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# Review of Recent Technologies for Prediction and Prevention of Relapse in Schizophrenia

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Patients with schizophrenia have a high rate of recurrent relapse episodes, with each subsequent relapse having a detrimental impact on clinical outcomes. To alleviate the substantial economic and humanistic burden, the availability of smartphones and the internet provides a crucial opportunity for collecting active (e.g., survey) or/and passive (e.g., sensor) data to monitor and assess the symptoms of relapse. This paper reviews the published literature that utilizes recent technologies (texting, telemedicine, apps, surveys, sensors) to predict and prevent a subsequent episode of relapse in schizophrenia. Our study provides an updated overview of the variety of technologies available for predicting and preventing relapse in people with schizophrenia. The effectiveness of technology, its limitations, and future direction are discussed based on the data from studies.

**Keywords:** Schizophrenia, Relapse, Technology, mHealth, Digital Phenotyping, ITAREPS

## Review of Recent Technologies for Prediction and Prevention of Relapse in Schizophrenia

The rate of recurrent episodes of relapse is high in patients with schizophrenia, with 40% of patients relapsing within one year. (Barnett, et al., 2018) and 80% within five years (Spaniel, et al., 2015). Each subsequent relapse is associated with a detrimental effect on cognition, social and occupational functioning, and mortality. The damaging impact of schizophrenia can be moderated or mitigated by interceding before an ensuing episode of relapse to reduce a substantial economic and humanistic burden. Prediction and prevention of relapse in schizophrenia provide an essentially attainable opportunity, as the relapse is preceded by early warning signs (EWS).

The critical approaches for EWS detection use evaluation of symptoms through rating scales and in-person interviews, which require in-person interaction. This approach has the limitations of being time and resource-intensive, susceptible to inaccuracies and interpretive errors, less accessible, and scalability. (Buck, et al., 2019) The need for innovative approaches and recent technologies for schizophrenia is evident owing to the heterogeneity and complexity of schizophrenia, along with the requirement for accurate and holistic observations of the patient's experiences. Schizophrenia affects approximately 24 million people (0.32%) worldwide, prompting WHO's Mental Health Gap Action Programme (mhGAP), which uses evidence-based technical guidance, tools, and training packages to expand service in resource-poor settings.

The ubiquitous presence of mobile phones, the internet, and technology provides an effective and affordable opportunity to monitor, record, and assess the gradual changes in the individual and aggregate symptoms preceding relapse.

Patients with schizophrenia increasingly have a high overall mobile ownership, the majority of whom are willing to receive technology-enabled mental health services via their mobile phones. (Firth, Cotter, Elliott, French, & Yung, 2015) Thus, it is essential to explore its ability to identify and monitor patient symptoms, predict and prevent relapse, and encourage medication adherence.

Self-reporting, fundamental to the existing approach, can accurately capture patients' symptoms using technological approaches (e-mail, SMS, App) to assess symptoms without direct contact with a trained professional. It can provide insight into the patient's regular assessment of aggregate EWS (daily, bi-weekly, tri-weekly, weekly), usually more frequently than an in-person assessment.

Additionally, technology has the potential to augment self-report with real-time insight into physiology, sleep, and social patterns. The technological facilitation of existing technology is an advancement. Still, the urgent necessity for a real-time objective assessment of the longitudinal profile of patients' symptoms drives the technological innovation in mental health. Passive data collection allows real-time capturing of digital behavior of human behavior, also known as digital phenotyping. It automatically collects data from smartphones and wearables, which can analyze both passive (e.g., sensor) and active (e.g., survey) data. This ecological momentary assessment (EMA) helps understand the relationship between active and passive data, which may yield personalized relapse signals and adaptive intervention. Existing studies have established the potential of EMA to predict relapse and characterize changes that occur in the post-relapse period. Additionally, apps for self-monitoring and self-management purposes may extend the reach of mental health services in a more personalized domain through technology. Machine learning is yet another technology that may offer the potential to bridge the gaps in future clinical states.

Thus, in this paper, we aim to thoroughly review existing studies on technologies that predict and prevent relapse in patients with schizophrenia to explore the current potential of evidence-based assessment and intervention of clinical care. With the ever-increasing ease, accessibility, and cost-effectiveness of technologically facilitated mental health services, academic research in this area is crucial to explore future possibilities. Owing to the prevalence of smartphones, the barriers to the collection of schizophrenia-related data are diminishing, which prompts a variety of technology-related studies in relapse prediction and prevention of schizophrenia. The literature has yet to be reviewed to examine these studies and deepen the understanding for future research.

The paper is arranged as follows: Method with search strategy, screening criteria, and study selection for this review are discussed. Then, the results of our narrative review, discussion, and conclusion are discussed in detail.

