg, adherence therapy), have produced mixed findings at best.<sup>15-16</sup> However, behavioral tailoring strategies that incorporate medication taking into the daily routine and use environmental supports (eg, reminders, medication packaging), monitoring, and reinforcement (including

monetary) are increasingly showing promise, and the results of selected studies employing these approaches are reviewed here. In addition, certain emerging interventions utilizing novel technologies, including electronic monitors and mobile phones, for the purpose of improving medication adherence (and often other domains of functioning) via behavioral tailoring are also described.

## Non-technology-based behavioral tailoring strategies for improving medication adherence

### Environmental supports in the home

Cognitive adaptation training (CAT) uses compensatory strategies and environmental supports tailored to a person's specific cognitive impairments in order to prompt several adaptive behaviors, including grooming, independent living skills, social and role performance, and medication adherence in the home environment. Both Full-CAT (CAT focused on many aspects of functioning, also including medication adherence) and Pharm-CAT (CAT focused only on medication and appointment adherence) employ supports for medication taking such as pill organizers, signs, missed-dose alarms, activity checklists, and other personalized approaches maintained in weekly 30- to 45-minute home visits from a CAT therapist. In a randomized controlled trial (RCT) in which 95 individuals with schizophrenia or schizoaffective disorder were randomized to Full-CAT, Pharm-CAT, or usual care for 9 months, percent adherence to antipsychotic medication was objectively evaluated by unannounced pill counts conducted in the home and through pharmacy refill records. On the basis of pill counts, both Full-CAT and Pharm-CAT were associated with improvements in antipsychotic adherence after 9 months of treatment relative to usual care ( $P=0.001$  and  $P=0.0001$ , respectively), effects that persisted 6 months after treatment was withdrawn ( $P=0.001$  and  $P=0.002$ , respectively). This corresponded to large effect sizes for both Full-CAT (1.09) and Pharm-CAT (1.05), with medication adherence approximating 80% in both treatment groups when averaged across the 15-month study period. The results using pharmacy refill records to measure adherence were only somewhat attenuated, with average effect sizes of 0.51 for Full-CAT ( $P<0.006$  vs usual care) and 0.33 for Pharm-CAT ( $P<0.07$  vs usual

care) over 15 months. Although there were no differences across study groups in positive psychotic symptoms ( $P$ 's > 0.09), both Full-CAT and Pharm-CAT were associated with reduced relapse ( $P < 0.004$  and  $P < 0.005$ , respectively), and at 9 months, Full-CAT was associated with improved functional outcome relative to Pharm-CAT ( $P = 0.0001$ ) and treatment as usual ( $P = 0.0001$ ), with no significant differences between the latter two groups.<sup>17</sup>

### Pharmacy-based reminders

Meds-Help is a pharmacy-based intervention consisting of unit-of-use medication packaging, a medication education session, and mailed refill reminders for patients, and notifications to clinicians when patients fail to fill prescriptions on time. A total of 118 veterans with schizophrenia, schizoaffective disorder, or bipolar disorder were randomly assigned to receive Meds-Help or usual care for 12 months. Pharmacy refill records were used to objectively measure the primary outcome, antipsychotic adherence, via the medication possession ratio (MPR), which indicates the percentage of time an individual has an adequate supply of medication for continuous treatment. A composite adherence measure (CAM) combining the MPR, patient self-report, and a blood test indicating the presence of some antipsychotic medication was also analyzed. Relative to usual care, participants receiving Meds-Help experienced significant improvements in adherence to antipsychotic medications, with average MPRs increasing from 0.54 ( $\pm 0.20$ ) at baseline to 0.86 ( $\pm 0.30$ ) after 12 months, compared with average MPRs of 0.55 ( $\pm 0.19$ ) at baseline and 0.62 ( $\pm 0.33$ ) at 12 months in the control group ( $P < 0.0001$ ). Furthermore, the percentage of individuals considered adherent on the CAM increased from 0% to 34.0% after 12 months in the Meds-Help group, while only increasing from 0% to 17.7% in the control group (adjusted odds ratio [AOR], 5.41; 95% confidence interval [CI], 1.61-18.12). No differences were observed in psychiatric symptoms ( $P = 0.67$ ), quality of life ( $P = 0.65$ ), or patient satisfaction ( $P = 0.39$ ) between the groups, though power to detect small effects was limited.<sup>18</sup>

