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Digital Technology Use in Schizophrenia: A Systematic Review

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Digital Technology Use in Schizophrenia: A Systematic Review

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Ao meu pai, Francisco.

Resumo

Objetivo: O uso das novas tecnologias tem aumentado entre as pessoas com doenças do espetro da esquizofrenia e tem sido amplamente considerado em diferentes tipos de intervenção. O rápido desenvolvimento das tecnologias aumenta a necessidade de confirmar a sua viabilidade e eficácia. Este estudo tem como objetivo rever e sintetizar os diferentes tipos de ferramentas digitais e tecnologias usadas para o tratamento de pessoas com esquizofrenia e outras condições do respetivo espetro, para além da sua viabilidade e aceitabilidade. ***Métodos:*** Seguindo as normas de PRISMA, foi feita uma pesquisa a 1 de março de 2021 em diferentes bases de dados, encontrando 71 artigos, após análise de título e resumo. Os critérios de inclusão foram aplicados. ***Resultados:*** Seis estudos foram incluídos e os principais objetivos das intervenções doram défices motivationais ($n = 2$), alucinações auditivas verbais ($n = 2$) e sintomas cognitivos ($n = 2$). ***Conclusões e implicações para a prática:*** A aceitabilidade e viabilidade das technologias digitais foram confirmadas, apesar de ainda não ser clara a sua exata eficácia. Estudos futuros devem considerer o aumento do tamanho das amostras e criar intervenções mais longas para reforçar a evidência e permitir a generalização dos resultados pararealçar a eficácia destas intervenções.

Palavras-chave: tecnologia; esquizofrenia; alucinações auditivas verbais; funções cognitivas; intervenções motivacionais

Abstract

Objective: The use of digital technologies has been increasing among people with schizophrenia spectrum disorder and it has been widely considered in different types of interventions. The fast development of technologies increases the need for confirming their feasibility, effectiveness, and efficacy. This study aimed to review and synthesize the different types of digital tools and technologies used to treat people with schizophrenia and other conditions of the respective spectrum, besides its feasibility and acceptability. ***Method:*** Following the PRISMA guidelines, a search was conducted on 1 March 2021 on several databases with 71 articles retrieved for the title and abstract screening. The inclusion criteria were applied. ***Results:*** A total of six studies were included and the principal targets of the interventions were motivational deficits (n = 2), auditory verbal hallucinations (n = 2), and cognitive symptoms (n = 2). ***Conclusions and Implications for Practice:*** The acceptability and feasibility of digital technologies were confirmed, although their exact efficacy is still unclear. Future studies need to consider increasing the size of the samples and create longer interventions to empower the evidence and allow the generalization of the results to enhance the efficacy of these interventions.

Keywords: digital technology; schizophrenia; auditory hallucinations; cognitive functions; motivational intervention

Índice

1. Introduction

In the last decade, digital technologies in health care have increased with computers, tablets, mobile phones, and other devices like wearable sensors. This use of technologies provides several advantages, such as lower health care costs, step up and reinforce the access of health care and can also provide not only innovative types of intervention, but also prevention, detection, and diagnosis of several diseases (Fernández-Sotos et al., 2019; Gay et al., 2016; Yu et al., 2020). The role of technology in healthcare, currently named Mobile Health (mHealth), specifically for mental disorders, such as psychosis and schizophrenia, has highly increased (Onwumere et al., 2018; Yu et al., 2020). In addition to mobile apps, used to assess mood functioning and symptoms, interactive short message service text messages are commonly used, as well as Web-based psychological interventions, computerized interventions, and wearable technologies with real-time feedback on well-being and functioning (activity and sleep quality for example) (Arnberg et al., 2014; Ben-Zeev et al., 2014; Cella et al., 2019; Granholm et al., 2012; Naslund et al., 2016; Onwumere et al., 2018; Reeder et al., 2016). A systematic review of Alvarez-Jimenez and colleagues (2014) stands online, social media, and mobile phone-based interventions are effective in reducing the severity of positive symptoms and depression, the number of hospitalizations, and improve medication adherence and social contacts in patients with schizophrenia. The feasibility, effectiveness, and efficacy of this technology with a retention rate of 92% in people with Schizophrenia is confirmed with other benefits referred in other studies, such as enhanced self-monitoring and self-management, increased self-esteem and empowerment, decreased stigma due to their condition, remote monitoring and tracking of functioning and relapse prevention (Lindhiem et al., 2015; Naslund et al., 2016; Välimäki et al., 2016; Yu et al., 2020). It is suggested that high levels of symptom-related distress and poor coping abilities are factors that can be beyond a relapse (Lardinois et al., 2007). Once regular monitoring by clinicians is challenging to implement and the resources are limited, it is suggested to use mHealth for frequent monitoring on symptoms fluctuation (Kumar et al., 2013; Narayan & Manji, 2016). For all of this, mHealth can address all the aspects of the recovery of people with Schizophrenia which goes beyond symptom reduction and functional improvement (Schwartz, 2011; Yu et al., 2020). These technologies can assure continuity of care during all the course of the disease-focused on improving well-being; besides, help individuals to empower them to be active in their recovery, a crucial aspect for an improved intervention (Gay et al., 2016; Lim & Penn, 2018; Treisman et al., 2016).

Digital technology access and use of people with schizophrenia have been discussed through the last years and over different countries. A considerable number of people with schizophrenia, around 84%, are increasingly owning mobile devices such as mobile phones and use them for their mental health care, according to the years between 2014 and 2015 in the United States of America (Firth & Torous, 2015). In addition to mobile phones, people have access to landlines, smartphones, personal computers, and tablets which 90% indicate the access of more than one of these devices. Information referent smartphones use states around 54% (Gay et al., 2016). This changes by age with a pronounced number of 68% in ages between 18 and 34, 48% in ages between 35 and 46, 44% in ages between 47 and 64, also 37% with more than 65 years.

It is stated that although the use of devices is still lower in patients with schizophrenia when compared with healthy individuals, the age range of early adulthood reveals a greater use of technologies that usually present prodromal or first episode symptoms and early-stage illness (Fernández-Sotos et al., 2019; Gay et al., 2016). It is also known that this population has a strong interest in using technology to cope and care for their illness (Gay et al., 2016; Lal et al., 2015).

Thus, it is crucial to consider the use of current devices such as smartphones and computers in the moment of designing intervention programs which have been recently investigated its use in areas such as neurocognitive remediation (Garrido et al., 2017), adherence to pharmacological treatment (Batra et al., 2017), social cognition remediation (Fernandez-Gonzalo et al., 2015), treatment of refractory auditory hallucinations (Craig et al., 2017), or training in social skills (Rus-Calafell et al., 2014).

This study aims to review and synthesize the different types of digital tools and technologies used to treat people with schizophrenia and other conditions of the respective spectrum, besides its feasibility and acceptability. The fast development of technologies is a challenge for the empirical search to confirm their feasibility, effectiveness, and efficacy. For this reason, it is essential to review the evidence related to the use of these technologies on mental health (Molina et al., 2021).

2. Methods

Preferred Reporting Items for Systematic Reviews and Meta-Analyses(PRISMA) was used for reporting this systematic review (Rethlefsen et al., 2021).

2.1. Search Strategy

A search was conducted on databases, such as PubMed, Cochrane Library and Web of Science, on 1st March 2021 using the search string with keywords ((("digital therapies") OR ("digital technology")) AND (schizophrenia)) with the filter of ten years applied.

2.2. Eligibility and Study Selection

Inclusion criteria included studies such as Randomized Controlled Trials (RCT), articles published in English, adults with more than 18 years old and diagnosed with schizophrenia and other conditions of schizophrenia spectrum illness, such as schizoaffective, schizophreniform, delusional disorder and psychosis.

For exclusion criteria were considered studies focused on individuals with comorbid conditions such as attention deficit hyperactivity disorder and autism spectrum disorder.

2.3. Data Extraction and Synthesis

The final search results of three databases were exported to software manager Mendeley and the duplicates reports were removed. After this, two reviewers started to analyze the articles independently. One reviewer analyzed the titles of all the articles and the second reviewer focused on the abstracts ir order to check whether articles met the inclusion criteria. If the two reviewers could not agree on the admissibility of an article, a third reviewer was requested to contribute for a final decision.

The full texts of the potential articles were obtained from all of the databases and then full read in order to analyze their admissibility taking in account the inclusion and exclusion criteria. The process of selection of the articles is illustrated in the PRISMA flowchart in Figure 1.