## Methods

The review utilizes a narrative approach to compile and analyze the available data on relapse prediction and its prevention utilizing digital technology amongst people with schizophrenia.

### Search Strategy

The critical databases of PubMed, EMBASE, PsycINFO, Web of Science, Scopus, and the Cochrane Library are employed to identify the relevant peer-reviewed publications. The systematic search strategy encompasses the search terms about the research question for technologies in predicting and preventing relapse in schizophrenia, as seen in Table 1.

The search method was adapted according to individual databases through Boolean operators to ensure the inclusion of all pertinent research available. Only the publications in English between January 1, 2008, and July 26, 2022, were made available as deemed to be a suitable timeframe.

Table 1: Search terms.

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| Technologies in relapse of schizophrenia. | (schizophrenia) AND ((relapse) OR ("relapse prevention") OR ("relapse-prevention")) AND (("treatment-resistant schizophrenia") OR ("treatment-resistant schizophrenia") OR (digital) OR ("digital phenotyping") OR ("digital-phenotyping") OR ("m health") OR ("m-health") OR ("information technology") OR ("information-technology") OR ("e-health") OR ("e-health") OR ("mhealth") OR (internet) OR ("mobile health") OR ("mobile-health") OR ("technology")) |

**Screening Criteria**

**Inclusion Criteria:**

1. Studies on the target group of age e"16 years.
2. Publication originally in English or translated into English.
3. Published between January 1st, 2008 and July 26th, 2022.
4. Studies on technology use in relapse prediction and/or prevention of schizophrenia.
5. Studies on the target group with a diagnosis of schizophrenia spectrum disorder by the Diagnostic and Statistical Manual of Mental Disorders (DSM).
6. Studies regarding the implementation of technologies in relapse prediction and/or prevention of schizophrenia.
7. Studies having a target group with a minimum of one psychiatric hospitalization for psychosis before the enrolment.

**Exclusion Criteria:**

1. Studies that did not report a diagnosis of schizophrenia spectrum disorder on the target group by the Diagnostic and Statistical Manual of Mental Disorders (DSM).
2. Studies not focused on schizophrenic spectrum disorder only.
3. Studies on developing the technology utilized in relapse prediction and/or prevention of schizophrenia.
4. Studies with participants in another relapse prevention program.
5. Conference Paper or Preprints.
6. Protocols for research studies.
7. Studies on technology use in schizophrenia are not focused on relapse prediction or prevention.

**Study Selection**

The initial screening involved the review of abstracts to filter the 192 publications, with further scrutiny of the full text for unavailable or ambiguous abstracts. Twenty-two articles met the initial inclusion criteria, and a hand search uncovered eight additional articles. This paper thus discusses only fourteen of the articles that met the comprehensive criteria after the full-text review of the articles.

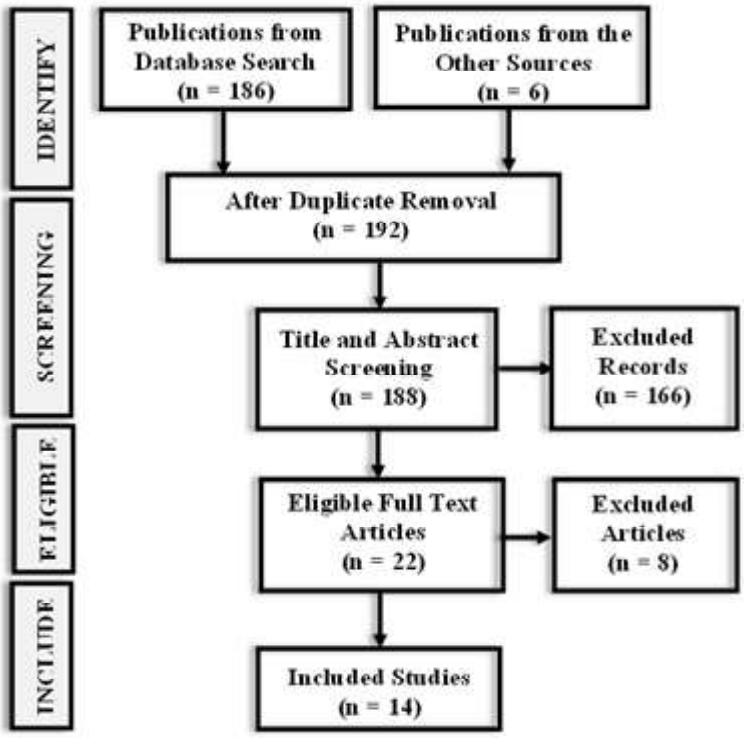


Figure 1: PRISMA Flow Diagram.

