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DIGITAL HEALTH TECHNOLOGIES IN THE PSYCHOSOCIAL TREATMENT OF CORE SYMPTOMS OF PSYCHOTIC DISORDERS – LITERATURE REVIEW AND PRACTICAL ASPECTS

ABSTRACT

The use of various digital health technologies is increasing in the treatment of psychotic disorders, as well as in psychiatry in general. In this review we present key studies on how technology is practically used to treat cognitive deficits, hallucinations and delusions of psychotic patients. The goal of this literature review is to provide the reader a comprehensive understanding on how technology is currently being utilized in the treatment of psychotic disorders, and to discuss how technology can pave the way towards a more integrative approach of treating psychotic disorders. The search for each symptom category was performed through PubMed and Google Scholar databases over the last 10-15 years. Computer-based cognitive rehabilitation seems to be as effective as the non-computerized equivalent, but has several additional advantages. AVATAR therapy and virtual reality-based treatments show promise in treating both hallucinations and delusions, but more research in this area is required. Digital solutions offer new ways to monitor and assess the different symptoms of psychotic disorders and to administer self-management in the daily lives of patients. Digital health technology belongs to the treatment of psychotic disorders, but it should be further studied in order to more fully understand the underlying psychological mechanisms involved, and to further validate the approaches that will be the most beneficial for large scale clinical use.

KEY WORDS: SCHIZOPHRENIA, EHEALTH, VIRTUAL REALITY, AVATAR-THERAPY, HALLUCINATIONS, PARANOIA, COGNITIVE DEFICITS

INTRODUCTION

Digital technology in the context of mental health includes, but not limited to, telemedicine, virtual reality, mobile apps, patient portals, electronic health records and computerized therapy. Digital technology has been harnessed to create new, accessible and scalable forms of mental healthcare and represents an innovative opportunity to improve existing services [1,2]. Different digital solutions have been found to be effective in the treatment of a variety of psychiatric disorders, including depression and anxiety, with the potential of increasing quality of life [3]. In addition to creating novel ways to treat patients, these solutions also have the potential to enhance the assessment, diagnostic accuracy and follow-up monitoring of psychiatric disorders by augmenting the objectivity and reliability of existing protocols [2].

Although these new innovations have to date most often been used in the treatment of less severe forms of psychopathology, recent studies have also suggested that they provide additional benefit in the treatment of more severe disorders, including schizophrenia and other psychotic disorders [1,2,4]. Despite advances in pharmacological and psychological treatment, almost one third of patients with schizophrenia do not respond to treatment and are denoted as treatment resistant, and evidently need new and innovative treatment options [5]. Digital solutions have been demonstrated to be feasible in both early and later stages of the trajectory of psychotic disorders. They can also be deployed in conjunction with the treatment received in hospitals and outpatient departments, or remotely as a form of self-help [4,6,7]. In addition to creating new treatment options, methods based upon established treatment frameworks, including Cognitive Behavioural Therapy (CBT), can be delivered to patients via different digital platforms [8,9].

The use of various digital tools, such as web- and mobile device-based interventions and virtual reality applications, in relation to psychotic symptoms have been deemed acceptable and feasible from a clinical perspective [10,11]. The use of mobile phones, computers and the internet are generally similar between patients and the general population, as 84.8% of people with a psychotic disorder have access to the internet and 88.6% own a device capable of accessing the internet, although access to technology may be more restricted especially with patients from older age groups and ethnic minorities [12,13,14]. In a study using Finnish data from patients with schizophrenia spectrum disorder in psychiatric inpatient units, the researchers concluded that the level of access to computers and the internet was quite good and that patient functioning was not associated with the frequency of internet and computer use [15]. Overall, the ownership of mobile devices in this patient cohort has been increasing since 2007, and most patients are willing to use mobile devices as a part of their treatment and self-management [16]. The use of digital tools has been associated with numerous potential benefits. These include a reduction in the time required by staff in delivering interventions, better standardization of the content of the interventions, more user choice regarding content, more options for data collection and symptom prevention and unlimited access to care [13]. These potential benefits make exploring and researching the topic from a clinical perspective highly worthwhile.

The goal of this literature review is to offer the reader an extensive look on how digital technology is being used in the treatment of psychotic disorders. We focus on all core symptom categories of psychotic disorders: cognitive disorders, hallucinations and delusions, and examine how technology can add value in the treatment of different symptoms alongside more established treatment options. Because of the wide scope of the paper, and still a very early phase of the research in some areas, our review is descriptive not systematic. More definitive descriptions are given at the beginning of each chapter. We discuss the need for further research, and propose how future research efforts can be aligned towards a more intergrative approach.

COMPUTERIZED REHABILITION OF COGNITIVE DEFICITS

COGNITIVE DEFICITS AND REHABILITATION

Cognitive deficits represent one of the core symptoms of schizophrenia, and it is suggested that they are the fundamental reason for the functional impairment underlying the disorder [17,18,19]. The Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative, developed by The US National Institute of Mental Health (NIMH), has suggested that seven cognitive domains should be assessed when evaluating treatment efficacy in schizophrenia: processing speed, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem solving and social cognition [20,21,22]. It is estimated that 61-78% of patients with schizophrenia manifest a severe cognitive deficit characterized by performance of one

to three standard deviations below the age group average [23,24]. Although diagnoses are categorical, psychotic disorders have been suggested to reflect a dimensional continuum, with respect to which cognitive and functional impairment vary. Schizophrenia has been suggested to reflect one extreme of this continuum [25]. Neurocognitive deficits have also been found to be present in individuals who present with an elevated risk for psychosis, termed the "clinical high-risk state". Impaired cognitive functioning in the domains of verbal fluency, verbal and visual memory and working memory have been suggested to associate with increased risk of transition to overt psychosis in high-risk states. This finding emphasizes the importance of early interventions that target cognition [26,27].

Cognitive remediation therapy (CRT) refers to a heterogeneous group of rehabilitative methods, which are designed to teach thinking and to improve mental skills among patients presenting with cognitive deficits [28]. Typically, CRT consists of weekly or biweekly 60-90-minute sessions which can include a combination of drill and practice exercises (e.g. training progressively more difficult memory tasks), strategy training (e.g. focusing on the strategies or mnemonics which help with memory tasks), action-based tasks and conversations with the therapist or between training group members [18,29,30].

