Systematic Literature Review of Text Messaging Interventions to Promote Medication Adherence Among People With Serious Mental Illness

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Objective: Mobile health tools are feasible options to encourage behavior change among patients with serious mental illness. Mobile health tools vary widely, both in platforms used and content delivered. This literature review assessed the use of text messaging interventions to promote medication adherence among patients with serious mental illness.

Methods: A systematic literature review using PRISMA guidelines examined short message service (SMS) text messaging interventions promoting medication adherence to people with a serious mental illness diagnosis. Databases included PubMed, Cochrane, CINAHL, and PsycINFO. Data extraction included demographic information, participant diagnoses, intervention components, medication class, adherence measures, research design, and study outcomes. Study quality was also assessed.

Results: Of 114 full-text articles screened, 10 articles were selected from nine unique interventions (N=937 people with serious mental illness). Study durations ranged from 30 days to 18 months, with frequency of SMS ranging from twice weekly to 12 times daily. Of the nine unique trials, most reported using an automated server to deliver SMS messages (N=7), two-way SMS capabilities (N=6), customized message content or timing (N=7), and additional components (e.g., provider contact, educational content, and monetary rewards) (N=7). Seven of the 10 articles reported statistically significant improvement in medication adherence and in at least one clinical outcome.

Conclusions: Evidence to date indicates that text messaging interventions are feasible and appear to improve medication adherence and clinical outcomes among patients with serious mental illness. Future research should assess implementation approaches and how to scale up efforts in nonresearch settings.

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Serious mental illness can have an impact on cognitive, social, and occupational functioning; add stress to family units; and ultimately decrease quality of life (1–5). The scientific literature maintains that adherence to evidence-based medications can dampen symptomatic disease and, in turn, improve global functioning and quality of life (6–10). However, medication nonadherence is a pervasive problem for individuals with serious mental illness, with rates of partial or total nonadherence between 40% and 50% (11–14). Drivers of nonadherence are complex, including unintentional nonadherence factors (i.e., forgetfulness), which in part stem from illness symptoms and poor baseline functioning (e.g., poor insight into illness, impaired cognition, and apathy), and intentional nonadherence factors (e.g., negative attitudes toward medications, aversion to side effects, and past treatment ineffectiveness) (11, 12, 15).

Furthermore, defining what constitutes nonadherence is also complex. For example, categorizing patients into binary

HIGHLIGHTS

- This systematic review demonstrated that use of short message service (SMS) platforms to increase medication adherence among people with serious mental illness is feasible and effective.
- One- and two-way messaging, customized and standardized content, and frequency of messaging ranging from infrequent messages to several daily messages led to appreciable improvement in medication adherence.
- Of 10 selected articles, seven reported a significant improvement in medication adherence after the intervention and at least one significant improvement in a clinical outcome.
- Research is needed to assess implementation approaches and how to scale up interventions in a clinical setting.

adherent versus nonadherent groups fails to capture the difference between those who take none of their medications versus those who take them 50% of the time. It also neglects other potentially clinically relevant dimensions, such as the timing of taking medications or what circumstances surround missing doses. Indeed, expert consensus on capturing adherence suggests that using multiple methods to capture adherence and quantifying the proportion of missed drug or doses are useful approaches (16).

Technological platforms are increasingly utilized to promote patient wellness and treat disease across many diverse illnesses and patient populations (17–20). Given the potential for downstream effects on patient and clinical outcomes, medication adherence has been a target of such platforms. In the era of the COVID-19 pandemic, the normativity and culture around remote health care delivery are rapidly shifting, with long-term implications (21, 22). However, "technological platforms" represent a heterogeneous group of services—from mobile applications, video conferencing, and Web browsers to smart-home technology and wearable devices (23–26)—with equally diverse intervention content and goals. This variety creates a practical challenge for researchers and clinicians interested in implementing technological platforms effectively.

A large body of research suggests that mobile health, or mHealth, interventions are feasible, acceptable, and efficacious for persons with serious mental illness (27–38). In an early systematic literature review on mobile and Web-based text messaging in mental health, a notable rise in efforts to implement mHealth platforms was observed across several diverse patient populations, starting around 2006. These studies predominantly assessed feasibility and acceptability by patients (27). Similarly, another systematic literature review reported acceptance and feasibility of online, social media, and mobile technologies in treating psychosis (28). Earlier systematic literature reviews also reported on the expansion of technology to address medication adherence specifically among patients with mental health concerns, such as schizophrenia (31–33). Furthermore, more recent systematic literature reviews provided greater evidence for improved outcomes, such as increased clinical engagement and medication adherence, through mHealth interventions in populations with serious mental illness (30, 35, 38).