## Narrative Results

Table 2: Characteristics and main findings of identified studies.

| Study | Intervention | Design | Duration (month) | Sample | Age Group | Data Collection | Collection Frequency | Preventive Tool | Result | Limitation |
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| **(Spaniel, et al., 2008)** | ITAREPS Home Telemonitoring (PC to Phone SMS) (EMA for Relapse Prevention) | Double-blind, randomized trial, mirror follow-up | 12 | 45 | 18-65 years. | Active (10-item Early Warning Sign Questionnaire (EWSQ)) | Weekly (Thursdays) Twice weekly (Thursdays and Mondays) during the alert period. | Notification to the psychiatrist for Early Intervention Algorithm (EIA). Raises the antipsychotic dosage by 20% from the baseline maintenance level within the following 24 | EWSQ scores from patients in 88 instances and family member reports throughout the follow-up period in 47 cases; the ITAREPS system reported the development of EWS. The only significant factors were medication compliance, ITAREPS program adherence, and family member participation in the study. | Lack of a control group Relatively small population of patients. |

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| | | | | | | | | hours. | For a mean follow-up of 283.3±111.9 days, there was a 60% decrease in hospitalizations during the ITAREPS program (sign test, p<0.004). Hospitalizations amongst extremely cooperative patients, including family members, and 70+% of SMSs replied reduced by 100%. | |
| **(Spaniel, et al., 2008)** | **ITAREPS Home Telemonitoring (Phone-to-PC SMS) (EMA for Relapse Prevention).** | **Double-blind, randomized trial, mirror follow-up** | **12** | **73 (Original = 45, New =28).** | **>18 years.** | **Active (10-item EWSQ)** | **Weekly** | **Notification to the psychiatrist for Early Intervention Algorithm (EIA).**<br><br>**Raises the antipsychotic dosage by 20% from the baseline maintenance level within the following 24 hours.** | **For a mean follow-up of 396.8 ± 249.4 days, there was a 77% reduction in hospitalizations during the ITAREPS program (Wilcoxon-signed ranks test (WSTP) p < 0.00001). Hospitalization from 991 days before to 365 days after the ITAREPS (WSTP, p < 0.003). Hospitalizations amongst extremely cooperative patients and family members were reduced by 100%. Hospitalization has no significant difference in the patients.** | **Limitation to the mirror-image design method. Lack of a control group Absence of blinding and randomization. Inability to account for the patient's risk of rehospitalization. Unable to document the intervention during the alert states.** |

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| **(Španiel, et al., 2012)** | ITAREPS (EMA for Relapse Prevention). | Parallel group, randomized, double-blind, controlled trial | 12 | 146 (Active = 75, Control = 71). | 18-60 years | Active (10-item EWSQ) | Weekly | Notification to the psychiatrist for Early Intervention Algorithm (EIA).<br><br>Raises the antipsychotic dosage by 20% from the baseline maintenance level within the following 24 hours. | No variation in the hospitalization-free survival rate across groups.<br>Absence of pharmaceutical management leads to an eleven times higher risk of hospitalization after a PIRE.<br>ITAREPS Algorithm Adherers (IAAs, n = 25) have nine times less risk of hospitalization than their counterparts.<br>Compared to the ITAREPS Non-interventional group, there was a nine-fold decrease in the probability of hospitalization for ITAREPS Algorithm Adherers (IAAs, n = 25). | Adherence by increase of the antipsychotic dosage in only 39% of PIREs.<br>Implementation in clinical practice requires acceptance of computerized methods. |
| **(Komatsu, et al., 2013)** | **ITAREPS Home Telemonitoring (PC to Phone SMS)** | **RCT** | **12** | **45 ITAREPS = 22, Control = 23)** | **20-65 year** | **Active (10-item EWSQ)** | **Weekly** | **Raises the antipsychotic dosage by 20% from the baseline maintenance level within the following 24 hours.<br><br>Home visits by nurses within the duration of the alert.** | **Lower probability of rehospitalization in the ITAREPS group (2 [9.1%]) compared with the control group (8 [34.8%]).<br>Reduced mean number of inpatient days from 88.8 to just 18.5 days. (p = 0.036).<br>Lower ratio of the number of rehospitalizations to relapses (p = 0.035) and a considerably smaller mean change in total BPRS scores at relapse from baseline (p = 0.019) in the ITAREPS group.** | **Small sample size.<br>Brief observation period.** |

