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When do psychiatric interventions work? An argument for using functional outcomes when evaluating the effectiveness of treating schizophrenia

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Review

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Abstract

Schizophrenia is known to be a disabling psychiatric condition with wide reaching impact on everyday functioning and outcomes. These functional outcomes include increases in all-cause mortality (especially suicide and injury), cognitive and functional capacity deficits, lower reported levels of quality of life (QoL), increased incarceration, higher risk for violence and victimization, and homelessness. Studies have shown that medications and outpatient services can improve each of these functional outcomes in individuals with schizophrenia. However, most studies of pharmacological treatment utilize rating scales that do not reflect these real-world outcomes. This review looks at available studies focused on real-world outcomes and argues for an expansion of this body of research.

Introduction

Schizophrenia is considered one of the most disabling psychiatric illnesses in the world.[1,2] Schizophrenia is incredibly complex and impacts not only the individual suffering from this illness, but also the families and communities who often struggle with finding ways to support and care for them.[3] Schizophrenia is most often associated with the presentation of its positive symptoms (eg, hallucinations, delusions, thought disorganization, and paranoia) and negative symptoms (eg, alogia, blunted and flat affect, stereotyped behaviors and thinking, and social withdrawal) that are used to diagnose the psychiatric illness. Thus, many outcome studies focus on the reduction of these symptoms as measured by such instruments as the Positive and Negative Syndrome Scale[4] (PANSS) or the Brief Psychiatric Rating Scale[5] (BPRS) for measuring the presence and severity of symptoms associated with psychiatric disorders such as schizophrenia. While these instruments have strong psychometric properties and measure an important aspect of the illness, the impact of schizophrenia on functional outcomes goes beyond just the symptomatology of the illness. For instance, individuals with schizophrenia have higher mortality rates and experience more health issues, cognitive deficits, and functional capacity limitations. These individuals have greater involvement in the criminal justice system, increased risk of being both the victims and perpetrators of violence, increased rates of homelessness, and often struggle with everyday functioning. Moreover, they report lower levels of QoL.

While these topics have been researched by others, to this author's awareness, there has not been a paper that synthesizes the mortality, cognitive, criminal justice, violence, and QoL-related functional outcomes of schizophrenia. Moreover, this paper will discuss the impact that pharmacology and outpatient services can have on improving these broader functional outcomes. The author posits that to promote a more holistic, integrated, and meaningful life, clinicians, researchers, and policymakers need to have a broader conceptualization of "real-world" functional outcomes in individuals diagnosed with schizophrenia that extend beyond just management of psychosis symptomatology.

Mortality rates and health status

The diagnosis of schizophrenia is associated with one of the highest mortality risks of all psychiatric disorders.[6] Studies have suggested that individuals diagnosed with severe mental illness (including schizophrenia) die 15–20 y prematurely compared to the general population.[7] While the reduced lifespan with individuals diagnosed with schizophrenia is well documented, the underlying causes are less understood. In a systematic review and meta-analysis of 135 cohort studies comparing 4.5 million individuals with schizophrenia to 1.11 billion individuals in the general population, Correll and colleagues examined the risk and attenuating factors associated with mortality in people with schizophrenia.[8] Their findings revealed that the all-cause mortality

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rates in individuals diagnosed with schizophrenia was 2.9 times higher when compared with the general population.[8] A lower but still statistically significant 1.6-fold increase in all-cause mortality was observed when compared with diseased-matched general population controls.[8]

Suicide was identified as the highest relative risk factor for individuals diagnosed with schizophrenia. Specifically, Correll and colleagues identified a 9.7-fold increase in relative risk in mortality by suicide, as well as a 7.4-fold increase in relative risk for all-cause mortality for first episode schizophrenia when compared with the general population.[8] The suicide-related mortality risks were higher for those individuals who were under the age of 40 y.[8] While not examined specifically in this study, others have highlighted that suicide attempts increase with severity of psychotic and depressive symptoms at first psychotic episode.[9]

