



Digital Interventions for Relapse Prevention, Illness Self-Management, and Health Promotion In Schizophrenia: Recent Advances, Continued Challenges, and Future Opportunities

Anand Chukka, A.B.

Soumya Choudhary, M. Phil

Siddharth Dutt, PhD

Ameya Bondre, MSPH, MBBS

Preethi Reddy, MD

Deepak Tugnawat, MSW

Abhijit R. Rozatkar, MD

Urvakhsh Mehta, MD, PhD

Narayana Manjunatha, MD

Matcheri Keshavan, MD

Vikram Patel, PhD, MBBS

Suresh Bada Math, MD, PhD

Channaveerachari Naveen Kumar, MD

Jagadisha Thirthalli, MD

Anant Bhan, MHSc, MBBS

John Torous, MD

*John A. Naslund, PhD**

Address

*Department of Global Health and Social Medicine, Harvard Medical School, Boston, USA

Email: john_naslund@hms.harvard.edu

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Abstract

Purpose of Review Schizophrenia presents a significant mental health challenge requiring innovative solutions for relapse prevention, self-management, and health promotion. Patients face an excess mortality gap, driven by increased rates of chronic health conditions, exacerbated in low-resource settings. Digital interventions are a promising avenue to address the multifaceted needs of individuals with schizophrenia. This narrative review synthesizes evidence from digital intervention trials for schizophrenia published from January 2020 to June 2023.

Recent Findings 23 studies were identified, encompassing smartphone applications and web-based platforms to mitigate symptom severity, prevent relapse, and promote physical health. Key developments thus far have shown reduced symptom burden, and enhanced medication adherence and physical activity engagement. Despite more than a decade of research on digital interventions, many trials in this review continued to focus on acceptability and feasibility, with emphasis on patient uptake. This suggests the field has shown limited advancement in effectiveness studies of digital interventions.

Summary As the field evolves, further fully powered effectiveness studies, greater emphasis on implementation studies for digital tools for schizophrenia, and attention on digital health equity and evidence generation among those in lower-income countries are warranted. These findings hold implications for clinicians, researchers, and policymakers towards optimizing digital care for individuals with schizophrenia.

Introduction

Schizophrenia is a chronic disease with an immensely high disease burden, affecting 24 million people worldwide [1]. Often a debilitating condition, those who are affected by schizophrenia can have severe compromises in their functioning and ability to participate in broader communal and societal activities [2, 3]. In the United States alone, it is estimated the average life-lost for people with schizophrenia is 28.5 years [4]. Excess mortality in schizophrenia is driven by high rates of co-occurring chronic medical conditions, increased risk of suicide and self-harm, poor access to mental and physical health care, and lifestyle factors that increase risk of death [5]. The excess mortality due to substance-use is equally steep; in the United States, studies show that 62–80% of people with schizophrenia are active tobacco users and 24–36% have an alcohol use disorder [6]. Co-occurring substance-use

disorders are known contributors to the excess cardiovascular and cirrhotic risk, among other chronic diseases that affect people with schizophrenia [5, 7, 8]. This burden of disease, however, is not equally distributed – it is estimated that greater than 80% of all people with mental health conditions, including schizophrenia-related disorders, reside in low- and middle-income countries (LMICs) [9, 10] and disproportionately experience structural inequality such as low socioeconomic status, migration [11], racism [12], poverty, housing insecurity [13], and reside in settings with greater income inequality [14]. These risk factors worsen positive psychotic and depressive symptoms. Structural inequalities are exacerbated by global gaps in access to quality psychiatric care and community mental health services. Globally, there are roughly 4 psychiatrists per 100,000 people, however, most LMICs

are well below that threshold with estimates ranging from 0.04 to 1.55 psychiatrists per 100,000 [9]. Mental health services are often not available in many countries, making early identification, linkage to care, and follow-up lacking.

In recent decades, promising digital interventions have emerged to address the large treatment access gaps and excess morbidity and mortality among individuals living with schizophrenia [15]. Previous reviews of digital interventions for schizophrenia and other serious mental disorders have shown innovations in relapse management (i.e., recurrence of symptoms after remission), symptom tracking, and psychosocial rehabilitation [16–22]. Young people, in particular, are digital natives and recent studies have demonstrated that there are many applications of digital health ranging from daily medication reminders and momentary ecological assessments to caregiver support and coping-skill practice that can improve individual self-management of schizophrenia [16]. Digital technology has been proposed and studied at the individual and systems-level to address chronic health conditions and poor health behaviors among those with schizophrenia. At the individual level, one area of focus has been on wearable technologies and digital coaching to encourage lifestyle modification around tobacco use, exercise, among other health behaviors [23]. At the systems level, there has been a push to leverage electronic medical records and other systems-integrations to monitor physical health symptoms [15]. Digital technology has also shown promise to scale psychiatric community-based care in LMICs [17]. The focus of these interventions has similarly been on symptom

management and relapse prevention and have been adapted to fit low-income settings, leveraging community health workers, adapting language needs, and involving caregivers. Digital technology has afforded opportunities for promoting self-management of schizophrenia-related disorders and thus empowering patients to take greater control of their disease.