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| **(Spaniel, et al., 2015)** | ITAREPS-Telemedicine Program (Early Warning Sign Questionnaire by SMS). | RCT (Randomized controlled trial) | 18 | 146 (Active =74, Control =72) | 18 – 60 years. | Active (10-item EMA self-report scale). | Weekly. | 20% dose increase in medication within 24 hours of alert.<br><br>Investigator visits following 72 hours post-alert. | Detection of EWS by ITAREPS at least once in 52% of participants in the active arm (n= 43). The hospitalization-free survival rate (Active = 12/74, Control = 14/72) did not differ between the groups. The risk of hospitalization was only elevated by ITAREPS-related factors (Alerts without pharmaceutical intervention, Hazard Ratio [HR], and patient non-adherence to ITAREPS). | Twenty-six (35%) patients of the active arm satisfied the predetermined criteria for ITAREPS non-adherence. Inadequate adherence of the active group's investigators. Information technology-based warning systems are relied on by psychiatrists. |
| **(Ben-Zeev, et al., 2017)** | **CrossCheck** | **RCT (Randomized controlled trial)** | **12** | **5** | **>18 years** | **Active (10-item self-report) symptoms of Psychosis, general mental health, and functioning<br><br>Passive: Multi-modal behavioral sensing<br><br>Device use Data** | **Multiple times a week (Monday, Wednesday, and Friday).** | **-** | **Distinct digital indications of each individual's psychotic relapse. Significant variation in the digital remnants of the participants' psychotic relapses. Self-reports gave some people a precise account of their symptom aggravation before being admitted to the hospital. Others experienced changes evidenced effectively by behavioral sensing data trends or device usage patterns.** | **The data set is from an ongoing investigation. There is a chance that certain data don't accurately reflect the behavior of the target user. Some data may not reflect user behavior accurately. • The desired construct may not always be captured by sensed data.<br><br>Data sets presented in this paper were drawn from a study still underway. Possibility that some data do not represent the intended** |

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| | | | | | | | | | | user's behavior. Sensed data may not always capture the intended construct. |
| (Barnett, et al., 2018) | Beiwe App (Open-Source platform) | - | 3 | 15 | - | Active (Bi-weekly in-app symptom survey).<br><br>Passive (GPS, accelerometer, anonymized call, text message logs, screen on/off time, and phone charging status). | Bi-weekly. | - | The rate of behavioral anomalies was 71% higher two weeks before relapse.<br>The mobility, sociability, and self-report of clinical outcomes samples have anomalies of 1.8, 1.7, and 1.4, respectively.<br>The variability of the anomalies varied depending on the subjects within the range of twice of others.<br>On the day with reported anomalies, the patients struggled with moderately strong anxiety and depression as on the Warning Symptoms Scale. Extreme sleeping problems and extreme levels of psychosis were also reported. | Small sample size and infrequent relapse limits the accurate estimate of the sensitivity and specificity.<br>Insufficient anomaly data before the test.<br>Ideally, the frequency of detected anomalies should match actual relapses. |

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| (Buck, et al., 2019) | CrossCheck behavioral sensing system | RCT (Randomized controlled trial) | 12 | 45 | >18 years. | Passive (Digital Social Functioning Incoming & outgoing call counts, their total duration, SMS messages, frequency & duration of nearby human speech. | - | - | The average relapse rate was more significant than one for each patient during the study. (Twenty-seven relapse for twenty) The collected data indicates the variation in social functioning over smartphones. Thirty days before the psychiatric relapses, the digital indicators differed from their typical patterns. The anomaly in behavioral pattern, which is most closely related to the relapse, is a decrease in SMS text messages in the evening (i.e., after 6 pm) and late at night (after midnight). Another behavioral anomaly in social functioning is the decrease in the outgoing calls at nearly all-time windows. Also, a reduced call duration in outgoing was closely related to relapse at spaced epochs (i.e., 12 pm to 6 am and 12 am to 6 am). | Analysis was exploratory and involved multiple statistical tests. Thus, results should be interpreted with potential Type-I error. Some participants did not use the provided device as their primary mobile phone. Lacks insight into the causation of the effect, i.e., behaviors that might function as primary causal factors. |

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| **(Eisner, et al., 2019)** | **ExPRESS ( obile phone app to monitor basic symptoms and conventional early signs of psychosis relapse).** | **Framework Analysis.** | **6** | **16** | **22-57 years.** | **Active (Self-Reported BSC, i.e., Basic Symptoms Checklist)** | **Weekly (1:30 pm on Wednesdays).** | **-** | **This study highlights that participants use a symptom-monitoring app for significantly longer with less frequent monitoring; this helps develop effective apps for relapse prevention. It also facilitates self-management, which seems to aid an integrative recovery style through a symptom monitoring app that enables patients to understand their psychosis and has therapeutic results.** | **Small sample size It is not a representative sample** |
| **(Ybarra, Rodriguez , Madison, Mojtabai, & Cullen, 2019)** | T4RP (Texting for Relapse Prevention) | RCT (Randomized controlled trial) | - | 25 | >18 years. | Active (Text messaging). | Daily. | Automated alert to the provider to reach out. | More accessible and Cost-effective. T4RP as a supplement and not an alternative to current care. Facilitates communication between patient and provider. Daily monitoring and management of symptoms for personalized coping ways. | The programs only involved English-speaking patients. The patient sample was majority female. |