EFFICACY OF COMPUTERIZED COGNITIVE REMEDIATION

The search for relevant meta-analyses was done from PubMed and Google Scholar databases using the keywords 'cognitive remediation', 'schizophrenia', 'psychotic disorder', 'meta-analysis' and 'systematic review'. The search was done during April 2020 and reviews and meta-analyses from the last 15 years were included. Early CRT programmes were carried out as paper and pencil training, but digital variants of the programmes have been developed where the training is executed with the help of a computer. There are numerous proposed benefits in computer-based CRT compared to conventional CRT. These include favouring neural plasticity, being helpful in learning compensatory strategies, providing unlimited training possibilities and exercise repetitions, multisensory presentation, objective scoring of exercises, automatic scaling of difficulty, immediate structured feedback and potentially enhancing motivation through stimulating and entertaining applications [31]. Digital implementations have also improved the accessibility of the programmes and made it possible to offer more tailored services [30].

Various meta-analytical studies have examined the efficacy of cognitive training and CRT in the treatment of psychotic disorders (*Table 1, Figure 1*). These wtreatment methods have been associated with significant improvements in improving cognitive performance, symptoms and psychosocial functioning in psychotic disorders. The reported effect sizes range from small to medium and the efficacy of computer-based methods are comparable to conventional methods. Higher effect sizes for cognitive improvements are associated with a treatment model combining drill and practice exercises and strategic coaching. Better functional outcomes are achieved when cognitive training is combined with wide-ranging psychiatric rehabilitation [32]. There is also preliminary evidence for the effectiveness of CRT in the clinical high-risk state [33]. In addition to positive changes in cognition, studies have reported improvements in different functional outcomes, such as in social functioning, self-reported social adjustment and different productivity outcomes [33,34]. It has been suggested that improvements in cognitive abilities trigger a rehabilitative process in functional capabilities which, in turn, aid the clinical improvements [35].

Research article	Findings
McGurk et al. (2007). A meta-analysis of cognitive remediation in schizophrenia. [32]	Both computerized and non-computerized cognitive remediation therapy (CRT) were examined. CRT was associated with significant improvements in cognitive performance and psychosocial functioning with medium effect sizes (ES) of 0.41 and 0.36 as well in symptoms with small ES of 0.28. The effect of CRT on psychosocial functioning was increased when adjunctive psychiatric rehabilitation was offered.
Wykes et al. (2011). A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. [36]	Both computerized and non-computerized CRT were examined. CRT was associated with elevated global cognitive functioning and functioning with medium ES of 0.45 and 0.41. CRT was also associated with decreased symptoms with a small ES of 0.18. In follow-ups 6 to 12 months after treatment, all changes except the changes in symptoms remained. There were no significant differences between computer or no computer groups in outcomes.
Grynszpan et al. (2011). Efficacy and specificity of computer-assisted cognitive remediation in schizophrenia: a meta-analytical study. [31]	16 randomized controlled trials evaluating the efficacy of computerized CRT were examined. Significant changes in cognition were reported with a mean ES of 0.38 in verbal memory, working memory, attention and processing speed. Most notable change of the interventions was in social cognition where medium ES of 0.64 was found.
Anaya et al. (2012). A Systematic Review of Cognitive remediation for schizoaffective and affective disorders. [37]	CRT was associated with a positive change in cognitive function across 16 studies with a medium ES of 0.32. The researchers concluded that CRT with schizoaffective disorders may have comparable benefits to patients with schizophrenia.
Chan et al. (2015). Can computer-assisted cognitive remediation improve employment and productivity outcomes of patients with severe mental illness? A meta-analysis of prospective controlled trials. [34]	Nine trials examining computer-assisted CRT efficacy on selected productivity outcomes of severe mental illness patients were examined. Receiving the treatment was associated with enhanced productivity outcomes including higher employment rate, longer duration of work and higher income.
Revell et al. (2015). A systematic review and meta-analysis of cognitive remediation in early schizophrenia. [38]	Several trials with 615 participants were evaluated in both conventional and computer-based CRT. Non-significant effects of CRT on global cognition were found. Significant positive effects were found on verbal learning and memory. Participants taking part in CRT showed significant improvements in functioning and symptoms with medium ES (0.36 for both). Conclusions were made that CRT in early schizophrenia is associated with similar improvements compared to chronic patients but to a lesser degree. The use of computer in the rehabilitation was not associated with cognitive outcomes.
Cella et al. (2017). Cognitive remediation for negative symptoms of schizophrenia: a network meta-analysis. [39]	CRT was associated with significant decrease in negative symptoms of schizophrenia with small to moderate effect sizes (mean ES 0.30). Both computerized and non-computerized CRT were included.
Glenthøj et al. (2017). The effect of cognitive remediation in individuals at ultra-high risk for psychosis: a systematic review. [33]	Six studies providing computer-based CRT were identified. Significant improvements were found in the domains of verbal memory (0,61,1.23), attention (0.69) and processing speed (0.50, 0.63, 0.84). Some studies also reported improvements in social functioning (3.09) and social adjustment (1.04).

Prikken et al. (2019). The efficacy of computerized cognitive drill and practice training for patients with a schizophrenia spectrum disorder: A meta-analysis. [40]	Compared to control groups, patients receiving computerized drill and practice training showed significantly more improvement on attention (0.31), working memory (0.38), positive symptoms (0.31) and depressive symptoms (0.37).
Kambeitz-Ilankovic et al. (2019). Multi-outcome meta-analysis (MOMA) of cognitive remediation in schizophrenia: Revisiting the relevance of human coaching and elucidating interplay between multiple outcomes. [35]	67 studies were included in the meta-analysis where computerized CRT was administered to patients with schizophrenia, alone or in combination with human guidance. CRT was associated with improvements in cognitive function, functioning and clinical symptoms (small to moderate ES). Human guidance strengthened the effect the intervention had on verbal and working memory.

Table 1. Systematic reviews and meta-analyses evaluating the effectiveness of cognitive remediation across various outcome measures.

Computerized and non-computerized variants of CRT are typically pooled together in research articles. The difference in effectiveness of computerized and non-computerized has been tested and no significant differences between the two methods have been found [38]. To our knowledge, research articles dedicated to comparing these two methods of CRT have not been published. To further deepen the understanding regarding the effectiveness of computerized cognitive remediation alone, we made a visual representation comparing the effectiveness between computerized and non-computerized CRT from the studies included in *Table 1*. First, all individual research articles included in a singular meta-analysis were divided into two groups based on what kind of CRT was included in the study (computerized vs. non-computerized). An average effect size of cognitive measures (a mean including all cognitive domains included in each study) from each study was either extracted directly or calculated. Calculations were made if a study included in the meta-analysis did not report an effect on 'global cognition' or a 'mean effect' from cognitive measures but rather effect sizes on specific cognitive functions. In these cases, we calculated a global mean effect from existing measurements. If the confidence intervals were not reported, they were calculated using the 'cohen.d.ci' function from the 'psych' library in RStudio. Comparisons between the effect sizes on computerized and non-computerized CRT can be viewed in *Figure 1*.