On the whole, most of the previous reviews have included a variety of intervention delivery platforms, treatment goals, and clinical diagnoses. This systematic literature review aimed to supplement the current literature on mHealth platforms targeting treatment of individuals with serious mental illness by focusing on a specific subset of intervention delivery methods, treatment goals, and clinical conditions—namely, mobile text messaging, or short message service (SMS), to promote medication adherence among patients with serious mental illness. This focus may be particularly practical considering favorable estimates of cell phone ownership, a relatively low skill set required for usability (39), and the importance of daily medication adherence among people with serious mental illness. In this systematic literature review, serious mental illness was defined as one of the following diagnoses: schizophrenia spectrum disorders, bipolar disorders, major depressive disorder, and otherwise unspecified psychosis, because there is clear evidence of the need for pharmacotherapy in the treatment of these conditions (40–42). We used the systematic approach outlined below to answer four questions: What is the literature on the use of text messaging to promote medication adherence? What properties of a text messaging intervention have been shown to be efficacious in enhancing medication adherence? What are common limitations or pitfalls to using text messaging to promote adherence? What questions or next steps in research are suggested by the current body of work?

METHODS

Literature Search

The search protocol outlined below followed PRISMA guidelines (43). PubMed (MEDLINE), Cochrane, CINAHL, and PsycINFO databases were searched in February 2021. Boolean logic was used to combine search terms to find relevant indexing to represent adherence promotion interventions with text messaging. The literature search used the following terms: "medication adherence," "serious mental illness," and "text-messaging," along with other closely related or synonymous words.

Inclusion and Exclusion Criteria

Inclusion of articles was based on the following criteria: peer-reviewed literature written in English; original research reports; prospective interventional studies; research involving humans only; research involving any age group; and research involving patients with a serious mental illness diagnosis, which was defined as major depressive disorder, bipolar disorder, schizophrenia or schizoaffective disorder, or other psychotic disorder based on self-report, clinical evaluation, standardized diagnostic interview, or medical record diagnosis. Additionally, the study intervention must have assessed or promoted medication adherence by using a standardized medication questionnaire or quantitative measure of medication—and not solely by assessing changes in attitudes about medication or endorsing yes or no regarding taking medications as prescribed at only two time points. The intervention must also have included a text messaging component that offered the following: medication reminders, health education, encouragement or health promotion, or prompts to which a patient could respond; the intervention consisted of more than appointment reminders or data collection. The SMS component could be automated or delivered by a clinician, nurse, researcher, etc., and participants could have additional comorbid diagnoses. Similarly, medication adherence did not need to be specific to medications prescribed for serious mental illness (i.e., adherence to hypertension medications by patients with major depressive disorder was permissible).

Exclusion criteria from the study included the following: studies in which the SMS intervention was a simple notification regarding an appointment or for the sole purpose of data collection; interventions in which patients used mobile applications to receive messages or interact but in which no SMS was used; studies that assessed medication adherence based only on patients' opinions or attitudes toward medication, without any measurement of how often the patient was taking any given medication; opinion pieces or editorials; other literature reviews; literature that described only research methods, with no interventional component; case studies (fewer than five were found); studies that reported only on access or availability of technology; reports that described only methods (no outcome data); book chapters; and posters or conference abstracts.

Data Extraction

Data extracted included the components of the intervention, psychiatric disorder, care setting, number of participants, primary outcomes, secondary outcomes, comorbid conditions, adherence measurements, duration of the intervention, medication class, one-way versus two-way SMS, frequency of SMS, automated versus care provider–generated messages, SMS content, research design, medication adherence change, and the demographic characteristics age, gender, race-ethnicity, and socioeconomic status (SES) or employment. Both qualitative and quantitative data were collected regarding text messaging and medication adherence.

Study Quality Assessment

Quality assessment of the studies was completed by using the adapted Methodological Quality Rating Scale (MQRS) (44). The MQRS is a widely used tool to evaluate the quality of studies on the basis of several components: study design, replicability, baseline characteristics, quality control, follow-up length, intervention dosage, collaterals and objective verification, attrition, statistical power, independent outcomes assessment, statistical analyses, and number of study sites. Scores on the MQRS can range from 0 to 17, with higher scores indicating greater methodological quality.

RESULTS

Study Characteristics

Of 114 publications identified, 11 met initial inclusion criteria. One publication was excluded because it was an additional analysis of the same study sample and no new adherence data were reported. One publication represented an extension of a previously reported intervention that was included because it provided additional medication adherence data. Thus, 10 publications, including nine unique interventions, underwent data extraction (a CONSORT diagram is provided in an online supplement to this article) (45–55). Characteristics of the 10 publications are shown in Table 1. Seven of the 10 publications were randomized controlled trials (RCTs) (45, 47, 48, 50, 51, 53, 54), including one stepped-wedge RCT (54). One publication was a prospective cohort study (52), and one publication piloted an intervention without a comparison group (49). Finally, one publication employed nonrandomized allocation of participants into intervention or comparison groups (46).