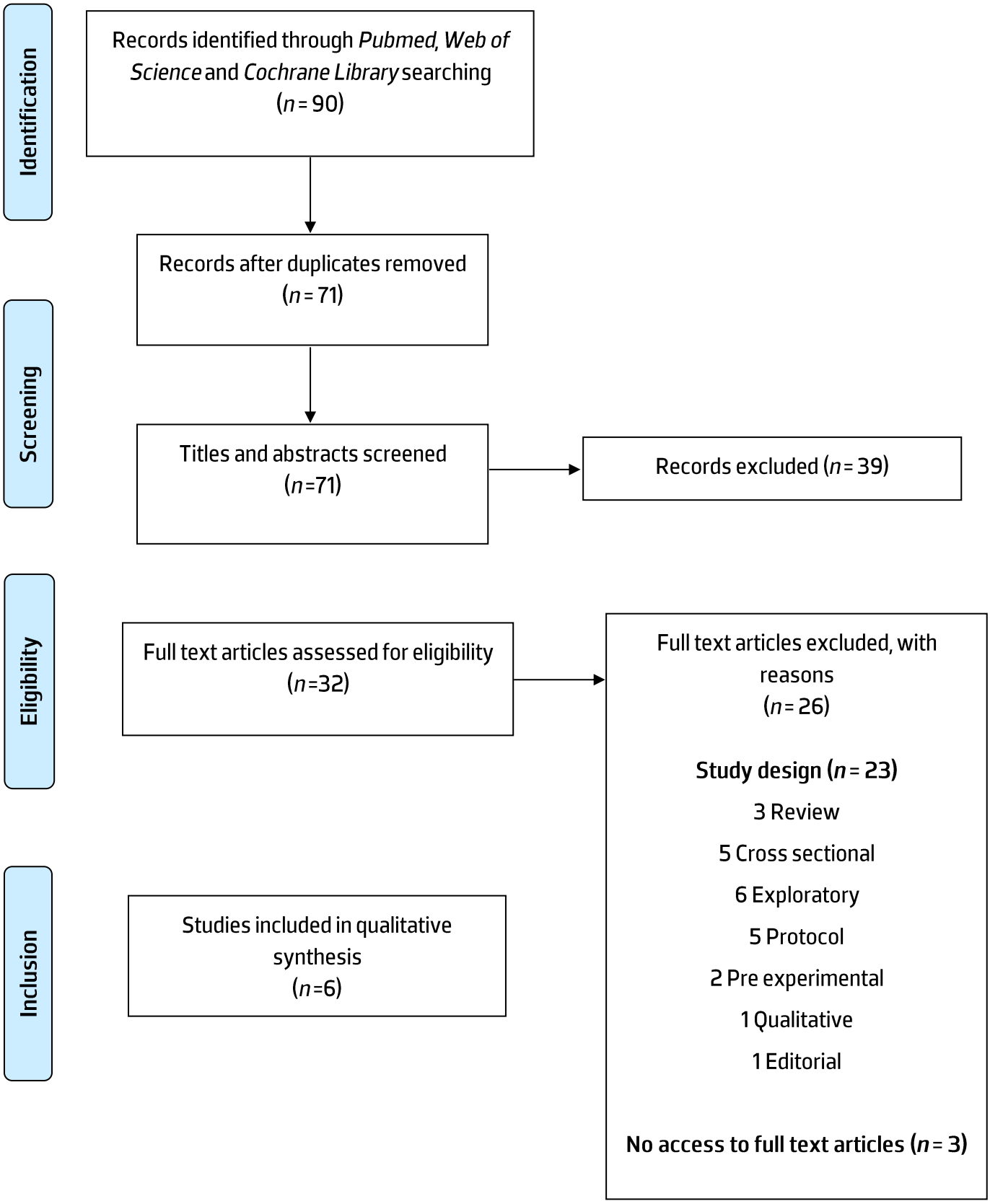

Figure 1

Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) diagram

2.4. Assessment of Risk of Bias

The risk of bias of each study was assessed using The Risk of Bias 2, an update to the original risk of bias tool Cochrane Risk of Bias Tool launched in 2008 (Sterne et al., 2019). This tool was specifically designed to assess RCTs, composed of 5 bias domains, such as randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each domain has signaled questions that have responses to answers such as "Yes", "Probably yes", "Probably no", "No" and "No information". These signaling questions are answered using different algorithms which allow determining the risk of bias judgment of each domain as "Low risk of bias", "Some concerns" or "High risk of bias". *RevMan* software was used to determine the risk of bias of each study.

3. Results

3.1. Search results

The searches resulted in 90 studies across all the databases. First, the duplicates were removed, leaving 71 papers for the title and abstract screening. Following this step, a total of 32 full-text papers were assessed for eligibility using the specified inclusion criteria. 26 articles were excluded with reasons, such as study design (three reviews, five cross-sectional studies, six exploratory studies, five protocols, two pre-experimental studies, one qualitative and one editorial); also, three articles were excluded because the authors could not access the full respective full text. After this analysis, a total of six studies were included in this review.

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3.2. Risk of Bias

Each study was assessed for risk of bias by two reviewers using the software RevMan, and it is summarized in Figure 2. All studies showed, in general, a low risk of bias, with 100% in random sequence generation (selection bias), blinding of outcome (detection bias) and incomplete outcome data (attrition bias), more than 75% in allocation concealment (selection bias) and selective reporting (reporting bias) and more than 50% in blinding of participants and personnel (performance bias). Details of the analysis of each of the seven studies are illustrated in Figure 3.

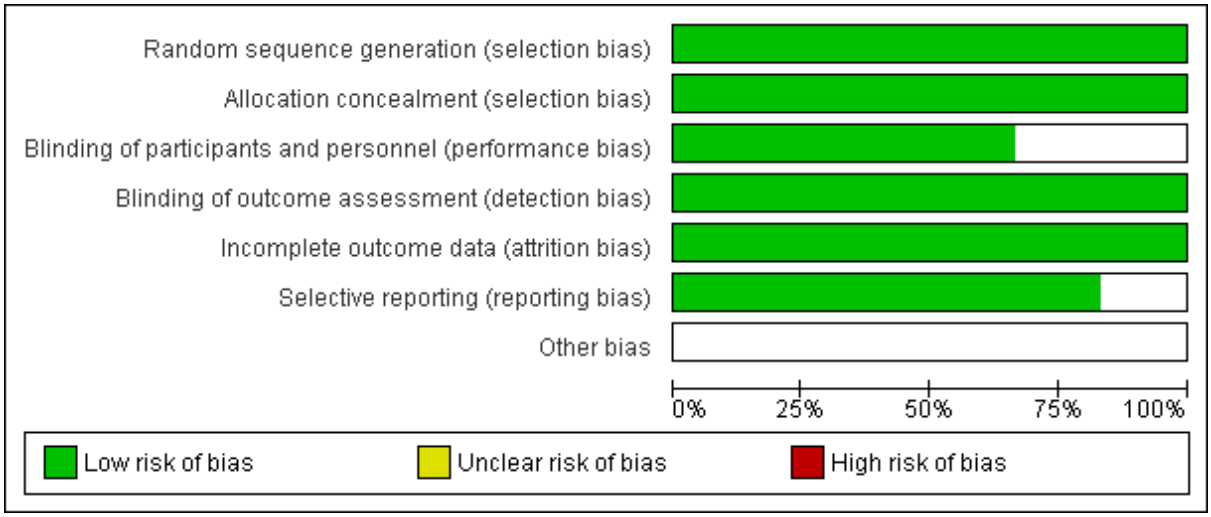

Figure 2

Risk of Bias Graph of the included studies

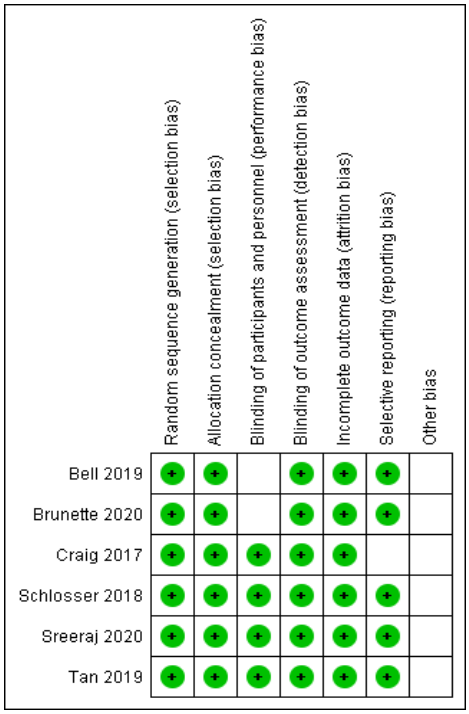

Figure 3

Risk of Bias Summary of the included studies

3.3. Study Characteristics

In this review were analyzed a total of six RCTs, the respective characteristics are presented in Table 1. These studies took place in the United States of America (n = 2), Australia (n = 1), United Kingdom (n = 1), and India (n = 1) between the years of 2017 and 2020. Study participant's numbers ranged from 23 to 311 and ages from 16 to 65 years. Most of the studies (n = 4) require as an inclusion criteria participants being fluent in English and with ages up to 18 years (n = 2), with the exceptions of two studies indicating ranges from 16 to 36 and 20 to 60 years. Most of the studies (n = 4) used DSM–IV to diagnose schizophrenia spectrum disorders (SSDs). In addition, some studies assessed psychotic symptoms with Psychotic Symptom Rating Scale – Auditory Hallucinations (PSYRATS–AH) (n = 2), and Scale for Assessment of Positive Symptoms and Scale for Assessment of Negative Symptoms (n = 1). Intellectual disability and cognitive impairment were also assessed using the Wechsler Test of Adult Reading (WTAR) (n = 2) and Wisconsin Card Sort Test (WSCT), and WAIS – R Digit Span Backward Test (n = 1).

Regarding to the types of interventions, computerized therapy (n = 3), apps were used (n = 2), and transcranial direct current stimulation (tDCS) (n = 1).