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| **(Adler, et al., 2020)** | **CrossCheck System (Android app with a cloud-based data collection and storage platform).** | **RCT**<br><br>**Encoder-Decoder neural network model and clustering-based local outlier factor model** | **12** | **60** | **>18 years** | **Active (Self-report EMA).**<br><br>**Passive (Passive Sensing Data: Acceleration, App use, call, conversation, location, screen activity, sleep, and text).** | **Every 2 to 3 days.** | **-** | **Passive data indicates an increase in deviations from typical patterns the thirty days before relapse.**<br>**The median sensitivity and specificity are 0.25 (IQR 0.15-1.00) and 0.88 (IQR 0.14-0.96.**<br>**The anomaly detection system effectively indicates an increase of 108% near relapse within the thirty days before relapse. This increase in anomaly was restricted to specific days within the defined NR30 period.**<br>**Identifying patient-specific behaviors that alter from their typical patterns before relapse allows clinicians to intervene early. The anomaly detection system allows measurement of these behaviors, indicating the specific patient's declining state.** | **Limited sample size (18/60 relapse).** |
| **(Buck, et al., 2021)** | CrossCheck (Integrated mobile-monitoring system)<br><br>Embedded sensors, GPS, and accelerometer. | Randomized | 12 | 61 | >18 years. | Active (10-item EMA self-report scale).<br><br>Passive (Sensors, accelerometers, and GPS). | Three times per week (Monday, Wednesday and Friday). | - | On the days of relapse, the EMA system found increases in negative mood anxiety, persecutory ideation, and hallucinations with d equal to 0.34, 0.49, 0.35, and 0.34.<br>Over the hundred days before relapse, there was a gradual emergence in both persecutory ideation and hallucinations with d equal to 0.05 per week. | Small size of relapse sample (20).<br>Possibility to align missing data periods with the greatest risk.<br>Attenuated strength between EMA symptoms and relapse due to reaching out. |

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| **(Gumley, et al., 2022)** | **EMPOWER** | **Cluster design-randomized controlled trial.** | **12** | **73 (EMPOWER = 42, Control = 31)** | **>16 years.** | **Active (22-item Questionnaire)** | **Daily** | **Messages tailored to questionnaire responses designed to improve self-management and independence.** | **After a year, the EMPOWER group had lower relapse fear compared to the in-treatment group, with a mean difference of 7.53, indicating that the frequent monitoring did not increase hypervigilance and worry regarding the illness.** | **The EMPOWER group had a higher attrition rate, which was associated with the increased burden and detrimental impacts of self-monitoring.** |
| **(Zhou, Lamichhane, Ben-Zeev, Campbell, & Sano, 2022)** | CrossCheck (Mobile Sensing Data for Relapse Prediction). | Clustering-based behavioral categorization. (GMM, i.e., Gaussian Mixture Model, and PAM, i.e., Partition Around Medoids). | >12 | 63 | 18 – 65 years. | Passive (21 passive sensing features: acceleration, distance traveled, sleep duration, ambient light and sound, conversation duration, mobile unlock duration, call and SMS log, and app use). | Daily | - | 27 Relapse (20 Patients) during the monitoring period. The higher the number of days of sensor inactivity, the greater the risk of relapse. Relapse occurrences not signaled by sensor inactivity revealed no significant alterations in any particular characteristic before the relapse. | The F2 score of 0.23 is a relatively poor performance of relapse prediction. |

**Characteristics of included studies**

Table 2 presents the summarized vital findings and research characteristics of the fourteen included studies that satisfied the requirements for inclusion were included. The included studies incorporated several types of predictive and preventive tools for relapse in schizophrenia. This includes ITAREPS, CrossCheck, ExPRESS, EMPOWER, BEIWEI app and T4RP. Information Technology-Aided Program of Relapse Prevention in Schizophrenia (ITAREPS) and CrossCheck, employed in ten studies, were the tools most often utilized in these studies. Smartphones and other devices were recognized as the technology used to track activity in the research. Of the fourteen investigations, two gathered just passive data, eight gathered active data, and the remaining studies gathered both active and passive data.

