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EPA Guidance on the Quality of eMental Health Interventions in the Treatment of Psychotic Disorders

Wolfgang Gaebel^{1,2,3*}, Isabell Großimlinghaus^{1,2,3*}, Ariane Kerst^{1*}, Yoram Cohen⁴, Bert Johnsson⁵, Davor Mucic⁶, Ionela Petrea⁷, Wulf Rössler⁸, Graham Thornicroft⁹, Jürgen Zielasek^{1,2,3*}.

¹Department of Psychiatry and Psychotherapy, Medical Faculty, Heinrich-Heine-University, Düsseldorf, Germany

²LVR Institute for Healthcare Research, Düsseldorf, Germany

³WHO Collaborating Center for Quality Assurance and Empowerment in Mental Health, Düsseldorf, Germany

⁴GAMIAN Europe, Brussels, Belgium

⁵European Federation of Associations of Families of People with Mental Illness, Leuven, Belgium

⁶Little Prince Psychiatric Center, Copenhagen, Denmark

⁷Trimbos Instituut, Utrecht, The Netherlands

⁸Leuphana University, Lüneburg, Germany, and University of Zürich, Switzerland

⁹Institute of Psychiatry, King's College, London, UK

*These authors contributed equally to this work.

Corresponding author:

Prof. Dr. Wolfgang Gaebel,
LVR Institute for Healthcare Research
LVR-Klinikum Düsseldorf,
Bergische Landstr. 2,
D-40629 Düsseldorf,
Germany.

Phone +49 211 922 2001

FAX +49 211 922 2020.

E-mail: wolfgang.gaebel@uni-duesseldorf.de

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Abstract

The main aim of this study was to develop recommendations on eMental health interventions for the treatment of psychotic disorders. A systematic literature search on eMental health interventions was performed and twenty-four articles about interventions in psychotic disorders were retrieved and systematically assessed for their quality. Thirteen studies were selected for this guidance. Web-based and mobile devices-based interventions mostly addressed psychoeducation and showed the feasibility and acceptability of the interventions. Evidence for beneficial clinical effects was weak. Studies were characterized by a large heterogeneity with regard to study type, sample sizes, interventions, and outcome measures. Five graded recommendations were developed.

Keywords

Mental healthcare, eMental Health, mobile health, psychotic disorders, schizophrenia, severe mental illness, treatment

1. Introduction

Mental disorders are one of the major challenges in public health in Europe with regard to prevalence, burden of disease and resulting disability. Within the spectrum of mental disorders, psychotic disorders belong to the most severe illnesses with a lifetime prevalence of 3-4% of the population [1]. According to the World Health Organisation (WHO), the group of neuropsychiatric disorders ranks as the leading cause of years lived with disability (YLD) in Europe. Within this group, schizophrenia ranks fifteenth with 1.8% [2]. It is one of the most severe and disabling mental illnesses and characterized by psychotic symptoms like hallucinations, delusions and thought disorder [3] and negative symptoms like anhedonia, lack of drive and depressed mood, which may lead to severe psychosocial impairments. The majority of patients has relapsing-remitting or chronic courses. Schizophrenia can be treated with antipsychotic drugs, psychosocial therapy and rehabilitation [4]. It is estimated that only approximately 10-50% of the mentally ill, including psychotic disorders, receive treatment [5]. The costs of schizophrenia treatment are related to the treatment itself (direct costs) and more important to indirect costs associated with lost productivity at work, early retirement, public support payments, and others [6]. Besides these costs, psychotic disorders are also associated with an increased prevalence of somatic disorders, leading to additional costs and further reduced quality of life, and with discrimination and stigma [7, 8].

A pressing issue is the improvement of access to care for people with mental disorders [9]. In addition to the impairments negatively affecting help-seeking, long waiting times and limited financial resources are strong arguments to develop innovative treatment concepts. One novel technological opportunity to close the treatment gap may be to provide mental health services via the internet [9]. The use of such “eMental Health” technology to care delivery has developed rapidly. E-mental health interventions have a number of advantages: They are easily accessible, provide anonymity to the user and are less expensive than personal patient-provider contacts [9]. The elimination of social cues and distinctions such as race, disability and facial expressions through text-based communication can help people to communicate more freely and feel more confident [9]. However, there is still no consensus as to a common definition of eMental health, but pragmatic approaches are available (Box 1).

BOX: E-Health and eMental-Health – Definitions

Currently, there is no general consensus on the definition of e-health and while many different definitions have been proposed, there is thus far no universal agreement about what may be included and excluded in this term [10]. E-health can be defined in multiple ways using narrow or broad definitions. Broad definitions often encompass administrative

healthcare systems, electronic prescribing, electronic health records and direct clinical care [11]. Definitions of e-health and its subdomains are formed either by the inclusion or exclusion of specific information technologies, such as the internet and smartphone apps, as well as by the need to update the definitions as new technologies are developed and used, and old technologies become obsolete [11]. In its glossary, the WHO defines e-health as “the transfer of health resources and healthcare by electronic means”.

