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REVIEW

Optimizing psychosocial interventions in first-episode psychosis: current perspectives and future directions

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Abstract: Psychotic-spectrum disorders such as schizophrenia, schizoaffective disorder, and bipolar disorder with psychotic features are devastating illnesses accompanied by high levels of morbidity and mortality. Growing evidence suggests that outcomes for individuals with psychotic-spectrum disorders can be meaningfully improved by increasing the quality of mental health care provided to these individuals and reducing the delay between the first onset of psychotic symptoms and the receipt of adequate psychiatric care. More specifically, multicomponent treatment packages that 1) simultaneously target multiple symptomatic and functional needs and 2) are provided as soon as possible following the initial onset of psychotic symptoms appear to have disproportionately positive effects on the course of psychotic-spectrum disorders. Yet, despite the benefit of multicomponent care for first-episode psychosis, clinical and functional outcomes among individuals with first-episode psychosis participating in such services are still suboptimal. Thus, the goal of this review is to highlight putative strategies to improve care for individuals with first-episode psychosis with specific attention to optimizing psychosocial interventions. To address this goal, we highlight four burgeoning areas of research with regard to optimization of psychosocial interventions for first-episode psychosis: 1) reducing the delay in receipt of evidence-based psychosocial treatments; 2) synergistic pairing of psychosocial interventions; 3) personalized delivery of psychosocial interventions; and 4) technological enhancement of psychosocial interventions. Future research on these topics has the potential to optimize the treatment response to evidence-based psychosocial interventions and to enhance the improved (but still suboptimal) treatment outcomes commonly experienced by individuals with first-episode psychosis.

Keywords: first-episode psychosis; multicomponent care; psychosocial treatment; personalized medicine

Introduction

Psychotic-spectrum disorders such as schizophrenia, schizoaffective disorder, and bipolar disorder with psychotic features are devastating illnesses accompanied by high levels of morbidity and mortality. Under usual systems of care, these disorders are characterized by repeated symptomatic relapses,[1–3] elevated rates of psychiatric comorbidities such as anxiety, depressive, and substance use disorders,[4,5] reduced rates of participation in competitive occupational and educational activities,[6–8] severe deficits in cognitive abilities,[9–11] rates of death by suicide up to 12 times greater than population norms,[12,13] and a life expectancy reduced by up to 25 years[14,15] due primarily to cardiovascular, infectious, and pulmonary diseases.[13,16] The severity of these disorders was recently highlighted within the Global Burden of Disease (GBD) Study.[17–19] As part

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of a larger effort to quantify the deleterious effects of various health conditions worldwide, the GBD Study assigns a disability weight to over 300 illnesses and injuries – a numerical value indicating where a particular health state exists on a range from 0 (i.e., a state of perfect health) to 1 (i.e., a health state equivalent to death). Within the two past iterations of the GBD study, the acute presentation of schizophrenia – the prototypical psychotic-spectrum disorder – where active hallucinations and delusions are present was assigned the highest disability weight among all illness and injuries.[20,21] In fact, while achieving remission of hallucinations and delusions is often considered a "treatment success" for individuals with schizophrenia,[22,23] this health state (i.e., schizophrenia in its residual state) was assigned the ninth highest disability weight among all illnesses and injuries in the GBD study.[20,21] When a "successful" treatment outcome equates to the ninth worst health state that humans can experience other than death, there is significant room for improvement in existing treatments for a given disorder.

Growing evidence suggests that outcomes for individuals with psychotic-spectrum disorders can be meaningfully improved by increasing the quality of mental health care provided to these individuals and reducing the delay between the first onset of psychotic symptoms and the receipt of adequate psychiatric care.[24,25] More specifically, multicomponent treatment packages that 1) simultaneously target multiple symptomatic and functional needs and 2) are provided as soon as possible following the initial onset of psychotic symptoms, appear to have disproportionately positive effects on the course of psychotic-spectrum disorders.[26,27] To date, numerous trials of multicomponent treatment packages for individuals early in the course of a psychotic-spectrum disorder – a period frequently referred to as "first-episode psychosis"[28] – have been completed by independent research teams across four continents. Although there is some variation in the results, overall, these studies suggest that multicomponent care for first-episode psychosis may produce improved outcomes across numerous psychiatric (e.g., positive symptoms, negative symptoms, and depressive symptomatology) and functional domains (e.g., cognition, social functioning, and participation in competitive work and school).[29–40] In response to these findings, multicomponent care provided as soon as possible following the first onset of psychotic symptoms is now recognized as the new "gold standard" in the treatment of psychotic-spectrum disorders. Such treatment programs are now available in every continent with the exception of Antarctica,[41,42] and several countries have launched federally-supported efforts to disseminate multicomponent care for first-episode psychosis nationwide.[43–45] For example, between fiscal year 2014 and 2016, the federal government of the USA dedicated nearly $100 million to support the dissemination of Coordinated Specialty Care for first-episode psychosis – a multicomponent treatment program comprised of individual psychotherapy, family psychoeducation, medication management, and supported employment and education.[46]