Despite the early promise of digital interventions for relapse prevention, symptom management, and improving access to quality care for patients with schizophrenia, adoption of these innovations has been disappointingly low. Following numerous feasibility and acceptability studies, there appear to have been few adequately powered and rigorously conducted large-scale effectiveness trials. Digital mental health continues to evolve rapidly, and in many instances, without adequate regulation [24]. This raises concerns about the clinical quality [25] and safety of emerging mobile applications and digital platforms. The purpose of this narrative review is to assess whether the initial promise of digital tools has met expectations of the nascent field and to understand whether the gap to clinical practice is closing with the development of new digital techniques. Specifically, we expanded on recent literature reviews by synthesizing evidence from trials of digital interventions for schizophrenia published from January 2020 to June 2023. Our goal was to consider recent developments in the use of digital interventions for mental health, physical health and functional outcomes in individuals living with schizophrenia, limitations with the latest studies, remaining challenges to the field, and new opportunities to advance digital innovation use for schizophrenia.

Methods

We relied on the PRISMA guidelines for scoping reviews, which informed our methodological approach in this rapid narrative review. To find English studies that used digital technology for schizophrenia, we used a broad search on PubMed and Google Scholar. The main search terms that were used included (“schizophrenia” OR “psychosis”) AND (“digital technology” OR “mHealth”) AND (“physical health” OR “rehabilitation” OR “substance-use”), as well as keywords such as “ecological momentary assessment”, “digital intervention”, “smartphone-based” and “web-based” (as examples).

We narrowed our focus to include studies of clinical trials published from January 2020 to June 2023. We chose this date range to expand on numerous

previous reviews on digital technology for schizophrenia that covered studies through 2019 [16–19, 21, 22]. We restricted our review to empirical studies that evaluated a specific digital intervention targeting individual clinical care, excluding health workers or caregivers, and illness self-management, thus excluding reviews, cross-sectional studies, meta-analyses, and commentaries.

Our team extracted the data from the included studies and summarized these findings in a table. We grouped the included studies according to broad clinical focus: 1) relapse prevention; 2) symptom tracking and illness self-management; and 3) health promotion. The identified studies primarily used interventions such as digitally integrated platforms, smartphone-based self-management tools, digital phenotyping, ecological momentary assessments and interventions, digital medicine and wearables, and observational studies.

Given our objective to offer a rapid synthesis of digital intervention developments for schizophrenia, we conducted a narrative review; this review does not offer a comprehensive summary of the literature or a meta-analysis of quantitative findings. This review should be seen as a broad overview of recent developments in the field, and a commentary on the challenges and opportunities ahead.

Findings

We found a total of 23 studies, from 9 countries. Characteristics of these studies are summarized in Table 1, and broad findings are summarized in the sections that follow.

Relapse Prevention

Relapse prevention has long represented a key target for digital interventions in schizophrenia. This trend continued, as 7 studies described recent developments focused on relapse prevention. The Scotland and Australia-based EMPOWER trial piloted a smartphone application that combined self-monitoring of symptoms and real-time peer and clinician-based support. This feasibility RCT showed high acceptability rates, treatment adherence; decreased participant fear of relapse; and increased self-empowerment [26••]. Similarly, the ARIES trial from England [27••] combined psychiatric services and a digital platform called “My Journey 3.” This platform encouraged self-management techniques to prevent relapse via planning, symptom tracking, and medication tracking. While high acceptability and feasibility with the platform were also observed, there was significant long-term discontinuation. In contrast to the EMPOWER trial, this study highlighted concerns around ensuring regular clinician support alongside the digital intervention. In a U.S.-based outpatient program, the Improving Care and Reducing Cost (ICRC) study [28••] combined a digital platform, smartphone application, and provider-facing pharmacy decision-agent to reduce the number of hospital days. This study found that this multi-pronged intervention was successful

Table 1. Table summarizes the digital interventions studies included in this review (linked in separate document)

Theme	Trial Name	Authors	Country	Study aim	Design	Participants	Findings
Relapse Prevention	Early Signs Monitoring to Prevent Relapse in Psychosis and Promote Wellbeing, Engagement, and Recovery (EMPOWER)	Gumley et al., 2022	UK and Australia	To investigate the effectiveness of an intervention called Early signs Monitoring to Prevent relapse in psychosis and promote Wellbeing, Engagement, and Recovery (EMPOWER), using peer support and clinical triage, to recognize and promptly manage early warning signs of relapse in schizophrenia with the aim of preventing relapse as compared to treatment as usual	A multicenter, two-arm, parallel-group cluster randomized controlled trial involving eight community mental health services, with 12-month follow-up	73 in total. 42 in EMPOWER group and 31 in treatment as usual	A trial of digital technology to monitor early warning signs to detect and prevent relapse is feasible. EMPOWER-intervention arm had a lower rate of relapse over 12 months than the control group and was found to be cost-effective
	the App to support Recovery in Early Intervention Services (ARIES)	Steaere et al., 2020	UK	To test the feasibility and acceptability of a RCT to evaluate a smartphone-based self-management tool called My Journey 3 for use in Early Intervention in Psychosis (EIP) services as compared to treatment as usual. The study also aimed to test procedures for evaluating engagement and outcomes from participants on such apps	A two-arm unblinded feasibility RCT	40 total, 20 in active group with the app and 20 TAU only in TAU only group	Recruitment and retention were feasible as 75% of the participants were retained at the 12 months. Within a trial context, "My Journey 3" could be successfully delivered to adults using EIP services; however, the application had relatively low usage rates