E-mental health is one subdomain of e-health. Like for e-health, there is no single general definition of the term. It may be considered to include initiatives delivered directly to mental health service users and only on the Internet (and not just via stand-alone computers). Broad definitions may include delivery activities related to screening, mental health promotion and prevention, provision of treatment, staff training, administrative support and research. Mucic and Hilty [12] describe eMental health as “the use of telecommunication and information technologies to deliver mental health services at a distance”. According to the National Health Service (NHS) Network, eMental Health is “the use of information and communication technologies to support and improve mental health, including the use of online resources, social media, and smartphone applications”. Christensen and Evans [13] describe eMental health as “mental health services and information delivered or enhanced through the internet and related technologies”. This definition is closest to the research question of this paper which is the investigation of the evidence on internet- and mobile-based therapeutic eMental health interventions for schizophrenia and other psychotic disorders. There is a number of studies that explore the use of technology for common mental disorders like depression. In contrast, the use of eMental health interventions for psychotic disorders and schizophrenia is still scarce. The aim of this study is to give an overview of the existing evidence on these interventions and give recommendations for their application and future research.

The use of eMental health applications may be especially important for patients without access to traditional mental healthcare. For example, with the rising numbers of refugees in Europe, providing telemental health in the patients’ own languages becomes a reasonable alternative to interpreter-based treatment, and initial studies show that this increases patient trust [14]. Especially for the most severely mentally ill like most persons with psychotic disorders, internet-based therapy may provide a way of approaching mental healthcare anonymously avoiding stigmatization and obviating the need to leave one’s home to seek help. Also, providing internet-based interventions may lower costs of mental healthcare. While such effects have been shown for common mental disorders like depression and

anxiety [15, 16], the main purpose of this guidance was to review the evidence of the feasibility and efficacy of internet-based interventions for patients with psychotic disorders as an example of severe mental illnesses. Further guidances in the future will deal with other mental illnesses.

The following five hypotheses were formulated:

1. E-mental health interventions increase mental health literacy about psychotic disorders (for the public or in patient-oriented psychoeducation)
2. E-mental health interventions are efficacious to treat the positive and negative symptoms of psychotic disorders (primary psychotic disorders like schizophrenia, schizoaffective disorders, delusional disorders, acute and transient psychotic disorders, and secondary psychotic disorders)
3. There are quality assurance methods for assessing the efficacy of eMental health applications for psychotic disorders
4. There are ethical standards for eMental health interventions in psychotic disorders
5. There is a legislative framework for eMental health interventions in psychotic disorders

2. Methods

2.1 Guidance development process

In order to identify evidence for this guidance, we performed systematic literature researches. We searched the databases Medline (PubMed), PsychINFO and Scopus. A time limit as of 2000 was set and language filters were set to include English, German and Dutch publications. The detailed search strategy is shown in Table 1.

- Insert Table 1 here –

The following inclusion and exclusion criteria were used:

Inclusion criteria:

1. Studies providing information about the causes, symptoms, diagnosis and treatment of mental disorders (mental health literacy for the general population, psychoeducation for patients) (hypothesis 1)
2. Studies about the use of eMental health applications (i.e. computer-based, internet-based, smartphone or tablet-based applications) as interventions in mental disorders (hypothesis 2)
3. Papers addressing quality assurance methods for assessing the efficacy of eMental health applications for psychotic disorders (hypothesis 3)

4. Publications addressing the ethical or legislative aspects of eMental health applications (hypothesis 5)
5. Manuals about eMental health applications (hypotheses 1-5)
6. After screening of results of the initial broad literature searches using the title and abstract format, studies focusing on psychotic disorders only were further considered. This initial search served not to overlook studies dealing with psychotic disorders, which were performed together with other disorders.

Exclusion criteria:

1. Conference abstracts, editorials, pure opinion papers and papers addressing general mental healthcare questions without empirical data
2. Computer-aided systems, i.e. systems which use computer- or internet-based technologies to address study participants or retrieve and/or collect information from study participants, but which have no clear focus on eMental health applications (like the use of a computerized version of a depression test without any further eMental health aspect of the study)
3. Studies dealing with television, radio, telephone, videoconferencing, video telephone services and print materials
4. Studies dealing with the prevention of or diagnostic processes of mental disorders
5. Descriptions and evaluations of computer- or internet-based systems exclusively used to collect or analyze routine healthcare data (like hospital information systems or descriptions of algorithms used to analyze mental health datasets) or solely used as a communication tool between patients and healthcare providers
6. Technical descriptions of eMental health systems without evaluation of their efficacy (like descriptions of the design stages of eMental health product developments or conceptual papers about the potential uses of e mental health applications)
7. Studies about information retrieval systems (like analyses about the use of computers to store medical information or analyses of database use, but studies were included if they analyzed the use of eMental health applications)
8. General electronic information applications provided by healthcare providers, patient organizations or medical specialty societies
9. Applications not dealing with mental health services or mental disorders
10. Publications about principles of eMental health applications but without empirical or other research data allowing an assessment of the efficacy of the eMental health application
11. Internet/computer use and addiction: studies on computer use (for example its relation to sleep problems) and on the concept of internet addiction, epidemiology, diagnosis and

classification, and non-eMental health based interventions for internet or computer use and addiction were not included

12. Radiologic studies without eMental health aspects (like clinical studies on the use of “computer tomography”)

13. Virtual reality studies, unless these used internet-based presentations of virtual reality applications in the framework of an eMental health application

Classical setting-specific mapping of mental healthcare studies (in-patient vs. out-patient) does not pertain to eMental Health-related studies and was not considered in this guidance. Three authors (IG, AK and JZ) independently screened the retrieved documents in three stages, at first on the title level followed by the abstract and the full-text levels. Discrepancies between the raters were resolved by discussion. The details of the selection process are shown in Figure 1.