### Telephone reminders

In a study by Montes et al,<sup>19</sup> psychiatric nurses provided once-monthly telephone calls in which medication ad-

herence and attitudes toward antipsychotic treatment were assessed, reports were provided to prescribing psychiatrists, and additional psychiatrist visits were scheduled when nonadherence was detected. A total of 928 clinically stable individuals with schizophrenia were randomized to receive the monthly telephone calls or routine care for 4 months, and for the primary outcome, participants were classified as adherent ( $\geq 60\%$  of doses taken) or nonadherent ( $< 60\%$  of doses taken) to antipsychotic treatment; this classification was made by their psychiatrists and the study nurses, who were not blind to treatment assignment. Among those receiving monthly telephone calls, the percentage of participants classified as adherent increased from 88.2% to 96.7% at 4-month follow-up, compared with an increase from 90.0% to 91.2% in the control group ( $P = 0.0007$ ). In multivariable analysis, receipt of telephone calls was associated with a higher likelihood of being considered adherent to antipsychotic treatment (AOR, 3.3; 95% CI, 1.6-6.6;  $P = 0.0001$ ). In addition, subjective attitudes toward medication ( $P < 0.0001$ ) and clinician ratings of the degree of change in positive ( $P = 0.0088$ ), depressive ( $P = 0.01$ ), cognitive ( $P = 0.02$ ), and global ( $P = 0.0099$ ) symptoms were significantly better at the 4-month follow-up in the intervention group than in the control group. There were no significant differences in hospital admissions or quality of life between the groups. Limitations of this study included the subjective measure of medication adherence, non-blind raters of outcomes, and the relatively high rates of adherence throughout the study.

### Financial incentives

Priebe et al<sup>20</sup> conducted a RCT in which 141 individuals with schizophrenia spectrum or bipolar disorders who were prescribed long-acting injectable antipsychotic medications but had received 75% or less of prescribed injections were randomized to receive modest financial incentives (\$22) for each injection received or to usual care over 12 months. This study showed that participants that were provided the monetary incentives received a significantly higher percentage of prescribed injections, with adherence increasing from 69% ( $\pm 16\%$ ) at baseline to 85% ( $\pm 15\%$ ) after 12 months, compared with 67% ( $\pm 16\%$ ) at baseline and 71% ( $\pm 22\%$ ) at follow-up among those randomized to treatment as usual ( $P = 0.0003$ ). Furthermore, the percentage of individuals

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achieving  $\geq 95\%$  adherence increased from 7% to 28% in those receiving financial incentives, compared with an increase from 2% to 5% in the control group ( $P=0.003$ ). Those receiving financial incentives also had significantly better subjective quality-of-life ratings ( $P=0.002$ ), but clinician-rated clinical improvement ( $P=0.174$ ), patient satisfaction with medications ( $P=0.610$ ), and hospital admissions, which were infrequent, did not differ between the groups.

## Summary

The results of several methodologically robust studies suggest that behavioral tailoring strategies that are incorporated into a person's daily life, including tailored environmental supports in the home that cue medication taking—such as specialized medication packaging, prescription refill reminders, periodic telephone reminders by mental health providers, monetary reinforcements, and providing adherence information to clinicians—address several important risk factors for adherence problems and can improve adherence to psychiatric medications in individuals with serious mental illness. However, because implementation of these strategies in the real world may prove labor intensive (eg, use of specially trained providers for weekly home visits or periodic telephone contacts) and costly (eg, through provision of ongoing financial incentives to patients), they may prove unsustainable in regular clinical practice.