Table 1. (continued)

Theme	Trial Name	Authors	Country	Study aim	Design	Participants	Findings
	Improving Care and Reducing Cost	Homan et al., 2023	USA	To compare whether the "Health Technology Program," an individualized relapse prevention plan compared to standard relapse prevention care, would decrease re-admission in the hospital days during the 6-month intervention period after a recent hospitalization for schizophrenia	Two-arm. Quasi-experimental study design	438 total. 89 in control group and 439 in HTP group	During the 6 months, 43% of the controls and 24% of the intervention group had a relapse. The study found that days of hospital re-admission was reduced by 5 days in the intervention group as compared to control in a 6 month follow up period
	HORYZONS trial	Alvarez-Jimenez et al., 2021	Australia	The aim of the study was to examine if adding HORYZONS, an online social media therapy, could enhance first-episode psychosis specialty services	Single-blind RCT	170 pts with FEP assigned to 2 groups	The study found that social functioning was higher than baseline in both the groups at the 18 th month follow up. The group on Horyzons had better educational and vocational outcomes and reduced hospitalizations than the TAU only group
	m-RESIST	Eva Grassa et al., 2023	Spain, Hungary, and Israel	To assess the feasibility, acceptability, and usability of the m-RESIST integrated smartwatch, mobile app, and web-based digital intervention among patients with treatment resistant schizophrenia (TRS) after using this intervention across 3 sites	Prospective multicenter feasibility study, 1 arm	39 patients with Treatment Resistant Schizophrenia	The m-RESIST intervention is a feasible, acceptable, satisfactory, and potentially useful tool for a population with TRS who usually have poor clinical outcomes and low adherence to treatment. Patient satisfaction was also high with 78% reporting the quality of service as good or excellent. The study had a dropout rate of 18%

Table 1. (continued)

Theme	Trial Name	Authors	Country	Study aim	Design	Participants	Findings
	mHealth-Assisted Detection of Precursors to Relapse in Schizophrenia	Buck et al., 2021	USA	To determine whether a brief ecological momentary assessment delivered by CrossCheck system administered to patients with schizophrenia spectrum disorders can capture changes happening before, during and after psychiatric relapses	Two-arm RCT	61 in the intervention group with 20 pts with relapse	Patients reported an increase in negative mood, anxiety, persecutory ideation, and hallucinations on relapse days as compared to other days in the study. Elevations in these symptoms were also gradually increasing in the 100-day period preceding relapse. EMA were able to detect significant signals of relapse before they occur
	Smartphone Health Assessment for Relapse Prevention (SHARP)	Cohen et al., 2023	USA and India	To determine the feasibility of using anomaly detection as a statistical technique in predicting relapse in patients with psychosis using the MindLAMP app across 3 sites	Two Arm Observational Study	20 patients with relapse	Anomalies were 2.12 times more frequent in the month before a relapse and 2.78 times more frequent in the month preceding and following a relapse compared to time periods without relapses. Relapse prediction models using data gathered by a smartphone app can create alerts to the clinician and patient of a potential schizophrenia relapse
Symptom Management	Capturing Clinical Symptoms with Ecological Momentary Assessment	Harvey et al., 2021	USA	The aim was to examine deployment and usage of EMA to capture clinical symptoms in patients with bipolar disorder and Schizophrenia and match them with structured clinical ratings	1 arm, Observational study	71 pts with bipolar disorder and 102 with schizophrenia	The study collected 12,406 EMA samples with a prompt adherence rate of 80%. EMA reported psychotic symptoms were converging with equivalent PANSS items. Repeated assessments of up to 90 times in 30 days did not lead to a change in symptom severity scores

Table 1. (continued)

Theme	Trial Name	Authors	Country	Study aim	Design	Participants	Findings
	PeerTECH	Fortuna et al., 2022	USA	To examine the feasibility, acceptability, and initial validity of using smartphone-based peer-supported ecological momentary assessment (EMA) called PeerTECH as a tool to assess loneliness and functioning among adults with a serious mental illness diagnosis	Single-Arm Pre/Post Study	30 with Severe Mental Illness and one medical comorbidity	The study reported EMA acceptability of 15.9%; use of EMA was correlated with higher levels of hope, social support, and self-efficacy among participants. Participants were able to use the peer support function on days of high loneliness to good effect. Findings also indicate EMA-measured loneliness and functioning are significantly predicted by baseline variables, and thus, baseline variables may impact engagement
	Texting Mobile Interventionist Augmentation	Ben-Zeev et al., 2020	USA	To determine whether patients with severe mental illness receiving Assertive Community Treatment (ACT) have better clinical outcomes when combined with a peer-based "mobile interventionist," who checks-in via mobile texting regularly	Assessor-blind, two-arm, randomized controlled trial	51 with Severe Mental Illness	Exploratory post-treatment clinical effect estimations suggest significant reductions in the severity of paranoid thoughts (Cohens $d = -0.61$) and depression (Cohens $d = -0.59$; improved illness management; and recovery in the mobile interventionist group. Augmentation of care with a texting mobile interventionist proved to be feasible, acceptable, safe, and clinically promising

