Editor

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Handbook of Schizophrenia Spectrum Disorders, Volume III
Therapeutic Approaches, Comorbidity, and Outcomes

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Schizophrenia Spectrum Disorders: Insights from Views Across 100 years

Schizophrenia spectrum and related disorders such as schizoaffective and mood disorders, schizophreniform disorders, brief psychotic disorders, delusional and shared psychotic disorders, and personality (i.e., schizotypal, paranoid, and schizoid personality) disorders are the most debilitating forms of mental illness, worldwide. There are 89,377 citations (including 10,760 reviews) related to “schizophrenia” and 2118 (including 296 reviews) related to “schizophrenia spectrum” in PubMed (accessed on August 12, 2010).

The classification of these disorders, in particular, of schizophrenia, schizoaffective and mood disorders (referred to as functional psychoses), has been debated for decades, and its validity remains controversial. The limited success of genetic studies of functional psychoses has raised questions concerning the definition of genetically relevant phenotypes.

Many researchers around the world have investigated schizophrenia spectrum, and related disorders from the perspectives of diagnostics, early detection of psychotic disorders, genetics, neuroscience, prognosis, and treatment. Therefore, these fields have considerably expanded with new findings that were obtained through clinical and longitudinal observations and neuropsychological, neurophysiological, neuroimaging, neuroanatomical, neurochemical, molecular genetic, genomic and proteomic analyses, which have generated a necessity for syntheses across the functional psychoses.

The present three-volume handbook is a collection that continues to achieve my goal of providing a comprehensive up-to-date state of the art overview of the literature that addresses the challenges facing clinical and biological psychiatry. This series follows four recently published books:

- Quality of Life Impairment in Schizophrenia, Mood and Anxiety Disorders. New Perspectives on Research and Treatment. Ritsner, Michael S.; Awad, A. George


  
  **Volume I: Neuropsychological Endophenotypes and Biomarkers.** 231pp.
  **Volume II: Neuroanatomical and Neuroimaging Endophenotypes and Biomarkers.** 244pp.
  **Volume IV: Molecular Genetic and Genomic Markers.** 232pp.


This handbook offers a broad synthesis of current knowledge about schizophrenia spectrum and related disorders. It is based on methodological pluralism regarding psychiatric nosology and raises many controversial issues, and limitations of categorical nosology of functional psychoses covering the ongoing debate on key conceptual issues that may be relevant for the development of DSM-V and ICD-11.

Reflecting the copious amount of new information provided, the handbook has been divided into three volumes. Volume I contains 20 chapters and serves as an introduction and overview of theoretical issue, and neurobiological advances. The chapters in this volume review the schizophrenia construct, diagnosis and classification of the schizophrenia spectrum disorders, and schizotypy concept; present proof-of-concept Multidimensional Continuum Model of functional psychoses and evolutionary models of autism; new findings regarding neurodevelopmental, neurodegenerative, and neurochemical abnormalities; genetic and environmental influences; changes in gene expression; neurotransmitter activity; brain imaging and morphological abnormalities in subjects with schizophrenia and other psychotic disorders, methamphetamine psychosis as a model for biomarker discovery in schizophrenia and advances in proteomics. Our knowledge of the genetics of schizophrenia and its borderlands is heavily indebted to the research and writings of Professor Irving Gottesman. The chapter that summarizes his contributions in that historical context is an invaluable contribution to the handbook.

Volume II contains 19 chapters focusing on phenotypic and endophenotypic presentations of schizophrenia spectrum and related disorders. The authors discuss psychopathology, stress, social anxiety, neuropsychological, neurocognitive and neurophysiological findings, endophenotype and neuroethological approaches, quality of life deficits, and risk for cancer morbidity and mortality. The authors also review advances and challenges in mapping the prodromal phases of psychosis, in the prediction and early detection of first-episode psychosis, early- and late-onset schizophrenia, the longitudinal course of these disorders, as well as the interface of acute transient psychoses, the association of metacognition with neurocognition and
function in schizophrenia, neurophysiology of cognitive dysfunction in schizophrenia, schizo-obsessive states, and risk for cancer morbidity and mortality in schizophrenia spectrum disorders.

*Volume III* includes 18 chapters that provide a wealth of information regarding treatment approaches, comorbidity, recovery, and outcomes of schizophrenia and spectrum disorders; in particular, recovery-based treatment approaches, antipsychotic and neuroprotective-based treatment; prevention and early intervention in at-risk states for developing psychosis, psychotherapy, cognitive remediation, cognitive behavior therapy; and interventions targeting social and vocational dysfunction in schizophrenic spectrum disorders. Furthermore, therapeutic approaches to schizophrenia with medical illness, comorbid substance abuse, suicidality, implications for treatment and community support, the relationship between religiosity/spirituality and schizophrenia, and the ethical ramifications of biomarker use for mood disorders are also reviewed and discussed.