## Technology-based behavioral tailoring strategies for improving medication adherence

### Computerized relational agents

Bickmore et al<sup>21</sup> developed a home-based computerized system consisting of an animated relational agent capable of conducting simulated face-to-face conversations in order to promote medication adherence in individuals with schizophrenia by establishing an emotional relationship with the person and providing consistent social support. During a 1-month uncontrolled pilot study, 20 individuals with schizophrenia were provided with laptop computers and were expected to have daily 10-minute interactions with the agent in the home, coinciding with the time a dose of antipsychotic medica-

tion was due, for 31 days. During each session, the agent inquired about medication taking/adherence behavior, provided positive reinforcement or tips for solving adherence problems tailored to the reason for nonadherence, reviewed charts tracking self-reported adherence over time, assisted in setting behavioral goals, and provided reminders to refill prescriptions. Users interacted with the agent by selecting from a menu of preformatted responses. Twice during the study, the system also provided brief educational modules on topics including managing side effects of medications and using cues to schedule medication taking. Regarding the 13 out of 20 participants who used the system for at least 4 days, individuals interacted with the agent on 66% of available days. Adherence to antipsychotic medication was assessed through self-reports provided during interactions with the agent, with daily adherence averaging 85% ( $\pm 26\%$ , range=8% to 100%) during the study. Satisfaction with the system was high, though a few participants had difficulties using it, including one person experiencing paranoia related to interacting with the agent.

Although promising, additional investigation of these types of systems is needed in order to augment the findings of this initial pilot work.

### Electronic monitors

Frangou et al<sup>22</sup> evaluated the effects of a medication-adherence telemonitoring system (@HOME) that included an electronic dispenser that fit on standard prescription bottles and recorded the date and time of bottle openings. Adherence data were automatically transmitted electronically to a Web site accessible by patients and their caregivers, as well as by their clinicians, who received alerts from the system if adherence dropped below 50% within a given week. In this study, 108 individuals with schizophrenia who were prescribed oral antipsychotic medication were randomized to one of three groups for 8 weeks. Adherence among those randomized to @HOME was objectively measured via the system's electronic medication dispenser. Participants could also be randomized to a pill-counting group in which hospital pharmacists assessed adherence via counting the number of pills returned versus dispensed, or to a control group, which received usual care and for whom medication adherence was assessed via the self-reported Morisky Medication Adherence

Scale (MMAS).<sup>23</sup> The respective methods of measuring adherence were used to produce estimates of the percentage of medication doses taken as prescribed over the study period for each group. Average medication adherence after 8 weeks was found to be 92.3% ( $\pm 4.8\%$ ) in the @HOME group, which was significantly higher than that in the pill-counting ( $78.5\% \pm 14.0\%$ ;  $P=0.007$ ) and control ( $77.3\% \pm 22.1\%$ ;  $P=0.001$ ) groups. In addition, after 8 weeks, the @HOME group had significantly greater improvement in psychotic symptoms than the control group ( $P=0.04$ ), significantly greater improvements in Clinical Global Impression Scale ratings relative both to the pill-counting ( $P=0.04$ ) and control groups ( $P=0.01$ ), and fewer medical ( $P's=0.01$ ) and crisis ( $P's=0.0001$ ) visits than both other groups. Limitations of this study included its relatively short duration and that adherence was measured differently, and not always objectively, across the three groups.