Table 1. (continued)

Theme	Trial Name	Authors	Country	Study aim	Design	Participants	Findings
	Smartphone-Assisted coping focused interVention for Voices (SAVVy)	Bell et al., 2020	Australia	To investigate the potential clinical utility of smartphone based EMA/I called Savvy to augment coping-based therapy for auditory hallucinations	Single-blinded, parallel group, pilot RCT	34 pts who heard distressing and frequent voices	Findings supported the feasibility and acceptability of the approach, with good engagement and satisfaction rates, and clinical outcomes showed the intervention holds promise for improving coping, overall severity of voices and to some degree their negative impact
	SlowMo	Garety et al., 2021	UK	To investigate whether a digital therapy app called SlowMo (consisting of CBT for psychosis, face-to-face sessions, digital games and storytelling) is able to reduce paranoia and improve reasoning in patients with psychosis when compared with treatment as usual	Parallel group randomized clinical trial	362 in total, 181 to the SlowMo group and 181 to the treatment as usual group	SlowMo did not demonstrate significant improvements in the primary measure of paranoia at 24 weeks; however, a beneficial effect of SlowMo on paranoia was indicated by the results on the primary measure at an earlier point and on observer-rated paranoia and self-reported persecution at 12 and 24 weeks. The app did have improvements in reasoning, including high therapy uptake and adherence. Serious adverse events were reported in both the groups

Table 1. (continued)

Theme	Trial Name	Authors	Country	Study aim	Design	Participants	Findings
CORE		Ben Zeev et al., 2021	USA	To test the feasibility of CORE, a smartphone intervention that comprises daily exercises designed and secondly to promote reassessment of dysfunctional beliefs in multiple domains. recruiting and engaging individuals The other aim was to check for the ability to recruit patients in a full-remote trial	Remote Randomized Controlled Crossover Trial	315, Various severe mental illness	CORE was a usable, acceptable, and effective tool for reducing the severity of psychiatric symptoms and disability while improving recovery and self-esteem as compared to the waitlist control group. 33.1% of participants in the active group and 40.3% in the control group were retained at the 60-day assessment period
Longitudinal symptom changes and association with home time in people with schizophrenia		Ranjan et al., 2022	USA	To investigate the longitudinal changes in symptoms of schizophrenia and their association with "home-time" using digital phenotyping in a naturalistic and longitudinal manner	Observational Study	86 participants with schizophrenia and schizoaffective disorder	The results suggest that smartphone data capture can be used toward the quantification of personal symptom/behavioral trajectories. The study also found that physical location (home vs not-home) could be a predictor of mood, sleep, psychosis; these differences were not statistically significant in the current dataset

Table 1. (continued)

Theme	Trial Name	Authors	Country	Study aim	Design	Participants	Findings
	PEAR-004	Ghaemi et al., 2022	USA	The aim of this study was to determine whether PEAR-004, a smartphone-based digital therapeutic, which includes cognitive restructuring, illness self-management training, and social skills training, can improve the symptoms of an acute psychotic exacerbation of schizophrenia when it is added to standard treatment protocols	Multicenter, randomized, sham-controlled, rater-blinded, parallel group, proof-of-concept trial	112, divided into 2 groups 56 each. Pts with schizophrenia	PEAR-004 did not demonstrate an effect on the total PANSS score when compared to the control group. The treatment difference between PEAR-004 and sham was 2.7 points, in favor of the sham at a key endpoint. No significant results were noted in the secondary and exploratory outcomes except for possible small improvement in depressive symptoms
	Creating Live Interactions to Mitigate Barriers (CLIMB)	Sawson et al., 2021	USA, Canada, France, India, and the UK	To test the feasibility of CLIMB, a smartphone app using CBT for psychosis, moderated peer to peer instant messaging, social cognition training and ecological momentary assessments in improving social cognition, social functioning, and reducing negative symptoms among patients with schizophrenia-spectrum disorders	2-Arm, Randomized Trial	24 patients, 12 in each arm	CLIMB did not prove to be better than the control intervention as both groups improved equally on social cognition outcomes

Table 1. (continued)

Theme	Trial Name	Authors	Country	Study aim	Design	Participants	Findings
	Hummingbird	Cohen et al., 2022	USA	The aim of the study was to investigate whether aripiprazole tablets with sensor (AS; system includes ingestible event-marker sensor, wearable sensor patches, and smartphone application) could reduce psychiatric hospitalizations compared with oral standard-of-care (SOC) antipsychotics	Phase 3b, multi-center, open label, mirror image trial	277 pts with schizophrenia on medication	Compared with oral standard of care, AS reduced inpatient psychiatric hospitalization rates for adults with mild-to-moderate schizophrenia. The AS system aided medication ingestion by 26.5% and is associated with improvements in symptoms, potentially reducing acute-care needs among patients with schizophrenia. The intervention arm, however, had an adverse event rate of 70%
Health Promotion	Fit Forward Trial	Aschbrenner et al., 2022	USA	To evaluate the effectiveness of a group lifestyle intervention (PeerFit) with digital peer-to-peer support, group workout sessions, and self-monitoring as compared to basic education and activity training (BEAT) in addressing cardiovascular health among young adults with serious mental illness	Two arm randomized controlled trial	150 participants with serious mental illness who were overweight or obese	The study found no significant differences between PeerFit and BEAT in reducing cardiometabolic risk factors in young adults with serious mental illness. More than half the population in both the groups were below their baseline weight at 6th and 12th month follow-up, and both the groups had significant CVD risk reduction

