Early Detection and Intervention in Psychosis
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State of the Art and Future Perspectives

Volume Editors

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Foreword

The Near Future

The care and study of persons with psychotic illness has a rich history. The acquisition of knowledge has accelerated, and application with life-altering potential for patients is now established in expert centers and ready for broader application in health care systems. Material in this book details the relevant advances in knowledge and understanding and enables the reader to view the near future with optimism. Presented in this Foreword is a brief outline of how the field has arrived at this point. Knowledge developed in the context of schizophrenia is critical, but so is the extension across disorders associated with psychosis or psychotic-like experiences. The reader will gain an appreciation of rapidly changing concepts in mental illness research and the implications for clinical application.

Kraepelin defined two fundamental psychotic disorders, dementia praecox and manic-depressive illness, providing a profound conceptual framework still influential in current classification, research, and clinical care. But the combination of ‘weakening the well-springs of volition’ with dissociative thought and a poor prognosis set the stage for 100 years of pessimism regarding clinical course. Bleuler’s view of dissociative pathology as fundamental and primary in all cases reinforced the disease entity concept even while the ‘group of disorders’ seemed to suggest a syndrome. Decades later, Schneider’s symptoms of first rank suggested that true schizophrenia was identified with special forms of reality distortion. This emphasis did not deny the importance of what we now term negative symptoms and disorganized thought and behavior, nor did it change presumptions regarding poor prognosis. These concepts, combined with limited effectiveness of treatment and concern about stigma, resulted in emphasis on schizophrenia as a brain disease where antipsychotic medication for symptom control and relapse prevention was the central issue, and expectations were of a chronic course for most patients.

A very different picture emerges from careful consideration of the actual data available for over a half century. First, schizophrenia has never been validated as a disease entity. The diagnostic class is a heterogeneous clinical syndrome. With various pathophysiologies, substantial individual variation is expected. This was shown
to be the case with onset, manifestations, and course data in long-term studies including Manfred Bleuler’s 40-year follow-up of his father’s patients. More recent studies have shown that not all patients have a poor developmental history and many do not have a chronic course. Despite psychotic symptoms being unifying at the level of diagnostic criteria, the nature of the psychotic experience and associated features have also varied between cases. In short, there is a profound heterogeneity that is not addressed in public or clinical concepts of schizophrenia, nor is it addressed in treatment guidelines or therapeutic discovery.

If the above snapshot generally captures our history (and, of course, there are many exceptions), it is about to change. This change is driven by a combination of new concepts and accumulated knowledge of early morbid/prodromal pathologies in the schizophrenia spectrum.

The following concepts are relevant to the care of persons with a psychotic illness: clinical syndromes are not adequately informative about individual patients, clinical targets for treatment go well beyond psychotic symptoms, recovery as a personal process and recovery as a goal of medical treatment, stress reduction, emphasis on the individual’s resilience and support network, and reduction in adverse factors such as substance abuse. These and other issues related to understanding the individual patient provide a basis of personalized and integrated therapeutics. These concepts are not new, but what has changed the landscape is a body of work focused on detecting clinical high risk in persons before full psychosis. It is the personalized application of these therapeutic concepts at the earliest point in a psychosis and moving clinical intervention to a prepsychosis phase of illness that will enable young people vulnerable to psychosis to gain a better future.

Much is known about early morbid features such as impaired cognition, declining social engagement, negative symptoms, aggressive and inappropriate behaviors, deteriorating role performance, and the experience of psychotic-like phenomena. These manifestations of psychopathology were traditionally viewed as prognostic factors or the developmental pathway to schizophrenia. The paradigm shift involves viewing this early phase as defining the need for clinical care with the goal of secondary prevention of psychosis. Throughout medicine, early detection and intervention is time honored as an approach to reducing morbidity/mortality. Clinical scientists such as this book’s editors and its contributors have produced an astounding growth in knowledge over the past quarter century that includes identifying at-risk individuals, organizing model programs for clinical care, validating the clinical high-risk construct with the full range of methods used to study established illness including electrophysiology, neuroimaging of structure, function and biochemistry, phenotypic information, associated negative symptoms, impaired cognition, and more. In addition to reliable and valid methods for identifying cases of clinical high risk, the initial random assignment controlled clinical trials support efficacy for symptom reduction, secondary prevention of full psychosis, and perhaps improved function. This is accomplished with minimum-risk therapeutics reserving risk/
benefit decisions for antipsychotic medications to a stage where full psychosis is emerging.

Specialized clinical care programs are growing internationally at a rapid rate. Model programs creating friendly clinical environments for young people and staging treatment according to what is wrong and where in the pathway to psychosis the individual fits provides a common-sense approach, but one that is challenging in traditional clinical care systems.