Velligan et al<sup>24</sup> conducted a RCT to compare the effects of 9 months of the previously described Pharm-CAT intervention, an electronic Med-eMonitor (MM), and treatment as usual on adherence to antipsychotic medication among 142 individuals with schizophrenia or schizoaffective disorder. In the MM group, a therapist trained and assisted participants in accurately filling the MM in the home, after which the device had to be refilled by participants when new prescriptions were obtained. This particular electronic device cued the taking of medication, provided warnings if the wrong medication was taken or a medication was taken at the wrong time, and automatically transmitted adherence data via a secure Web site to alert staff of failures to take medication, after which the MM therapist intervened via telephone using a standardized script to address common adherence barriers. For all participants, medication adherence was assessed objectively by monthly unannounced in-home pill counts and by electronic monitors, which measured both container openings and participants' reports of ingesting pills, but were only activated to cue adherence in the MM group. Based on electronic monitoring, adherence to antipsychotic-medication regimes in both Pharm-CAT and MM groups was significantly higher at all time points relative to usual care (all  $P's < 0.0001$ ); there were no differences between the two active treatments (all  $P's > 0.43$ ). This corresponded to large effect sizes for both Pharm-CAT (1.03) and MM (0.98), with medication adherence averaging 91% for MM, 90% for Pharm-CAT, and 72%

for usual care across the 9-month study. Based on pill counts, average medication adherence was significantly higher in the Pharm-CAT group (91%) than in both the MM (86%;  $P=0.04$ ) and control (80%;  $P=0.0001$ ) groups, with no significant difference between the MM and control groups ( $P=0.072$ ). There were no significant differences across the three groups in symptoms or functioning ( $P's > 0.09$ ) or use of emergency services ( $P=0.77$ ).

Most recently, Sajatovic et al<sup>25</sup> described the usability and feasibility of a technology-enabled AEI in five individuals with bipolar disorder during a 15-day pilot study. The intervention consisted of an electronic pill cap intended for use with standard medication bottles; it recorded all openings and displayed for the user's information the hours since the last opening and total openings in the last 24 hours. Completion of interactive-voice-response calls were required to transfer adherence data from the pill cap to a report for providers. The intervention also included a multimedia adherence-enhancement program designed to educate participants about illness knowledge and self-management skills, and financial incentives were provided when various components of the intervention and study assessments were completed. Though only three out of five (60%) participants made complete use of the system over the 15 days due to difficulties arising from the sensors not adequately fitting medication containers, usability and acceptability ratings of the system were high. A full analysis of the impact of the system on other outcomes (eg, self-reported adherence, bipolar disorder symptoms, treatment knowledge) was not possible due to the small sample included in this pilot study, which focused on the feasibility of the intervention.

## Summary

Electronic medication monitors represent a mostly usable and acceptable method to measure and cue medication-taking behaviors among individuals with serious mental illness. The available studies provide suggestive evidence that these features, in conjunction with the data they provide clinicians, play a role in improving medication adherence, though extension and replication of these findings is needed, particularly in individuals with bipolar disorder. Although the use of such monitors has the potential for increasing the reach of AEIs, the available devices remain relatively cost pro-

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hibitive for individuals with serious mental illness and for public mental health systems.<sup>26</sup> Also, it is not entirely clear from the available studies if the observed benefits of electronic monitors can be achieved only when they are used in combination with other supports—eg, a case worker who intervenes when problems with adherence arise—which would add to the costs and complexity of the deployment of these devices. Also, in some cases medications must be transferred to the electronic dispensers by the individuals themselves, who may have cognitive or motivational difficulties in repeatedly completing this task, prefer traditional medication containers or pill boxes, or require childproof containers.<sup>24-25</sup> Furthermore, not all monitors track bottle openings remotely, requiring return visits or periodic downloading of data from medication vials in order for clinicians to access and track adherence data.<sup>25</sup> Practically, the devices are often too bulky to keep on one's person and separate dispensers are needed to accommodate polypharmacy.<sup>26</sup> These and other characteristics of these devices limit their current utility in regular clinical practice.