Table 1. (continued)

Theme	Trial Name	Authors	Country	Study aim	Design	Participants	Findings
	Acceptability and Usability of two smartphone apps for smoking cessation	Gowarty et al., 2021	USA	To evaluate the usability and acceptability of two smartphone apps (QuitGuide and quitSTART) for smoking cessation among young adults with serious mental illness based on UX design for patients with SMI	User centered, mixed-method study	17 participants with severe mental illness	Both QuitGuide and quitSTART were well-received and practical among young adults dealing with significant mental health issues. QuitSTART showed a higher level of user-friendliness and approval which remained consistent as time went on. Users responded to 18.5 notifications, did 41 interactions and spent an average of 10.8 days on QuitSTART app as compared to QuitGuide. The users appreciated positive and encouraging language, motivational quotes, and information about saved money
	Learn To Quit	Villardaga et al., 2020	USA	The aim of the study was to examine feasibility, acceptability, and preliminary efficacy of Learn to Quit compared to an active app control (NCI QuitGuide) in patients with SSD with high tobacco use	Pilot parallel randomized controlled trial	62 participants in Learn to Quit and 29 in QuitGuide group	Learn to Quit had higher number of app interactions, almost double duration of app use and higher usability scores as compared to QuitGuide. At the week 16 outcome, Learn to Quit led to greater reduction in the number of cigarettes per day (12.3 vs 5.9)

Table 1. (continued)

Theme	Trial Name	Authors	Country	Study aim	Design	Participants	Findings
	Let's Talk about Smoking	Brunette et al., 2020	USA	To test the appeal and efficacy of an interactive, digital motivational decision support system intervention ("Let's Talk About Smoking") as compared to a static, digital education pamphlet from the National Cancer Institute (NCI) among smokers with schizophrenia	Randomized Control Trial	173 participants with schizophrenia	The dynamic multimedia digital approach ("Let's Talk About Smoking") was not more successful than a fixed digital approach (NCI Education) at reducing mental effort among individuals with schizophrenia who smoke. The mean satisfaction and usability index score was higher for Let's Talk About Smoking than NCI Education. The digital approach was rated more appealing
	Technology-Based Psychological Interventions for Young Adults with Early Psychosis and Cannabis Use Disorder	Tatar et al., 2021	Canada	To explore psychological intervention practices and intervention targets relevant for treating Cannabis Use Disorder (CUD) in individuals with early psychosis and to explore factors related to the development and implementation of a technology-assisted psychological intervention	Qualitative Study	10 patients with psychotic disorders and CUD, 10 clinicians	The findings demonstrated that the nature and strength of in-person psychological treatments for CUD differed and relied on the clinician's training, expertise, and willingness to modify their cannabis use played a central role in psychological interventions and influenced the selection of a specific approach

Table 1. (continued)

Theme	Trial Name	Authors	Country	Study aim	Design	Participants	Findings
Evaluating preferences for online psychological interventions to decrease cannabis use in young adults with psychosis		Tatar et al., 2023	Canada	To evaluate patient preferences related to the structure and content of app-based psychological interventions for the treatment of CUD and to explore the associations between app preferences, sociodemographic, and cannabis use	Cross-sectional design	121 participants with CUD and psychosis	The findings indicate that patients have a greater inclination towards a moderately intense app-driven intervention, consisting of 15-min modules scheduled on a weekly basis. Participants favored app-based interventions over in-person sessions, due to the enhanced accessibility and convenience offered by remote sessions

in significantly reducing the number of hospitalizations and the number of days hospitalized when compared to usual care. These findings were similar to those found in the Horyzons study, which examined a novel digital platform that combined peer support, clinician support, and therapeutic interventions to target relapse and social functioning. The findings were significant for promoting vocational recovery and had a non-significant reduction in hospital emergency service usage. However, there was not a significant improvement in social functioning, a key marker of relapse prevention [29••].

Ecological momentary assessments (EMAs) and interventions (EMIs) offer a unique avenue to assess real-time risk of relapse. One U.S.-based study looked at specific EMA markers that preceded and followed relapses among 20 patients to better understand how these digital tools can be tailored to detect when a patient is headed toward a relapse [30]. This study found that patients experienced increases in negative mood, anxiety, persecutory ideation, and hallucinations in the days before a relapse. This principle was applied in the SHARP trial [31], which used mindLAMP, a multimodal application, to test the feasibility, acceptability and potential clinical utility of digital phenotyping across sites in India and the US [32–34]. Digital phenotyping was achieved through passive data collection in the app, active EMA/EMIs, cognitive games, and was supplemented with psychoeducation resources. The application showed high levels of engagement and potential for demonstrating scalability across multiple, demographically distinct, study sites. The mResist [35] trial, which builds on previous wearable technology trials [30], found that people with schizophrenia had a mixed-view of combination therapies. The intervention used an integrated smartwatch, for monitoring deviations in physical health indicators; a mobile-based application; and a web-application approach to prevent relapse. While there was a favorable view of the smartphone-based application, participants felt that the smartwatch was not usable to manage their condition. This trial is unique in that it attempted to connect multiple different modalities of treatment, finding that there was an overall mixed view of the total intervention.