- Insert Figure 1 here -

Evidence evaluation tables were adapted from SIGN50 (Scottish Intercollegiate Guidelines Network) templates (<http://www.sign.ac.uk/methodology/checklists.html>) [17].

Recommendations were developed by four authors of this manuscript (WG, IG, AK and JZ) and reviewed by the EPA Guidance Committee, the EPA Board and the coauthors of this manuscript including representatives of patients and families.

2.2 Evidence and recommendation grading

Recommendations were developed by the authors of this article and reviewed by the EPA Guidance Committee and the EPA Board. Both evidence and recommendations were systematically graded following previous EPA Guidance procedures (Tables 2 and 3; [17]) based on assessment protocols by Daly and coworkers [18] and the SIGN grading system (1999-2012 version)[19].

- Insert Table 2 here –

- Insert Table 3 here -

3. Results

3.1 Characteristics of included studies

The systematic literature search identified four systematic reviews, two randomized controlled trials, four open uncontrolled trials, two unsystematic literature reviews and one focus group study that were eligible according to the inclusion and exclusion criteria. The evaluation summary of the 13 included studies is shown in Table 4.

- Insert Table 4 here -

The following types of eMental Health interventions were identified in these studies:

- Web-based interventions (websites, online feedback tools, discussion rooms, internet diaries, social media, online therapy) (thematized in 10 of 13 studies)
- Mobile-devices based interventions (text messaging, use of smartphones and other mobile devices) (thematized in 9 of 13 studies)

3.2 Study description: Web-based interventions

Naslund and coworkers [20] summarized the types of remote technologies used in different eHealth interventions for severe mental illnesses and showed that mostly web-based interventions (n=12) had been developed thus far. There were five studies using internet-based schizophrenia interventions. Two studies were pilot trials and showed the feasibility of online platforms as psychosocial interventions and some positive effects on depressive symptoms. One randomized controlled trial used the internet to improve parenting skills of mothers with severe mental disorders including schizophrenia, and led to improved parenting skills and decreased parental stress. Another randomized controlled trial showed no effects of an unmoderated peer support internet forum for schizophrenia patients. A randomized controlled trial with a 12-months follow-up period using an online website-based psychoeducational intervention that provided information about schizophrenia, its prognosis and treatment and coping strategies to persons with schizophrenia and their supporters, led to a significant reduction in positive symptoms for persons with schizophrenia and a significant increase of knowledge about schizophrenia for both, persons with schizophrenia and their supporters [21, 22]. A limitation of this study was its small sample size (31 patients and 24 supporters) [21]. Kasckow and coworkers [23] conducted a systematic literature review and reported on another study on the feasibility of an online group program designed for relatives of persons with schizophrenia [24]. Participants (n=26) in the intervention group were compared to archival data from persons receiving treatment as usual (n=26). Most participants attended more than 50% of the core online support sessions and showed high levels of satisfaction. However, there was only little impact on relatives' distress. Another systematic review showed that two pilot studies pointed to high rates of patient satisfaction (75-92%) with web-based psychoeducation both in terms of usability and helpfulness [25]. The review identified a single uncontrolled trial using web-based cognitive-behavioural therapy for persistent auditory hallucinations and found significant improvements in hallucination severity and general psychopathology [26].

A focus group study of siblings of persons with schizophrenia showed that siblings were eager for information and peer support [27]. Another study developed a web-based program to empower patients with schizophrenia to discuss treatment options with their clinicians [28]. Patients in the intervention group used an interactive web-based intervention with video clips of actors, who simulated a patient discussing treatment concerns showing the performance of communication strategies and skills. The control group was shown educational videos about the treatment of schizophrenia before a routine follow-up appointment. Results showed that the ensuing clinician visits in the intervention group were longer (24 versus 19 minutes, $p < .05$), and patients had a proportionately greater contribution to the dialogue ($p < .05$) with less verbal dominance by the clinician ($p < .05$). Moreover, patients in the intervention group asked significantly more questions (2 versus .9, $p < .05$), provided more lifestyle information (76 versus 53 statements, $p < .05$) and more often made sure that they had understood the information provided by the clinician (3.6 versus 2.1 checks, $p < .05$). In addition, with intervention group patients, clinicians interacted in a more patient-centered manner, made more empathic statements and provided more cues of interest. The emotional tone of the visits of the intervention group in comparison to the control group was rated as more dominant and respectful for patients ($p < .05$) and more sympathetic for clinicians ($p < .05$). A limitation of this study was the small sample size and therefore limited generalizability. In addition, there was a self-selection bias, since less than one-third of clinicians at the study sites participated. Thereby, results may have represented clinicians and patients who were generally more interested in communication and patient empowerment [28].

A further systematic review concluded from few studies that participation in unmoderated and unstructured online peer support groups was not associated with clinical or psychological benefits [22]. Formal supervision or guidance in online peer support therefore seemed to be pivotal [22]. Research on online peer support groups is still sparse and a randomized controlled trial showed that unmoderated and unstructured internet-based peer support (including patients with schizophrenia spectrum disorders and affective disorders) was not efficacious to improve recovery, quality of life, empowerment, social support and distress [20, 29].