Tabel 1

Summary of the six included studies

Citation and Country	Aims	Sample	Measures	Intervention	Main Results	Limitations/Recommendations
Bell et al. (2019) Australia	To test the feasibility, acceptability, and estimated clinical effects of Ecological Momentary Assessment/Intervention (EMA/I) with standard face-to-face therapy to improve coping with hearing voices (Smartphone-Assisted coping focused intervention for Voices [SAVVy];	Adult participants (*n* = 34) SAVVy + Treatment-as-usual (TAU) (*n* = 17) TAU (*n* = 17)	Mini-International Neuropsychiatric Interview for DSM-5 mental disorders at baseline; Structured Clinical Interview for DSM-5 for borderline personality disorder diagnosis at baseline; Scale for Assessment of Negative Symptoms (SANS) at baseline; Wechsler Test of Adult Reading (WTAR) to assess intellectual ability at baseline; Credibility and Expectancy Questionnaire (CEQ) after informed consent procedure; Working Alliance Inventory – Short Revised (WAI-SR) to assess rapport with the therapist of participants of treatment group; Psychotic Symptom Rating Scales – Auditory Hallucinations (PSYRATS-AH) to assess frequency and distress hearing voices at baseline and after the intervention; Depression, Anxiety and Stress Scale-21 (DASS-21) to assess secondary clinical outcomes; Subjective Experiences of Psychosis Scale – Negative Impact Subscale (SEPS) to assess secondary clinical outcomes; Two visual analogue scales (VAS) to assess (1) confidence in coping with voices day-to-day and (2) awareness of patterns in voices and two multiple-choice items measuring the frequency of use of coping strategies and the number of strategies used;	Four sessions, two phases: - Initial assessment and EMA monitoring for functional analysis; - Identifying and implementing individualized coping strategies supported by personalized EMI reminders in daily life; The existing app called *MovisensXS* was used and in the first session the introduction and training in how to use this app was explained to the participants; A total of six days of EMA monitoring involving the completion of a 39-item questionnaire (measure common antecedents to voices, voice-related variables, and coping responses to the voices), ten times per day; Participants worded short sentences related to their individual coping strategies and programmed them into the app; Participants received five personalized EMI prompts per day for the following ten days after session two and view their reminders on-demand; Eight evening EMA questions were to monitor changes in the voices and helpfulness of the coping strategies with feedback of this information then reviewed in session three and coping strategies could be updated if needed; after session three another ten-day EMI period and evening EMA questions were introduced with the final session with a review and at the ending of the intervention;	Results enhance the feasibility and acceptability of this brief coping-focused intervention for distressing voice-hearing experiences which blended standard face-to-face psychological therapy with EMA/I between sessions; Completion rates of the EMA questionnaires were high, leading to the EMA-derived feedback and good engagement with prompted and user-initiated EMI coping reminders; Moderate effects in the treatment group were observed for PSYRATS-AH; Regarding SEPS negative impact scale there were no significant effects in favoring the treatment group; Also, regarding DASS-21, non-significant effects favoring the control group; Large effect favoring treatment group for the VAS coping with voices item and significant differences between groups; Significant group differences for the VAS coping with voices, although non-significant for the VAS awareness of patterns in voices item; Significant pre-post increase in the number of coping strategies; No correlations were found in the confidence of using smartphone apps with any scores on clinical or process measures on treatment group;	Unclear if the effects of the intervention were maintained since there was no follow-up point; Multiple components in the intervention, which could have limited inferences on specific therapeutic mechanisms; future trial should carefully consider an active comparison group with the recently highlighted digital placebo effect; Small sample size interferes with the generalizability of the results; Future studies should involve more streamlined programming of EMI content and the use of context-aware systems for a better understanding of the timing and nature of tailored EMI prompts.

Brunette et al. (2020) United States of America	To test whether the *Let's Talk About Smoking* was more effective and more appealing than *National Cancer Institute Education (NCI Education)* for increasing use of smoking cessation treatment, quit attempts, and abstinence among smokers with schizophrenia, accounting for the level of cognitive functioning.	Adult smokers with schizophrenia (*n* = 162) *Let's Talk About Smoking* (*n* = 84) *NCI Education* (*n* = 78)	Structured in-person interview for demographics and smoking history; Diagnostic and Statistical Manual for psychiatric and substance use disorder diagnosis; Brief Psychiatric Rating Scale for psychiatric symptom severity at baseline; Fagerström Test to assess the level of nicotine dependence at baseline and 3 and 6 months; Treatment Motivation Scale-Revised to assess attitudes about using cessation treatment; Structured interview to assess the primary outcome, all self-reported use of cessation treatment at any time during each past 3-month period; Timeline Follow-Back method to assess the amount of smoking and other tobacco product use each day, going back week-by-week over the past 3 months; Perceived Usefulness and Ease of Use Scale to assess perceptions of usability and satisfaction with the intervention; Cognition: Continuous Performance Test to assess sustained attention, Hopkins Verbal Learning Test to assess verbal learning, Trail Making Test Part A to assess processing speed, Trail Making Test Part B to assess cognitive flexibility, Delis-Kaplan Executive Functioning System Color-Word Interference Test to assess inhibitory control, and Wide Range Achievement Test Reading subtest fourth edition to assess word recognition	*Let's Talk About Smoking is* a Web-based intervention, a linear, modularized, and interactive program which takes 30 to 90 minutes to complete. Users can choose one video host who is an ex-smoker with mental illness and access through 3 different modules (module 1 of assessment/feedback, module 2 of quit intention, and module 3 of education about cessation treatments, feedback, and referral) with assessments and exercises used in motivational interviewing and health decisions aid systems; *NCI Education* computerized version of NCI patient educational handout which provides information about risk factors and protective factors for cancer and other smoking-related diseases and smoking cessation treatments; Static intervention by a laptop computer in a similar format of *Let's Talk About Smoking*, with large black font on a white background with no images and one concept per page in a short paragraph or bulleted sentences.	Treatment outcomes did not differ between intervention conditions, although participants from *Let's Talk About Smoking* considered it more appealing; more than one-third (38,9%) of participants used any verifiable cessation treatment during 6 months follow up period and respective initiation was significantly predicted by older age, higher levels of education, lower positive symptom scale scores; Regarding self-reported abstinence during the follow-up period, a greater level of education, greater positive affect, better overall cognitive functioning, and use of any cessation treatment significantly predicted abstinence.	Used an active and computerized control condition, which did not unable to determine the level of advantage these interventions could provide in usual care, such as doctor's advice; No detailed information about the frequency and intensity of the community-delivered cessation medication and behavioral interventions, which would have facilitated a better understanding of abstinence outcome; Study participants were recruited from three communities in three states and included patients from several racial and ethnic groups which may not be representative of all smokers with schizophrenia in the USA or other countries.
Craig et al. (2017) United Kingdom	To test the clinical efficacy of AVATAR therapy on auditory verbal hallucinations compared with a supportive counseling control condition; to explore explanatory mechanisms of action and moderators for AVATAR therapy and to determine preliminary estimates of the cost-effectiveness of AVATAR therapy;	People with schizophrenia spectrum or affective disorder with psychotic symptoms (*n* = 150) AVATAR therapy (*n* = 75) Supportive counseling (*n* = 75)	Psychotic Symptom Rating Scales, auditory hallucinations subscale (PSYRATS-AH) to assess the primary outcome; PSYRATS-AH voice frequency and voice distress subscales, Revised Beliefs about Voices Questionnaire (BAVQ-R), perceived malevolence, omnipotence and benevolence subscales, and Voice Acceptance and Action Scale (VAAS) acceptance and action subscales, and Voice Power Differential Scale (VPDS) power and assertiveness subscales to assess secondary outcomes; Scale for Assessment of Positive and Negative Symptoms (SAPS and SANS), Psychotic Symptoms Rating Scale-Delusions (PSYRATS-DEL), Depression Anxiety and Stress Scale (DASS-21), Calgary Depression Scale, Rosenberg self-esteem, Manchester Short Assessment of Quality of Life (MANSA), and Maudsley Addiction Profile (MAP) to assess other secondary outcomes;	AVATAR therapy: Six sessions weekly with 50 min; Delivered by experienced clinicians skilled in psychological therapies, participants created a computerized representation of the entity they believed was the source of their main voice in the introductory session, including a comprehensive assessment of the voice(s) and included verbatim content; Participants sat in one room facing their avatar on a computer monitor while the therapist sat in a second room with a control panel which allowed them to speak in their own voice or as the avatar; Two phases: phase one (one to three sessions) with exposure to the avatar speaking the typical verbatim content of the participant's voices while the therapist encouraged assertive responding, and phase two (four to six sessions) where the dialogue gradually evolved as the avatar conceded ground and acknowledge the strengths and good qualities of the participant, with an explicit focusing on self-esteem and acknowledgments of the participant's strengths and capabilities; All sessions were audio-recorded and a copy of the avatar dialogue was provided on an MP3 player to the participant with	AVATAR therapy was feasible to deliver, acceptable to participants, and did not result in any adverse events; rapid and sustained reduction in the severity of auditory verbal hallucinations by the end of therapy at week 12 also significantly superior when compared to the supportive counseling; AVATAR therapy had a positive and significant on omnipotence and these positive effects on voices were sustained at 24 weeks, although no significant effect on the reported malevolence of voices;	The absence of treatment-as-usual control condition could have interfered in the interpretation of the absence of a significant difference between both groups at 24 weeks, although the large effect of AVATAR is maintained after therapy up to 24 weeks; AVATAR therapy was a very brief and tightly focused intervention; longer-term benefits might require additional sessions or effectiveness increased by a higher dose on potential effective mechanisms, such as increasing control and reducing perceived omnipotence; it would be relevant in future research to examine the contribution of different intervention components to the reduction in auditory hallucinations; The study was done in only one center by skilled therapists with substantial expertise in the psychological treatment of psychosis which could interfere with generalization to other centers or delivery by a wider mental health workforce.