A total of 937 people with serious mental illness were included in the 10 studies. Of the nine unique participant samples, the diagnostic breakdown included 610 with schizophrenia, 47 with schizoaffective disorder, 220 with bipolar disorder, and 60 with major depressive disorder. All participants were outpatients. Care settings included community-based mental health programs, psychiatric clinics, residential programs, and academic medical or research centers. Most of the nine samples were collected in the United States (47–49, 52, 53). The other studies were conducted in rural China (45, 54), urban Iran (46), Spain (50), and India (51).

The mean±SD age of participants was 44.6±6.2, and 44.1% of the participants were women. SES was reported for three of the study populations: in two, most participants were classified as having low SES (45, 51), and in the other study, most were classified as having moderate SES (46). The five samples from populations based in the United States included the following racial or ethnic data: in two studies, most participants were Black (85% [47] and 73.7% [52]); in one study, 50% of participants were Black (48); and in two studies, most participants were White (74% [49] and 54% [52]).

Study durations ranged from 30 days to 18 months (Table 1), with some studies capturing data after a period without the intervention, allowing for analysis of extinction or maintenance of study outcomes (45, 50, 51, 54). One intervention obtained baseline data for a month prior to implementing the intervention, providing more robust baseline data than self-report alone (52).

Interventions

SMS intervention delivery, structure, and frequency. Although all nine interventions used SMS, the format, timing, and frequency of these messages varied (Tables 2 and 3). Seven of the nine interventions reported use of an automated server to deliver messages (45–47, 49, 50, 52, 53) and allowed for or prompted a response from participants (i.e., six studies used two-way SMS capabilities [45, 47–49, 52, 53]). One of the interventions delivered messages via the principal investigator (48), and one did not report delivery method (51). In three of the interventions, no responses were provided by participants (i.e., one-way SMS capabilities) (46, 50, 51). In five interventions, participants were able to customize the content of the messages (47–49, 52, 53), and in six interventions, they were able to customize the timing for receipt of the messages (47, 49–53). Customization included simple choices, such as selecting reminder or reinforcement stems from a predetermined list (53), patient-created symptom surveillance (47), or reminder content (52, 53).

TABLE 1. Demographic, setting, and duration characteristics and quality scores of 10 articles included in the systematic review[a]

Article	Mean age	Women N	Women %	Socioeconomic status	Race-ethnicity	Location	Recruitment care setting	Study duration	MQRS score[b]
Xu et al., 2019 (45)	46.0	154	55.4	Low	nr	China (rural)	Enrolled in community treatment program	5.5 months	13
Mohammadi et al., 2016 (46)	33.1	37	61.7	Moderate	nr	Iran (urban)	Outpatient psychiatric clinic(s)	6 weeks	9
Cullen et al., 2020 (47)	49.1	17	42.5	nr	Black, 85%; White, 7.5%; other, 7.5%	United States	Enrolled in community treatment program	6 months	11
Beebe et al., 2014 (48)	48.7	19	63.3	nr	Black, 50%; White, 50%	United States (Southeast)	Enrolled in community treatment program	3 months	10
Granholm et al., 2012 (49)	48.7	13	31	nr	Black, 7%; White, 74; Hispanic, 10%	United States (San Diego)	Outpatient residential and treatment settings	12 weeks	8
Montes et al., 2012 (50)	39.6	85	33.5	nr	nr	Spain	Outpatient psychiatric clinic(s)	6 months; 3 months of intervention	13
Menon et al., 2018 (51)	37.9	63	47.7	Low	nr	India	Academic medical center, outpatient psychiatric clinic(s)	6 months; 3 months of intervention	12
Levin et al., 2019 (52)	51.5	20	53	nr	Black, 73.7%; White, 23.7%; other, 2.6%	United States (urban)	Academic medical center	3 months; 2 months of intervention	10
Moore et al., 2015 (53)	47.2	6	12	nr	White, 54%	United States (San Diego)	Research program at a university	30 days	11
Cai et al., 2020 (54)[c]	46.0	154	55.4	Low	nr	China (rural)	Enrolled in community treatment program	18 months; 6 or 12 months of intervention	13
Average or total	44.6	414	44.5						11

[a] nr, not reported.
[b] Methodological Quality Rating Scale. Possible scores range from 0 to 16, with higher scores indicating greater methodological quality.
[c] An extension of the study by Xu et al., 2019 (45); only duration and rating scale score differ.