Since many of the contributors to this handbook are internationally known experts, they not only provide up-to-date state of the art overviews, but also clarify some of the ongoing controversies and future challenges and propose new insights for future research. The contents of these volumes have been carefully planned, organized, and edited. Of course, despite all the assistance provided by contributors, I alone remain responsible for the content of this handbook including any errors or omissions which may remain. Similar to other publications contributed to by diverse scholars from diverse orientations and academic backgrounds, differences in approaches and opinions, as well as some overlap, are unavoidable.

This handbook is designed for use by a broad spectrum of readers including psychiatrists, neurologists, neuroscientists, endocrinologists, pharmacologists, psychologists, general practitioners, geriatricians, graduate students, and health care providers in the fields of mental health. It is hoped that this book will also be a useful resource for the teaching of psychiatry, neurology, psychology and policy makers in the fields of mental health.

I would like to gratefully acknowledge all contributors from 16 countries (Australia, Brazil, Canada, China, Czech Republic, Denmark, Germany, Ireland, Italy, Israel, Japan, Spain, Switzerland, Ukraine, United Kingdom, and USA) for their excellent cooperation. I wish to thank Professor William T. Carpenter, distinguished psychiatrist, who was willing to write the afterword for this handbook. I also wish to take this opportunity to thank the wonderful staff in my clinical department as well as in other departments in Shaar-Menashe Mental Health Center (Director – Dr. Alexander Grinshpoon) for their commitment, support, and cooperation. I would like to thank my wonderful and generous friends, particularly Boris Altshuler, Anatoly Polischuck, and Stella Lulinsky. They always took the time to listen, even when I was just complaining. The support they have given me over the years is the greatest gift anyone has ever given me. Finally, I thank Springer Science Business Media B.V. for the goodwill and publication of this book, particularly Mr. Peter Butler, and Dr. Martijn Roelandse, publishing editors, who did their utmost to promote this project and provided valuable assistance that made the book possible.

I sincerely hope that this handbook will further knowledge in the complex field of psychiatric disorders.
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1. Recovery in Schizophrenia: Perspectives, Evidence, and Implications

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Abstract
The recovery model of schizophrenia represents a paradigm shift in both the conceptualization and treatment of schizophrenia. However, the varied use of the term “recovery” in research and clinical settings has caused confusion about what it means in relation to schizophrenia. Two views of recovery appear in the literature including a medical model, having its origins in treatment outcome studies; and a consumer model of recovery, which was conceived from the writing and testimonials of former patients. The medical model of recovery suggests that there are many possible outcomes in the prognosis of schizophrenia and many patients do experience periods of symptom remission and improved functioning. On the other hand, the consumer model of recovery suggests that recovery involves integrating illness into a multifaceted sense of self that actively pursues goals, interests, roles, and aspirations despite the limitations imposed by the illness. This model emphasizes hope, empowerment, and overall wellness regardless of the status of symptoms and functional disability. The current chapter is an overview of the medical and consumer views of recovery and
studies supporting both models. Despite their distinct origins and focus, both models of recovery offer a hopeful view of recovery in schizophrenia; however, implementing the consumer model of recovery in mental health systems is fraught with challenges.

**Keywords** Schizophrenia – Recovery – Outcome – Process

**Abbreviations**

*Project GREAT*  Georgia Recovery-based Educational Approach to Treatment  
*SAMHSA*  The Substance Abuse and Mental Health Services Administration

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**Introduction**

In the last two decades, the concept of recovery in schizophrenia has emerged as an essential construct in the study and treatment of schizophrenia and schizophrenia spectrum disorders. Traditionally, “recovery” has primarily being viewed as an outcome characterized by symptom mitigation or reduction and improvements in functional capacities. This view draws from the medical model, which underscores the symptomatic experience of psychiatric illnesses and the role of targeted interventions to decrease symptoms and disabilities. Historically, schizophrenia had been viewed as a chronic condition marked by poor functional and therapeutic outcomes. With evidence emerging from recent studies of short-term and long-term outcomes, this view has evolved into one of a more positive medical conception of recovery. Current views of schizophrenia characterize the disorder as having a more, heterogeneous symptom course, including periods of good functioning for many patients. Emanating from a mental consumer/survival movement is a new paradigm for the concept of recovery. This consumer/survival perspective views recovery as a process rather than an outcome, and thus deemphasizes the role of symptom remission. Moreover, this paradigm of recovery focuses on the individual as a “whole person” with personal attributes and capacities and reframes the process of care around the individual’s long-term expectations and lifetime aspirations. Central to this view of recovery is the instillation of hope and empowerment, and a development of a self living a full life despite the limitations of illness.