PSYCHOLOGICAL MECHANISMS BEHIND COGNITIVE REMEDIATION

Neuropsychological Educational Approach to Cognitive Remediation (NEAR) is a method of cognitive remediation that has been widely implemented for patients with psychotic disorders in North America, Europe, Asia and Australia [29,41]. It is a group-based intervention consisting of 60-90-minute sessions performed at least twice a week. Every session starts with an individual computer-based training phase and is followed with a bridging group. Bridging groups include discussions, psychoeducation and action-based tasks, e.g. playing board games and problem solving in real-life situations. Each bridging group is carefully instructed to enhance motivation, learning and metacognition. The theoretical foundations of NEAR form the basis for planning and structuring every session to include carefully implemented instructional techniques [26].

Neuropsychological evaluation helps to understand the underlying neuronal basis of cognition, cognitive operations and effective remediation strategies. In addition, learning theory is needed to understand and enhance the best ways to practise and learn skills. The techniques widely used in cognitive remediation include errorless learning, shaping, prompting, demonstration and generalization. In errorless learning the difficulty level of tasks is carefully adjusted to guarantee positive experiences with increasing challenges [42,43]. Shaping refers to systematically reinforcing cognitive skills and behaviours that are targeted (e.g. giving positive feedback every time a person is attending a session on time or staying on task

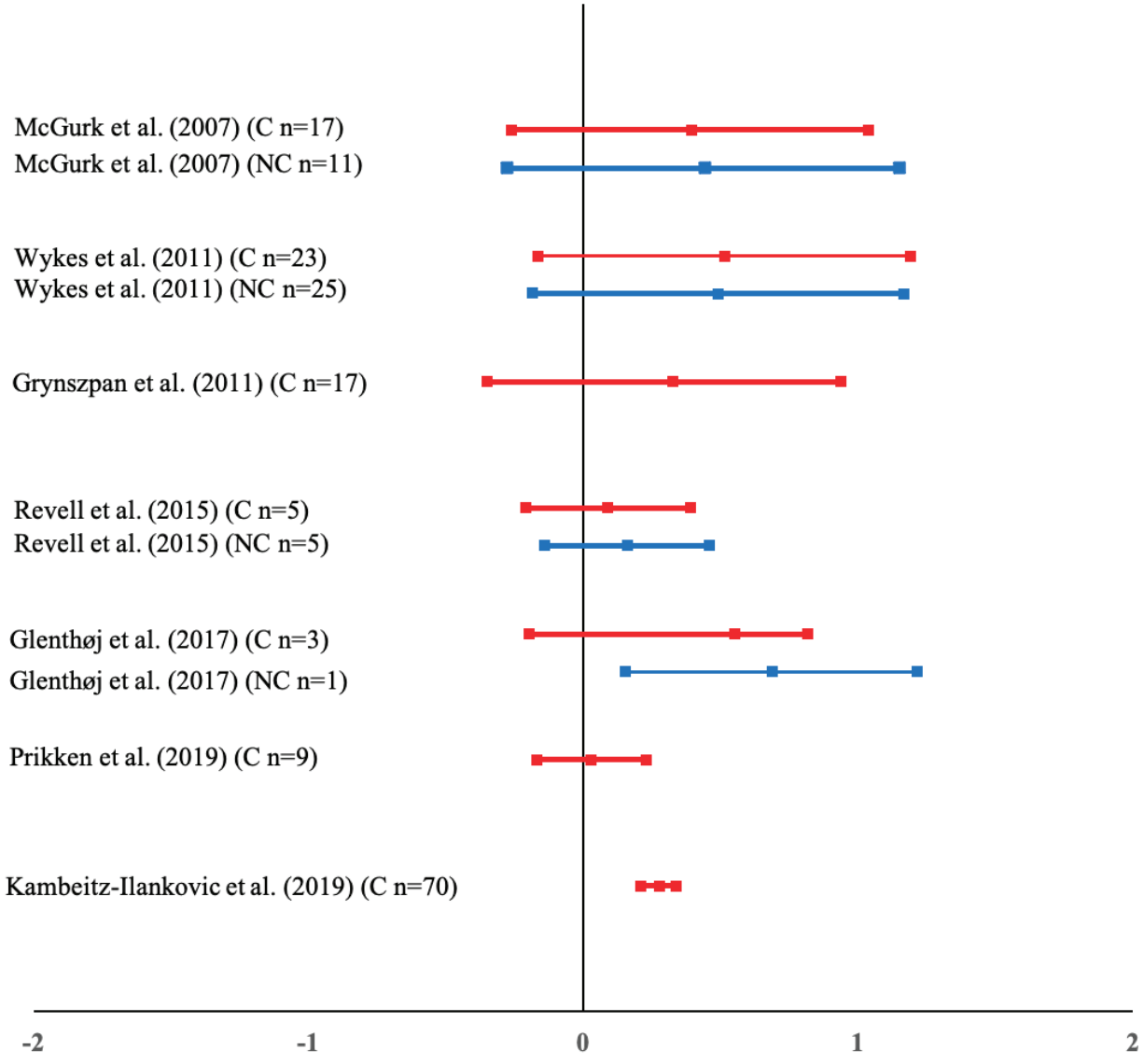

Figure 1. Mean effect sizes and 95% confidence intervals of both computerized (red) and non-computerized (blue) cognitive remediation therapy for cognitive measures from recent reviews and meta-analyses. The mean effect size for cognitive remediation across multiple reviews and meta-analyses is 0.36 and computerized and non-computerized remediation are overlapping and comparable.

as planned), and prompting to foster active learning style by asking open-ended questions to guide the person towards the correct solution [29,44]. Demonstrating a solution is used occasionally if needed and is done by modelling with verbal explanation towards an immediate goal. Generalization refers to doing various tasks in multiple contexts to transfer learning from clinical settings to everyday life (e.g. a bridging discussion where the goal is to connect the tasks done during the session to real-life situations) [29,41].

Educational psychology introduces the concept of intrinsic motivation that is essential to understand in ways to promote learning in remediation groups. A person with intrinsic motivation performs actions because it feels rewarding and has got an inherent inclination to explore and learn. In remediation groups, intrinsic motivation is enhanced with tasks that are contextualized, personalized and allow for learner control. There are several teaching techniques to foster intrinsic motivation and positive attitude about learning, which in turn have been associated with increased autonomy, self-determination, sense of well-being and commitment to treatment [29,41,45,46]. Another impact of educational psychology on remediation is the multisensory presentation of learning material [29].