## Mobile health (mHealth) technologies

### Personal digital assistants

Wenze et al<sup>27</sup> described a mobile technology-based intervention focused on improving adherence to both medications and appointments in bipolar disorder. The intervention consisted of ecological momentary assessments (EMAs) of common prodromal symptoms of bipolar disorder and other risk factors for nonadherence; the EMAs were delivered on personal digital assistants (PDAs) at 10:00 AM and 5:00 PM daily. The risk factors included knowledge about and trouble remembering appointments and medications, and self-report of adherence behaviors, concerns about medication side effects, and doubts regarding overall helpfulness of treatment or need for treatment when feeling well. Preformatted feedback was provided when problems or concerns were reported. Fourteen individuals with bipolar disorder were enrolled in a 2-week pilot feasibility trial of the intervention and were reimbursed \$1 for each of the 28 EMA surveys completed. All 14 participants completed the trial and self-reported not taking medications in only 3% ( $\pm 4\%$ ) of EMAs of adherence behaviors, which did not change over the course of the study ( $P=0.16$ ). Clinical assessments of depressive

( $P=0.05$ ), but not manic ( $P=0.80$ ), symptoms decreased significantly from baseline to follow-up. To incorporate participant feedback on the intervention derived from this pilot study, a larger RCT of an expanded version of the intervention delivered via smartphones and augmented with in-person sessions is currently underway.<sup>27</sup>

### Text messaging

Granholm et al<sup>28</sup> developed Mobile Assessment and Treatment for Schizophrenia (MATS), a text-messaging intervention incorporating cognitive behavioral therapy (CBT) techniques that challenge unhelpful beliefs and provide personalized behavioral coping strategies for medication adherence, socialization, and auditory hallucinations. In an uncontrolled pilot trial, 55 individuals with schizophrenia or schizoaffective disorder received three sets of four text messages that used CBT techniques to assess and intervene on each of the three domains at random times 6 days a week for 3 months. Participants received modest monetary incentives every 2 weeks for responding to the sets of text messages. For the purpose of analysis, medication adherence was assessed via responses to the text-message assessments of whether participants self-reported taking their medications each day. Thirteen participants (23.6%) with more severe negative symptoms, lower functioning, and lower premorbid IQ did not complete the trial. Among the 42 completers, self-reported medication adherence improved over the 3-month study, but only in participants living independently who did not receive assistance with medication administration ( $P=0.003$ ). Whereas number of social interactions self-reported via text messaging also increased ( $P=0.033$ ) and self-reported severity of auditory hallucinations decreased significantly ( $P=0.020$ ), there were no changes in laboratory-based assessments of symptoms and functioning during the study.

Telephone Intervention Problem Solving (TIPS) is a manualized, provider-initiated intervention in which nurses provide weekly support by telephone to community-dwelling individuals with schizophrenia; support involved six domains, including taking medications, attending appointments, coping with symptoms, abstaining from drugs and alcohol, getting along with others, and other problems specified by the individual. During the calls, nurses guide individuals through a problem-solving process to identify difficulties in each domain,

and suggest and assess the effectiveness of coping strategies or other solutions for addressing difficulties.<sup>29</sup> A daily text-messaging adaptation of TIPS was also developed, in which individuals receiving text messages are asked to respond to a different multiple-choice question daily, addressing each of the aforementioned domains, with questions repeating every 6 days. In a recent study, 30 individuals with schizophrenia or schizoaffective disorder were randomized to receive weekly TIPS calls (TIPS only), daily text messages (texting only), or both (TIPS plus texting) for 3 months. Percentage adherence to oral psychiatric and nonpsychiatric medications was objectively assessed by monthly scheduled in-home pill counts, and percentage adherence to intramuscular antipsychotic medication was assessed via medical record review. Whereas those in the TIPS-plus-texting group had significantly lower psychiatric symptom scores than those in the other two groups after 3 months ( $P=0.005$ ), there were no significant differences in psychiatric ( $P=0.31$ ) or nonpsychiatric ( $P=0.71$ ) medication adherence across the three groups. Difficulties in detecting differences in medication adherence across three active interventions may have been further heightened by the modest group sample sizes and because almost half of the sample was receiving intensive case-management services that included daily home delivery of medications by treatment staff.<sup>30</sup>