One of the more complex and diverse elements of the study interventions was the frequency of text messages. Frequency of SMS messages ranged from as low as twice weekly (51) to 12 times daily (49). Some customization was designed to meet specific patient needs. Two of the studies—both variations of the individualized texting for adherence building (iTAB) technology—determined the number of reminders on the basis of individual medication schedules (52, 53). Additionally, these interventions created a system using outreach messages or telephone calls to reengage participants who had not responded to several messages. One of the interventions had algorithmic systems that modified the frequency and message content on the basis of participant responses (47).

SMS themes and content. Beyond the mechanics of intervention delivery, the thematic elements of the messages delivered varied, both within a given intervention and across studies. Generally, the themes included the following: medication reminders, coping strategies or educational content, symptom surveillance, and encouragement or reinforcement (Table 2). All of the interventions included some form of medication reminder, with two interventions using medication reminders as their only SMS content (50, 51). Medication reminders varied from simple, closed-ended remarks ("Please remember to take your medication" [50]) to more complex, personalized messages ("John, your meds r important. It is time to take ur meds. Take ur big blue pill now. Pls reply (A) took (D) didn't (G) snooze" [53]).

Coping strategies, such as incorporation of cognitive-behavioral therapy techniques in messages, or education was provided in five of the nine interventions (Table 2) (45–47, 49, 52). Educational content focused on medication side effects (45–47); symptom management and relapse prevention ("If I don't take my meds, I may become manic/hypomanic or very irritable" [52]; "Adhering to your medication on time and on the prescribed dose is the key to control your symptoms. We are here to help you." [45]); and self-care and social resources (45).

Symptom surveillance or relapse monitoring was provided in five of the nine interventions (45, 47–49, 52) (Table 2). The content was disease or patient centered. For example, Granholm et al. (49) included inquiries about hallucinations and socialization, both components of schizophrenia spectrum disorders, and Cullen et al. (47) created patient-selected signs of relapse. Conversely, in two

TABLE 2. Delivery of short message service (SMS) texting messaging interventions in 10 articles included in the systematic review[a]

Article	One-way vs. two-way SMS	Automated vs. manual	Message customizing		Frequency minimum	Follow-up		Content	
			Content	Timing		Text	Provider	Themes	Details
Xu et al., 2019 (45)	2	Automated	No	No	Once daily	No	Yes	Medication reminder, education or coping strategy, symptom and relapse surveillance	Medication reminder and education or coping strategy, daily; symptom and relapse surveillance, monthly
Mohammadi et al., 2016 (46)	1	Automated	No	nr	Twice daily	No	No	Medication reminder, education or coping strategy, encouragement-reinforcement	Medication reminder or education or coping strategy, daily; encouragement-reinforcement, daily
Cullen et al., 2020 (47)	2	Automated	Yes	Yes	Twice daily	Yes	Yes	Medication reminder, education or coping strategy, symptom and relapse surveillance, encouragement-reinforcement	Medication reminder, education or coping strategy, symptom and relapse surveillance, or encouragement-reinforcement, once daily minimum
Beebe et al., 2014 (48)	2	Manual	Yes	nr	Once daily	Yes	No	Medication reminder, symptom and relapse surveillance, encouragement-reinforcement	Medication reminder, symptom and relapse surveillance, or encouragement-reinforcement, once daily
Granholm et al., 2012 (49)	2	Automated	Yes	Yes	12 times daily	Yes	No	Medication reminder, symptom and relapse surveillance, education or coping strategy	Medication reminder, symptom and relapse surveillance, and education or coping strategy, each 4 times daily (total of 12 messages per day)
Montes et al., 2012 (50)	1	Automated	No	Yes	Once daily	No	No	Medication reminder	Medication reminder, once daily
Menon et al., 2018 (51)	1	nr	No	Yes	2 per week	No	No	Medication reminder	Medication reminder, once daily
Levin et al., 2019 (52)	2	Automated	Yes	Yes	3 or more daily[b]	Yes	No	Medication reminder, education or coping strategy, symptom and relapse surveillance, encouragement-reinforcement	During month 1: education or coping strategy, symptom and relapse surveillance, each once daily; during month 2: medication reminder, once daily for each medication; symptom and relapse surveillance and encouragement-reinforcement, each once daily
Moore et al., 2015 (53)	2	Automated	Yes	Yes	3 or more daily[b]	Yes	No	Medication reminder, encouragement-reinforcement	Medication reminder, once daily for each medication; encouragement-reinforcement, once daily minimum
Cai et al., 2020 (54)[c]	2	Automated	No	No	Once daily	No	Yes	Medication reminder, education or coping strategy, symptom and relapse surveillance	Medication reminder, once daily; education or coping strategy, once every other day; symptom and relapse surveillance, monthly

[a] nr, not reported.
[b] Baseline minimum dependent on number of medications.
[c] An extension of the study by Xu et al., 2019 (45).

of the interventions that centered on individuals with bipolar disorder, surveillance focused on monitoring participants' daily mood (52, 53).