According to the NEAR framework and rehabilitation psychology, cognitive deficits can also be seen as a social cognitive dysfunction, and thus cognitive remediation is offered in the context of rehabilitation of educational, vocational, social and independent living skills. At best, cognitive remediation is individually planned and integrated in comprehensive psychiatric rehabilitation [29,41,47]. Related to this, the goals for cognitive remediation are derived from overall treatment goals. Goal setting is an efficient process to help people to achieve a better quality of life, sense of well-being and higher self-efficacy [48]. One way to address the goals for cognitive remediation is to ask how cognitive deficits interfere with attainment of overall treatment goals. Involving the entire treatment team and relevant family members makes the goal setting and monitoring more efficient [29].

Client-centred therapy has influenced the way clinicians relate to clients in cognitive remediation. A client-centred approach refers to a method where the clinician acts as a facilitator whose main objective is to convey genuineness, acceptance and empathy [49]. Empathetic, non-judging understanding of the client's reactions to the learning process is a key component in facilitating learning. A clinician who meets the client without a facade, values the client's individuality, relates in a caring way and has trust in the capacity of the client is likely to create an optimal environment for exploring and learning [29,41].

A method that is gaining popularity is Action-Based Cognitive Remediation (ABCR), where the clinician's role is to assist clients to bridge computerized cognitive training to real-life situations. This is achieved through simulated tasks, behavioural activation techniques, role plays and repeated multimodal practice with computers to actively and warmly coach clients to navigate through both computer-based and real-life tasks which allows transfer of learning to happen [41,50].

CASE DESCRIPTION: SKILLED THINKING GROUP

Helsinki University Hospital has developed a form of computerized cognitive remediation therapy as a group-based intervention called the Skilled Thinking Group (STG), which is based on the NEAR model. The software used as the learning tool is Cognitive Interactive Remediation of Cognition and Thinking Skills (CIRCuiTS), a web-based remediation therapy programme which has been translated into Finnish [51,52]. The programme targets metacognition and promotes strategy use to strengthen the transfer of practiced cognitive skills to everyday life [53]. Details of the STG are presented in *Table 2*.

DIGITAL INTERVENTIONS IN THE TREATMENT OF HALLUCINATIONS

PSYCHOLOGICAL TREATMENT OF HALLUCINATIONS

The search for relevant studies was done from PubMed and Google Scholar databases using the keywords 'psychotherapy', 'schizophrenia', 'psychotic disorders', 'effectiveness/efficacy', 'meta-analysis', 'systematic review' and 'hallucinations' for psychological treatments, and 'AVATAR therapy', 'hallucinations', 'self-help' and 'digital treatment/intervention', 'schizophrenia' and 'psychotic disorders' for digital treatments. The search was done during April 2020 and again during October 2020. Latest meta-analytical studies covering psychological treatments were included in the review and all relevant studies covering technological solutions were included as broadly as possible.

In cognitive terms, a hallucination can be defined as "a sensory experience, which occurs in the absence of corresponding external stimulation of the relevant sensory organ, has a sufficient sense of reality to resemble a veridical perception, over which the subject does not feel

Theoretical background	Neuropsychological Educational Approach to Cognitive Remediation (NEAR)
Practical implementation	STG was implemented in 2015, and it is now used widely in the HUS area. It consists of 20 biweekly 90-minute long sessions. Each session begins with an individual computer-based practice and is followed by a bridging group. STGs are multidisciplinary led. There are several psychologists, occupational therapists and psychiatric nurses who have been educated to run the CIRCuiTS programme and to facilitate bridging groups. In one group there are at least two clinicians working together.
Evaluation and outcomes	STG has been evaluated qualitatively from the beginning of its implementation. Clients have given systematic feedback after every group and have reported an increased amount of self-confidence and better capability to function in everyday activities. A quantitative study of the effects of STG on the clients' cognitive skills, different psychiatric symptoms and functioning will be conducted in the HUS area during 2020-2021.

Table 2. Theoretical background, practical implementation and evaluation of the Skilled Thinking Group operated in the HUS area (HUS refers to Helsinki University Hospital).

s/he has direct and voluntary control, and which occurs in the awake state" [54]. Hallucinations can occur in any sensory modality and different types of hallucination can also co-occur. In schizophrenia spectrum disorders, auditory hallucinations are the most common form of hallucination [55]. Hallucinations are typically associated with significant distress [56].

Cognitive behavioural therapy (CBT) has been utilized to treat hallucinations in many patient cohorts, including treatment-resistant patients [57]. A meta-analysis by van der Gaag, Valmaggia and Smit [58] examined 18 RCT studies regarding the use of CBT to treat auditory hallucinations, in which the mean effect size was 0.44. By 2020, the effect of *CBT for psychosis* (CBTp) in treating hallucinations had been deemed sufficient and stable across multiple studies [59]. The central focus of CBT is to restructure the power imbalance between the hallucinations in relation to the individual's experience of them and to normalize different symptoms and psychotic phenomena [60,61]. Other psychological interventions that are researched and clinically used in the treatment of hallucinations, as well as in the treatment of psychotic disorders in general, include person-based cognitive therapy (PBCT), metacognitive therapy (MCT), acceptance and commitment therapy (ACT) and compassion-focused therapy (CFT) [62,63,64,65,66,67,68,69]. Short descriptions of these interventions can be viewed from *Table 3*.

Despite being a highly recommended treatment option for hallucinations, only around 10% of patients with a psychotic disorder receive CBT, or any other therapeutic approach as a treatment [70]. There is a growing body of evidence suggesting that elements of CBT can be successfully conveyed through digital platforms [8,9]. A wide use of technology might be a partial solution for the poor implementation of conventional therapeutic treatments.

Intervention	Description	Potential outcomes
Person-based cognitive therapy (PBCT)	Intervention that has been developed to reduce stress of people with psychotic disorders. Combines behavioural experiments, mindfulness practice and working with schematic beliefs [62].	An RCT study by Chadwick et al. examined the effect of PBCT with patients distressed by hearing voices. The results were in favour of PBCT in voice-related distress and in the controllability of voices [63].
Metacognitive therapy (MCT)	Focuses on cognitive bias, or thinking errors, which are related to psychotic symptoms [64].	Current results of MCT's efficacy in treating the symptoms of psychotic disorders are mixed [64,65,66].
Acceptance and commitment therapy (ACT)	Focuses on changing the patients' attitude towards negative experiences and tries to foster behaviours which are consistent with the patients' values [67].	Recent meta-analytic studies have concluded that patients who take part in ACT may experience a decrease in distress associated with hallucinations [68,69].
Compassion-focused therapy (CFT)	Focuses on fostering skills of compassion as a way to influence affect regulation [64].	Research on the effectiveness is still in its infancy, but initial case studies have revealed that CFT may lead to reduction in the frequency of positive symptoms and making the auditory hallucinations less malevolent and persecuting and more reassuring [64].