Schlosser et al. (2018) United States of America	To test the efficacy of the mobile intervention PRIME (Personalized Real-time Intervention for Motivational Enhancement) and compare to a treatment-as-usual/waitlist (TAU/WL) control group; to test the feasibility of conducting a remote clinical trial for individuals with schizophrenia.	Partici-pants with schizo-phrenia, schizo-phreniform or schizo-affective disorder (*n* = 43) PRIME (*n* = 22) WL condition (*n* = 21)	Structured Clinical Interview for DSM-IV-TR Disorders for a diagnosis of schizophrenia spectrum disorder at baseline; Wechsler Test of Adult Reading (WTAR) to assess IQ at baseline; Chlorpromazine (CPZ) equivalents to calculate the antipsychotic burden ate baseline; Trust Task to assess changes in components of motivated behavior at baseline and 12-week time point (post-trial); Motivation and Pleasure-Self Report Scale (MAP-SR) to assess self-reported defeatist beliefs and change in motivation atbaseline and 12-week time point (post-trial); Role Functioning Scale (RFS) to assess real-world functioning in independent living, work, family, and social domains and 12-week time point (post-trial); Quality of Life Scale – Abbreviated (QOL-A) to assess the quality of life in social and vocational domains and 12-week time point (post-trial); Dysfunctional Attitudes Scale (DAS) to assess defeatist beliefs about successfully performing goal-directed behavior and 12-week time point (post-trial); Beck Depression Inventory, Second Edition (BDI) to assess depression symptom severity and 12-week time point (post-trial); Revised Self-Efficacy Scale (R-SES) to assess self-efficacy and 12-week time point (post-trial);	instructions to listen at home, especially when they heard the voice(s); Therapists used a detailed therapy manual written for the trial by the team, developed from an earlier guide provided by JPL, who also provided initial training and consultation during periodic attendance at weekly group supervision meetings; The control condition, supportive counseling: Six sessions weekly with 50 min, delivered by graduate assistant psychologists; Manual-based and face-to-face supportive counseling approach adapted with permission form that employed by the SoCRATES Trial Group; inherited manual proposed activities, such as board games and listening to music together to deliver an emotion-focused psychological intervention which facilitated exploration of issues of fundamental importance in the person's life; typical themes of the counseling included improving quality of life, issues of identity or belonging, coming to terms with past trauma and identifying personal resources and qualities; At the end of each session participants recorded a weekly positive message onto an MP3 player to listen back to during the week; At the end of the therapy in both groups was given a therapy summary letter and a copy was sent to their responsible clinician; Supportive online environment selected by participants and documented progress on small and self-determined goals in the domains of health/wellness, social relationships, creativity, and productivity; Participants should select long-term goals from a 36-item list and later choose one of them, which triggers a display of brief challenges that contribute to that goal; For each long-term goal, there is an average of 15 suggested challenges which participants sequentially view and could create a custom challenge which they could manually enter; Automatic reminders were given and indicated when participants completed the challenges they selected; at this time. Participants had the opportunity to post a quick "accomplishment moment" with their coach and the PRIME community; Were provided motivation coaches who use evidence-based interventions from	Results showed PRIME is a feasible, acceptable, and efficacious intervention for improving mood and motivation in young people with SSD, very well tolerated with a retention rate of 74%; overall satisfaction with PRIME was rated highly; Significant improvements in depression, defeatist beliefs, self-efficacy, and important components of motivation (reward learning, anticipated pleasure, and effort expenditure) which confirms the use of PRIME as a behavioral activation intervention;	Relatively small sample size which may not be representative of people with SSD nor strong enough results to determine whether PRIME would successfully improve other important clinical outcomes, like social functioning; The use of TAU/WL condition did not allow for an understanding of the relative effect of PRIME compared with other types of mobile interventions or treatment approaches; The relatively short follow up 3 months may not have been long enough to conclude the effects of PRIME would induce longer-term and clinically meaningful outcomes; Further research is needed to improve knowledge about moderators of outcomes and refine the understanding of who may benefit more or less from this intervention approach.

			Positive and Negative Syndrome Scale (PANSS) to assess positive and negative symptoms and 12-week time point (post-trial); PRIME Acceptability assessed by rating satisfaction with the specific features, such as the ability to interact with peers and the different goal categories at the 12-week time point (post-trial); Feasibility assessed using metrics, such as login frequency, the average number of challenges completed, challenge completion percentage, and average number of peer and coach interventions;	Cognitive Behavioral Therapy (CBT), behavioral activation, mindfulness, and psychoeducation to help participants overcome the obstacles that affect goal progress; Also, a PRIME community which provided a platform for users to interact with one another and enabled users to send messages directly to each other and share positive moments of daily life with the whole PRIME community;		
Sreeraj et al. (2020) India	Compare the effect of online-tDCS and offline-tDCS on Working Memory (WM) and its transferability to other cognitive functions (digit-symbol substitution, emotional matching/labeling, and anti-saccade eye movement) in a crossover sham-controlled design; Evaluate the effect of tDCS on Sternberg's task performance.	Patients with schizo-phrenia (*n* = 23) Online group (*n* = 11) Active-tDCs (*n* = 6) Sham-tDCs (*n* = 5) Offline group (*n* = 12) Active-tDCs (*n* = 6) Sham-tDCs (*n* = 6)	Mini-International Neuropsychiatric Interview (MINI) plus for the diagnosis of schizophrenia (DSM-IV-TR) at baseline; Digit Symbol Substitution Test (DSST) paper-pencil and Animal fluency test to assess cognitive deficits at baseline; Hindi Mental State Examination and Global Assessment of Functioning (GAF) to assess the absence of profound impairments at baseline; Scale for Assessment of Positive Symptoms, Scale for Assessment of Negative Symptoms, Calgary Depression Rating Scale, and Simpson-Angus Neurological Rating Scale, all administered at baseline; Outcome measures: Computerized numerical n-back (NNB) test with two different versions for pre and post-session; Computerized Digit Symbol Substitution Test (cDSST), Computerized Emotional Matching and Labelling Task (cMALT) along with eye movement tracking of prosaccade and anti-saccade tasks, all before and after a session; Adverse Effect Questionnaire related to tDCS after each session; Intrinsic Motivation Inventory to assess motivation in doing the Sternberg's WM Task in the online group; 10-point Likert scale ranging from "Not at all" to "Very much" to assess attentiveness during the task and cognitive fatigue by participants and investigator; 5-point Likert scale to assess patient's subjective judgment of the activeness of the session;	One session of active tDCS and one session of sham tDCS with a gap of 2 – 7 days and almost at the same time of the day; tDCS was conducted using a standard device Neuroconn DC Stimulator Plus; The anode was placed with the center of the electrode over a point midway between F3 and FP1 (left DLPFC, corresponding to Brodmann's areas [BA] 8, 9, 10, and 46) and cathode over midway between T3 and P3 (left temporoparietal junction [TPJ], corresponding to BA 22, 39, 40, 41 and 42); The stimulation level was set at 2 mA for 20 minutes; tDCS stimulation parameters were followed in both groups; only the online group completed Sternberg's task during the session whereas the offline group maintained a resting wakeful state; Sternberg's WM Task was in a three-block design using E-Prime 2.0 professional version; it was presented a set of numerical digits (0 – 9) sequentially and after a latency of 2 seconds, target stimuli is presented; Participants had to respond to the target digit by pressing "Yes" or "No" to indicate whether the target digit had been presented in the earlier set and feedback appeared after the response;	Mild to moderate side effects were noted in one or both sessions; Improvement in reaction time in the 2-back test only in the online-sham session in comparison to the offline-sham session, schizophrenia patients were able to perform 2-back test faster after completing Sternberg's task during a sham tDCS; Change in 2-back performance after active tDCS (with/without Sternberg's task) was comparable to that of sham stimulation; The practice of Sternberg's task improved the performance in the 2-back task, but it was observed when anodal stimulation was combined; The effect was restricted to 2-back alone and was not transferred to other cognitive functions; WM improvement was noted in the offline-tDCS session along with online-sham tDCS sessions, both tDCS and WM task enhanced the WM performance across sessions when provided independently; No significant differences were noted in any of the other neurocognitive and eye-tracking measures of saccade and anti-saccade tasks;	A relatively small sample prevented the power of the study to note the statistical difference in the other neurocognitive tests; One single session showed insufficient to show a significant change in cognitive functions and could not be easily generalizable to therapeutic tDCS; Cathodal electrode placement at left in this study to target cognitive deficits while other studies usually use extracranial or right supraorbital region, which could involve a different neural circuitry and a possibility of inadvertent inhibition of temporoparietal areas involved in WM could result in an undermining effect of tDCS in this study; Future studies should compare the same with healthy controls, larger sample size, optimal montage placement, focused stimulation techniques, and multiple tDCS sessions.
Tan et al. (2019) China	To test the efficacy of a new Chinese cognitive remediation computerized program, Computerized Cognitive Remediation Therapy (CCRT) for cognitive performance and whether these improvements contribute to improved	Patients with schizo-phrenia (*n* = 311) CCRT (*n* = 196) Active control (*n* = 115)	Wisconsin Card Sort Test (WCST) or WAIS-R Digit Span Backward test to assess cognitive impairment at admission; Three moments of assessment at baseline, post-treatment, and 3-month follow-up: Cognition assessed with ten tests in seven domains (MATRICS Consensus Cognitive Battery, MCCB total score): - Speed of processing: Category Fluency Test, Trail Making Test, Symbol Coding Test; - Attention/Vigilance: Continuous Performance Test-Identical Pair (CPT-IP); - Working memory: Spatial Span Test (Wechsler Memory Scale-Third Edition, WMS-III), Digit Sequencing Test;	Cognitive remediation (50 sessions): Computer software (CCRT) developed from principles in Wykes and Reeder, consists of 30 exercises which dynamically change in difficulty as accuracy reaches 80%; treatment was provided in four to five 45-min sessions per week over 12 weeks; supervised by experienced therapists at a ratio of one therapist to four participants; The therapist teaches participants to use CCRT in the first two weeks and	Participants have demonstrated a benefit of CCRT in the overall MCCB total score, but no specific moderators of CCRT improvements; nevertheless, both groups showed Wisconsin Card Sort Test improvement mediated a positive effect on functional capacity and Digit Span benefit mediated decreases in positive symptoms; Younger and older participants showed cognitive improvements on different	Short follow-up, for that reason results may have been underestimated in long term functioning benefits; further studies should include environmental supports which would allow the exploration in real-life functioning; Results related to age moderating CCRT benefit only for individual cognitive tests rather than general cognitive function needs replication because the sample did not include individuals living in the community which limits generalization.