A key contribution of the recent movement toward multicomponent treatment programs for first-episode psychosis is increased recognition of the value of psychosocial interventions for psychotic-spectrum disorders. Although existing treatment guidelines typically identify pharmacological treatment as the "cornerstone" or "first-line" treatment of psychotic-spectrum disorders,[47–49] there is growing recognition that medication alone cannot fully ameliorate the morbidity and mortality associated with these disorders.[50–53] For example, while antipsychotic medications have clear efficacy with regard to the treatment of psychotic symptomatology,[54,55] available evidence suggests that such symptoms may account for <1% of the illness-related disability experienced by individuals with first-episode psychosis (Moe and Breitborde, unpublished data, 2017). Effects of antipsychotic medication on other meaningful outcomes in psychotic-spectrum disorders (e.g., employment, cognition, and social functioning) are small and may not be clinically significant.[11,51,56,57] Current multicomponent treatment programs for first-episode psychosis emphasize a combination of psychosocial and pharmacological interventions as first-line treatment[58,59] and available data have demonstrated that such combined treatment produces improved outcomes among individuals with psychotic-spectrum disorders – including first-episode psychosis – when compared with medication alone.[60–62]

Yet, despite the benefit of multicomponent care for first-episode psychosis, clinical and functional outcomes among individuals participating in such services are still suboptimal.[26,63,64] Among such individuals, inpatient psychiatric hospitalizations are common,[31] substance use – especially tobacco – is high,[29] poor physical health outcomes are the norm,[65] and rates of participation in competitive employment remain lower than their age-matched peers without psychotic-spectrum disorders.[30] Consequently, there is still significant room for improvement in the treatment of first-episode psychosis.[26,63]

Thus, the goal of this review is to highlight putative strategies to improve care for individuals with first-episode psychosis with specific attention to optimizing psychosocial interventions. To address this goal, we highlight several optimization strategies with the potential to enhance the benefits associated with these interventions. In particular, we focus our review on burgeoning areas of research with regard to optimization of psychosocial interventions for first-episode

psychosis and avoid reviewing strategies that are already clearly documented elsewhere (e.g., building a strong therapeutic alliance[66] and addressing the comorbid psychiatric symptoms, functional deficits, and cognitive decline that accompany first-episode psychosis[67–73]).

Strategy 1: reduce the delay in receipt of evidence-based psychosocial treatments

Within the first-episode psychosis literature, there is a clear association between the duration of untreated psychosis (DUP; i.e., the time between the first onset of psychotic symptoms and the receipt of adequate mental health care) and the course of psychotic-spectrum disorders. More specifically, a longer DUP is associated with a worse course of illness and poorer response to treatment.[25,31,32,74] Many studies have defined the endpoint of the DUP (i.e., the receipt of adequate mental health care) as participation in some duration of antipsychotic medication.[75,76] However, time until the start of evidence-based psychosocial interventions may also be an important endpoint following the first onset of psychotic symptoms. For example, in a seminal paper, de Haan et al[76] examined the association between the duration of time between the first onset of psychotic symptoms and the first receipt of intensive psychosocial treatment (i.e., delay in intensive psychosocial treatment [DIPT]) and the course of schizophrenia. Given the limited availability of evidence-based psychosocial treatments for psychosis in usual care settings,[77] it is not surprising that de Haan et al found that the mean DIPT (19 months) was nearly twice as long as the mean DUP (8.6 months). Among their sample, there were positive univariate associations between negative symptoms at 6-year follow-up and both DUP and DIPT (i.e., greater negative symptoms associated with longer DUP and DIPT, respectively). However, in multivariate analyses simultaneously examining DUP and DIPT, only DIPT was found to be a statistically significant predictor of negative symptoms at 6-year follow-up. These results raise the possibility that reducing the delay between the first onset of psychotic symptoms and the receipt of evidence-based psychosocial care may be a modifiable risk factor through which providers can improve the course of psychotic-spectrum disorders. This hypothesis comports with data suggesting that individuals earlier in the course of psychotic-spectrum disorders have a greater response to psychosocial treatments when compared with individuals with more longstanding illnesses.[78–80]

Despite the potential importance of DIPT to the course of psychotic-spectrum disorders, we are unaware of any subsequent studies that have investigated this concept in the 13 years since the paper by de Haan et al.[76] Consequently, there is a great utility for additional research to clarify the association between delay in access to psychosocial treatments and the course of psychotic-spectrum disorders. In addition, psychiatric service research may benefit from examining how evidence-based psychosocial services can be incorporated within inpatient psychiatric settings. Although the inpatient psychiatric unit is often the first care setting for individuals with first-episode psychosis,[81] evidence-based psychosocial treatments for first-episode psychosis are typically available in outpatient settings only. Thus, incorporating specialized psychosocial treatments in inpatient settings may be an important strategy in reducing delay of appropriate psychosocial care.