3.3. Mobile - based interventions

Mobile device-based interventions in the reviewed studies were used in a variety of ways: monitoring symptoms and detecting early warning signs of incipient psychosis, providing interactive feedback, assisting in symptom management or providing prompts for increasing treatment adherence. In one study, a mobile text messaging intervention assessed medication adherence and clinical status and provided feedback and support to the

participants. It suggested various coping strategies in response to participants' replies to the text messages [30]. Furthermore, this study assessed the usability and satisfaction with the intervention. The study was only a small scale (n=17) trial but it showed that the mobile text messaging intervention had a good response rate and was well received by the participants.

Another study offered individuals with schizophrenia or schizoaffective disorder prescheduled and on-demand resources to facilitate symptom management, mood regulation, medication adherence, social functioning, and improved sleep. Approximately 90% of participants rated the intervention as highly acceptable and usable. After one month there were reduced psychotic and depressive symptoms and a decline in general psychopathology (PANSS total; $P = .002$). The mobile phone intervention in this study showed feasibility, acceptability, and preliminary efficacy for a small scale group (n=30) [31].

Ben-Zeev and coworkers [32] examined predictors of self-stigma in schizophrenia by using mobile technologies. They tracked momentary levels of self-stigma, psychotic symptoms, negative affect, positive affect, activity, and the immediate social and physical environment in twenty-four individuals with schizophrenia. The levels of self-stigma were tracked multiple times daily for a one-week period in this uncontrolled short-term feasibility trial. The study intended to show how both external/contextual (i.e., location, activity, social company) and internal (i.e., psychiatric symptoms, mood) factors were related to the presence of self-stigma. It was shown that only the participants' current activity was associated with changes in self-stigma ($\chi^2 = 10.53$, $p < 0.05$). Furthermore, the study showed that increases in negative affect and psychotic symptom severity predicted increases in the intensity of self-stigmatizing beliefs of participating individuals. Psychotic symptoms were found to be an antecedent and a consequence of increased levels of self-stigma.

A review by Kasckow and coworkers [23] described an intervention by Spaniel and coworkers [33], which used a mobile phone-based telemedicine system to monitor early warning signs of psychosis in order to prevent hospitalizations. A clinician was provided with an analysis of the patients' symptoms. In the group of 45 patients with psychosis, the intervention showed a significant 60% decrease in hospitalizations one year after enrollment compared to one year prior to enrollment.

Alvarez-Jimenez and colleagues (2014)[25] systematically analyzed the evidence on the acceptability, feasibility, safety and benefits of online and mobile phone-based interventions for psychosis. In their review, they included one mobile intervention using text messages targeting auditory hallucinations, medication adherence and socialization for patients with

chronic schizophrenia delivered in a real world setting [34]. The majority of the patients (76%; n=42) completed the 3-months-intervention. Compared to the non-completers, completers had comparably less severe negative symptoms, higher premorbid IQ and better self-reported living skills.

Naslund and coworkers [20] found a number of mobile-based interventions when they reviewed mHealth and eHealth interventions for serious mental illnesses. The interventions for psychotic disorders focused on disease management, medication adherence and support, relapse control, managing psychiatric instability as well as detecting early warning signs. Preliminary evidence showed that mobile-based interventions may lead to improved outcomes regarding positive and negative symptoms, depressive symptoms, rates of hospital admissions and numbers of inpatient days, emergency room visits, medication adherence and attendance of clinical appointments, social interactions, suicidal ideation, quality of life, and somatic comorbidity [20]. Included in this review was also a study that we found in our search. Spaniel and coworkers [33] investigated a mobile-phone based telemedicine solution that allows for regular monitoring of the exacerbation of psychotic symptoms. This kind of weekly relapse monitoring via a PC-to-phone SMS platform was found to be possibly efficacious in enabling early intervention and reducing hospitalizations in people with psychotic disorders. This study included 45 patients in a one year follow-up.

These and most other studies included in the review by Naslund and coworkers [20] showed the feasibility and acceptability of the intervention for people with serious mental illness, including psychotic disorders. Some of these studies showed that remotely-delivered interventions may be efficacious for people with serious mental illness. However, the review did not find sufficient evidence to draw conclusions with regard to the effectiveness of the interventions.

In our search, we also identified a Cochrane review that evaluated information and communication technology based prompting to increase the treatment compliance of people with serious mental illnesses [35]. The study included mobile text messages, e-mail or other electronic device-interventions for prompting. The study found 32 references which included 25 trials. The analyses included 358 people with the diagnosis of serious mental illness, like schizophrenia, schizoaffective disorder and delusional disorder, serious/chronic mental illness' or 'psychotic illness'. The authors found no clear evidence for or against using modern technology prompting systems for treatment compliance for people with schizophrenia and suggested that future developments need to be followed in great detail by the involved groups.