Montes et al<sup>31</sup> conducted one of the only RCTs to date of an intervention exclusively targeting antipsychotic-medication adherence, in which 340 individuals with schizophrenia were randomized to receive either text message reminders to take their medication—at their choice of either 11:00 AM or 2:00 PM daily—or usual care for 3 months. Changes in self-reported adherence to antipsychotic treatment were assessed using the 4-item MMAS, with higher scores indicating worse adherence.<sup>23</sup> Among the 340 individuals enrolled in the study, 25% ( $n=86$ ) were excluded from analyses due to major protocol deviations or not properly receiving the text messages on their phones for 7 consecutive days. After 3 months, individuals receiving daily text messages had significantly greater mean reductions in MMAS total scores ( $-1.0$ ; 95% CI,  $-1.02$  to  $-0.98$ ) compared with usual care ( $-0.7$ ; 95% CI,  $-0.72$  to  $-0.68$ ) ( $P=0.02$ ), an effect that was maintained 3 months after the intervention concluded ( $P=0.04$ ). Additionally, those randomized to receive text messages had significantly better ratings of attitudes toward medication ( $P=0.0003$ ) and quality of

life ( $P=0.03$ ) and a greater degree of change in negative ( $P=0.02$ ), cognitive ( $P=0.01$ ), and global ( $P=0.012$ ), but not positive ( $P=0.1$ ) or depressive ( $P=0.07$ ), symptoms than in the control group after 3 months.

### Smartphone applications

Recently, Ben-Zeev et al developed<sup>32</sup> and pilot tested<sup>33</sup> the first smartphone-based illness self-management system for individuals with schizophrenia spectrum disorders. The application, FOCUS, provides both pre-scheduled and on-demand resources to facilitate self-management of psychotic symptoms, mood problems, medication adherence, social functioning, and sleep disturbances. In a 1-month uncontrolled trial, 33 individuals with schizophrenia or schizoaffective disorder were prompted to complete assessments three times daily on medication adherence and two other relevant domains among auditory hallucinations, mood, social interactions, and sleep difficulties; if difficulties were endorsed, the system provided brief, tailored feedback including self-management strategies. This study showed that individuals with schizophrenia spectrum disorders can feasibly use smartphone applications like FOCUS, which received high ratings on acceptability and usability from participants. On-demand, user-initiated interactions accounted for greater use of the application (62.5%) than responses to prescheduled prompts (37.5%). While there were no changes in beliefs about medications, negative symptoms, or sleep difficulties, there were significant within-group reductions in Positive and Negative Syndrome Scale (PANSS) total ( $P=0.002$ ), positive ( $P<0.001$ ), and general psychopathology ( $P<0.001$ ) scores, as well as significant reductions in depressive symptoms ( $P=0.003$ ) after 1 month of use of FOCUS.

With funding from the National Institute of Mental Health (under award number R34 MH0945555; principal investigator: J. Kreyenbuhl), we developed MedActive, a smartphone intervention for improving adherence to antipsychotic treatment in individuals with schizophrenia. The MedActive smartphone application delivers personalized reminders to individuals to take their antipsychotic medications at the prescribed times each day. Positive reinforcement/motivational feedback is provided when medications are taken as prescribed; otherwise, individuals are queried about reasons for not taking their medications and provided with brief,

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motivational feedback tailored to the reason for non-adherence. Once daily, individuals are also prompted to report on the occurrence of common antipsychotic side effects and the presence of positive psychotic symptoms, and tips for self-management and talking to one's doctor about medication concerns are provided. Summaries of these EMAs of adherence, side effects, and symptoms are made available to the individual on the smartphone and to their prescriber through a secure, online clinician interface, which enables both patients and prescribers to track the effects of the medication over time and facilitates shared decision making regarding antipsychotic treatment. Pilot testing of MedActive demonstrating its feasibility and acceptability in both individuals with schizophrenia and their prescribers has been completed, and will be described in more detail in separate reports.