functional capacity or symptoms;	– Verbal learning: Brief Visuospatial Memory Test-Revised (BVMT-R); – Reasoning and problem solving: Mazes Test (Neuropsychological Assessment Battery-Mazes, NAB-MAZES); – Social cognition: Mayer–Salovery–Caruso Emotional Intelligence Test (MSCEIT): Managing emotions; Secondary cognitive outcomes: Verbal Working memory (Wechsler Adult Intelligence Scale III Digit Span Test) and executive function (WSCT); Secondary symptom and function outcomes: – UCSD Performance-based Skills Assessment (UPSA) Chinese version to assess functional capacity – Nurse's Observation Scale for Inpatient Evaluation (NOSIE-30) Chinese version to assess behavior and functional capacity; – Rosenberg self-esteem scale to assess global feelings of self-worth or self-acceptance; Positive and Negative Syndrome Scale (PANSS) Chinese version to symptom assessment;	subsequent treatment is mainly performed by the participant; Active control (50 sessions): Two different activities, such as learning to play a fairly easy instrument (usually xylophone) and learning to dance; the therapist encouraged to these activities and took part actively in every session;	tests: younger, on Symbol Coding Test, and older, on the Spatial Span Test; Only the older age group showed MSCEIT benefits at post-treatment; Participants whose baseline total score was around 31 seem to derive the most benefit of the intervention;

3.4. Thematic analysis

Following the systematic analysis of the studies, three themes were identified: motivational interventions, auditory verbal hallucinations, and cognitive symptoms.

3.4.1. Motivational interventions

The studies of Brunette and colleagues (2020) and Schlosser and colleagues (2018) were focused on two different motivational interventions, mobile intervention Personalized Real-Time Intervention (PRIME) and *Let's Talk About Smoking*, respectively.

Cigarette smoking is a common comorbidity in people with schizophrenia, leading to smoking-related diseases and early mortality (Lasser et al., 2000; Taghizadeh et al., 2016). However, community clinics seem to have scarce resources to support cessation treatments (Olfson, 2016) adequately. For this reason, the solution can be using digital tools to deliver behavioral interventions to cessation smoking treatments. However, the issue with these digital tools is the cognitive impairment frequently observed in people with schizophrenia which can interfere with the best use, mainly because of their complex design (Ferron et al., 2017; Rotondi et al., 2017).

To solve this problem, Brunette and colleagues (2020) designed a multimedia and decision support system for smokers with schizophrenia to encourage the use of a smoking cessation treatment, *Let's Talk About Smoking,* comparing with a standard educational pamphlet from the National Cancer Institute (NCI Education). The designed web-based intervention did not reveal better results as expected; both interventions were rated highly, although the *users indicated the Let's Talk About Smoking intervention* to be more appealing than NCI Education.

Motivational deficits are frequent in people with Schizophrenia Spectrum Disorders (SSDs), in adaptive goal-directed with component processes, such as difficulty learning from rewarding outcomes (RO), diminished anticipation of pleasure for RO, and reduction in effort expanded to obtain rewarding outcomes (Kring & Barch, 2014; McCarthy et al., 2016; Strauss et al., 2014).

Once these impairments are observed to be less severe in the early course of illness and digital tools seem to be feasible and effective approaches to early intervention in psychosis (Alvarez-Jimenez et al., 2014; Ben-Zeev et al., 2014), Schlosser and colleagues (2018) tested the mobile intervention PRIME, designed to improve motivational impairments in people with SSDs. Therefore, these interventions may become easier and more accessible care than traditional engagement in weekly psychotherapy sessions, for example.

In concrete, PRIME is an app mobile that targets the motivational system utilizing social reinforcement to engage and sustain goal-directed behavior, using Cognitive Behavioral Therapy (CBT) based coaching. Feasibility, acceptability, and efficacy were confirmed, PRIME has increased learning from positive outcomes, anticipated pleasure for positive outcomes, and expenditure of effort to obtain future positive outcomes, all components of motivation. These components typically do not improve with medication nor in-person psychotherapy and, for this reason, PRIME can work as an adjunctive intervention to treatment approaches usually more focused on treating only the positive symptoms of people with SSD.

3.4.2. Auditory verbal hallucinations

The study of Bell and colleagues (2019) is focused on the use of a Smartphone-Assisted coping-focused intervention for Voices (SAVVy), while the study of Craig and colleagues (2017) is focused on an AVATAR therapy, both dedicated on the coping for hearing voices experiences.

CBT for psychosis is frequently recommended as a core piece of treatment for auditory verbal hallucinations, but its effects and access are limited (Jauhar et al., 2014; Van der Gaag et al., 2014), with high costs and complex to delivery (Berry & Haddock, 2008; Haddock et al., 2014; Ince et al., 2016). Thus, innovative ways of intervention, shorter and capable of being delivered by a more comprehensive workforce, are urgent. A*pps* also play an important role in coping-focused on hearing voices.

The study of Bell and colleagues (2019) used the *app* MovisensXS to apply the Ecological Momentary Assessment/Intervention (EMA/I), approach to deliver questionnaires in daily life at repeated intervals across several days and electronic prompts that encourage therapeutic behaviors when needed, respectively, blended with standard face-to-face therapy. The feasibility and acceptability of this approach were confirmed with high completion rates of questionnaires and good engagement. Furthermore, the findings suggest that personalized EMI reminders of tailored self-management strategies defined during therapy may enhance the generalization of these strategies into daily life.

With the same aims, the AVATAR therapy in the study of Craig and colleagues (2017) allows a new way of face-to-face intervention and interaction with a digital representation whose speech closely marches with the tone of the persecutory voice described by the patient. The therapist presents in the sessions switched between speaking as a therapist and as an avatar and facilitates dialogue. Hence, the patient gradually gains more power and control over the

omnipotent voice, and it loses its control over the hearer and becomes more conciliatory over time.

Feasibility and acceptability were confirmed, and participants did not report any adverse event that could be related to the therapy. With AVATAR therapy, there were significantly greater reductions in auditory verbal hallucinations. Seven participants reported a complete absence of voices during the preceding week at the week 12 assessment, and eight reported an absence at 24 weeks follow-up.

3.4.3. Cognitive symptoms

Cognitive impairment is common in people with schizophrenia, in multiple domains (speed of processing, attention/vigilance, verbal learning, visual learning, reasoning, problem-solving, social cognition, and working memory [WM]), and can be a predictor of functional outcome and quality of life on illness (Green, 2006; Nuechterlein et al., 2008).

The study of Sreeraj and colleagues (2020) especially focused on WM performance using online tDCS, once neurocognitive deficits, such as processing inefficiency, emotional misperception, and cognitive disinhibition, are associated with WM deficits (Bachman et al., 2010; Mehta et al., 2014). With the lack of effective pharmacology to improve cognitive dysfunction, tDCS seems to be promising in this field in enhancing cognitive functions by augmenting neuroplasticity (Brunoni et al., 2012; J. Choi et al., 2010). Participants performed Stenberg's WM task (WM task) during the sessions. WM improvement was noted in offline-active tDCS sessions, and online-sham tDCS sessions reflecting both tDCS and WM task enhanced the WM performance when provided independently.

On the other hand, pharmacological treatments seem to not effectively treat cognitive impairment (Choi et al., 2013). For this reason, cognitive remediation techniques have been developed to moderate the significant effects on cognitive outcomes (attention, memory, executive function, social cognition, or metacognition) (Wykes et al., 2011) with different modes or in paper and pencil (Cella et al., 2014; Wykes, Newton, et al., 2007; Wykes, Reeder, et al., 2007) or computer (Kurtz et al., 2015).

The study of Tan and colleagues (2019) focuses on testing a Computerized Cognitive Remediation Therapy (CCRT) and investigate whether the improvements in cognitive function contribute to improving functional capacity or symptoms. Results showed significant benefit of CCRT in the overall MATRICS Consensus Cognitive Battery (MCCB) total score. In short, changes

in cognitive outcomes contribute to improved functional capacity and decreased positive symptoms. Age and basic cognitive level of participants as mediators that seem to interfere with the cognitive effects from CCRT.

4. Discussion

The main aim of this systematic review was to synthesize the different types of digital tools and technologies used in treating people with a schizophrenia spectrum disorder, besides its feasibility and acceptability. A total of six studies were analyzed, with three studies using computerized therapy, two studies using *apps,* and one study using transcranial direct current stimulation (tDCS).