These studies illustrate how a range of technologies can support various aspects of relapse prevention, and continue to show potential for real-time symptom monitoring, community-based detection, and targeted clinical care. These studies used self-report and autonomous data collection as the primary monitoring method, leading to richer detailing about patients' illness trajectory.

Symptom Tracking and Illness Self-Management

We found 10 recent trials of digital interventions for symptom tracking and illness self-management for individuals living with schizophrenia. As shown for relapse prevention, EMAs can also be used for symptom management. One study in the US [36] used EMA samples to show convergence with clinically validated symptom tracking scales. Similarly, in another study in the US, a digital peer-supported EMA intervention [37] showed lower rates of loneliness. Peer-supported participants reported higher rates of hope and social functioning after completing regular EMAs, demonstrating that peer-driven

EMAs offer a potentially effective blended therapy. A “mobile interventionists” acceptability and feasibility study [38] in the US corroborated the role of peer-supported digital symptom-tracking. Initial findings showed a clinically moderate reduction in the severity of paranoid thoughts, depression and improved illness management and recovery among the intervention arm. The SAVVy study [39] from Australia, builds on this work, using personalized EMIs, based on participant’s coping mechanism preference, chosen during face-to-face therapy and smartphone EMAs focused on coping with auditory hallucinations. The blended approach showed a reduction in the severity of and improved coping with auditory hallucinations; greater awareness of factors causing auditory hallucinations; and increased self-management skills. Peer-supported EMAs/EMIs offer a relatively simple digital intervention to monitor minute symptomology changes, building on literature that emphasizes that mobile “hovering” [40] can augment other treatment options.

In contrast, in a UK study, researchers investigated whether SlowMo [41••], a blended-digital therapy augmentation program that combines in-person therapy, a digital game, and storytelling platform, could help reduce paranoia, rapid jumping-to-conclusions thinking, and negative metacognition among participants. The SlowMo intervention was not effective in reducing paranoia at 24 weeks post-treatment; however, there were moderate effects on reducing fixed belief thinking, increasing reasoning and “Slow Thinking”, which mediate paranoia. Comparing SAVVy and SlowMo offers contrasting views on blended therapy options for symptom management. SAVVy builds on previous studies [30] that have solidified the importance of EMA/EMI mHealth interventions for symptom management. Additionally, the SlowMo intervention required more active participation from users, which may lead to greater difficulties in engagement and retention. Another US-based study evaluated CORE [42••], a smartphone application that intervenes on dysfunctional thought patterns via game-like exercises. Researchers found that the application was acceptable, usable, and effective in reducing depressive and anxiety symptoms and improving self-esteem, improvement toward recovery, and decreased incapacity due to disease. CORE was unique in that they also found that by incorporating design thinking for those with schizophrenia, there was a reduction in technical issues. The digital phenotyping aspect to be used in symptom-tracking of mindLAMP [43], the application studied in the SHARP trial mentioned above, was validated through an observational study in the US looking at active (self-report) and passive (automated) data collection. “Home-time,” a measure of time spent at home has been previously clinically validated as a marker of worsened mood and psychotic symptoms. Using GPS and accelerometer data, the study team found that these specific markers could be collected using a novel digital platform.

In contrast, the PEAR-004 trial [44] studied an adjunctive digital therapy for schizophrenia in a 6-site trial comparing a smartphone application for cognitive restructuring against a sham-control. The PEAR-004 application focused on illness self-management via modules on behaviors such as sleep, exercise, meditation, social activity. The application did not show a significant reduction in symptoms when compared with a sham application and at best, demonstrated a transient improvement in depression symptoms. The limited impact of some digital interventions was further reflected in the CLIMB trial

[45], which combined established mHealth aspects—social cognition training, EMAs, smartphone-based messaging, and group teletherapy—against an unmoderated digital therapy and messaging system. In the CLIMB trial, the intervention arm showed no improvement in psychotic or mood symptoms compared to the control. These randomized trials are among the few trials comparing a digital intervention against a control digital application, prompting questions of whether other smartphone-based digital studies have buoyed benefits against standard treatment due to the presence of an application rather than the actual content of the digital application [46, 47]. These studies indicate a need to understand the mechanisms of action that contribute to even modest benefits from digital therapeutic interventions.

Digital tools have also been tested for improving medication adherence, an important aspect of schizophrenia self-management. In the “Hummingbird” study conducted in the US [48••], researchers outfitted aripiprazole, a second-generation antipsychotic agent, with a digital sensor to assess medication adherence via a body-sensor. Despite the relatively small sample of 44 patients, digital medicine tracking showed high adherence from participants, and resulted in significant reduction in inpatient psychiatric hospitalizations and an increase in 6-month medication adherence. Further investigation is required to understand whether those with paranoid symptoms can use digital medicines without significant distress, but this innovation offers promise for improving medication adherence [49], which remains a challenge in clinical care for schizophrenia.

Physical Health Promotion

Digital technology offers opportunities to address risk factors for early mortality in persons with schizophrenia via health and lifestyle promotion, addressing substance use, and tracking and managing metabolic and chronic medical conditions. To date, however, there have been relatively few studies [50, 51] leveraging technology for these targets. In this review, we found 6 studies on digital technology targeting diet, exercise, tobacco-use, and cannabis-use.