## Summary

Several reviews of mHealth applications in general and text messaging specifically have shown them to be effective in changing health behaviors, including medication adherence, as well as improving clinical outcomes for a number of nonpsychiatric medical conditions (eg, diabetes, asthma, human immunodeficiency virus, obesity, smoking cessation).<sup>34-40</sup> Although experience is more limited, mHealth applications involving mobile phones and similar technologies are increasingly being developed for both the assessment and treatment of serious mental illnesses, including for improving adherence to antipsychotic treatment,<sup>41</sup> as reviewed above.

With the exception of a single large controlled study of text messaging,<sup>31</sup> most available mHealth AEs for serious mental illness have undergone only preliminary phases of evaluation. More research employing controlled designs in studies of durations longer than several weeks to a few months and that use objective measures of adherence are needed to establish more definitively whether these mHealth AEs improve medication adherence. Furthermore, while the vast majority of individuals with serious mental illness have not had difficulties operating mobile technologies, it appears that certain subgroups, eg, with significant cognitive impairments or motivational deficits, may require additional supports. In addition, whereas mHealth AEs seem to be most helpful in people for whom nonadher-

ence is unintentional (ie, related to forgetting), some interventions are necessarily employing CBT and motivational techniques to address intentional nonadherence (ie, related to not believing medications are helpful or needed) as well.

Mobile phone technologies possess a number of attributes that make them ideal for AEs for individuals with serious mental illness. Due in part to their relatively low cost, mobile phones are the most commonly used form of technology worldwide.<sup>42</sup> Recent research has shown that 85% of individuals with mood disorders and 63% with schizophrenia own mobile phones.<sup>28</sup> While these rates are somewhat lower than in the general population, research has shown that many of these individuals express interest in using mobile technology to receive reminders to take medications or about appointments, to communicate with providers, and to receive psychoeducation and information about mental health treatment and services.<sup>43</sup> Despite having some challenges that might impede their use of mobile technologies (eg, lower socioeconomic status, cognitive impairments), many people with serious mental illness own, are familiar with, and are interested in using these technologies for a variety of purposes, including for improving health.

Beyond their relatively low cost and growing accessibility, mobile phones are small and convenient to carry. They offer mobile computing functions, including advanced voice, text messaging, data, and media capabilities, yet require little technical expertise to operate. Two-way communication via voice or text messaging offers users a sense of privacy and comfort that may ameliorate traditional barriers in the treatment of psychiatric disorders, in particular.<sup>44-45</sup> Importantly, mobile phone technologies allow for in-the-moment, personally tailored health communication and reinforcement, and are particularly well suited for ecologically valid health-behavior change interventions. Such ecological momentary interventions are provided to people as they go about their daily lives, while they are in their natural settings, and at the specific times they are in need of assistance. In addition to serving as environmental supports (eg, by providing reminders to take prescribed medications), these interventions are well suited for monitoring the effectiveness of treatments, including the occurrence of side effects or other adherence barriers, and for prompting strategies for managing or surmounting them in real time.



## Conclusion

Psychoeducation and motivational strategies alone have proven largely ineffective in improving medication adherence among individuals with serious mental illness,<sup>12-16</sup> but accumulating research suggests that approaches employing behavioral tailoring that incorporate medication taking into the daily routine and/or use environmental supports and reinforcement show promise. For example, large controlled studies of interventions employing tailored environmental supports for medication taking in the home, specialized medication packaging and prescription refill reminders, periodic telephone reminders provided by mental health staff, modest monetary reinforcements, and provision of adherence information to clinicians have all shown positive effects on adherence and, in some studies, on related outcomes such as relapse. However, evaluations of the cost effectiveness of these somewhat intensive interventions have not been conducted to date and will probably be necessary before many payers will consider implementation.