Table 3. Descriptions of psychological interventions that are being developed and used to treat hallucinations.

AVATAR THERAPY IN THE TREATMENT OF HALLUCINATIONS

Perhaps the most widely recognized digital approach for the treatment of hallucinations to date has been AVATAR therapy, which was initially described in a case study by Leff et al. (2013) [71]. The method was subsequently evaluated in a larger single-blind RCT in which patients receiving AVATAR therapy were compared to a control group receiving supportive counselling. In the study, Craig et al. [72] used a combination of digital image and speech modulation software to create an animated avatar, which best fit the experience of the patient. The tone and pitch of the voice of the avatar was finely tuned to match the auditory hallucinations perceived by the patient. During the sessions, the therapist acted as the avatar from another room to facilitate dialogue between the patient and the avatar. This dialogue ultimately led to the patient gaining increasing power over the initially powerful and threatening voice, which via the therapist's intervention became less threatening during the treatment. The RCT confirmed the positive outcomes of the case study, with a significant reduction in the severity of persistent auditory verbal hallucinations, a reduction in the reported frequency of voices and reduced stress after 12 weeks. The omnipotence of voices also reduced, compared to the control group.

Since the publication by Craig et al. (2018), AVATAR therapy has been further researched. Dellazizzo et al. (2018) investigated the efficacy of AVATAR therapy with treatment-resistant patients and concluded that this patient cohort may benefit from AVATAR therapy in terms of decreased intensity of auditory hallucinations [73]. Different versions of AVATAR therapy have been piloted and researched. Stefaniak et al. [74] conducted a study using a modified version of the original approach in which the therapist was in the same room as the patient. This was performed to ensure a sense of safety during the sessions. The study included 23 patients with chronic auditory hallucinations and demonstrated a similar effect with respect to the alleviation of symptomology, in line with the original study. AVATAR therapy has recently been implemented in an immersive virtual reality (VR) setting by du Sert et al. [75], in which a significant improvement in the severity of auditory hallucinations and

depressive symptoms was observed, with an accompanying increase in quality of life at a 3-month follow-up.

AVATAR therapy has been associated with various therapeutic implications. Perhaps the most important is the elevation in a subject's sense of control and mastery in relation to the experienced auditory hallucination. The process involves the initiation and promotion of dialogue, discourse, and taking an increasingly assertive stance in relation to an "internal other" (IO). For example, the therapist may encourage the patient to explicitly tell the IO that "you have been threatening me for years, I don't believe you anymore". By reclaiming and re-establishing a subjective sense of power in the relationship with the IO, the level of malevolence and omnipotence of the auditory hallucinations has been suggested to decrease. AVATAR therapy has also been suggested to foster an increase in the self-esteem of the patient and influence factors related to internal attribution. Understanding that the auditory hallucination(s) may reflect a specific part of the self is a common theme in AVATAR therapy. AVATAR therapy may also present an opportunity to work around certain feelings that appear in relation to voices, e.g. the feeling of shame. Overall, the process in which the patient actively practices engaging the IO, promotes the assertive disengaging of the IO. The process is suggested to foster the patients' subjective experience of the relationship between the self and the IO, promoting the demarcation of boundaries and the equilibration and decreasing of deviant omnipotence vs. impotence, submissive vs. oppressive power struggles. Finally, AVATAR therapy may present a novel way to engage therapeutic processes involving the treatment of trauma and/or grief when the auditory hallucination more clearly represents an internalized object related to the patient's past experiences [76].

It is suggested that AVATAR therapy may be a more suitable and effective form of treatment among some patients compared to traditional CBT, especially if there is a need to concretize the hallucinations, or if the patient finds it difficult to engage in a conventional therapeutic relationship. In some cases, the patient may even find working with the therapist via digital-based solutions subjectively more familiar, if the patient is accustomed to computers, especially younger generations. Large effect sizes (0.8) have been reported in an RCT setting evaluating AVATAR therapy in the treatment of auditory hallucinations. The same study reported that full remission, with respect to auditory hallucinations, was observed in three patients with schizophrenia out of the total 26 participants in the study. Positive results were observed in a relatively short time frame (seven 30-minute sessions), which indicates that providing AVATAR therapy might also save time compared to traditional therapeutic methods [77].

TOOLS FOR SELF-TREATMENT

Technology creates new solutions for administering self-help. The clear benefit of these solutions is that they are scalable and so can be widely implemented. This may partially solve the limitations of traditional therapeutic interventions which are difficult to implement in a widespread basis [78]. So far, there are relatively few examples of self-help tools which have been published and implemented in a clinical setting. However, some preliminary positive results have been found, which we present here.

A notable pilot project has been the web-based intervention, 'Coping with voices' constructed by Gottlieb et al. [79]. The programme was built to meet the need for psychosocial treatment in patients with moderate to severe auditory hallucinations. The intervention included therapeutic modules delivered through text, video and interactive exercises focusing on self-monitoring, relapse prevention and the enhancement of different coping skills. The efficacy of the intervention has been evaluated in an RCT against treatment as usual. Taking part in 'Coping with Voices' equally decreased the severity of auditory hallucinations compared to usual care. Participation in the internet intervention was associated with significantly greater increase in social functioning and knowledge about CBTp. The patients' engagement and satisfaction towards 'Coping with voices' was high. Similar type mobile applications of a CBT-based intervention for patients with an early psychosis have shown to be acceptable and feasible with a potentially strong signal for treatment efficacy [80,81]. For example, Husain et al. [82] have formulated a feasibility study for a solution called 'TechCare' which will combine personalized guided self-help with symptom monitoring. Furthermore, Baumel et al. [83] have researched the service utilization and user satisfaction towards a health technology which has been in use with patients with schizophrenia after hospitalization to prevent relapse. The solutions included coping strategy training for auditory hallucinations. Their study indicated very high utilization, acceptance and satisfaction towards the solution.

DIGITAL INTERVENTIONS IN THE TREATMENT OF DELUSIONAL THINKING IN PSYCHOTIC DISORDERS

PSYCHOLOGICAL TREATMENT OF DELUSIONS

The search for relevant studies was done from PubMed and Google Scholar databases using the keywords 'psychotherapy', 'schizophrenia', 'psychotic disorders', 'effectiveness/efficacy', 'meta-analysis', 'systematic review' and 'paranoia/delusions' for psychological treatments, and 'virtual reality', 'paranoia/delusions', 'self-help' and 'digital treatment/intervention', 'schizophrenia' and 'psychotic disorders' for digital treatments. The search was done during April 2020 and again during October 2020. Latest meta-analytical studies covering psychological treatments were included in the review and all relevant studies covering technological solutions were included as broadly as possible.