Regarding the study of Brunette and colleagues (2020), a web-design intervention, *Let's Talk About Smoking*, was created as a smoking cessation treatment in smokers with schizophrenia. Compared with *NCI Education*, *Let's Talk About Smoking* is more attractive since it contained videos of ex-smokers chosen by the participants who identified him/herself and guided them through three modules, with assessments and exercises used in motivational interviewing and health decision aid systems. Although there were no significant differences between *Let's Talk About Smoking* and *NCI Education*, participants scored *Let's Talk About Smoking* higher in terms of satisfaction and said they would recommend their respective intervention to a friend. Some design features were used in both interventions. Still, the fact that *Let's Talk About Smoking* used a video media intervention, seemed to interfere with the comprehension and cognitive processing of participants who had cognitive impairment, which might be a disadvantage on intervention results.

In the study of Schlosser and colleagues (2018), was used the PRIME *app* for the intervention focused on the motivational system with social reinforcement to engage and sustain goal-directed behavior. PRIME showed high levels of acceptability and efficacy by increasing learning from positive outcomes, anticipated pleasure for positive outcomes, and effort to obtain future positive results. These components of motivation typically do not improve with medication nor in-person psychotherapy (Lieberman et al., 2005; Wykes et al., 2008). For this reason, PRIME can work as an adjunctive behavioral activation intervention and provide a more holistic approach to the intervention.

Regarding Bell and colleagues (2019) study, smartphone-based EMA/I was tested for coping-focused therapy for auditory verbal hallucinations. Feasibility was confirmed with a high completion level of questionnaires of EMA/I and good engagement with prompted and user-initiated EMI coping reminders. This fact might be related to the production of EMA-derived feedback combined with positive feedback from participants. Acceptability was confirmed with good satisfaction shown by the participants; all of them said they would recommend their

treatment to other patients. In addition, feedback related to the intervention was positive, with a decrease in positive symptoms in terms of frequency and intensity. Findings suggest that personalized EMI reminders of tailored self-management strategies defined during therapy may enhance the generalization of these strategies into daily life. Since CBT is usually recommended as a core treatment to treat hallucinations, but effect sizes are modest, the study suggests that smartphone technologies can support standard face-to-face therapies, performing as a blended therapy.

Focusing on Craig and colleagues (2017) study also focused on the coping-focused therapy for auditory verbal hallucinations, AVATAR therapy was used. In this therapy, patients have a dialogue with a digital representation of their presumed persecutor voiced by the therapist. The avatar responds less negatively, and patients gain more power and control over the omnipotent voice. Feasibility and acceptability were confirmed and a rapid and sustained reduction in persistent auditory verbal hallucinations severity.

Pharmacological therapy has been used to treat hallucinations, but it is still not effective for all the population experiencing hallucinations (Aleman & Larøi, 2011). CBT has also been used, but it must be delivered by highly trained therapists, leading to a scarce workforce and minor to moderate effects on hallucinations (van der Gaag et al., 2014). The study of Craig and colleagues suggests that patients would benefit from briefer therapies, such as AVATAR therapy, and focused on specific target processes by being incorporated into CBT or offered as a standalone approach. Although AVATAR therapy is presented as brief, it might be necessary to have additional sessions for longer-term benefits, like CBT or other auditory verbal hallucinations-focused interventions.

Focusing on cognitive impairment in people with schizophrenia, Sreeraj and colleagues (2020) focused on WM performance using online tDCS. Some cognitive deficits in this function are associated with people with schizophrenia (Bachman et al., 2010; Mehta et al., 2014). With the lack of effective pharmacology, combining performing a task during tDCS can enhance the benefits of post-stimulation WM (Brunoni et al., 2012; J. Choi et al., 2010; Hill et al., 2019; Martin et al., 2014). WM improvement was noted with this intervention, with better results by using only WM task than its combination with tDCS, probably because the intervention only included one session, becoming it insufficient to induce effects on cognitive function and due to the neural phenomenon of homeostatic plasticity present in people with schizophrenia (Keshavan et al., 2015).

Cognitive Remediation Therapy (CRT) seems to have moderate to large effects on improvement on cognitive function, and it has been used with different modes, such as paper and pencil (Cella et al., 2014; Wykes, Reeder, et al., 2007) or computer (Kurtz et al., 2015). However, health sources are limited, and, for this reason, it is essential to understand when some participants benefit more from CRT.

Tan and colleagues (2019) study investigated the use of Computerized Cognitive Remediation Therapy (CCRT) for cognitive improvement and identify moderators and mediators of treatment benefit. Results showed cognitive benefits in the overall MCCB total score, which improved functional capacity and decreased positive symptoms. Regarding the mediators, age seems to have different domain benefits between age groups, but it is not a barrier to cognitive improvement. In terms of cognition, evidence suggests that poorer cognition have more benefit of cognitive interventions. The principal disadvantage of this type of intervention is the lack of face-to-face interaction with the therapist, who usually provides social cues to improve the self-esteem of patients.

Focusing on the strong points of this review, the included studies were all RTCs; also its result of bias assessment was strongly positive, with a generally low risk of bias, and five of the six studies included follow-up in its procedures.

Regarding the limitations of this review, the number of included studies was low with only six studies; in the case of some studies, the small sample size may have prevented a generalization of the results and the power of the studies; finally, the heterogeneity of the instruments used to assess the outcomes of almost all studies.

5. Conclusion

The results of this review show there is some diversity of interventions with the same target and issue of a schizophrenia spectrum disorder, such as motivational deficits, auditory verbal hallucinations, and cognitive symptoms. Along with the growing interest of people with a schizophrenia spectrum disorder in the use of digital technologies, their acceptability and feasibility have been confirmed over time. Nevertheless, future studies need to consider increasing the size of the samples and create longer interventions to empower the evidence and allow the generalization of the results to enhance the efficacity of these interventions.

References

Aleman, A., & Larøi, F. (2011). Insights into hallucinations in schizophrenia: novel treatment approaches. *Expert Review of Neurotherapeutics*, *11*(7), 1007–1015. https://doi.org/10.1586/ERN.11.90

Alvarez-Jimenez, M., Alcazar-Corcoles, M. A., González-Blanch, C., Bendall, S., McGorry, P. D., & Gleeson, J. F. (2014). Online, social media and mobile technologies for psychosis treatment: A systematic review on novel user-led interventions. *Schizophrenia Research*, *156*(1), 96–106. https://doi.org/10.1016/j.schres.2014.03.021

Arnberg, F. K., Linton, S. J., Hultcrantz, M., Heintz, E., & Jonsson, U. (2014). Internet-Delivered Psychological Treatments for Mood and Anxiety Disorders: A Systematic Review of Their Efficacy, Safety, and Cost-Effectiveness. *PLoS ONE*, *9*(5), e98118. https://doi.org/10.1371/journal.pone.0098118

Bachman, P., Reichenberg, A., Rice, P., Woolsey, M., Chaves, O., Martinez, D., Maples, N., Velligan, D., & Glahn, D. (2010). Deconstructing processing speed deficits in schizophrenia: Application of a parametric digit symbol coding test. *Schizophrenia Research*, *118*(1–3), 6–11. https://doi.org/10.1016/J.SCHRES.2010.02.1029

Batra, S., Baker, R. A., Wang, T., Forma, F., DiBiasi, F., & Peters-Strickland, T. (2017). Digital health technology for use in patients with serious mental illness: A systematic review of the literature. *Medical Devices: Evidence and Research*, *10*, 237–251. https://doi.org/10.2147/MDER.S144158

Bell, I. H., Rossell, S. L., Farhall, J., Hayward, M., Lim, M. H., Fielding-Smith, S. F., & Thomas, N. (2020). Pilot randomised controlled trial of a brief coping-focused intervention for hearing voices blended with smartphone-based ecological momentary assessment and intervention (SAVVy): Feasibility, acceptability and preliminary clinical outcomes. *Schizophrenia Research*, *216*, 479–487. https://doi.org/10.1016/j.schres.2019.10.026

Ben-Zeev, D., Brenner, C. J., Begale, M., Duffecy, J., Mohr, D. C., & Mueser, K. T. (2014). Feasibility, Acceptability, and Preliminary Efficacy of a Smartphone Intervention for Schizophrenia. *Schizophrenia Bulletin*, *40*(6), 1244–1253. https://doi.org/10.1093/schbul/sbu033

Berry, K., & Haddock, G. (2008). The implementation of the NICE guidelines for schizophrenia: Barriers to the implementation of psychological interventions and recommendations for the future. *Psychology and Psychotherapy: Theory, Research and Practice*, *81*(4), 419–436.

https://doi.org/10.1348/147608308X329540

Brunette, M. F., Ferron, J. C., McGurk, S. R., Williams, J. M., Harrington, A., Devitt, T., & Xie, H. (2020). Brief, Web-Based Interventions to Motivate Smokers With Schizophrenia: Randomized Trial. *JMIR Mental Health*, *7*(2), e16524. https://doi.org/10.2196/16524

Brunoni, A., Nitsche, M., Bolognini, N., Bikson, M., Wagner, T., Merabet, L., Edwards, D., Valero-Cabre, A., Rotenberg, A., Pascual-Leone, A., Ferrucci, R., Priori, A., Boggio, P., & Fregni, F. (2012). Clinical research with transcranial direct current stimulation (tDCS): Challenges and future directions. *Brain Stimulation*, *5*(3), 175–195. https://doi.org/10.1016/J.BRS.2011.03.002

Cella, M., He, Z., Killikelly, C., Okruszek, Ł., Lewis, S., & Wykes, T. (2019). Blending active and passive digital technology methods to improve symptom monitoring in early psychosis. *Early Intervention in Psychiatry*, *13*(5), 1271–1275. https://doi.org/10.1111/eip.12796