3.4. Professional supervision/moderation

The 13 studies dealt differently with the question of professional supervision/moderation. Some did not address it at all [9, 23]. One study was a focus-group study performed by experts [27]. One intervention was developed by experts, but it was unclear from the published study whether professional supervision and moderation were provided [28]. In two interventions, experts supervised the feedback from patients [31, 32] and in three others, experts themselves provided feedback and/or moderation [21, 30, 33]. Alvarez-Jimenez and coworkers in their reviews recommended in order to optimize safety in internet-delivered interventions for people with psychosis to regularly monitor and moderate online interventions [22, 25] while Naslund and coworkers in their review only mention for one of their studies that it was an unmoderated internet forum, but did not further discuss the issue of professional moderation or supervision [20]. In the review by Kauppi and coworkers, only two studies were included and both were supervised by experts [33].

4. Recommendations

Recommendation 1. The European Psychiatric Association considers (Grade of recommendation: B) that web- and mobile-based interventions are feasible and acceptable for persons with schizophrenia and their relatives (evidence level I-III) [20, 22, 25].

Recommendation 2. The European Psychiatric Association considers (Grade of recommendation; B) that preliminary evidence shows that mobile-based interventions may lead to improved outcomes regarding positive and negative symptoms, depressive symptoms, rates of hospital admissions and numbers of inpatient days, emergency room visits, medication adherence and attendance of clinical appointments, social interactions, suicidal ideation, quality of life, and somatic comorbidity. (evidence level I-III) [20, 21, 25, 27, 30, 33, 35].

Recommendation 3. The European Psychiatric Association considers (Grade of recommendation: B) that web-based psychoeducational interventions are acceptable for family members and friends of patients with schizophrenia and may increase the knowledge about schizophrenia of both, persons with schizophrenia and their caregivers. They may also empower patients to discuss quality of care and treatment questions with their clinicians, may increase the parenting skills of patients with schizophrenia, increase knowledge about

schizophrenia and reduce positive symptoms (evidence level I-III). [20, 21, 22, 25, 27, 28, 31, 33, 35].

Recommendation 4. The European Psychiatric Association considers (Grade of recommendation: C) that online peer support groups are efficacious to address patients and caregivers. Moderation by mental health professionals is necessary in order to ensure efficacy (evidence level III) [20, 22, 27, 29].

Recommendation 5. The European Psychiatric Association considers (Grade of recommendation: D) that there is a need to develop quality standards, ethical guidelines and legal frameworks to regulate the provision of eMental health interventions for persons with schizophrenia and other psychotic disorders (evidence level IV) [9, 20, 22].

5. Discussion

The studies reviewed here show the feasibility and user acceptance of both web- and mobile-based interventions for people with psychotic disorders. The heterogeneity in study design, types of studies, outcome assessments, study quality and low sample sizes precluded any definite conclusions in terms of efficacy and effectiveness and efficiency of eMental health interventions for people with schizophrenia. Studies about other psychotic disorders were scarce except for bipolar disorder [20]. Alvarez-Jimenez and coworkers [22] discussed that online therapy for patients with psychosis may decrease social contacts, and that online interventions specifically designed to supplement existing mental health services and augment traditional relationships may be most promising. For online forum use, moderation by professionals was deemed to be necessary.

Preliminary evidence has shown that persons with psychotic disorders like schizophrenia use the internet in the same way as individuals not affected by mental disorders [36]. However, the use of the internet and mobile phones is differing among different social groups and income groups with an observed lower use among low-income and disadvantaged groups like individuals with severe mental illness. It needs to be considered that electronic (mobile) devices and internet access, which is a requirement for eMental health interventions, involve additional costs which may limit access for some groups [37]. Nevertheless, current research results show that people with severe mental illnesses are interested in using modern therapeutic technologies and perceive them as positive.

Moreover, the way of patient-professional communication has shifted from a paternalistic framework to a patient-centered, evidence based approach, in which patients are more

involved in medical decision-making and in which clinicians and patients interact as partners. Against this background, eMental Health interventions may support the autonomy, information and opportunity for bidirectional communication [9, 28].

There is a lack of specific studies or reviews addressing the aspects of quality assurance of eMental health products for people with schizophrenia or other psychotic disorders. While ethical issues were addressed in the discussion sections of some of the retrieved articles, a consensus development would be necessary about these questions. We did not identify studies about legislative aspects.

In summary, the studies reviewed here provide strong evidence that web- and mobile based interventions for people with schizophrenia and/or other psychotic disorders are feasible and acceptable both for patients and caregivers. There was moderate evidence that eMental health interventions may improve specific elements of mental healthcare processes, such as shared-decision-making, symptom monitoring, disease management, information provision, empowerment, and there was preliminary evidence that they may also improve outcomes by fostering symptom reduction and treatment adherence. E-mental health interventions hold promise to shape the future of mental healthcare delivery through increasing service accessibility, reducing stigma and self-stigma, and providing timely and flexible support to individuals with psychotic disorders and their caregivers. Nevertheless, it is important to also consider other aspects such as the lack of ethical guidelines and quality assurance mechanisms, and the need to analyse the legal framework about eMental health in different nations when developing and implementing eMental health interventions. We did not identify ethical guidelines or quality assurance systems specifically developed for eMental health interventions targeting people with psychotic disorders.