The severity of paranoid symptoms exists on a continuum ranging from brief passing thoughts that can appear in non-clinical populations to the longitudinally stable, systematic, severe ideation observed in schizophrenia [84]. In psychotic disorders, paranoia often manifests in a form of persecutory delusions, which means that the persecutory experience is held with increasing levels of certainty [85]. Delusions are associated with significant distress and an elevated risk for hospitalization and suicide [86,87].

As with hallucinations, CBTp represents a widely recommended and well-researched treatment option for the treatment of delusions [88]. The target of CBTp is often to focus on worry processes and certain thought patterns that are associated with delusions and paranoid thinking. These include 'jumping to conclusions', where conclusions are drawn from a very limited pool of information and belief inflexibility which manifests as an ineptitude to consider alternative explanations for the interpretations made concerning an individual's surrounding environment [89,90,91]. A significant difference in treatment efficacy between a group receiving CBTp and a group receiving treatment as usual was presented in a cumulative meta-analysis by Turner et al. [59] (g=.37). The researchers concluded that the evidence of CBTp in treating delusions is sufficient and stable.

From the third-wave CBT interventions, PBCT has been evaluated in two case studies. Initial results of the studies are positive in terms of reduced conviction and distress associated with paranoid beliefs [92]. Metacognitive therapy includes modules, which target delusions through processes related to jumping to conclusions, belief inflexibility, theory of mind and overconfidence in errors, but the current results of its efficacy in treating delusions are mixed [64,65,66]. Technology may create new opportunities to strengthen existing treatment approaches for delusions, including paranoid thinking, and has the potential to generate entirely new perspectives for treatment.

VIRTUAL REALITY IN THE TREATMENT OF DELUSIONAL THINKING

Virtual reality (VR) may be helpful when treating paranoia in psychotic disorders. VR refers to a practice where simulated environments are created using technology. With VR, users can experience a deeper level of immersion and interactivity than with traditional computer interfaces [7]. The use of VR in targeting paranoid ideation among psychotic patients has been suggested to be economically viable, and evidence indicating its effectiveness particularly in relation to paranoid thinking has been reported [93,94].

Pot-Kolder et al. [94] investigated the effect of VR-based CBT (VR-CBT) in relation to the severity of paranoid thoughts in a social context in a single-blind randomized controlled trial. VR-CBT was demonstrated to reduce momentary paranoid ideation (effect size –1.49) and momentary anxiety (effect size –0.75), but did not significantly increase the amount of time spent with other people. The researchers concluded that the change in paranoid ideation was mediated by changes in safety behaviour and social cognition. VR can also be utilized in treating impaired social cognition in psychotic disorders. Gainsford et al. [95] concluded in their article that both VR and non-invasive brain stimulation can be used independently, or in combination, to treat impaired social cognition in schizophrenia. Recently, Freeman et al. [96,97] have put forth plans to research a form of therapy which is conveyed through an automated VR coach, which can be used without the presence of a professional.

TOOLS FOR SELF-TREATMENT

Digital intervention, 'SlowMo', described by Garety et al. [98] is designed to treat paranoia. It aims to help people with paranoid thoughts by promoting the individual's ability to observe one's thoughts, and creating strategies for 'slowing down in the moment' in order to refine one's subjective ability to think more securely. The efficacy of the solution is being researched at the moment and results from the first trials are expected to be available in 2020. The researchers expect the solution to be highly acceptable and lead to clinically sound improvements in the severity of paranoid symptoms.

DIGITAL MONITORING AND ASSESSMENT IN PSYCHOTIC DISORDERS

The search for relevant studies was done from PubMed and Google Scholar databases using the keywords 'digital symptom monitoring, 'schizophrenia', 'psychotic disorders'. The search was done during April 2020 and again during October 2020. Relevant studies describing a digital solution for monitoring and assessing psychotic symptoms were included.

Self-monitoring positive and negative symptoms of psychotic disorders is feasible and may offer more detailed information compared to traditional methods, and might even help professionals to recognize behavioural patterns which are relevant for treatment [99,100]. Paranoid thinking, persecutory delusions and hallucinations can be monitored by combining self-assessment and physiological measurements such as heart rate variability and electrodermal activity. Both distressing hallucinations and delusions have been associated with significantly higher electrodermal activity levels, and it has been proposed that biosignatures could be used to identify signatures related to relapse [101].

'Crosscheck' is a smartphone application which has been designed as a tool for monitoring patients with psychotic disorders. It combines several methods for data collection including self-reports, device usage logs and different behavioural sensing methods. During usage, the application administers a 10-item self-report measurement focusing on the symptoms of psychosis (e.g. hallucinations), general mental health (e.g. anxiousness) and functioning (e.g. sleep). Physical activity, geospatial activity and speed frequency and duration are automatically collected using the sensors of the device. The software also tracks how the user is using the phone during the day (amount of telecommunication, app usage and phone unlocks). Ben-Zeev et al. [102] researched the application in a clinical setting in order to recognize indicators for a potential relapse. Participants showed unique indicators for a psychotic relapse and the researchers concluded that while the symptom monitoring and relapse detection are still in their infancy, innovations in data management and modelling may be essential in creating preventive methods for psychotic disorders. A solution combining monitoring and CBT methods called 'MATS' (Mobile Assessment and Treatment for Schizophrenia) which implements a text message approach has been associated with improvements in medication adherence, number of social interactions and in severity of hallucinations [103].

An RCT by Välimäki, Kannisto, Vahlberg, Hätönen and Adams [104] examined the effect of personalized short text messages on the rate of hospital readmissions with people with psychosis in Finland. The text message service did not reduce any service outcomes. The same researchers also conducted an RCT. A study by Kauppi et al. [105] later examined the potential benefits of text messaging across various demographic variables. They concluded that patients prefer messages which are encouraging, positive and humorous and that text messages may be useful especially for younger males. It has been suggested that SMS may play a crucial role in decreasing the number of relapses and hospitalizations in psychotic disorders. 'ITAREPS' is a SMS solution which assesses the possible prodromal symptoms of relapse with the EWSQ (Early Warning Signs Questionnaire). Weekly assessments have been associated with significantly lower hospital admissions [106].