Both perspectives are considerably independent, having distinct origins, focus, and ramifications for assessment, treatment planning, and research in schizophrenia spectrum disorders. The current chapter examines these divergent recovery constructs in schizophrenia. We begin with a conceptual review of the medical and consumer perspectives of recovery including research evidence pertinent to both views of recovery. We then discuss the implications of the consumer model of recovery.

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**What Is Recovery?**

Although the medical and consumer conceptions of recovery are virtually orthogonal in their origins, content, and ramifications, both views permeate the literature, causing well-documented confusion about the meaning of recovery [1–5]. Some conflation in the use of the term also results from articles which appear to cite the results of
longitudinal outcome studies in support of their discussions on the consumer view of recovery [6]; and articles discussing recovery from a medical/scientific perspective, which appear to cite the role of political forces such as the President’s New Freedom Commission in the genesis of the medical model of recovery [7]. The current chapter attempts to avoid such conflation by discussing the medical and consumer models of recovery as separate perspectives supported by distinct evidences.
Part I: The Medical Model of Recovery

The medical definition views recovery as an end state and focuses on symptom relief, alleviation, remission, and return to premorbid levels of functioning [5, 8]. This definition is grounded in the symptomatic experience of schizophrenia and spectrum disorders and recovery is generally viewed as akin to becoming asymptomatic, subthreshold with regard to meeting diagnostic criteria, regaining prior levels of premorbid functioning, or becoming literally cured [9].

Due to its emphasis on an “end state,” and its origin in treatment outcome studies, the medical definition is also synonymous with the “outcome definition” of recovery [5]. This definition emanated from changing conceptions of schizophrenia from one of a chronic psychiatric condition marked by functional deterioration to one characterized by heterogeneous outcomes [10, 11]. So pessimistic was the traditional view of schizophrenia that occasions in which individuals experienced marked improvements in symptoms or regained functional status were viewed as indicative of false positive diagnosis [11, 12]. Over the years, however, studies have emerged that have rebutted this pessimistic view. These include both short and long-term studies pointing to individuals experiencing significant remission and improved functioning with or without treatment [10, 13–15]. Various short-term studies have demonstrated that over 70% of individuals receiving standard treatments for schizophrenia experience “significant remission” to “full or complete remission” within the first year of treatment [16–19]. Some individuals receiving comprehensive treatments including medication management and psychosocial interventions have also experienced improvements in psychosocial functioning [16]. Longitudinal studies of outcomes in schizophrenia have demonstrated that only a fraction of individuals demonstrate a deteriorating course. Conversely, about 20–65% demonstrate moderate to good outcomes (although periods of symptom remission and exacerbation are common), and about 20% return to premorbid levels of functioning [13]. Recent studies have continued to support the heterogeneity of functional outcomes with longitudinal studies producing positive outcomes of up to 91% in a review of studies [14] when “positive outcomes” is defined as symptomatic remission.

Predictors of positive outcomes in these studies include good premorbid intellectual functioning, education, female biological sex, early discharge or short hospital stay, and younger age. Better educated participants also tended to have better cognitive functioning, and education was also associated with better social and vocational functioning. Early discharges or shorter hospital stays was associated with better community adjustment and better overall global functioning. Female participants tended to have better social outcomes than male participants, whereas younger participants tended to have better cognitive functioning. The socio-cultural context of individuals appears to have an impact on the course of schizophrenia symptoms [15]. The specific socio-cultural variables associated with heterogeneous outcomes are currently unknown but have been speculated to involve greater acceptance and tolerance of mental illness, and better social support networks usually involving family and members of the community [20].

Some have observed that improvement or recovery rates suggested in most studies
represent underestimates of the potential for recovery in schizophrenia spectrum disorders. It has been suggested that this is because many individuals who experience symptoms do not present in treatment settings [5, 10]. Evidence supporting this assertion is usually drawn from the disparities between prevalence rates identified in epidemiological studies and the number of people that actually present in treatment settings [21]. It may be that these individuals represent cases that did not require hospitalization because they experienced less severe forms of illness relative to those requiring hospitalization, or individuals who had developed abilities to cope with symptoms without need for clinical care. Including this group of patients in long-term outcome studies may increase the recovery rates obtained from these studies.