Regarding the five hypotheses, we found evidence to support the first hypothesis that eMental health interventions are efficacious to increase mental health literacy. Regarding the second hypothesis that eMental health interventions are efficacious to treat mental disorders, we found preliminary evidence for the field of the treatment of psychotic disorders. We did not find evidence to support the hypotheses 3-5 in the field of psychotic disorders (quality assurance, ethical standards, legal frameworks), but we found some statements indicating the need to address these aspects. These issues will need to be further developed in the future. Also, future research needs to provide controlled, sufficiently powered studies to provide definite answers as to the questions of clinical efficacy, efficiency and effectiveness of web- and mobile-based eMental Health applications for people with psychotic disorders and their caregivers. In addition, certification procedures will need to be developed to assess the

quality of web- or mobile-based interventions for people with psychotic disorders, and these quality assessments should be grounded in explicit scientific and ethical quality standards taking also into consideration the current legal frameworks in the different European countries.

Conflict of interest

W. Gaebel is President of the European Psychiatric Association (EPA), Chair of the EPA Guidance Committee and Chair of the World Psychiatric Association Section on Quality Assurance. He is the co-chair of the steering committee for the development of the German Association for Psychiatry, Psychotherapy and Psychosomatics (DGPPN) guideline on schizophrenia, and Vice President and member of the guideline commission of the Association of the Scientific Medical Societies in Germany. He has received support for symposia from Janssen-Cilag, Sanofi-Aventis Germany, Lilly Germany, and Servier Germany. He is a member of the faculty of the Lundbeck International Neuroscience Foundation.

I. Großimlinghaus is a member of the coordination group for the development of the DGPPN guideline on schizophrenia.

A. Kerst is affiliated to the European Psychiatric Association (EPA) as assistant to the President of the EPA.

Y. Cohen

B. Johnsson

D. Mucic

I. Petrea

W. Rössler

G. Thornicroft

J. Zielasek has received congress travel support from the DGPPN and is a member of the coordination group for the development of the DGPPN guideline on schizophrenia. He has received an author honorarium from Servier International for a review article.

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Figure 1: Flow of studies retrieved in the systematic literature search with the algorithm detailed in Table 1.

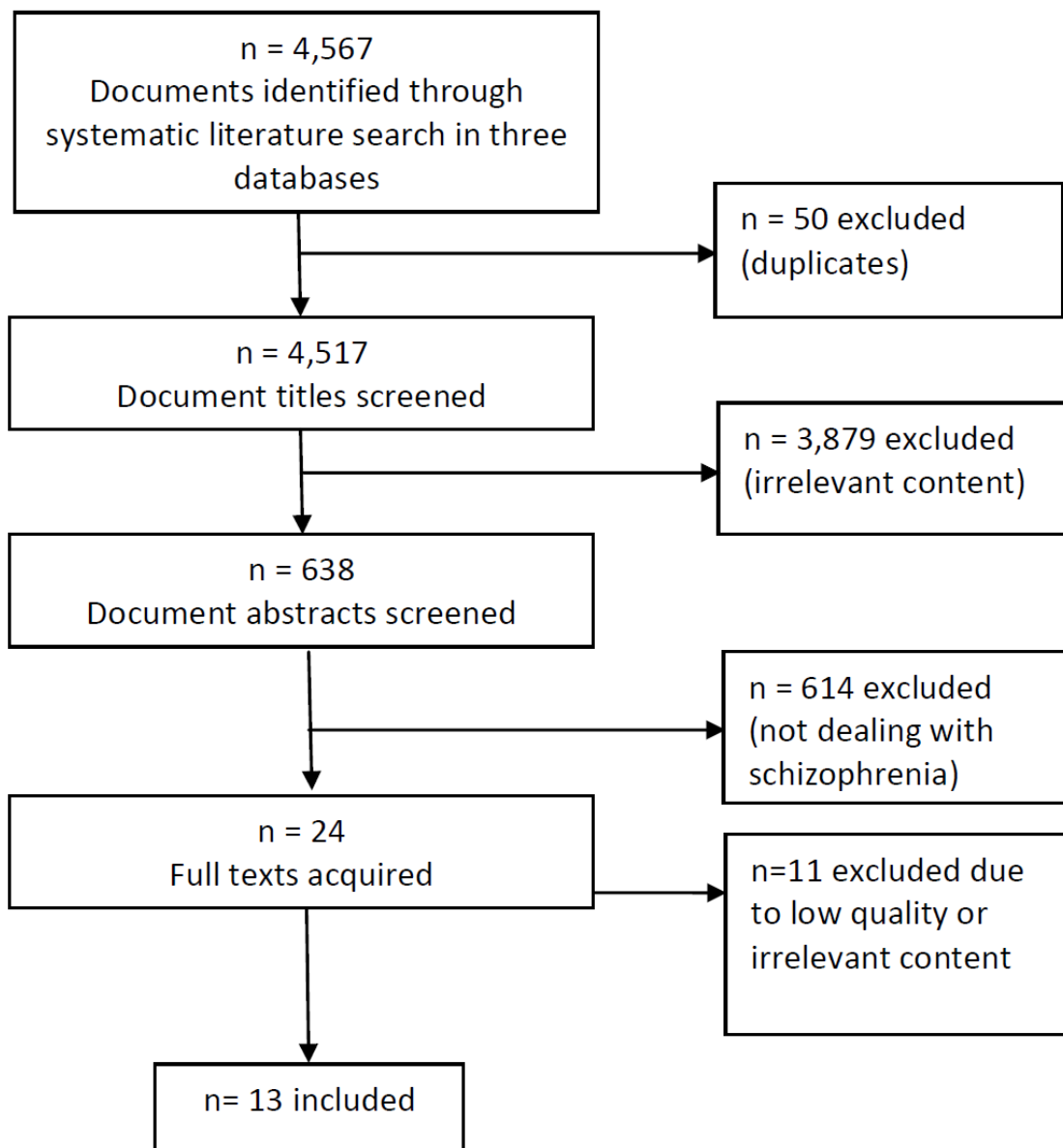


Table 1: Search terms and syntax of the systematic literature search.