Strategy 2: synergistic pairing of psychosocial interventions

Kern et al[62] have highlighted that although numerous evidence-based psychosocial interventions are available for psychotic-spectrum disorders, no single psychosocial intervention is sufficient to address numerous health and functional consequences associated with these disorders. Thus, there is growing interest in examining how best to pair psychosocial interventions to improve outcomes among individuals with first-episode psychosis. Although research in this area is still developing, promising results from the broader literature on psychotic-spectrum disorders are already available with regard to effective pairing of psychosocial interventions with cognitive remediation – an intervention defined by the 2010 Cognitive Remediation Experts Workshop as "a behavioral training based intervention that aims to improve cognitive processes (attention, memory, executive function, social cognition, or metacognition) with the goal of durability and generalization." To date, studies have examined the benefits of pairing cognitive remediation with several additional psychosocial interventions, including work therapy and supported employment programs,[82–84] functional skills training,[85] and even an aerobic exercise program.[86]

Bell et al[82] examined a combined cognitive remediation and work therapy program, which involved individuals with schizophrenia or schizoaffective disorder being randomly assigned to receive cognitive remediation – characterized by completion of computerized cognitive exercises and weekly processing groups – plus work therapy or work therapy alone for 6 months. Although both groups showed improvements, individuals in the cognitive remediation and work therapy group evidenced greater mean differences and larger effect-size changes on cognitive performance, including working memory, attention, and executive functioning. An additional

study by the same group[83] using the same methodology but with an extended treatment period of 1 year similarly revealed that individuals who received combined cognitive remediation and work therapy had significantly better performance on measures of executive functioning and working memory post-treatment compared with those who received work therapy alone. In a sample of 44 individuals with schizophrenia, McGurk et al[84] compared the effects of 12 weeks of supported employment and computerized cognitive training against supported employment alone. Post-treatment cognitive testing revealed that those in the combined cognitive training plus supported employed group performed significantly better on an overall composite cognition score than those receiving supported employment alone, and that these individuals in the combined condition also showed significant reduction in depression and autistic preoccupation and better work outcomes compared with individuals in the supported employment-alone condition. The functional outcome improvements, particularly in work functioning, can be directly attributed to the addition of cognitive remediation in this case, as all other aspects of treatment were matched. Although work training and supported employment programs target work functioning directly, the addition of cognitive training led to greater levels of employment, more hours worked, and better functioning at work in individuals with schizophrenia. In addition, those receiving cognitive remediation also showed improvement in other domains (i.e., symptom levels and neurocognitive functioning).

In an additional study, Bowie et al[85] randomly assigned individuals with schizophrenia to receive cognitive remediation, functional adaptation skills training, or a combination of both treatments. Although improvements in neurocognition were observed in both the cognitive training and combined treatment groups and social competence significantly improved in the functional skills and combined treatment group, the combined treatment group showed significantly greater improvements in functional competence and real-world community activities than either the functional skills training and cognitive remediation-only groups. Importantly, the durability of these gains was greatest in the combined treatment group. Taken together, these results suggest that a combined treatment approach may produce better gains across domains that are more likely to persist over time.

The utility of combining cognitive remediation and physical activity has also been explored. In a recently published pilot study,[86] individuals early in the course of a schizophrenia-spectrum disorder were randomly assigned to 10 weeks of either cognitive training alone or cognitive training combined with aerobic exercise sessions. Even with a small sample and short training period, individuals receiving combined cognitive training and exercise demonstrated larger gains in overall cognitive abilities compared with participants receiving cognitive training alone. These preliminary data suggest that a combination approach including both exercise and cognitive remediation allows for even larger gains in cognition than cognitive remediation alone.