With regard to the notion of “cure,” a number of authors have highlighted the problems with adopting such a standard for chronic conditions such as schizophrenia [5, 8, 9]. First, in schizophrenia, similar to other chronic medical conditions, the notion of recovery as cure may be untenable, given that a disease process may be persistent even when symptoms undergo significant remission. For example, given their episodic nature positive psychotic symptoms can undergo significant remission, yet underlying cognitive impairments tends to be more unrelenting in nature. Thus cognitive impairments limit the ability to fully regain premorbid functioning even with full resolution of positive symptoms [9]. Second, the concept of cure is difficult to operationalize in schizophrenia [5]. For example, many patients experience loss of functions (e.g., increased asociality) even before the first psychotic episode; consequently, determining return to premorbid functioning may be indeterminate for an adult patient. Some studies do suggest that a fraction of patients experience “full recovery,” characterized by complete symptom remission and return to premorbid levels of social and occupational functioning [10]. However, it is unclear if this constitutes cure, given that outcome studies primarily focus on symptom remission and psychosocial functioning, while ignoring other domains of illness such as neurocognitive functioning.

In addressing symptom status, realistic medical notions of recovery generally focus on remission of symptoms or decreased severity of symptoms. For example, Andreason and colleagues [9] in their definition focused on decreased severity of symptoms rather than complete absence of core signs or symptoms of disorder. The symptoms are subthreshold, not enough to meet diagnostic criteria, and they are not severe enough to cause marked impairment. Liberman and colleagues’ [3, 22] definition also focused on decreasing symptom severity, which they conceptualized to be indexed on a continuous scale such as the Brief Psychiatric Rating Scale (BPRS), the Schedule for Affective Disorders and Schizophrenia (SANS), or the Positive and Negative Syndrome Scale (PANSS). A number of outcome studies have established various remission criteria based on these measures. For example, Liberman et al. [23] defined remission based on a positive symptom item threshold score of ≤ 3 on the SANS; and Clinical Global Impression (CGI) severity scale score of ≤ 3. Additional criteria include a CGI global impression of change score of no more than 2; scores of ≤ 2 (mild) on all SANS negative symptom global items, and a “full remission” categorization when there are no residual positive symptoms. Liberman et al. [3] established a threshold score of ≤ 4, indicating minimal to moderate severity for positive and negative symptom items on the BPRS. Yen et al. established remission
criteria of a mean score of \( \leq 2 \) on positive, negative, or general psychopathology subscales of the PANSS [24]. Some studies of early psychosis have established strict criteria for remission defined as “absence of symptoms” or “full remission” [23, 25]. It should be noted, however, that the cited studies also included symptom severity as an outcome variable.

With regard to psychosocial functioning, outcome studies have used various criteria including operational definitions and global assessment of functioning scales. One example is found in the Liberman et al. [3, 23] definition, which emphasizes evidence of social interactions with others outside of the individual’s immediate family members and treatment providers (at least once a week). It also requires involvement in age and culturally appropriate educational or vocational activities (at least part-time), and activities of daily living including management of medications and financial responsibilities. Studies have also used global assessment scales such as the Global Assessment Scale (GAS) and Global Assessment of Functioning (GAF) Scale to indicate levels of psychosocial functioning [26, 27]. Harding et al.’s [26] seminal study of recovery outcome categorized good functional outcomes as GAS scores \( \geq 61 \) and the Torgalsbøen and Rund [27] study defined GAF scores \( \geq 65 \) as indicative of adequate psychosocial functioning. None of these definitions require a return to premorbid levels of functioning; rather, they underscore improvements in psychosocial functioning.

Given that psychotic disorders are episodic by nature, extended periods of symptom remission and normal functioning would be necessary operational criteria to suggest recovery. Thus, attaining recovery from schizophrenia requires that a sufficiently extended period of time has passed during which symptoms are maintained at subthreshold severity with substantial improvements in functional status. For example, Liberman and colleagues [3, 22, 23] suggest two continuous years of sustained remission and normal functioning as reasonable standard for defining recovery from schizophrenia, whereas others suggest shorter or longer period of recovery (e.g., a 5-year period in the Torgalsbøen and Rund [23] study, and a 1-year period in the Harrow and colleagues [7] study).

In summary, outcome definitions of recovery incorporate both symptom remission and adequate psychosocial functioning for a specified duration as criteria. Although some studies incorporate the criterion of “absence of symptoms,” this is not required in most definitions of recovery. Definitions do require that there is evidence of “normal”, “good”, or “improved” psychosocial functioning in the domains of social relationships, vocational or educational involvement, and activities of daily living, as indicated by GAS or GAF scores greater than 60. It is likely that the variability in recovery criteria established in individual studies also contributes to differences in recovery rates.

Of course, the more heterogeneous and positive outcomes reported for individuals with schizophrenia may be very well attributable to recent advances in interventions for the disorder. The effect of treatment programs on course and outcome is schizophrenia is well illustrated by the classic Vermont-Maine longitudinal studies [26, 28–30]. These series of studies suggested that Vermont participants had better long-term outcomes compared to Maine participants due to the Vermont hospital’s comprehensive treatment program of medication management and a host of