Database	Search algorithm (titles, abstracts, MESH terms)	Number of retrieved documents	Date of search
Medline (PubMed)	"mhealth" OR "mobile" OR "e health" AND "mental health" OR "mental disease" OR "mental disorders" OR "e mental health" OR "psychiatr*" OR "psychotic*" OR "psychotic disorders" AND "intervention" OR "application" OR "applicat*" OR "guideline" OR "guideline*" AND "effect" OR "effect*" OR "effic*" OR "evidence" OR "eviden*" OR "outcome"	3445	30.07.2015
Scopus	Available on request from authors	1015	27.08.2015
PsychINFO	Available on request from authors	107	11.09.2015

ZUSAMMENFASSUNG für MEDLINE PRÜFEN, ANGABEN für SCOPUS UND PSYCHINFO MÜSSEN EXPLIZIERT WERDEN

Table 2: Grading of evidence from quantitative studies, qualitative studies and reviews [17, 18, 19].

Study type	Features of qualitative research	Features of quantitative studies	Features of reviews
Level I Generalizable studies	Sampling focused by theory and the literature, extended as a result of analysis to capture diversity of experience. Analytic procedures comprehensive and clear. Results can be generalized to settings or stakeholder groups other than those reported in the study	Randomized controlled trials. Surveys sampling a large and representative group of persons from the general population or from a large range of service settings. Analytic procedures comprehensive and clear usually including multivariate analyses or statistical modeling. Results can be generalized to settings or stakeholder groups other than those reported in the study	Systematic reviews or meta-analyses
Level II Conceptual studies	Theoretical concepts guide sample selection, based on analysis of literature. May be limited to one group about which little is known or a number of important subgroups. Conceptual analysis recognizes diversity in participants' views	Uncontrolled, blinded clinical trials. Surveys sampling a restricted group of persons or a limited number of service providers or settings. May be limited to one group about which little is known or a number of important subgroups. Analytic procedures comprehensive and clear. Results have limited generalizability.	Unsystematic reviews with a low degree of selection bias employing clearly defined search strategies
Level III Descriptive studies	Sample selected to illustrate practical rather than theoretical issues. Record a range of	Open, uncontrolled clinical trials. Description of treatment as usual. Survey sampling not representative	Unsystematic reviews with a high degree of selection bias

	<p>illustrative quotes including themes from the accounts of “many”, “most”, or “some” study participants</p>	<p>since it was selected from a single specialized setting or a small group of persons. Mainly records experiences and uses only a limited range of analytical procedures, like descriptive statistics. Results have limited generalizability.</p>	<p>due to undefined or poorly defined search strategies</p>
<p>Level IV Single case study</p>	<p>Provides rich data on the views or experiences of one person. Can provide insight in unexplored contexts</p>	<p>Case studies. Provides survey data on the views or experiences of a few individuals in a single setting. Can provide insight in unexplored contexts. Results cannot be generalized</p>	<p>Editorials</p>

Table 3: Grading of recommendations [17, 18, 19].

Recommendation grade	Description
A	At least one study or review rated as I and directly applicable to the target population; or A body of evidence consisting principally of studies and/or reviews rated as I, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies and/or reviews rated as II, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies and/or reviews rated as I or II
C	A body of evidence including studies and/or reviews rated as II–III, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies and/or reviews rated as II–III
D	Evidence level III or IV; or Extrapolated evidence from studies and/or rated as III or IV; or Expert consensus

Table 4: List of included studies and reviews, their methods, the main results and evidence ratings.

Reference	Type of study	Main results	Evidence level
Alvarez-Jimenez et al. [22]	Non systematic literature review	Online family interventions showed acceptability but no consistent clinical effects. Preliminary evidence showed that online psychoeducation and the use of mobile-based devices was acceptable and feasible, but only few data on effectiveness (medication adherence, number of hospital admissions) were available.	III
Alvarez-Jimenez et al. [25]	Systematic review	Only 12 eligible studies were identified, of which two examined the acceptability of internet-based interventions, nine studies provided data on intervention effects (web-based psychoeducation, web-based therapy, web-based psychotherapy, personalized advice and mobile phone-based interventions). Study results supported the notion of acceptability and feasibility of internet and mobile-based interventions for psychosis. The intervention studies provided preliminary data showing that web-based cognitive behavioural therapy can reduce hallucinations, that psychoeducation for patients and caregivers may improve positive symptoms, and that individually tailored mobile phone-based interventions may reduce relapses and improve social contacts.	I
Ben-Zeev et al. [30]	Uncontrolled trial	Seventeen participants with dual diagnosis (schizophrenia/schizoaffective disorder and substance abuse) were enrolled in a twelve-week single-arm trial. A clinical social worker served as the mobile interventionist and sent daily text-messages to participants' privately-owned mobile phones to assess their medication adherence and clinical status. Participants received an average of 139 messages from the mobile	III