Besides symptom monitoring, digital technology offers new ways to collect important information from patients with psychotic disorders. Moore et al. [107] have developed and validated a mobile version of the UCSD Performance-Based Skills Assessment, which is a widely used tool in assessing functional capacity of patients with psychotic disorders. They concluded that the developed mobile version performed just as well as the standard version of the tool. Virtual reality offers another interesting interface for functional capacity assessment. A great example of this was a study by Ruse, Harvey, Davis, Atkins, Fox and Keefe [108], where a virtual reality assessment method simulating a shopping trip, 'Virtual Reality Functional Capacity Assessment Tool (VRFCAT)', was created. They compared results from the assessment between healthy controls and patients with schizophrenia. Patients with schizophrenia performed more poorly compared to the healthy controls and the researchers concluded that the results are highly correlated with standard cognitive assessment.

DISCUSSION

SUMMARY

This review compiled relevant digital solutions from recent years in the treatment of psychotic disorders. This descriptive review covers a relatively large scope of digital approaches in the treatment of psychoses. For cognitive remediation, the review was systematic since all meta-analytical studies and systematic reviews from the last 15 years were included in this review. Later parts of the review were more narrative

in nature, though we have compiled a big part of the most relevant studies, since the total number of research papers focusing on digital treatment and assessment of hallucinations and delusions is still quite low.

Various technical innovations are conquering a remarkable place in psychiatry, but their clinical relevance in the treatment of the most severe end of the spectrum of psychiatric disorders (e.g. schizophrenia) is still somewhat in its infancy. In this review we have presented a growing pool of evidence suggesting that these novel technological approaches will increasingly play an interesting role in the treatment of severe psychiatric disorders, perhaps in the not so distant future. It is additionally suggested that the described innovations present potential with respect to a group of patients, which arguably to date, have not basked in the limelight of conventional therapeutic considerations. The most notable technological solutions presented in this study are collected in *Table 4*.

COGNITIVE SYMPTOMS

Cognitive impairment is common in psychotic disorders and is typically less responsive to antipsychotic treatment. It is associated with decreased functional capacity, especially in relation to everyday functioning. On the grounds of our review of several systematic reviews and meta-analyses, there are no findings indicating that computer-assisted cognitive remediation therapy is inferior in comparison with conventional CRT. CRT is an established form of rehabilitation that can be effectively delivered in multiple settings and with the help of various software. Although CRT has shown positive results in rehabilitating cognitive abilities across multiple reviews, the intervention is not without its limitations and methodological problems. It can be argued that the different interventions which are called CRT form a group which is too heterogeneous. This makes it difficult or even impossible to compare different interventions to one another. This might also limit our ability to include all relevant studies in this review. Closer examination of the practices and mechanisms, which make the rehabilitation effective in each situation, would be a desirable addition to the corpus of literature. Comparisons between the software would yield interesting results on how different kinds of exercises may associate with changes in different cognitive domains, and thus potentially facilitate the development of increasingly optimized solutions. Standardizing the process on how the effectiveness of CRT is studied and monitored would ensure that future trials would include every cognitive domain stated by MATRICS as an outcome measure, and clinicians would have the means to more precisely evaluate the efficacy of the rehabilitation they are delivering. It must be noted here that we did not specifically search for digital interventions focusing on social cognition, which is also an increasing area in applications for psychosis treatment.

IS THE FUTURE VIRTUAL IN THE TREATMENT OF HALLUCINATIONS AND DELUSIONS?

It can be argued that utilizing technology is the only solution by which we can offer therapeutic interventions to every patient with a psychotic disorder, and thus meet the standards laid out by NICE and others. Having different technology-driven solutions for treating hallucinations and delusions allows us to better individualize and tailor the treatment process with respect to interventions that best suit the requirements of an individual patient. Self-help programmes conveyed through mobile devices are scalable solutions that can help patients to alleviate the distress caused by hallucinations and support everyday functioning. Patients, who do not significantly benefit from these low threshold solutions, or conventional treatment processes, can be directed towards novel technology-aided interventions, such as AVATAR therapy and VR-CBT-based solutions for the treatment of hallucinations and delusions, which are both promising.

The results of AVATAR- and VR-CBT-based therapies hold great promise in the treatment of auditory hallucinations and delusions (paranoia) [72,94]. However, it has been suggested that further multicentre studies are needed to more fully establish the clinical efficacy of these preliminary findings, which have so far been performed on a very limited number of individuals. In both studies, the intervention groups consisted of a relatively heterogeneous group of patients presenting with a primary psychotic disorder spectrum diagnosis (ICD-10 or DSM-IV). In addition, the AVATAR study included all affective disorders with psychotic symptoms (ICD-10). The follow-up time for the AVATAR study was 24 weeks [72], which is considered short and does not provide information concerning long-term efficacy. The study by Pot-Kolder [94] had a 6-month follow-up period, and the intervention demonstrated a significant alleviation of momentary paranoia and anxiety in relation to social situations, which persisted at 6 months, although the time spent with others did not increase relative to the control group. The control groups in both studies

Digital technology	Intended use	Description of effectiveness
Computerized cognitive remediation	Rehabilitating cognitive deficits associated with psychotic disorders.	Remediation is effective in improving cognitive skills and functioning of participating patients. Computerized remediation is comparable to traditional forms of rehabilitation.
AVATAR therapy	Decreasing the severity of auditory verbal hallucinations and the stress they cause.	AVATAR therapy has been associated with significant reductions in the severity of persistent auditory verbal hallucinations, reported frequency of voices and stress.
Coping With Voices	A web-based self-help intervention built to meet the need for psychosocial treatment in patients with moderate to severe auditory hallucinations.	Taking part in the intervention equally decreased the severity of auditory hallucinations compared to usual care.
TechCare	A combination of symptom monitoring and personalized guided self-help-based psychological intervention.	The feasibility and acceptability of the solutions is still being researched.
VR-CBT for paranoia	Decreasing the severity of paranoid thoughts in a social context.	VR-CBT has been demonstrated to reduce momentary paranoid ideation and momentary anxiety, but did not significantly increase the amount of time spent with other people.
SlowMo	Treating paranoia. A combination of face-to-face meeting via a digital platform and self-management.	The efficacy of the solution is being researched at the moment and results from the first trials are expected to be available in 2020.
Crosscheck	Tool for monitoring patients with psychotic disorders. Combines several methods for data collection.	Through the application it is possible to recognize unique indicators of patients for psychotic relapse.
ITAREPS	Assessment of the prodromal symptoms of relapse.	Weekly assessments have been associated with significantly lower hospital readmissions.
VRFCAT	Assessment of functional capacity of patients with psychotic disorders. A virtual reality solution.	Patients with schizophrenia perform more poorly in a 'shopping trip' task in the virtual environments, and the results were highly correlated with standard cognitive assessment.