(Spaniel, et al., 2008) presents ITAREPS to facilitate an early intervention for relapse prevention of schizophrenia. ITAREPS provides an easy and effective telemedicine system based on mobile phones, which provides greater accessibility. It monitors the behavior patterns of the patient remotely every week to identify the prodromal relapse symptoms. This program thus allows authorized physicians to intervene early to avoid needless hospitalizations. Preliminary findings of the study show that the number of hospitalizations was reduced by significant statistics of 60% during the ITAREPS participation period, compared to the days before the ITAREPS program.

(Spaniel, et al., 2008) presents a one-year extension of a previous study based on a mirror follow-up aimed at decreasing the number of hospitalizations. The ITAREPS study evaluating the clinical effectiveness shows that the number of hospitalizations dropped significantly by 77%, and there was a significant reduction in the number of hospitalization days. This decrease in the requirement for hospitalization care while participating in the ITAREPS program, compared to before the program, displays the effectiveness of this program. It highlights that the number and duration of relapses can be reduced through prediction and early intervention.

(Španiel, et al., 2012) indicated that there was no difference in the hospitalization-free survival rate between groups after a year post-evaluation of the effectiveness of the ITAREPS. In the absence of pharmacological intervention following a PIRE, there is a reported eleven-fold higher risk of hospitalization. Additionally, the study showed that ITAREPS Algorithm-Adherers had a nine-fold lower risk of hospitalization than the ITAREPS Noninterventional group.

(Komatsu, et al., 2013) assessed the efficacy of the ITAREPS without considering the impact of user adherence to the program's protocol. The ITAREPS group had a lower probability of rehospitalization than the control group. Comparing the ITAREPS group to the control group, the probability of rehospitalization and the mean number of inpatient days was considerably lower. Additionally, in the ITAREPS group, the mean change in total BPRS scores at relapse from baseline was much smaller, and the ratio of rehospitalizations to relapses was considerably lower.

(Spaniel, et al., 2015) presents a remote telemedicine system based on weekly monitoring, known as the ITAREPS program. It is used for relapse prediction and prevention through early detection and intervention in schizophrenia. The objective was to assess the program's effectiveness in lowering hospitalizations within the duration of the study. Furthermore, there was no difference between the groups for the hospitalization-free survival rate.

(Ben-Zeev, et al., 2017) describes and demonstrates CrossCheck, which utilizes a

smartphone to monitor and identify the indicators of relapse. The CrossCheck achieves this through participants' data collection through multimodal behavioral sensing. It reports that individuals with schizophrenia have digital markers of relapses that are unique to each individual. These unique indicators include behavioral trends (changes in geolocation patterns, decreased physical activity), device use patterns (increased use of apps during nighttime, cessation of smartphone use), and self-reports, clearly describing symptoms before hospitalization.

(Barnett, et al., 2018) conducted a pilot study for digital-phenotyping-based relapse prediction in schizophrenia. The reasonably available behavioral and other data gathered passively through the smartphone is, at present, an underutilized resource for remote monitoring and recognizing the early indicators of relapse. This allows an easy and early intervention before relapse to prevent further escalation. For a maximum of three months, seventeen schizophrenia patients undergoing active treatment utilized the Beiwe application on their smartphones for the study. The results show that the abnormalities before two weeks of the relapse were higher by 71% compared to any other period. Identifying deviations in behavioral tendency in real-time from the usual pattern will allow the prediction of relapse symptoms. Thus, intervening before the relapse occurs reduces care costs and patient suffering.

(Buck, et al., 2019) conducted a year-long study to determine the ability of the digitally measured social behaviors that are gathered through the smartphone to identify early signs of schizophrenia relapse. Smartphones equipped with the CrossCheck behavioral sensing technology were distributed to sixty-one patients with schizophrenia who were at high risk of relapsing. Exploratory mixed effects models analyzed the relationship of social behavior to relapse through digital socialization data of calls, texts, and microphones. Findings suggest that the relapses are related to decreased outgoing calls, duration, and text messages. However, there seems to be no relationship between incoming calls, their duration, and face-to-face interactions and relapses. Smartphone-enabled social behavior may be a valuable indicator for assessing the likelihood of a schizophrenia relapse.

(Eisner, et al., 2019) develop a smartphone app, ExPRESS, to track baseline symptoms and early indicators of schizophrenia relapse. Also, to assess the ExPRESS's long-term acceptance. It was found that the ExPRESS response for the long-term was appropriate for the priori themes, whereas minor adjustments were recommended for the subsequent iterations of ExPRESS. A posteriori themes provided further context for understanding people's experiences with ExPRESS. Since evaluations were more regular, anonymous, and did not require the person to express their sentiments in their own words, some reported finding it more approachable than clinical appointments.