Thus, research on cognitive remediation has highlighted strategies to increase the size, breadth, and durability of treatment effects via the deliberate pairing of psychosocial interventions. These findings are especially relevant to the treatment of first-episode psychosis given the improved, but still suboptimal benefits associated with current multicomponent treatment programs[64] and questions about the durability of these benefits after discharge from such multicomponent treatment programs.[87,88] Moreover, within most multicomponent treatment for first-episode psychosis, decisions with regard to psychosocial intervention uptake are typically individual preferences of providers and individuals with first-episode psychosis. Although such preferences are valuable – especially those of individuals with first-episode psychosis – future research exploring how specific psychosocial interventions can be synergistically paired may enhance clinical outcomes among individuals participating in multicomponent care for first-episode psychosis.

Strategy 3: personalized delivery of psychosocial interventions

Within the larger psychiatric literature, there is significant interest in advancing personalized medicine[89] – "the prescription of specific treatments and therapeutics best suited for an individual taking into consideration both genetic and environmental factors that influence response to therapy".[90] The treatment decisions resulting from these considerations fall under the categories of "macrotreatment" and "microtreatment" decisions.[91] Macrotreatment decisions are those that guide selection of specific interventions, whereas microtreatment decisions guide the delivery of specific aspects of an intervention. Given the heterogeneous presentation and course of psychotic-spectrum disorder,[92–94] personalized prescription of psychosocial intervention may help to maximize treatment outcomes among individuals with first-episode psychosis.

In recent years, there has been increasing focus on research suggesting that genetic variants associated with psychosis can be used to guide antipsychotic medication management decisions.[95] Genetic variants could also potentially be used to guide macrotreatment decisions concerning which psychosocial interventions are prescribed to specific individuals with first-episode psychosis. For example, growing

research has considered whether an individual's response to cognitive remediation may be moderated by genetic factors. To date, several studies have examined whether response to cognitive remediation may be predicted by the catechol-O-methyltransferase (COMT) gene via its putative influence on prefrontal dopamine functioning.[96–98] However, results from these studies are equivocal. There is some evidence that response to cognitive remediation among individuals with first-episode psychosis may be influenced by the expression of genes involved in memory and synaptic plasticity (e.g., activity-regulated cytoskeleton-associated protein [ARC]). In one recent study,[99] individuals identified as carriers of the ARC T allele showed significant improvement in overall cognitive functioning after participating in metacognitive remediation therapy, whereas non-T-carriers did not.

Another potential characteristic that could be used to personalize psychosocial intervention prescription for individuals with first-episode psychosis is personality traits. It has been demonstrated that non-pathological personality traits are associated with course of illnesss and subjective experiences of symptoms in individuals with psychosis,[100] as well as other relevant correlates of psychotic-spectrum disorders such as social cognitive abilities.[101] A framework for considering both research and theory of personality in first-episode psychosis intervention decisions has been proposed[102] that would first involve formal assessment of personality characteristics. These assessment data could then be used to inform macrotreatment decisions, such as choice of intervention formats (e.g., group interventions, caregiver involvement) and microtreatment decisions, such as how to tailor interventions for specific individuals to best address their unique symptomatology, functional deficits, and treatment goals.

Finally, the typical emergence of psychotic symptoms in the late teens to early 20's[103] raises the possibility that psychosocial interventions for first-episode psychosis may be enhanced by tailoring them to the unique needs of individuals in this developmental stage. In his seminal writings, Arnett has referred to this developmental stage as "emerging adulthood" and has described it as "a period characterized by change and exploration for most people, as they examine the life possibilities open to them and gradually arrive at more enduring choices in love, work, and worldviews."[104] Drawing on this research, McGorry et al have advocated for the development of youth-friendly mental health services that promote shared decision-making in treatment and emphasize social and vocational outcomes (as opposed to symptomatic remission) as key treatment goals.[105,106] Such characteristics are not only consistent with the norms of this developmental stage (e.g., movement toward greater autonomy and establishing the foundation for longstanding vocational and relationship roles) but may also play a role in whether emerging adults access and remain engaged in specialized services for first-episode psychosis.[105] For example, early evidence from existing youth-friendly mental health services suggests that they may be successful in increasing rates of youth and young adults from traditionally underserved populations who choose to access mental health services.[107,108]

Strategy 4: technological enhancement of psychosocial interventions

Another promising avenue for optimization of psychosocial treatment for first-episode psychosis involves integration of technological advances. Although clinical research has benefitted for several decades from emerging imaging and psychophysiological measurement technologies, these advancements are increasingly proliferated into people's typical, everyday activities (e.g., smartphones, digital streaming technologies, and fitness trackers equipped with heart-rate monitors). As these technologies continually interface with normative human activities, they represent an important avenue for advancement and expansion of health care and treatment. Interventions delivered via technology or technology-enhanced treatment may be a cost-effective way to provide personalized, flexible, and evidence-based interventions directly to individuals in their communities or homes.[109] The use of technology-enhanced treatment has a myriad of potential clinical benefits for individuals with first-episode psychosis, including the capability of providing real-time cues to engage in particular behaviors as a compensatory mechanism for memory deficits (e.g., to encourage medication adherence[110]), as well as the ability to alert individuals to physiological early warning signs of symptomatic exacerbations in a personalized manner (e.g., changes in heart-rate variability[111]).