Increasingly, novel technologies such as electronic medication dispensers and mHealth interventions delivered via mobile phones for improving adherence are being developed and have undergone preliminary feasibility testing. Although AEs utilizing these platforms have the potential for widespread dissemination to a broad range of individuals with serious mental illness, most require further empirical testing to determine their effects on medication adherence and other domains of functioning. In addition, although mobile phones in particular are relatively low cost and have the potential for replacing some face-to-face contact with health care professionals, formal economic evaluations of AEs employing these technologies are also needed, especially if additional supports (eg, ongoing assistance by mental health staff) are required for some individuals with serious mental illness to obtain maximum benefit. □

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# Clinical research

## Una revisión de estrategias conductuales para mejorar la adherencia en la enfermedad mental grave

La falta de adherencia a los tratamientos psicofarmacológicos constituye un desafío significativo para el éxito terapéutico de sujetos con enfermedad mental grave, dado que hay más del 60% de personas que no toma sus medicamentos psiquiátricos como son prescritos. La falta de adherencia está asociada con resultados adversos, incluyendo la exacerbación de los síntomas psiquiátricos, el deterioro funcional, el aumento de las hospitalizaciones y de la consulta en servicios de urgencia, como el aumento de los costos de salud. Mientras que las intervenciones que utilizan aproximaciones de psicoeducación o cognitivas, tales como la entrevista motivacional, han demostrado ampliamente la ineficacia para mejorar la adherencia, las aproximaciones que emplean ajustes conductuales incorporando la ingesta de medicamentos dentro de la rutina diaria y/o el empleo de soportes ambientales han mostrado ser prometedoras. Recientemente se han desarrollado intervenciones conductuales que refuerzan la adherencia mediante el empleo de nuevas tecnologías como son los monitores electrónicos y los teléfonos móviles. Aunque las intervenciones que utilizan estas plataformas tienen el potencial de una amplia diseminación a una gran cantidad de individuos, la mayoría requiere de más pruebas empíricas. Este artículo revisa estrategias conductuales que tienen como objetivo mejorar la adherencia a la medicación y otros resultados funcionales entre individuos con enfermedad mental grave.

## Les stratégies d'adaptation comportementale et leur utilisation pour améliorer l'observance médicamenteuse dans la maladie mentale grave

La non-observance des traitements psychopharmacologiques pose un problème important pour la réussite du traitement chez les personnes atteintes de maladie mentale grave, plus de 60 % des individus ne prenant pas les médicaments psychotropes tels qu'ils leur ont été prescrits. La non-observance est associée à des événements indésirables, y compris l'exacerbation des symptômes psychiatriques, la détérioration fonctionnelle, l'augmentation des hospitalisations et des passages aux urgences et l'augmentation des coûts des soins de santé. Les procédures utilisant des approches cognitives ou psychoéducatives, comme l'entretien motivationnel, se sont montrées largement inefficaces pour améliorer l'observance. Au contraire, les stratégies d'adaptation comportementale qui intègrent la prise de médicaments aux activités quotidiennes et/ou l'utilisation de différents supports facilitant l'observance, sont prometteuses. Récemment, des stratégies d'adaptation comportementale favorisant l'observance qui utilisent les nouvelles technologies, comme les moniteurs électroniques et les téléphones mobiles, se sont développées. Les procédures utilisant ces plateformes pourraient être diffusées de façon généralisée à un large éventail d'individus, mais la plupart d'entre elles ont besoin d'une vérification empirique complémentaire. Cet article analyse quelques stratégies d'adaptation comportementale dont le but est d'améliorer l'observance médicamenteuse et d'autres résultats fonctionnels chez les individus atteints de maladie mentale grave.

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