Non-natural causes of mortality, including poisoning (8- to 9-fold increase) and pneumonia (7-fold increase), were also higher when compared to the general population.[8] The mortality risk remained higher in individuals diagnosed with schizophrenia for infectious, respiratory, and endocrine diseases (3.7- to 3.8-fold increase), as well as injury or accidents (3.3-fold increase) when compared to the general population.[8] Unlike suicide-related mortality, natural cause mortality was not observed as being higher in those under the age of 40 y. Comorbid substance use disorder (SUD) increased all-cause mortality as well, which is most likely related to the adverse physical impact of substances, as well as the adverse impact related to injury and suicide-related behaviors.[8] Substance use in general, but particularly cannabis use, was associated with poorer antipsychotic medication adherence.[8]

Overall, these findings support the significant impact that schizophrenia has on outcomes related to all-cause mortality compared to the general population. The importance of early and accurate diagnosis, suicide and SUD screening, and treatment in individuals with schizophrenia is critical to reducing these relative risks.[8] Moreover, these findings highlight that earlier detection and treatment are critical for better health and mortality outcomes for individuals diagnosed with schizophrenia.

Functional capacity in everyday functioning

Aside from mortality rates and lifespan, arguably one of the most disabling impacts of schizophrenia is on an individual's ability to manage everyday life. While seemingly straightforward, operationalizing everyday functioning can be quite challenging as there are many abilities and factors that go into these daily activities, including stable employment, social connections, and independent living. To navigate the demands of daily living, a person must have the ability to perform the necessary life skills, the motivation to perform these skills, and the situational recognition to know when these skills are likely to be successful.[1] Undergirding the ability, motivation, and situational recognition of everyday functioning is a complex interconnection of cognitive performance, functional capacity, social cognition, clinical symptoms, fitness and health status, and environmental factors.[1] While all of these are important, this section will focus on the impact of schizophrenia on cognitive performance and functional capacity in daily life tasks.

Cognitive functioning, as measured by neuropsychological assessment, is comprised of specific domains including attention, language, memory and learning, processing speed, and executive functioning. Deficits in these areas can impact a person's ability to efficiently and effectively perform the daily tasks of life. As summarized in Harvey and Strassnig, several studies have shown small-to-moderate correlations between individual cognitive domains (eg, attention) and global indices of everyday functioning.[10] Composite scores (ie, multiple cognitive domains), on the other hand, show moderate-to-large correlations with everyday functioning.[10,11] Cognitive function is strongly associated with independent residential living,[12] which is a critical aspect of everyday functioning. While cognitive performance is clearly associated with everyday outcomes (eg, independent living), there is a growing body of literature on the concept of functional capacity as a more direct correlate of day-to-day functioning.

Functional capacity is defined as "an individual's capability, under controlled conditions, to perform tasks and activities that are necessary or desirable in their lives."[13 (p.13)] Given these elements, assessing functional capacity must take into consideration the specific task or ability, the context this is being performed in, and the nature of the disorder or disability that is impacting an individual's functioning.[13] Studies have found that measures of functional capacity are similarly correlated with performance-based neuropsychological measures on real-world functional outcomes.[1,12] While it is still unclear as to how exactly cognitive performance and functional capacity interact to impact everyday function, there is growing evidence that functional capacity has a more direct role.[1] Understanding the impact of cognitive and functional capacity deficits is critical, as there are specific cognitive rehabilitation interventions that can target these areas of challenge. Clinicians, researchers, and policymakers would be remiss if they did not consider cognitive and functional capacity dimensions when conceptualizing real-world functioning.

Criminalization, violence, and homelessness

It is well documented that individuals with serious mental illness (SMI; eg, schizophrenia, bipolar disorder, schizoaffective disorder) are at increased risk of arrest and incarceration.[14,15] Reports have indicated that approximately 14% of state prisoners, 8% of federal prisoners, and 26% of jail inmates have reported symptoms that are commensurate with "serious psychological distress."[16,17] Moreover, about 43% of state and 23% of federal prisoners had a history of mental health problems.[16] Individuals with schizophrenia who are incarcerated often experience disruptions in their treatment and can experience significant increases in symptomatology while languishing in jails and prisons. Much has been written on the topic of the criminalization of the mentally ill, and readers are encouraged to review those resources.[18]