Although the use of technological advancements in psychiatric treatment is in its relative infancy,[112] the ready availability and sophistication of these technologies is promising. This has been particularly true for smartphones and apps, which represent one of the most rapidly expanding and adopted forms of technology in human history.[113] Available research suggests that up to 90% of individuals with first-episode psychosis have access to smartphones.[114,115] Given the wide availability of this technology, these devices are ideal for assessment of in vivo experiences of individuals with psychosis. Ecological momentary assessment (EMA) – a method for collecting information on naturalistic behaviors

and experiences that has previously been done with paper-and-pencil methodology – has been enhanced by the use of smartphones. Smartphones offer participants the opportunity to record information about their symptoms, feelings, and thoughts in an immediately accessible forum that can automatically sync with an external database. This approach can mitigate the impact of cognitive deficits on memory and recall, and can also provide cues for individuals to engage in reflecting on internal processes and recording information that can minimize the impact of deficits in the initiation of behaviors that accompany psychotic-spectrum disorders. Further, research suggests that symptom ratings collected from individuals with psychosis via smartphone technology have greater concordance with clinician ratings compared with self-ratings made with paper and pencil.[116] In addition to being used to enhance treatment via self-monitoring, smartphone technology can also be used to deliver interventions directly to individuals with psychosis. Ben-Zeev et al[117] recently investigated the efficacy of a smartphone-based treatment to people with schizophrenia. This intervention was designed to provide automated real-time/real-place illness management support to individuals and was found to produce improvements in mood regulation, medication adherence, social functioning, and sleep. The demonstrated feasibility, acceptability, and preliminary efficacy of this smartphone intervention for schizophrenia offer promise for extending evidence-based treatment for first-episode psychosis beyond physical clinics and into the literal pockets of individuals via widely available smartphone technology. As the benefits of specialized care for first-episode psychosis may disappear when young adults return to usual care,[87,88] the extension of evidence-based psychosocial treatment via smartphone technology could potentially be leveraged to increase the durability of the benefits produced by such specialized, but typically time-limited, care.

Of note, the possibilities for integration of technology into psychosocial treatment for first-episode psychosis also extend to social media more broadly. For example, Alvarez-Jimenez et al[118] developed HORYZONS, an online intervention specifically for youth with first-episode psychosis. Individuals with first-episode psychosis could engage in a variety of interactive psychosocial interventions on this moderated forum and were also able to engage in peer-to-peer social networking. Results indicated that this approach was feasible, engaging, and safe for participants. The use of online forums to enhance other psychosocial treatments for first-episode psychosis is especially attractive, given its cost-effective nature, as well as its potential to provide ongoing support that may prevent disengagement from clinical services.

Technological advances are an evolving and exciting area for clinical service delivery. However, the importance of an evidence-based approach to treatment should not be forgotten. Thus, there is a great need for additional research of smartphone and other technology enhancements for first-episode psychosis. In the interim, mental health providers should strive to be both open-minded and prudent in the integration of technology into treatment for first-episode psychosis. Although many mental health apps are currently available, the vast majority have not been scientifically evaluated.[112,119] However, the literature on the use of apps for clinical treatment of psychotic-spectrum disorders – despite being limited – does provide strong evidence for the feasibility of this approach as well as high rates of patient engagement and interaction.[120]

Conclusion

Outside of the first-episode psychosis literature, Guralnick[121] has highlighted the distinction between first-generation and second-generation research – research designed to investigate the efficacy/effectiveness of an intervention versus research designed to investigate how to optimize outcomes associated with a proven intervention. With the efficacy and effectiveness of numerous psychosocial interventions for first-episode psychosis clearly established, scholars have noted the growing need for a shift toward second-generation research within the field.[122] The optimization strategies described above highlight some of the increasing corpus of second-generation research on the treatment of first-episode psychosis that is emerging internationally. Ultimately, such research has the potential to optimize the treatment response to evidence-based psychosocial interventions and to enhance the improved (but still suboptimal) treatment outcomes commonly experienced by individuals with first-episode psychosis. Moreover, as interest in intervention for psychosis before the first-episode grows,[123,124] continued research on the optimization of psychosocial interventions may also highlight ways to improve the prevention of psychotic disorders among those at clinical high risk.

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