Finally, encouragement or reinforcement messages were provided in five of the nine interventions (46–48, 52, 53) (Table 2). Many were reactionary to participants' responses. For example, the testing for relapse prevention intervention provided a supportive follow-up statement when a participant denied the presence of a relapse symptom (47). In iTAB-CV (iTAB-cardiovascular), the second month of intervention followed up medication reminders with messages such as "You're doing wonderfully with taking your meds," with the option to customize the reinforcement (52).

Additional intervention components. Table 3 provides a summary of additional components of the interventions. Only two of the interventions were solely SMS based, without another element to the intervention (50, 51). One study included a comparison group in which participants received both SMS and telephone calls to enhance medication adherence (48). Two interventions involved embedded additional support people in the design (45, 47, 54). The LEAN trial (for lay health supporters, e-platform, award, and integration) required a health supporter who could receive and send text messages for each participant and allowed for village doctors or psychiatrists to be contacted if signs of relapse were endorsed (45, 54). Similarly, the intervention by Cullen et al. (47) included a customized threshold of symptom endorsement that would trigger contact of a provider, who would then follow up with participants within 24 hours.

Three of the interventions provided participants with educational content in addition to the SMS intervention (46, 52, 53). Themes from these sessions included benefits of adhering to medications, coping with serious mental illness diagnosis, strategies for adherence, and medication side effects. Finally, two of the studies provided participants with small monetary rewards or gifts in response to engagement with the intervention (45, 49).

TABLE 3. Intervention components in the studies included in the systematic review

Article	Intervention or trial name[a]	SMS only	Additional interventions
Xu et al., 2019 (45), Cai et al. (54)	LEAN trial	No	Monetary rewards or gifts, provider or support person involvement
Mohammadi et al., 2016 (46)		No	Educational materials or sessions
Cullen et al., 2020 (47)	T4RP	No	Provider or support person involvement
Beebe et al., 2014 (48)	TIPS	No	Telephone calls
Granholm et al., 2012 (49)	MATS	No	Monetary rewards or gifts
Montes et al., 2012 (50)		Yes	None
Menon et al., 2018 (51)		Yes	None
Levin et al., 2019 (52)	iTAB-CV	No	Educational materials or sessions
Moore et al., 2015 (53)	iTAB	No	Educational materials or sessions

[a] iTab, individualized texting for adherence building; iTab-CV, individualized texting for adherence building–cardiovascular; LEAN trial, lay health supporters, E-platform, Award, and iNtegration; MATS, Mobile Assessment and Treatment for Schizophrenia; T4RP, Texting for Relapse Prevention; TIPS, Telephone Intervention Problem Solving for Schizophrenia (adapted to include short message service [SMS] texting messaging).

Medications and Measuring Adherence

The medication classes targeted for enhancing adherence included oral psychotropic medications (first- and second-generation antipsychotics, mood stabilizers, antiparkinsonism medications, hypnotics, anxiolytics, antidepressants, and anticonvulsants), long-acting injectables, oral medications for general medical illnesses (antihypertensives and antiretrovirals), or otherwise unspecified oral medications (Table 4). Studies differed in terms of how medication requirements affected participant inclusion or intervention target. For example, Montes et al. (50) specified that participants must be prescribed only one oral antipsychotic to be included. Conversely, both iTAB studies explicitly targeted a minimum of two medications, including an appropriate psychotropic medication and an appropriate medication to address the comorbid general medical condition of the study population (i.e., hypertension or HIV) (52, 53).

In terms of measuring medication adherence, most of the studies used self-report, either exclusively or in combination with objective measures (45–47, 49–54). Two used the Brief Adherence Rating Scale (45, 47), one used the Morisky Green Adherence Questionnaire (50), one used the Morisky Medication Adherence Scale–8 (51), one used the Tablets Routine Questionnaire (52), and the remaining three used study-specific measures (46, 49, 53). In addition to self-report, four of the studies also used objective measures, such as random pill counts (45, 48), medication refill records (45), number of pill bottle openings (52, 53), or proportion of injections received (47, 48). The study by Beebe et al. (48) was the only study to use exclusively objective data, using proportion of pills or injections received based on pill counts or injection schedule, respectively

Outcomes

Medication adherence. In seven of the 10 articles, significant improvement in medication adherence was observed from baseline to postintervention or in intervention groups compared with control groups (45, 47, 49–52, 54) (Table 4). Particularly robust results were observed in the LEAN trial. In this trial, a significantly greater proportion of pills taken by the intervention group, compared with the control group, was maintained in subgroup analysis of participants who were nonadherent at baseline, representing efficacy of the intervention for particularly vulnerable participants (45). Furthermore, after a 3-month hiatus from the intervention, reintroduction for an extended 3 months