While most individuals with schizophrenia are not violent, the presence of psychosis is a well-established risk factor associated with violence.[19] Specifically, individuals with schizophrenia had a 6-mo prevalence of 19%, with approximately 3.6% of those constituting "serious violent behavior."[20] Serious violent behavior was associated with positive psychotic symptoms (eg, persecutory ideation), depressive symptoms, childhood conduct problems, and victimization.[20] A similar prevalence of violence in 2–13% of outpatient individuals within a 6-mo to 3-y time frame has been observed by others.[21] While the public tends to be more concerned that individuals with schizophrenia are highly likely to commit acts of violence, the research indicates that individuals with SMI are more likely to be the victims of violence. Compared with 2–13% of individuals with SMI perpetrating violence, 20–34% had been violently victimized within the same time frame.[21] Studies that combined both inpatient and outpatient samples reported that

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12–22% had perpetrated violence in the past 6 to 18 mo as compared to 35% who were the victims of violence during that same period.[21]

Many factors contribute to homelessness, including victimization of violence (such as domestic violence), poverty, disability, unemployment, adverse childhood experiences, substance abuse, and the presence of SMI.[3] Individuals who are homeless have a higher prevalence of psychiatric disorders, including schizophrenia.[3] A meta-analysis of 31 studies involving 51,925 individuals worldwide showed a higher prevalence of psychosis (21.2%) and schizophrenia (10.3%) among homeless people.[3] Homelessness among those with schizophrenia was higher in developing (22.2%) as compared to developed countries (8.9%).[3] Overall, this meta-analysis highlights that schizophrenia has a significant impact on incarceration rates, being both the perpetrator and victim of violence, as well as homelessness.

Quality of life

Most of the research reviewed for this paper examined "objective" functional measures associated with a diagnosis of schizophrenia. However, an important overlooked perspective associated with schizophrenia is the subjective experience of the one diagnosed with this disabling psychiatric condition. The literature on QoL for those diagnosed with schizophrenia is complex and often contradictory due to a host of factors, including differing operational definitions, measurement methodology (eg, subjective QoL vs. "objective" measures of QoL), domains measured (eg, physical, psychological, social, and health-related), and the impact of symptom severity and the level of insight.[22,23] Early research raised doubt as to the "accuracy" of subjective QoL judgments due to the cognitive impairments and lack of insight related to schizophrenia[24] and findings of poor agreement in self-ratings as compared to the clinician and family members.[25] However, studies have shown that individuals with schizophrenia are able to accurately report on their social deficits and living situations,[26] and comparable convergent validity in perceptions of QoL between individuals and clinicians has been observed.[27] While there are many ways to define the concept, arguably the most recognized definition of QoL is "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns."[28] Relevant to the current paper, recent meta-analyses elucidate the relevance of QoL in the conceptualization of functional outcomes associated with schizophrenia.

There is considerable variability in the findings of published studies regarding QoL among individuals diagnosed with schizophrenia. Several recent studies, including two meta-analyses, examining individuals diagnosed with schizophrenia consistently report lower levels of QoL in domains of physical and psychological health, environmental domains (eg, accessing resources), and in social relationships when compared to the general population and healthy controls.[23,29,30] Longer durations of illness, symptom severity, poverty, and earlier onset of illness were associated with lower subjective reports of QoL.[23,31] While subjective ratings of QoL can vary significantly over a person's lifetime, one study found the most significant predictor of subjective QoL was age at time of illness onset, with later onset being associated with higher levels of QoL.[31] In this study, earlier age at onset of illness was associated with more relapses, hospitalizations, and poorer outcomes associated with social, occupational, and general functioning.[31]

Overall, these studies underscore the value of considering QoL when conceptualizing overall functional outcomes. As several studies observed, QoL ratings can fluctuate over the course of one's life and that despite all of the challenges associated with schizophrenia, some groups reported their subjective QoL to be good.[31] In the next section, we will examine the impact of pharmacological treatment and outpatient services on the functional outcomes reviewed in this paper.

The impact of medications and outpatient services on functional outcomes

As noted previously, individuals diagnosed with schizophrenia have higher mortality rates and health issues, significant cognitive deficits and functional capacity limitations, greater involvement in the criminal justice system, increased risk of being both the victims and perpetrators of violence, are overly represented among the homeless, and report lower levels of QoL. While there is no simple solution, there are some consistent interventions that have been shown to improve the functional outcomes reviewed in this paper.