Cella, M., Reeder, C., & Wykes, T. (2014). It is all in the factors: Effects of cognitive remediation on symptom dimensions. *Schizophrenia Research*, *156*(1), 60–62. https://doi.org/10.1016/J.SCHRES.2014.03.032

Choi, J., Mogami, T., & Medalia, A. (2010). Intrinsic Motivation Inventory: An Adapted Measure for Schizophrenia Research. *Schizophrenia Bulletin*, *36*(5), 966–976. https://doi.org/10.1093/SCHBUL/SBP030

Choi, K., Wykes, T., & Kurtz, M. (2013). Adjunctive pharmacotherapy for cognitive deficits in schizophrenia: meta-analytical investigation of efficacy. *The British Journal of Psychiatry : The Journal of Mental Science*, *203*(3), 172–178. https://doi.org/10.1192/BJP.BP.111.107359

Craig, T. K., Rus-Calafell, M., Ward, T., Leff, J. P., Huckvale, M., Howarth, E., Emsley, R., & Garety, P. A. (2017). AVATAR therapy for auditory verbal hallucinations in people with psychosis: a single-blind, randomised controlled trial. *The Lancet Psychiatry*, *5*(1), 31–40. https://doi.org/10.1016/S2215-0366(17)30427-3

Fernandez-Gonzalo, S., Turon, M., Jodar, M., Pousa, E., Hernandez Rambla, C., García, R., & Palao, D. (2015). A new computerized cognitive and social cognition training specifically designed for patients with schizophrenia/schizoaffective disorder in early stages of illness: A pilot study. *Psychiatry Research*, *228*(3), 501–509. https://doi.org/10.1016/j.psychres.2015.06.007

Fernández-Sotos, P., Fernández-Caballero, A., González, P., Aparicio, A. I., Martínez-Gras, I., Torio,

I., Dompablo, M., García-Fernández, L., Santos, J. L., & Rodriguez-Jimenez, R. (2019). Digital technology for internet access by patients with early-stage schizophrenia in Spain: Multicenter research study. *Journal of Medical Internet Research*, *21*(4), 1–15. https://doi.org/10.2196/11824

Ferron, J. C., Brunette, M. F., Geiger, P., Marsch, L. A., Adachi-Mejia, A. M., & Bartels, S. J. (2017). Mobile Phone Apps for Smoking Cessation: Quality and Usability Among Smokers With Psychosis. *JMIR Human Factors*, *4*(1). https://doi.org/10.2196/HUMANFACTORS.5933

Firth, J., & Torous, J. (2015). Smartphone apps for schizophrenia: A systematic review. *JMIR MHealth and UHealth*, *3*(4). https://doi.org/10.2196/mhealth.4930

Garrido, G., Penadés, R., Barrios, M., Aragay, N., Ramos, I., Vallès, V., Faixa, C., & Vendrell, J. M. (2017). Computer-assisted cognitive remediation therapy in schizophrenia: Durability of the effects and cost-utility analysis. *Psychiatry Research*, *254*, 198–204. https://doi.org/10.1016/j.psychres.2017.04.065

Gay, K., Torous, J., Joseph, A., Pandya, A., & Duckworth, K. (2016). Digital Technology Use Among Individuals with Schizophrenia: Results of an Online Survey. *JMIR Mental Health*, *3*(2), e15. https://doi.org/10.2196/mental.5379

Granholm, E., Ben-Zeev, D., Link, P. C., Bradshaw, K. R., & Holden, J. L. (2012). Mobile Assessment and Treatment for Schizophrenia (MATS): A Pilot Trial of An Interactive Text-Messaging Intervention for Medication Adherence, Socialization, and Auditory Hallucinations. *Schizophrenia Bulletin*, *38*(3), 414–425. https://doi.org/10.1093/schbul/sbr155

Green, M. (2006). Cognitive Impairment and Functional Outcome in Schizophrenia and Bipolar Disorder. *The Journal of Clinical Psychiatry*, *67*(10), 0–0. https://www.psychiatrist.com/jcp/schizophrenia/cognitive-impairment-functional-outcome-schizophrenia

Haddock, G., Eisner, E., Boone, C., Davies, G., Coogan, C., & Barrowclough, C. (2014). An investigation of the implementation of NICE-recommended CBT interventions for people with schizophrenia. *Http://Dx.Doi.Org/10.3109/09638237.2013.869571*, *23*(4), 162–165. https://doi.org/10.3109/09638237.2013.869571

Hill, A. T., Rogasch, N. C., Fitzgerald, P. B., & Hoy, K. E. (2019). Impact of concurrent task performance on transcranial direct current stimulation (tDCS)-Induced changes in cortical physiology and working memory. *Cortex*, *113*, 37–57. https://doi.org/10.1016/J.CORTEX.2018.11.022

Ince, P., Haddock, G., & Tai, S. (2016). A systematic review of the implementation of recommended psychological interventions for schizophrenia: Rates, barriers, and improvement strategies. *Psychology and Psychotherapy: Theory, Research and Practice*, *89*(3), 324–350. https://doi.org/10.1111/PAPT.12084

Jauhar, S., McKenna, P. J., Radua, J., Fung, E., Salvador, R., & Laws, K. R. (2014). Cognitive–behavioural therapy for the symptoms of schizophrenia: systematic review and meta-analysis with examination of potential bias. *The British Journal of Psychiatry*, *204*(1), 20–29. https://doi.org/10.1192/BJP.BP.112.116285

Keshavan, M. S., Mehta, U. M., Padmanabhan, J. L., & Shah, J. L. (2015). Dysplasticity, metaplasticity, and schizophrenia: Implications for risk, illness, and novel interventions. *Development and Psychopathology*, *27*(2), 615–635. https://doi.org/10.1017/S095457941500019X

Kring, A. M., & Barch, D. M. (2014). The motivation and pleasure dimension of negative symptoms: neural substrates and behavioral outputs. *European Neuropsychopharmacology : The Journal of the European College of Neuropsychopharmacology*, *24*(5), 725–736. https://doi.org/10.1016/J.EURONEURO.2013.06.007

Kumar, S., Nilsen, W. J., Abernethy, A., Atienza, A., Patrick, K., Pavel, M., Riley, W. T., Shar, A., Spring, B., Spruijt-Metz, D., Hedeker, D., Honavar, V., Kravitz, R., Craig Lefebvre, R., Mohr, D. C., Murphy, S. A., Quinn, C., Shusterman, V., & Swendeman, D. (2013). Mobile health technology evaluation: The mHealth evidence workshop. *American Journal of Preventive Medicine*, *45*(2), 228–236. https://doi.org/10.1016/j.amepre.2013.03.017

Kurtz, M., Mueser, K., Thime, W., Corbera, S., & Wexler, B. (2015). Social skills training and computer-assisted cognitive remediation in schizophrenia. *Schizophrenia Research*, *162*(1–3), 35–41. https://doi.org/10.1016/J.SCHRES.2015.01.020

Lal, S., Dell'Elce, J., Tucci, N., Fuhrer, R., Tamblyn, R., & Malla, A. (2015). Preferences of Young Adults With First-Episode Psychosis for Receiving Specialized Mental Health Services Using Technology: A Survey Study. *JMIR Mental Health*, *2*(2), e18. https://doi.org/10.2196/mental.4400

Lardinois, M., Myin-Germeys, I., Bak, M., Mengelers, R., van Os, J., & Delespaul, P. A. E. G. (2007). The dynamics of symptomatic and non-symptomatic coping with psychotic symptoms in the flow of daily life. *Acta Psychiatrica Scandinavica*, *116*(1), 71–75. https://doi.org/10.1111/j.1600-0447.2007.01022.x

Lasser, K., Boyd, J. W., Woolhandler, S., Himmelstein, D. U., McCormick, D., & Bor, D. H. (2000). Smoking and mental illness: A population-based prevalence study. *JAMA*, *284*(20), 2606–2610. https://doi.org/10.1001/JAMA.284.20.2606

Lieberman, J. A., Stroup, T. S., McEvoy, J. P., Swartz, M. S., Rosenheck, R. A., Perkins, D. O., Keefe, R. S., Davis, S. M., Davis, C. E., Lebowitz, B. D., Severe, J., & Hsiao, J. K. (2005). Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *The New England Journal of Medicine*, *353*(12), 1209–1223. https://doi.org/10.1056/NEJMOA051688

Lim, M. H., & Penn, D. L. (2018). Using Digital Technology in the Treatment of Schizophrenia. In *Schizophrenia bulletin* (Vol. 44, Issue 5, pp. 937–938). NLM (Medline). https://doi.org/10.1093/schbul/sby081

Lindhiem, O., Bennett, C. B., Rosen, D., & Silk, J. (2015). Mobile Technology Boosts the Effectiveness of Psychotherapy and Behavioral Interventions: A Meta-Analysis. *Behavior Modification*, *39*(6), 785–804. https://doi.org/10.1177/0145445515595198

Martin, D. M., Liu, R., Alonzo, A., Green, M., & Loo, C. K. (2014). Use of transcranial direct current stimulation (tDCS) to enhance cognitive training: effect of timing of stimulation. *Experimental Brain Research 2014 232:10*, *232*(10), 3345–3351. https://doi.org/10.1007/S00221-014-4022-X

McCarthy, J. M., Treadway, M. T., Bennett, M. E., & Blanchard, J. J. (2016). Inefficient effort allocation and negative symptoms in individuals with schizophrenia. *Schizophrenia Research*, *170*(2–3), 278–284. https://doi.org/10.1016/J.SCHRES.2015.12.017