TABLE 4. Measures and outcomes in the studies included in the systematic review

	Medication adherence				Other outcomes[a]		
Article	Medication of interest	Measure[a]	Significant improvement[b]	Outcome of interest	Medication attitudes	Standardized scales	Significant improvement
Xu et al., 2019 (45)	Oral psychotropic medications	Pill count, medication refills, BARS	Yes	Greater proportion of pills taken by the nonadherence subgroup of the intervention group (p=.047)	DAI-10	CGI, WHODAS	Reduction in risk of relapse and in risk of rehospitalization in intervention group
Mohammadi et al., 2016 (46)	Antidepressant medications	Self-report questionnaire	No	No significant difference in depression score or medication adherence (p=.06, p=.31, respectively)	None	BDI-II-Persian	
Cullen et al., 2020 (47)	Oral medications (not specified), long-acting injectable medications	Proportion of injections received, BARS	Yes	Long-acting injectables: significantly higher adherence at baseline (p=.09) and 6 months (p=.02) in intervention group but not at 3 months (p=.43); nonsignificant improvement in oral medication adherence at 3 and 6 months (p=.18, p=.11, respectively) in intervention group	None	PANSS, RAS-R, MADRS, BUES, YMRS	PANSS scores for positive symptoms lower (better) in intervention group at 6 months; RAS-R recovery scores significantly higher (better) at 3 months in intervention group
Beebe et al., 2014 (48)	Oral nonpsychiatric medications, oral and long-acting injectable antipsychotic medications	Pill count, proportion of injections received	No	No significant difference in medication adherence for psychiatric or nonpsychiatric medication (p=.31, p=.71, respectively)	None	BPRS	Significant main effect for group for BPRS scores (mean lower [better] scores on BPRS in TIPS and texting group, compared with TIPS-alone or texting-alone group)
Granholm et al., 2012 (49)	Second-generation antipsychotics, first-generation antipsychotics, antidepressants, mood stabilizers	Self-report, daily ambulatory monitoring of outcome assessment question	Yes	Significant improvement in medication adherence among participants living independently (p=.05)	Self-report	PANSS, BDI-II, ILSS, ANART	Time in the intervention increased the odds of having more social interactions and of reporting fewer auditory hallucinations
Montes et al., 2012 (50)	Oral antipsychotics	MAQ	Yes	Significant reduction in MAQ scores from baseline to 3 months (p=.02); maintenance of reduced MAQ scores at 6 months (p=.04)	DAI-10	CGI-SCH (SI and DC), SUMD, EQ-5D	In intervention group, reduction (improvement) in negative symptoms subscale of CGI-SCH-SI; greater improvement in negative, cognitive, and global symptom subscales of CGI-SCH-DC at 3 months; improvement in quality of life via EQ-5D

continued

TABLE 4, *continued*

Article	Medication adherence				Other outcomes[a]		
	Medication of interest	Measure[a]	Significant improvement[b]	Outcome of interest	Medication attitudes	Standardized scales	Significant improvement
Menon et al., 2018 (51)	Antipsychotic mood stabilizers	MMAS	Yes	Significant improvement in medication adherence from baseline to 3 months ($p<.001$); maintenance of improved medication adherence at 6 months for both intention-to-treat and completer analyses ($p<.001$)	DAI-10	WHOQOL	
Levin et al., 2019 (52)	Antipsychotic mood stabilizers, anticonvulsants, antihypertensives	eCAP, TRQ	Yes	Significant decrease from screening to baseline after 2 months of intervention for both bipolar disorder and antihypertensive medication nonadherence ($p<.001$); no significant decrease between any time points for eCAP.	None	BPRS, MADRS, YMRS, SRHI	Decreased systolic blood pressure, improved BPRS scores, lower (better) MADRS scores, and higher habit formation between screening and follow-up time points during intervention
Moore et al., 2015 (53)	Psychotropics, antiretrovirals	eCAP, self-report, visual analogue scale	No	No significant difference in adherence to psychotropic or antiretroviral medications	None	YMRS, BDI-II	
Cai et al., 2020 (54)[c]	Oral psychotropic medications	Pill count, medication refills, BARS	Yes	Greater proportion of pills taken during extended intervention period ($p=.004$)	DAI-10	CGI, WHODAS	Decrease in illness severity as measured by CGI and reduction in hospitalizations during intervention periods, compared with control period