Correll and colleagues showed that prescribing antipsychotic medications can protect against all-cause mortality in individuals diagnosed with schizophrenia.[8] Moreover, the second-generation antipsychotics (SGAs), long-acting injectables (LAIs), clozapine, and SGA–LAIs offered the most significant reductions in mortality rates.[8] The impact of LAIs and clozapine has been shown to improve continued treatment with cardiometabolic medications, such as statins, antidiabetic, and hypertensions medications.[32] Moreover, LAIs have been shown to improve medication adherence, relapse prevention, and psychotic symptoms control, as well as improved cognitive functioning in first-episode schizophrenia patients.[33]

Even the simple possession of consistent medication prescriptions, especially during the first 90 d post discharge, as well as routine outpatient services, offers one of the most significant protections against reincarceration for adults with schizophrenia.[14] High medication possession, which was defined as having medication to cover 80% or more of the days in a 30-d period, was associated with a reduction in arrest.[14] Interestingly, the reduction in arrests for medication possession was not observed for individuals who had medication possession for less than 90 d post discharge, indicating that consistent medication possession is critical for the observed reductions in arrests.[14] Also, monthly routine outpatient services were associated with the reduction of misdemeanor arrests.[14] Those who were arrested utilized systems (eg, psychiatric hospitalizations and emergency services) associated with higher acute care costs as compared to those who were not arrested; those who were not arrested had higher outpatient and pharmacological costs, which were still considerably lower than the more expensive acute care costs.[14] Economic modeling of the Van Dorn and colleagues'[14] study shows that the potential fiscal impact to state government, with a hypothetical 20% increase of antipsychotic medication upon release from incarceration, could lead to direct cost savings of $1.7 million over a 3-y period.[34] Thus, consistent medication possession among this population could result in direct cost savings for local and state governments by improving efficiency and reducing unnecessary expenditures.

Van Dorn and colleagues have demonstrated that violence perpetration was a positive indicator of both itself and victimization, drug use, and affective symptoms, while cognitive disorganization was associated with a decrease in violence perpetration.[35]

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Violent victimization was positively indicated by itself and violence perpetration, as well as affective symptoms and alcohol.[35] Their study also showed that violent victimization, alcohol or drug use, and inpatient hospitalization were associated with an increased likelihood of homelessness. The findings of this study support the use of outpatient services (eg, trauma informed therapy and cognitive behavioral therapy) and pharmacological interventions that target the affective symptoms associated with schizophrenia, which can reduce events of violence.[35] Similarly, combined pharmacological and psychotherapeutic treatment, well-managed medication side effects, and integration into community programs (as opposed to being institutionalized) have been associated with higher subjective reports of QoL.[23]

Conclusion

While symptom identification and monitoring are critical for diagnostic clarification and treatment, the findings of this brief literature review highlight the critical need to incorporate functional outcomes associated with schizophrenia that extend beyond just symptom management and reduction. The key point of these studies is that *consistent matched treatment that includes both pharmacological and outpatient services* has been shown to improve all functional outcomes. Consistent matched treatment and outpatient services that prioritizes improved medication adherence with SGAs, clozapine, and LAIs can significantly improve mortality rates (most notably related to suicide and injury), everyday functioning, and QoL in individuals disabled by schizophrenia. Clinicians are strongly encouraged to incorporate brief health measure screenings to identify illness risk and reduce mortality. Furthermore, consistent matched treatment and outpatient services that incorporate substance abuse screenings and treatment, trauma informed therapy, cognitive behavioral therapy, and pharmacological treatment that targets both psychosis and affective symptoms have been shown to reduce arrests, violence (both perpetration and victimization) rates, and homelessness. And finally, consistent matched treatment and outpatient services that include neurocognitive and social cognitive training have been shown to improve cognitive and functional capacity dimensions, which are essential for managing everyday life. Better community integration, managed symptoms, improved health, and purposeful living have been shown to improve QoL. Clinicians, researchers, and policymakers need to broaden their conceptualizations of "outcomes" to go beyond the management of psychosis symptomatology. This paper presents a conceptual framework for advancing more holistic, real-world functional outcomes that promote enhanced community integration and safety, as well as meaningful life experiences for individuals diagnosed with schizophrenia.

Author contribution. Conceptualization: S.E.E.

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