		<p>interventionist and responded to 87% of the mobile interventionist's messages when required. More than 90% of the participants thought the intervention was useful and helped them to be more productive and effective in their lives. The therapeutic alliance ratings were higher for the mobile interventionist than for the community team clinicians.</p>	
Ben-Zeev et al. [31]	Uncontrolled feasibility trial	<p>This smartphone-based system offers both prescheduled and on-demand resources to facilitate symptom management, mood regulation, medication adherence, social functioning, and improved sleep via apps. 33 individuals with schizophrenia or schizoaffective disorder used the system over a 1-month period in their own environments. Participants had to complete an assessment 3 times daily based on three apps: one app prompts users to engage, one app generates brief assessments and interventions, and a third app allows users to access illness-self management resources and coping strategies. Results show reductions of pre- vs. post trial symptom severity (PANSS positive, PANSS total, Beck Depression Inventory). Acceptability and usability of the system was rated highly positive by users.</p>	III
Ben-Zeev et al. [32]	Uncontrolled feasibility trial	<p>Mobile technologies were used to longitudinally track momentary levels of self-stigma, psychotic symptoms, affect, activity, and immediate social and physical environment in twenty-four individuals with schizophrenia, multiple times daily, over a one-week period. Multi-level modeling showed that current activities were associated with changes in self-stigma. Increases in negative affect and psychotic symptoms severity predicted</p>	III

		increases in self-stigmatizing beliefs. Psychotic symptoms were both antecedents and consequences of increased self-stigma.	
Kasckow et al. [23]	Systematic literature review	A total of 18 articles were relevant for this review. Regarding internet-based therapy for patients with psychotic disorders, studies only had addressed the feasibility of an online portal as an information source and one study provided data on the experiences of only nine patients with another web-based information portal. A further identified study was by Rotondi et al. (2010) discussed further below. A final study by Glynn et al. (2010) addressed relatives of persons with schizophrenia and showed limited effects on hospital admission frequency, carer distress and satisfaction. Based on the limited data available, the use of modalities involving the telephone, internet and videoconferencing appears to be feasible in patients with schizophrenia. In addition, preliminary evidence suggests these modalities appear to improve patient outcomes. The overall conclusion was that more research was needed.	I
Kauppi et al. [35]	Cochrane review	The objective was to investigate the effects of internet- and communication-technology based prompting to support treatment compliance in people with serious mental illness compared with standard care. Only two studies were included. The evidence base was found to be inconclusive.	I
Moock et al. [9]	Non-systematic review	The main conclusion was that in spite of much uncertainty about the impact of eMental health on the efficiency and effectiveness of mental health services, health care providers may be able to supply more clients using fewer resources through the use of eMental health.	III
Naslund et	Systematic	46 studies on mHealth and eHealth interventions	I

al. [20]	literature review	for serious mental illnesses were included. The study covered the diagnoses schizophrenia, schizoaffective disorder and bipolar disorder. 23 studies dealt with schizophrenia, but most in conjunction with schizoaffective disorder and/or bipolar disorder. The studies were also heterogenous regarding outcome measures, type of technology used and study design. In summary, the systematic review showed that such technologies are acceptable and usable for patients with psychotic disorders. However, it was not possible to draw firm conclusions from this review about the effectiveness of these interventions. Remotely-delivered interventions appear highly promising for reaching the target patient group as indicated by preliminary findings of efficacy.	
Rotondi et al. [21]	Randomized controlled trial	Comparison of an online intervention with treatment as usual to deliver a psychoeducational intervention for persons with schizophrenia (n=31) and their supporters (n=24). Persons with schizophrenia in the web-intervention condition had a larger and significant reduction in positive symptoms and increase in knowledge of schizophrenia compared with the treatment-as-usual condition.	I
Sin et al. [27]	Focus group study	14 siblings of patients with psychotic disorders were interviewed about their views on designing an online psychoeducational resource. Siblings were eager for focused information and peer support for themselves, as existing statutory and nongovernmental services tend to focus on key caregivers/parents. Siblings wanted a dynamic and flexible resource that was supported and moderated by mental health professionals to ensure the quality and credibility of the source materials and information exchanges.	III

Spaniel et al. [33]	Uncontrolled follow-up evaluation	This was a mobile phone-based telemedicine solution for weekly remote patient monitoring and disease management in schizophrenia and psychotic disorders (n=45 patients, pre-post comparison). The system provided clinicians with home telemonitoring via a PC-to-phone SMS platform. This was used to identify prodromal symptoms of relapse, to enable early intervention and prevent unnecessary hospitalization. The preliminary analysis after one year showed that there was a statistically significant 60% decrease in the number of hospitalizations (mean follow up 283 days).	III
Steinwachs et al. [28]	Randomized controlled trial	50 patients with schizophrenia used an interactive web-based intervention featuring actors simulating a patient discussing treatment concerns (n=24) or were shown an educational video about schizophrenia (n=26). Subsequent visits of the patients to their treating physicians (including psychiatrists and other clinicians) were analysed. Patients of the intervention group were more verbally active during mental health visits, visits were longer and patients contributed more to the medical dialogue. They asked more questions and gave more information. They were more likely to check understanding and appeared more dominant and respectful, but also more distressed.	I