[a] ANART, American National Adult Reading Test; BARS, Brief Adherence Rating Scale; BDI-II-Persian, Beck Depression Inventory-II–Persian; BPRS, Brief Psychiatric Rating Scale; BUES, Boston University Empowerment Scale; CGI, Clinical Global Impression; CGI-SCH, SI, and DC, Clinical Global Impression–schizophrenia, –severity of illness, and –degree of change; DAI-10, Drug Attitude Inventory–10; EQ-5D VAS, Euroqol 5D, visual analog scale; ILSS, Independent Living Skills Survey; eCap, a pharmacy bottle cap that tracks each opening with date and time; MADRS, Montgomery-Åsberg Depression Rating Scale; MAQ, Morisky Green Adherence Questionnaire; MMAS, Morisky Medication Adherence Scale; PANSS, Positive and Negative Syndrome Scale; RAS-R, Recovery Assessment Scale–Revised; SRHI, Self-Report Habit Index; SUMD, Scale to Assess Unawareness of Mental Disorder; TRQ, Tablets Routine Questionnaire; WHODAS, World Health Organization Disability Assessment Schedule 2.0; WHOQOL, WHO Quality of Life Instrument; YMRS, Young Mania Rating Scale.

[b] For at least one analysis related to medication adherence.

[c] An extension of the study by Xu et al., 2019 (45).

reaffirmed significant improvement in adherence, albeit to a smaller magnitude (54). Two publications, which reassessed adherence 3 months after the intervention, found maintenance of adherence gains after intervention completion (50, 51).

Of the three publications that did not find significant improvement in medication adherence (46, 48, 53), lack of study power was cited as a potential contributor (46, 48). Additionally, in an attempt to create a rigorous control group, researchers in one study sent a daily text message, albeit not the full intervention, to the control group, which was suggested by the authors as driving the high adherence (compared with pilot data in similar populations) in both the intervention and the control conditions (53). Similarly, in the study by Granholm et al. (49), only the subset of individuals living independently showed significant improvement in medication adherence, which was likely a function of high baseline medication adherence secondary to staff support given to individuals in assisted living.

Attitudes toward medication. Five of the 10 articles assessed participant attitudes toward medication (45, 48, 50, 51, 54) (Table 4). Four used a version of the Drug Attitudes Inventory (DAI), including both LEAN trial studies (same study sample but reported on different time intervals) (45, 50, 51, 54). Granholm et al. (49) used self-report data collected directly via the intervention. The two LEAN trial reports (45, 54) did not find a significant change in attitudes via DAI, but the other two studies (50, 51) reported significantly improved attitudes, one of which saw maintenance of effects 3 months after intervention completion (50). Finally, a significant decrease in negative attitudes was observed via self-report data by Granholm et al. (49).

Clinical outcomes. All 10 papers measured at least one clinical outcome, such as serious mental illness symptoms, mood, quality of life, hospitalizations, and rate of suicide (Table 4). Of these, seven reported at least one statistically significant improvement in clinical outcomes or reduction in symptomatology (45, 47–50, 52, 54).

Study quality assessment. The MQRS results are shown in Table 1. Scores for the included studies ranged from 8 to 13, with a mean score of 11. Strengths in study quality included the predominance of RCTs (N=7) (45, 47, 48, 50, 51, 53, 54) and inclusion of preintervention baseline and postintervention follow-up analysis (N=4) (50–52, 54). Lack of randomization or lack of inclusion of a control group limited three of the studies (46, 49, 52), and underpowered analyses or ceiling effects were cited in studies that lacked significant findings in regard to medication adherence (46, 53). Finally, although most of the studies collected data over the course of several months, medication adherence among persons with serious mental illness is a typically lifelong commitment. Thus, study duration limited the validity of the results on the long-term time scale.

DISCUSSION

The delivery of clinical interventions using mobile technology is increasingly commonplace, including for persons with serious mental illness (39). Furthermore, the demands of the current COVID-19 pandemic have accelerated the delivery of health care services via mobile technology (56). However, the heterogeneity in the platforms of mobile technology (SMS, telephone calls, Web browsers, smartphone applications, video meetings, etc.), the content delivered (appointments, reminders, and education), and the goals of the interventions (medication adherence, health care delivery, and disease surveillance) create a challenge to those interested in utilizing remote delivery services in terms of how to be most effective. Among persons with serious mental illness, this challenge is exacerbated by the interaction of the patients' underlying illness with treatment engagement (11, 57).

Improvement in attitudes toward medications was observed across several studies (50, 51, 55). This finding has potential implications as to how the interventions are driving increased medication adherence. Although in its simplest form, text messaging can serve as a reminder to take medications, targeting unintentional nonadherence alone (i.e., forgetfulness) addresses only one of the drivers of patient behavior. Attitudes and beliefs around medication, side-effect profiles, and insight into illness have been proposed as prominent components of medication nonadherence in populations with serious mental illness (12, 58). Of note, two of the studies that reported improved attitudes toward medication, Montes et al. (50) and Menon et al. (51), represented the most minimalist interventions of those included. Both used a one-way SMS messaging model, with medication-reminder-only content, provided no additional interventional components, and messaged only once daily or twice weekly, respectively. Furthermore, both included a 3-month follow-up and showed maintenance of the improved adherence. Given that the other interventions included multiple content themes and supplemental interventional components, these two studies offer evidence that even simple SMS messaging has the potential to drive robust changes in patient behavior.