Mehta, U., Thirthalli, J., Bhagyavathi, H., Keshav Kumar, J., Subbakrishna, D. K., Gangadhar, B., Eack, S., & Keshavan, M. (2014). Similar and contrasting dimensions of social cognition in schizophrenia and healthy subjects. *Schizophrenia Research*, *157*(1–3), 70–77. https://doi.org/10.1016/J.SCHRES.2014.05.018

Molina, R., Porras-Segovia, A., Ruiz, M., & Baca-García, E. (2021). eHealth tools for assessing psychomotor activity in schizophrenia: a systematic review. *Brazilian Journal of Psychiatry*, *43*(1), 102–107. https://doi.org/10.1590/1516-4446-2019-0867

Narayan, V. A., & Manji, H. K. (2016). Moving from "diagnose and treat" to "predict and pre-empt" in neuropsychiatric disorders. In *Nature Reviews Drug Discovery* (Vol. 15, Issue 2, pp. 71–72). Nature Publishing Group. https://doi.org/10.1038/nrd.2015.20

Naslund, J., Aschbrenner, K., Scherer, E., McHugo, G., Marsch, L., & Bartels, S. (2016). Wearable devices and mobile technologies for supporting behavioral weight loss among people with

serious mental illness. *Psychiatry Research*, *244*, 139–144. https://doi.org/10.1016/j.psychres.2016.06.056

Nuechterlein, K., Green, M., Kern, R., Baade, L., Barch, D., Cohen, J., Essock, S., Fenton, W., Frese, F., Gold, J., Goldberg, T., Heaton, R., Keefe, R., Kraemer, H., Mesholam-Gately, R., Seidman, L., Stover, E., Weinberger, D., Young, A., … Marder, S. (2008). The MATRICS Consensus Cognitive Battery, Part 1: Test Selection, Reliability, and Validity. *Https://Doi.Org/10.1176/Appi.Ajp.2007.07010042*, *165*(2), 203–213. https://doi.org/10.1176/APPI.AJP.2007.07010042

Olfson, M. (2016). Building The Mental Health Workforce Capacity Needed To Treat Adults With Serious Mental Illnesses. *Health Affairs (Project Hope)*, *35*(6), 983–990. https://doi.org/10.1377/HLTHAFF.2015.1619

Onwumere, J., Amaral, F., & Valmaggia, L. (2018). Digital technology for caregivers of people with psychosis: Systematic review. *Journal of Medical Internet Research*, *20*(9). https://doi.org/10.2196/mental.9857

Reeder, C., Pile, V., Crawford, P., Cella, M., Rose, D., Wykes, T., Watson, A., Huddy, V., & Callard, F. (2016). The Feasibility and Acceptability to Service Users of CIRCuiTS, a Computerized Cognitive Remediation Therapy Programme for Schizophrenia. *Behavioural and Cognitive Psychotherapy*, *44*(3), 288–305. https://doi.org/10.1017/S1352465815000168

Rethlefsen, M. L., Kirtley, S., Waffenschmidt, S., Ayala, A. P., Moher, D., Page, M. J., & Koffel, J. B. (2021). PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. *Systematic Reviews*, *10*(1), 39. https://doi.org/10.1186/s13643-020-01542-z

Rotondi, A. J., Spring, M. R., Hanusa, B. H., Eack, S. M., & Haas, G. L. (2017). Designing eHealth Applications to Reduce Cognitive Effort for Persons With Severe Mental Illness: Page Complexity, Navigation Simplicity, and Comprehensibility. *JMIR Human Factors*, *4*(1). https://doi.org/10.2196/HUMANFACTORS.6221

Rus-Calafell, M., Gutiérrez-Maldonado, J., & Ribas-Sabaté, J. (2014). A virtual reality-integrated program for improving social skills in patients with schizophrenia: A pilot study. *Journal of Behavior Therapy and Experimental Psychiatry*, *45*(1), 81–89. https://doi.org/10.1016/j.jbtep.2013.09.002

Schlosser, D. A., Campellone, T. R., Truong, B., Etter, K., Vergani, S., Komaiko, K., & Vinogradov, S. (2018). Efficacy of PRIME, a mobile app intervention designed to improve motivation in

young people with schizophrenia. *Schizophrenia Bulletin*, *44*(5), 1010–1020. https://doi.org/10.1093/schbul/sby078

Schwartz, M. A. (2011). *Recovery From Disability: Manual of Psychiatric Rehabilitation* (Vol. 28). Psychiatric Times. https://www.psychiatrictimes.com/view/recovery-disability-manual-psychiatric-rehabilitation

Sreeraj, V. S., Bose, A., Chhabra, H., Shivakumar, V., Agarwal, S. M., Narayanaswamy, J. C., Rao, N. P., Kesavan, M., Varambally, S., & Venkatasubramanian, G. (2020). Working memory performance with online-tDCS in schizophrenia: A randomized, double-blinded, sham-controlled, partial cross-over proof-of-concept study. *Asian Journal of Psychiatry*, *50*. https://doi.org/10.1016/j.ajp.2020.101946

Sterne, J. A. C., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., Cates, C. J., Cheng, H. Y., Corbett, M. S., Eldridge, S. M., Emberson, J. R., Hernán, M. A., Hopewell, S., Hróbjartsson, A., Junqueira, D. R., Jüni, P., Kirkham, J. J., Lasserson, T., Li, T., … Higgins, J. P. T. (2019). RoB 2: A revised tool for assessing risk of bias in randomised trials. *The BMJ*, *366*, 1–8. https://doi.org/10.1136/bmj.l4898

Strauss, G. P., Waltz, J. A., & Gold, J. M. (2014). A review of reward processing and motivational impairment in schizophrenia. *Schizophrenia Bulletin*, *40 Suppl 2*(Suppl 2). https://doi.org/10.1093/SCHBUL/SBT197

Taghizadeh, N., Vonk, J. M., & Boezen, H. M. (2016). Lifetime Smoking History and Cause-Specific Mortality in a Cohort Study with 43 Years of Follow-Up. *PloS One*, *11*(4). https://doi.org/10.1371/JOURNAL.PONE.0153310

Tan, S., Zhu, X., Fan, H., Tan, Y., Yang, F., Wang, Z., Zhao, Y., Fan, F., Guo, J., Li, Z., Quan, W., Wang, X., Reeder, C., Zhou, D., Zou, Y., & Wykes, T. (2019). Who will benefit from computerized cognitive remediation therapy? Evidence from a multisite randomized controlled study in schizophrenia. *Psychological Medicine*, *50*(10), 1633–1643. https://doi.org/10.1017/S0033291719001594

Treisman, G. J., Jayaram, G., Margolis, R. L., Pearlson, G. D., Schmidt, C. W., Mihelish, G. L., Kennedy, A., Howson, A., Rasulnia, M., & Misiuta, I. E. (2016). Perspectives on the use of eHealth in the management of patients with schizophrenia. In *Journal of Nervous and Mental Disease* (Vol. 204, Issue 8, pp. 620–629). Lippincott Williams and Wilkins. https://doi.org/10.1097/NMD.0000000000000471

Välimäki, M., Athanasopoulou, C., Lahti, M., & Adams, C. E. (2016). Effectiveness of social media

interventions for people with schizophrenia: A systematic review and meta-analysis. *Journal of Medical Internet Research*, *18*(4), e5385. https://doi.org/10.2196/jmir.5385

van der Gaag, M., Valmaggia, L. R., & Smit, F. (2014). The effects of individually tailored formulation-based cognitive behavioural therapy in auditory hallucinations and delusions: a meta-analysis. *Schizophrenia Research*, *156*(1), 30–37. https://doi.org/10.1016/J.SCHRES.2014.03.016

Van der Gaag, M., Valmaggia, L., & Smit, F. (2014). The effects of individually tailored formulation-based cognitive behavioural therapy in auditory hallucinations and delusions: A meta-analysis. *Schizophrenia Research*, *156*(1), 30–37. https://doi.org/10.1016/J.SCHRES.2014.03.016

Wykes, T., Huddy, V., Cellard, C., McGurk, S. R., & Czobor, P. (2011). A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *The American Journal of Psychiatry*, *168*(5), 472–485. https://doi.org/10.1176/APPI.AJP.2010.10060855

Wykes, T., Newton, E., Landau, S., Rice, C., Thompson, N., & Frangou, S. (2007). Cognitive remediation therapy (CRT) for young early onset patients with schizophrenia: an exploratory randomized controlled trial. *Schizophrenia Research*, *94*(1–3), 221–230. https://doi.org/10.1016/J.SCHRES.2007.03.030

Wykes, T., Reeder, C., Landau, S., Everitt, B., Knapp, M., Patel, A., & Romeo, R. (2007). Cognitive remediation therapy in schizophrenia: randomised controlled trial. *The British Journal of Psychiatry : The Journal of Mental Science*, *190*(MAY), 421–427. https://doi.org/10.1192/BJP.BP.106.026575

Wykes, T., Steel, C., Everitt, B., & Tarrier, N. (2008). Cognitive behavior therapy for schizophrenia: effect sizes, clinical models, and methodological rigor. *Schizophrenia Bulletin*, *34*(3), 523–537. https://doi.org/10.1093/SCHBUL/SBM114

Yu, Y., Li, Y., Li, T., Xi, S., Xiao, X., Xiao, S., & Tebes, J. K. (2020). New path to recovery and well-being: Cross-sectional study on wechat use and endorsement of wechat-based mhealth among people living with schizophrenia in China. *Journal of Medical Internet Research*, *22*(9), 1–14. https://doi.org/10.2196/18663