To target cardiovascular risk [52••] among patients with serious mental illness (SMI), including schizophrenia, a randomized control trial studied the difference between a digital group lifestyle intervention versus digital individualized coaching. This study found no in-group difference in weight loss, cardiorespiratory fitness, or cardiovascular risk reduction, however both trial arms had statistically significant changes in these metrics indicating that digital health interventions can target obesity among people with SMIs. This trial found greater engagement [53] with one-on-one remote coaching versus an intensive in-person and digitally augmented group lifestyle intervention.

Tobacco-use is an important risk factor for early mortality among patients with schizophrenia, and thus, expanding access to treatment via digital interventions is crucial [54]. There are numerous digital technology-based applications designed for smoking cessation, however, not many of them have been adapted for use by people with schizophrenia. A US-based study [55] looked at the efficacy of the National Cancer Institute’s official smoking cessation applications, quitGUIDE and quitSTART, among young people with serious

mental illnesses. This study found that while both applications had high levels of usability and mixed levels of acceptability, quitSTART was favored due to its user-friendly design. A similar study [56] compared the efficacy of “Learn to Quit,” an application designed for people with SMIs, against quitGUIDE. There were clinically significant findings of non-abstinent reductions in cigarette use and in thirty-day abstinence, however, long-term abstinence was not found. The application did have high acceptability and usability among patients with SMIs. These two studies emphasized, and showed clinical relevance of, schizophrenia driven UX design, similar to the CORE study, for symptom management. In contrast, another study [57] found that an interactive digital curriculum was not necessarily more effective than a static, text-based digital intervention. Both digital interventions studied in this trial were non-inferior in engagement and abstinence attempts to in-person interventions. Smoking cessation among patients with schizophrenia is a promising digital frontier with high levels of acceptability, usability, and has been shown to be non-inferior to standard in-person therapeutic interventions.

Clinically, it has been established that cannabis use, especially in adolescence [58], has a relationship with the development of schizophrenia-spectrum related disorders and worsening of positive psychotic [59] symptoms. Thus far, mHealth and digital technology research has primarily focused on augmenting CBT and other psychotherapeutic interventions to address cannabis use. However, these studies [60] have not borne clinically or statistically significant results, drawing focus back to application design for patients with schizophrenia. Two studies [61, 62] examined the specific characteristics that patients and addiction psychiatrist providers want. Participants expressed broad interest in digital technology, but concern that these applications would replace direct clinical care. In terms of design, participants expressed interest in digital video elements and blended gamification elements. Clinicians expressed that digital health may help track other substances, increase functional health and quality of life, and emphasize relationships with others. Both patients and providers hoped that digital health interventions would focus on blended approaches to addressing cannabis-use and schizophrenia. There are currently two on-going trials from Canada [63] and Australia [64] studying digital interventions (digital CBT and a web-based reduction program) for cannabis use among those with psychotic-spectrum disorders.

Discussion

Our review synthesizes recent digital intervention studies for schizophrenia, highlighting key advancements in the field, but also limitations and challenges going forward. Previous reviews expressed significant potential about digital interventions. 6 key reviews published in 2019 and 2020 primarily summarized and highlighted several acceptability, usability, and feasibility trials [16–19, 21, 22]. For instance, a review focused on the role of peer-driven digital [18] health interventions identified preliminary studies that showed great promise for blended digital approaches. Digital phenotyping and machine learning [19], to predict symptom worsening

and potential disease relapse, have also been highlighted as key developments for passive symptom management and relapse prevention. Digital technology was seen as a significant way to target patients, caregivers, and to support-tasking sharing [17] in LMICs, especially during the COVID-19 pandemic. Though there have been a significant growth of digital applications and in acceptability and feasibility trials, in this current narrative review, we note that the field has seen few recent large-scale studies; similarly, few studies have reported on the adoption of digital interventions for schizophrenia in clinical practice. In our review, we found that the greatest advancements were in the quality of studies conducted on digital tools, focus on low-technology interventions, and in the diversity of different digital approaches to address schizophrenia.

There were important recent trials that demonstrated significant findings for both relapse prevention and symptom management such as EMPOWER, Health Technology, Horyzons SlowMo, CORE, Hummingbird, and Fit Forward [26••, 28••, 29••, 41••, 42••, 48••, 52••]. Previous reviews identified the need for greater numbers of participants and difficulties in conducting large, randomized trials. Thus, the inclusion of these recent trials is significant advancement to the field. It was previously seen, as well, that blended interventions are highly acceptable and feasible [18]; recent studies continue this trend with advances showing that blended therapies also have significant symptom and relapse management effects [26••, 39]. Studies showed that incorporating UX design based on participant preference was crucial to higher usage; this was predominantly highlighted in the tobacco-use studies which focused on design choices acceptable to people with schizophrenia [55, 56].