In contrast, two of the interventions provided evidence that inclusion of providers and support persons for patients with mental illness is a feasible and efficacious extension of texting platforms (45, 47, 54). Xu et al. (45) integrated local physicians, psychiatrists, and personal support members into their intervention in the LEAN trial. The integration of support was particularly compelling, given the rural setting of the study, where technology such as SMS can have an even greater impact on enhancing connectivity. Beyond improved medication adherence, risk of relapse and rates of rehospitalization were significantly reduced in this integrated

model. Provision of support aligns with general treatment ideologies for serious mental illness and schizophrenia in particular (the diagnosis of patients in the LEAN trial), in which intradisciplinary approaches to treatment have been encouraged (59), including integration of family members (60). Cullen et al. (47) incorporated direct contact with patient providers when a predetermined, patient-specific threshold of symptom endorsement was met via SMS responses. The opportunity for providers to intervene at early signs of relapse is an exciting prospect in disease management. It conceptually aligns with best-care strategies for treating schizophrenia, in which higher rates of relapse have been demonstrated among persons with medication nonadherence in both placebo-controlled trials and reviews of hospitalization records (61).

Another promising expansion of more recent interventions includes targeting comorbid conditions beyond serious mental illness through SMS platforms. In the iTAB and iTAB-CV studies, antiretroviral and antihypertensive medication adherence, respectively, was also integrated into the model (51, 52). Antiretrovirals were taken closer to their intended time window by participants in the iTAB intervention group. In iTAB-CV, significant reduction in systolic blood pressure was observed from baseline to postintervention. High rates of cardiovascular disease have been reported among those with bipolar disorder (62), and there is a disproportionate prevalence of HIV among those with psychiatric conditions (63). Nonadherence to medications for chronic general medical conditions have their own consequences in terms of well-being, which can affect patients' ability to manage their mental health. Furthermore, having to take multiple medications creates increased demands on patients in terms of organization and routine; thus, platforms that address multiple conditions or medications offer a low-cost, high-yield collaborative care model, particularly for high-need patients.

Our review illustrated that many practical questions remain in terms of how to most effectively deliver an SMS intervention to individuals with serious mental illness. Despite a rather narrow set of inclusion criteria, the interventions varied widely, and few clear themes emerged in terms of what was most effective. One- and two-way messaging, customized and standardized content, and frequency of messaging ranging from infrequent messages to several daily messages led to appreciable improvement in medication adherence. Additionally, measurement of medication adherence, although captured in each study, was largely via self-report or by methods that allowed for introduction of additional confounding variables. Furthermore, study limitations, such as poorly powered studies, lack of a control group, ceiling effects, and relatively short study durations (particularly in light of the chronic nature of medication therapy required for most of the included conditions) hindered interpretation of what is likely to make a clear impact on clinical outcomes.

Future studies are needed to address remaining limitations, both in terms of study methodology and real-world application. Creating multiple study conditions, each of which captures a single dimension of an intervention, would allow for more clarity about which specific components are effective. For example, having two groups, one that receives one-way messaging and one that receives two-way messaging, or having groups that receive varying numbers of messages a day would aid in finding the "sweet spot" between sufficient reminders and fatiguability. In terms of real-world application, studies that follow participants for years (with or without continual interventional support) would illuminate the durability of study effects, the time scale for habit formation, and the potential need to reinstate interventions after certain intervals without them. Finally, increasing the objectivity of the measure of "improved adherence" by using automated pill counts or patient-recorded video clips of taking medications may strengthen the quality of the data but must be balanced with proper controls to reduce the risk of introducing potential confounders.

CONCLUSIONS

This review has provided evidence that increasing medication adherence via SMS platforms among people with serious mental illness is likely feasible and achievable. Most interventions resulted in significant improvement in medication adherence with SMS and associated improvement on clinical measures, including reduced rehospitalization, improved quality of life, and decreased symptom burden (45, 50, 52, 54). A strength is that these findings were for several diverse patient populations across the included studies, with differing geographical locations, races, ethnicities, and SES. However, caution should be used in presuming the robustness of these findings, because many of the measures of improved medication adherence were subjective.

Future studies are needed with better controls for confounds to allow for identification of what is driving study outcomes, longer study durations to confirm durability of effects, more objective measurement of medication adherence, and methodology that evaluates the minimal time needed to establish a habit of medication adherence and how to maintain it once it has been established.

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