(Ybarra, Rodriguez, Madison, Mojtabai, & Cullen, 2019) detail the development of "Texting for Relapse Prevention," an affordable, scalable text messaging platform that asks patients about their "early warning signs" daily. Findings from content advisory teams and development focus groups with 25 patients and 19 physicians indicate that patients were excited about the application and believed that getting daily updates about their symptoms would make them feel supported. Although providers were enthusiastic about the concept, they expressed concern that if patients believed the messages were from them, the program would obstruct patient-provider contact. Patients thought the information was valuable and practical.

(Adler, et al., 2020) use behavioral abnormalities and passive sensing data from a smartphone to develop "early warning signs" for relapse prediction. This suggested approach may be utilized to identify behaviors of an individual that alter before relapse and predict a greater rate of abnormalities in patients with SSDs throughout the thirty-day near-relapse duration.

(Buck, et al., 2021) examined the Precursors to Relapse in Schizophrenia by mHealth-Assisted Detection of EMA measurements. Findings report that the participants had higher levels of anxiety, depressive mood, persecutory ideation, and hallucinations on relapse days than they did on study-wide averages. Over the 100 days before the relapse, there was a notable and consistent rise in persecutory ideation and hallucinations, which eventually led to these increases on average. This implies that evaluations of psychotic symptoms could identify important cues that exist well in advance of psychiatric relapses.

(Gumley, et al., 2022) aim to establish the feasibility of determining the efficacy of a mixed digital intervention (EMPOWER) for relapse prevention. According to the year-long results of the study, thirty, i.e., 71% of the participants randomly assigned to EMPOWER, satisfied our predetermined criterion of more than 33% adherence to daily monitoring, which was predicated on practicality. In the EMPOWER group, there were 29 adverse events, while in the treatment-as-usual group, there were 25. Eleven individuals were affected by the 13 app-related adverse events, one of which was rather significant. At 12 months, the EMPOWER group experienced less fear of recurrence than the treatment-as-usual group.

(Zhou, Lamichhane, Ben-Zeev, Campbell, & Sano, 2022) this study aims to develop and identify a clustering model representing behavior for relapse prediction from continuous multimodal mobile sensing. It used GMM and PAM-based models representing different behavioral patterns. In this study, significant changes were observed near the relapse periods.

## Discussion

### Implications for design and implementation

We distinguished between active versus passive data collection because it highlights the difference between self-report and objective assessments of the patient's symptomology. The interventions used in the studies ranged from 3 months to 18 months, though the effectiveness of the intervention was reduced due to lower relapse occurrence. The range of study designs, varying analytic approaches of predicting or preventing, and small sample sizes demonstrate significant variation in the methodological quality of included studies. The following general categories were used to group all studies that satisfied the inclusion criteria to understand the results:

### ITAREPS

Five studies utilizing ITAREPS evaluated the symptoms through an active (10-item Early Warning Sign Questionnaire) to detect changes in the patient's symptoms to prevent any subsequent relapse. Each included an alert period that mandated a 20% increase in anti-psychotic drugs, often accompanied by confirmation by trained individuals (in-person or through the web). The home telemonitoring system (PC to Phone SMS) is highly effective in most cases with greater adherence, which may be owed to less weekly-frequent assessments (up to tri-weekly in alarm periods only). The participants were mainly between 18 and 65 years of age. However, the sample size varied greatly.

(Spaniel, et al., 2008), (Spaniel, et al., 2008) used the double-blind, randomized trial, mirror follow-up design and found a significant reduction in hospitalization. The follow-up study confirmed that the only factors that statistically significantly contributed to fewer hospitalizations were medication compliance, adherence to the ITAREPS program, and family member participation in the project. The studies were prone to methodological limitations as they included 45 and 73 participants only and for the duration of 12 months without a control group.

These limitations were extradited by (Španiel, et al., 2012), which utilized parallel-group,

randomized, double-blind controlled trial with146 participants (Active = 75, Control = 71). It confirmed the previous findings, but the adherence to the implementation of the clinical practice of a 20% dosage increase was still low and challenging. These findings were later confirmed by (Komatsu, et al., 2013) and (Spaniel, et al., 2015) by utilizing a random controlled trial with control groups for 12 months.