Table 4. Digital technology solutions that were presented in this study which are used and researched in the context of psychotic disorders.

consisted of patients receiving treatment as usual. In future studies it may be beneficial to compare the efficacy of these interventions to other specific interventions with known efficacy in relation to the treatment of psychotic disorders, e.g. conventional CBT-based methods and family interventions [109,110,111]. Longer follow-up periods are required to assess the potential influence of AVATAR- and VR-CBT-based interventions in relation to other clinically relevant outcome measures, including overall functioning, relapse prevention and quality of life.

AVATAR therapy has paved the way for the advent of increasingly immersive virtual reality-based interventions, which as its name suggests, may provide a greater degree of depth and understanding into the patient's overall experience, which for many psychotic patients may be difficult to explicitly verbalise and thus convey in a traditional psychotherapeutic setting. For instance, the social stress environment provides the potential to directly access the implicit domain of patient experience, which can be shared in the *here-and-now* situation, promoting explicit dialogue. From a therapeutic perspective, VR-CBT-based interventions may foster the opportunity to cultivate the observational and reflective domain of the patient, which has been suggested to reflect a common meta-level denominator in the process of varying psychotherapeutic orientations [112].

NEW PERSPECTIVES ON PSYCHOTHERAPY THROUGH DIGITAL TECHNOLOGY

A fundamental question, which is still widely debated in the field of psychotherapy, is whether cognitive schemas are secondary to emotions or vice versa. A unitary model for understanding human behaviour cannot be understood based on the context of cognition or emotion alone [113]. At present, psychosocial treatment options in relation to psychotic disorders have widely been grounded on cognitive perspectives. Many traditional forms of psychotherapy, which emphasize emotions and the patient's overall experience, have found it difficult to gain traction in the treatment of psychotic disorders. VR-based systems thus exhibit the additional potential of integrating the investigation of both the emotional and cognitive dimensions of experience in the *here-and-now* situation, and thus in the future may facilitate a more integrated approach in the psychosocial treatment of psychotic disorders. Digital solutions can also help researchers and clinicians alike to more intricately understand the individual therapeutic elements of treatment methods. Methods and exercises conveyed through technological interfaces strike an interesting mixture of flexibility and objectivity. An exercise which is built using technology is always based on prior robust theoretical understanding and its execution is always identical between patients, and is not influenced by fatigue. Technology also offers a way to make many treatments scalable and with it we can approach the recommendations stated by established authorities (e.g. NICE). Self-help solutions and active monitoring through technology may also bridge the treatment often received in outpatient departments with the daily life of the patients. Close monitoring of the incrementally different responses of a vast number of different patients may help us to iterate the methods towards optimal implementation.

MORE HOLISTIC TREATMENT THROUGH DIGITAL TECHNOLOGY

Different technological solutions seem to be capable to help treat the core symptoms of psychotic disorders, which cause the most distress to the patients and lead to disability. In addition to the core symptoms, technology can be used to treat conditions that are often comorbid with psychotic disorders, e.g. sleep disorders. Sleep disorders and symptoms of disturbed sleep (difficulties initiating sleep, maintaining sleep, early morning awakenings or poor sleep quality) are highly prevalent in patients with schizophrenia. Sleep disruption occurs often before the onset of first psychosis episode [114]. It may also predict later paranoia and hallucinations as well as transition to a psychotic disorder [115,116,117]. Cognitive behavioural therapy for insomnia, CBT-I, is the treatment of choice for insomnia, with a plenitude of evidence from clinical trials [118,119]. CBT-I can be applied via internet, with effects comparable to those found for face-to-face CBT-I [120]. Recent data evidence for the effectiveness of CBT-I in treatment of insomnia as a comorbid disorder for other psychiatric traits, notably depression, where treatment of comorbid insomnia and depression has shown the superiority of internet-based CBT-I to CBT for depression and to online sleep education [121,122]. A trial on university students suffering from insomnia resulted in small improvements in paranoia and hallucinatory experiences following digital CBT for insomnia [123]. CBT-I has also been used in the context of schizophrenia (clinical populations or adolescent patients at ultra-high risk for studies), where studies have shown a large effect for improvement of insomnia and a medium effect on hallucinations in some studies [124,125,126]. So

far, there is no published data on utilizing digital CBT-I on comorbid insomnia and schizophrenia. However, given the encouraging results on digital CBT-I in insomnia, with or without comorbid psychiatric traits, it also provides a promising approach for patients with comorbid insomnia and schizophrenia. The initial experiences of its application in digital format have been encouraging (RCT NCT04144231). In the Helsinki University Hospital, a randomized clinical trial of CBT-I in first-episode psychosis patients with sleep problems is being started.

At present there are various digital-based solutions, which have either been implemented or are currently being investigated in the treatment of psychosis in HUS Psychiatry. For instance, a "virtual ward" model has been employed for the treatment of schizophrenia patients presenting with overt psychotic symptoms living in supported housing units, to decrease the rate of hospitalizations. In this model, video conferencing services directly link supported housing units to specialists of a psychiatric ward. Patients, who would otherwise be sent to the ward for evaluation, are directly evaluated via video conference, allowing swifter implementation of interventions aimed to reduce psychotic symptoms. Another innovation, which is currently being evaluated for possible clinical use, includes the use of an electronic pill box, which reminds patients to take their medication through an audio signal. Information on whether the pill box has or has not been opened is transmitted to healthcare workers, who gain valuable information concerning adherence to medication.

CONCLUSIONS

This review presented an opportunity to examine a wide array of digital solutions simultaneously in the context of psychotic disorders. Many previous review articles have taken a 'technology first' approach and discussed the effectiveness of treatments carried out through a specific technology (e.g. virtual reality). Such reviews are of course of great value, since they evaluate extensively the safety and suitability of the technology itself. Our review found no findings indicating that the use of digital technologies with patients with psychotic disorders would undermine the patient's safety. Since the use of technology can be denoted as being ethical, we can move past the detailed description of the technology itself towards an integrative approach, where the technology is not in the limelight. User-centric and iterative development of technology allows us to create focused interventions for specific symptom dimensions which cause the patients the most distress or functional impairment.

However, during our review process it soon became apparent that these new digital interventions simultaneously influence multiple symptom dimensions. In several studies an integrative approach seemed to be most effective. The specific psychotherapies should carry on with overall rehabilitation and practice. It is unlikely that digital services will ever eliminate the pivotal role of relational aspects underlying the authentic *person-to-person* engagement of our clients.

In conclusion, digital health interventions are already succesfully implemented and will be implemented further in the treatment of psychotic disorders. The rate of implementation will increase expansively because of various technological opportunities and epidemiological demands. Besides continuous research endeavours, we need education for both healthcare staff and patients about the possibilities of different technological innovations, as well as access to relevant equipment to fully harness the potential of these solutions in the routine treatment of psychotic disorders.

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