Low-technology interventions and non-individualized treatments often fared as well as more intensive digital interventions that had a multimodal, complex, features. As an example, there were multiple EMA/EMI studies that showed significant symptom reduction and relapse prevention findings [30, 31, 36, 37, 39]. Similarly, a study focused on the role of mobile interventionists [38] who sent regular text messages to participants showed clinically significant reductions in paranoia and depression. This was also observed in the Fit Forward [52••, 53] study and a smoking cessation study [57] which showed that remote coaching and a simple, web-based intervention had clinically-significant findings and were superior to multimodal interventions. This principle of leveraging simple and basic forms of technology is important to consider for developing cost effective, scalable, and equitable interventions that can reach lower-income population groups, as shown in Fig. 1. While the field has moved toward complex integration of smartphone, web-based, and other technologies there remains a need to refine low-tech interventions, such as text messaging, and consider approaches for supporting widespread adoption of low-tech interventions given the promising results demonstrated thus far.

A key challenge in the field is progressing from acceptability and feasibility studies; our narrative review identified several preliminary trials. Study design additionally remains a challenge in the field. A few large-scale RCTs notwithstanding, most trials had less than a hundred participants and stringent inclusion criteria. Study endpoints were often

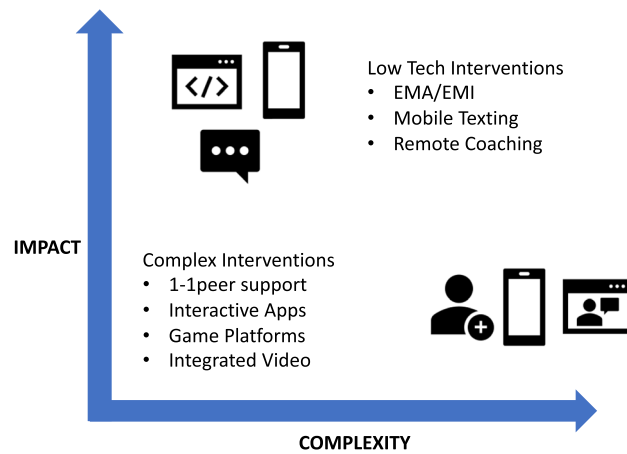


Fig. 1 The range of complexity of interventions against the observed impact in this review

less than a year, a significant limitation in understanding whether digital interventions can be used for a chronic relapsing–remitting disease. Many studies did not use active digital control conditions and the two primary studies [44, 45] that used digital controls showed minimal change in primary outcome between study arms, raising a question of whether a sham digital application is sufficient to address symptom reduction and disease self-management.

Digital health equity is also an important consideration in the digital mental health care field [20]. Patients with schizophrenia often face greater social and economic determinants of their health which make consistent digital access a challenge; this is especially true among those who are experiencing homelessness, incarcerated, and in assisted living facilities. Exacerbating the digital gap, these patients are often excluded from large trials given the inconsistency in access and thus, are under-represented in trials. For example, in the CORE study, roughly one-tenth of its study population was either homeless or in assisted living, which is not representative of the population [65]. To close this digital gap, in one example, a team [66] in Boston, has designed an open-access curriculum to teach those with schizophrenia how to effectively use mHealth applications, focused on digital literacy, digital safety, and evaluation of effective applications.

Digital technology is often seen as a solution to the global mental health gap [67] as a mechanism to scale psychiatric services to rural, and often neglected, parts of LMICs. This requires a greater focus on ensuring high-quality and consistent global digital access and incorporation of global patients to effectively scale these interventions. To ensure quality access to care, especially in LMICs, attention should be paid to internet access, quality of smartphone use, and designing lightweight, easy to use applications. Additionally, given the rapid proliferation in data from these applications, there needs to be an increased focus on safe use, data privacy, regulation, and ethical data collection.

New Opportunities

Future directions for digital mental health should include greater engagement of patients with schizophrenia, providers, and their caregivers in design, evaluation, and delivery of digital interventions. Clinicians and caregivers have expressed an interest [68, 69] in using digital applications to enhance self-management of behavioral and physical comorbidities and in integration with community behavioral health teams.

Alcohol and other drug-use remains an area for future growth. There have been a few digital studies, using methods such as virtual-reality based CBT [70], EMA/EMI delivery focused on alcohol-use [71, 72], and digital training for community health workers [73] to address problematic alcohol-use; however, none have focused specifically on people with schizophrenia. Studies in high-income countries further demonstrate that addressing opiate-use and stimulant use among people who have schizophrenia is important to close the mortality gap [74].

Leveraging task-sharing as a method to scale community-based psychiatric care is a key area of further study and has shown great promise in “last mile” psychiatric care. Studies from India [75, 76] have shown that digital training holds promise as an approach to build capacity of community health workers to identify and triage rural patients with schizophrenia. This is an area of future growth which has the potential to help close the mental health gap among LMICs.

Conclusion

Digital mental health interventions have expanded over the last decade; however, uptake and implementation remain slow. Large-scale randomized control trials are necessary to identify key interventions that show clinically relevant results. Future innovations should also look toward scaling low technology interventions, digital medicine, digital phenotyping, and digital training for task-sharing.

Author Contributions

All authors contributed to the study conception and design. The first draft of the manuscript was written by Anand Chukka and John Naslund. The data collection, revision, and final edits of the study table was completed by Soumya Choudhary and Siddharth Dutt. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Competing Interests

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Human and Animal Subjects

This article does not contain any studies with human or animal subjects performed by any of the authors.

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- Of importance
- Of major importance

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