**CrossCheck**

Five CrossCheck studies evaluated the symptoms through active and passive data to detect changes in the patient's symptoms and predict relapse. CrossCheck was developed by Ben Zeev et al. in 2017. It employed a randomized controlled trial on merely five participants for 12 months. The program collected both Active and passive data. The active data was collected multiple times a week (Monday, Wednesday, and Friday) through a 10-item self-report focusing on symptoms of functioning (socialization, sleep), general mental health (stress, depression, hopefulness, calmness, clarity of thought), and psychosis (hallucinations, persecutory ideation). Furthermore, the passive data collection utilized multi-modal behavioral sensing (physical & geospatial activity, speech frequency, and duration) and device use data (call and text activity, app use). The program identified that participants had individual digital indicators of their relapse, which were unique to each person. However, there was considerable heterogeneity in the digital indicators predicting their relapses. Such a small sample size was not very representative. (Buck, et al., 2019) reiterated the study with 45 participants focusing exclusively on passive data (Digital social functioning: number of incoming & outgoing calls, call duration, SMS messages, frequency & duration of nearby human speech). The study found that social functioning deviated from the set behavior pattern in the 30-day preceding psychiatric relapses, and decreases in SMS text message behavior late in the day, outgoing calls, and outgoing call duration were related to relapse at spaced epochs. (Zhou, Lamichhane, Ben-Zeev, Campbell, & Sano, 2022) CrossCheck was also employed on 63 patients using clustering-based behavioral categorization. (GMM, i.e., Gaussian Mixture Model, and PAM, i.e., Partition Around Medoids). The relapse prediction was relatively low, and sensor inactivity did not indicate the events. It also found no non-trivial changes in any specific feature before relapse.

(Adler, et al., 2020) CrossCheck was also used with active and passive data, using an "Encoder-Decoder neural network model" and a "clustering-based local outlier factor model" on 60 patients. It identified patient-specific behaviors that alter solely before relapse and, using passive data, exclusively predicted an increase in anomalies within the 30 days preceding relapse. Using EMA evaluation by CrossCheck on 61 patients (Buck et al., 2021) found increases in negative mood, anxiety, persecutory ideation, and hallucinations on relapse days.

### Apps

*Bewei App* is an open-source platform used by (Barnett, et al., 2018) to collect active and passive data bi-weekly to predict relapse in patients. Two weeks before a relapse, the rate of behavioral abnormalities was found to be 71% greater. Subject diversity was also seen, with some participants exhibiting nearly double the rate of anomalies discovered compared to others. Since the app is an open-source platform, it may be used to validate the obtained results in the future.

*EMPOWER* was used by (Gumley, et al., 2022) through cluster design- a randomized controlled trial with preventive messages tailored to questionnaire responses designed to enhance self-management and autonomy. However, higher attrition from the EMPOWER group appeared to be related to additional burden and adverse effects of self-monitoring.

*ExPRESS* is a smartphone app designed to track the typical early indicators of psychosis relapse as well as basic symptoms. Framework analysis was used to investigate it (Eisner et al., 2019). This study shows that individuals are willing to use a symptom-monitoring app for noticeably longer when there is less frequent monitoring. An app for tracking symptoms can help patients understand their psychosis and achieve treatment outcomes. As a result, facilitated self-management supports an integrated recovery approach.

### T4RP

Within the context of our review, “mobile technologies” encompasses a wide range of gadgets, including laptops, tablets, smartphones, and other devices that provide remote digital interventions. Most mHealth tools are smartphone applications since they are widely available, well-researched, and simple to download. From the initial physician-oriented PDAs (personal digital assistants) to patient-oriented mobile applications, we saw a change in how technology develops in our study. (Ybarra, Rodriguez, Madison, Mojtabai, & Cullen, 2019) explored T4R (Texting for Relapse Prevention) through RCT (Randomized controlled trial) on 25 patients. The program collects active data through text messaging daily, which sends an automated alert to the provider to reach out if it crosses the threshold. It is the most accessible and cost-effective prevention, recommended as a supplement, not an alternative to current care.

## Conclusion

This narrative review presents a comprehensive analysis of the literature about technologies for schizophrenia relapse prediction and prevention. To conclude, the review deems the existing and emerging technologies as effective and acceptable. SMS-based interventions, specifically ITAREPS, appear highly effective with more adherence, which is promising for future interventions. Implications for apps such as SHARP and ReMind are warranted, which promote self-monitoring and self-management of relapse symptoms.

Despite the mindfulness of authors, there may have been phrases that were not recognized and included in the search method; even though the writers made sure to utilize several versions of the concept “Technology” and were aware of its abundance of synonyms, there may have been terms that were not identified and included in the search strategy. Studies analyzing the experiences of schizophrenia spectrum disorder with other psychotic illnesses may have been disregarded since this review focused exclusively on the experiences of individuals with schizophrenic spectrum disorders. Furthermore, the search technique was limited to publications written

in English, which might have implied bias in the material found.

Future research agenda should include the development of apps and technologies for prediction, prevention, treatment, and adherence personalized to the individual patient's symptoms, focusing on the implications of using the technologies for mental disorders. In the development of these technologies, ethical considerations should be highlighted before broad acceptance and public use, particularly for people with schizophrenia spectrum disorder.

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