I think our field can make the future for persons who may be on a path to psychotic illness substantially better. To date we have no therapeutic approach that cures the pathology once established. We know that early intervention in the first psychotic episode is better for the person and for society. There are proven advantages to reducing the duration of untreated psychosis. Identifying and providing care for clinical high-risk individuals may benefit each person with the psychopathology already present and, for those who are on the path to full psychosis, may delay or prevent a first episode. If psychosis emerges, institution of treatment specific for psychosis will be immediate rather than the usual delay of months or years.

We do not yet know if intervention in the prepsychotic phase will alter the long-term pathophysiology. If so, this will be an unparalleled accomplishment. But if not, clinical intervention may enable the person to be successful with life milestones that are essential to future well-being such as successful education, being employed, having a love relationship, and supportive social network.

The field does not yet have the knowledge base to launch large-scale public health initiatives at primary prevention. But the knowledge base reviewed in this book provides the basis for an aggressive shift in the timing and nature of clinical care for persons who merit clinical attention and may be vulnerable to a psychotic disorder.

*William T. Carpenter, Baltimore, Md.*
Preface and Introduction

“I was extremely scared when the symptoms occurred for the first time. From one moment to the next, everything changed massively. That was extremely bizarre and scary at the time – this change in perception. At that time, the fear was predominant. What can I do about it? Why did this happen now and as suddenly? I consulted my family doctor a couple of times hoping to be referred to psychiatric services. But from what I felt, he thought that I just did not feel like going to work and wanted a sick note. He then put me on sick leave for a couple of days each time. After moving, I saw an advertisement of a psychiatric emergency service in the tram. I called and got an appointment for the next day. From there I got referred to the early intervention service very quickly – and finally, I felt that I was being taken seriously for the first time. I was really seeking help before. There was something seriously wrong with me and I had not been taken seriously. I felt desperate.

Prior to my first appointment at the early detection clinic, I was insecure. What is next? What will happen to me there? But to not do anything would not have been the solution either, and my symptoms were very severe at the time. That’s why I said to myself: ‘I need to seek help now! I do not want to continue like this!’ You go to the hospital too when you break an arm or a leg, and in my case something else was broken. After my first appointment at the early detection clinic, I felt seen for the first time and at last taken seriously, which I was very glad about.

When I was informed that I had a risk of developing psychosis and received information about the possible outcomes and about psychosis and schizophrenia in general, I could finally evaluate myself again. Up to the time I received this information, there had always been a certain insecurity that felt like an empty space in which I didn’t know where I stood. I knew a lot from my education as a health care worker, but I had not been able to integrate the information properly. To know what was happening to me was a great relief. It took a lot of the fear away. Afterwards, my energy increased, I took back control over my life, I cleaned up my apartment and dedicated myself to my hobbies again. I thought that since I had completed my education and performed well so far despite my symptoms, I would not let myself down now! I knew chronically ill patients with schizophrenia from work and I could see the difference between them and myself, standing with both feet on the ground – despite the insecurity and everything that I had been through! Some insecurity stayed – I knew that I could possibly slide down into schizophrenia. But then I thought that the probability was not that high, and that, if the symptoms stayed as they were I could live with them quite fine. Step by step, with successive appointments at the early detection clinic, I found explanations and answers for the changes I perceived. Then, I slowly managed to cope with them. From the initial exhausting additional burden of the symptoms on top of my everyday stress, they became with time something that I perceived as less and less scary and in the end as interesting, even. I perceived the support I received from the early detection center as friendly, enjoyable and obliging – exactly what I had so often needed. While I was dealing with what had happened to me, someone was standing behind me the whole time. Someone neutral, who I could call if something happened. That support in the background helped me a lot in my search for answers. I am a lot better now compared to how I was half
a year ago when I first came to the early detection clinic. I still suffer from certain problems, but I can cope quite well. After long days, I get tired faster than before, but I can live with that. I was really glad for the support I got and would like to express a great thank you for it!"

Patient of the FePsy Early Detection Clinic, Basel, Switzerland

Psychiatry during the last decades has achieved enormous progress. One of the major steps certainly was the overdue recognition of the concept of early detection and intervention as in other medical disciplines.

Interest first arose in the field of schizophrenia research. In these disorders, it had been described for some decades that they do not arise all of a sudden but, in most cases, very slowly with early subthreshold features. Kraepelin and Bleuler both described this pattern of onset, but the first to focus on it specifically was Harry Stack Sullivan [1] in 1927. Later, German authors recognized the so-called ‘Vorposten’ (outpost syndromes) and prodromal symptoms as well as a new concept of basic symptoms [2, 3]. Influenced by these early descriptive clinical studies, Häfner et al. [4] developed a semistructured interview to assess the prodromal phase of schizophrenia, the IRAOS. In 1986, they started a first representative study in a population of 232 first-admitted psychosis patients in and around Mannheim, Germany, and found that in 73% of all patients the disorder had begun with a prodromal phase which lasted on average for 5 years [5, 6]. An emerging research focus on first-episode patients through the 1980s (Crow, Kane, Lieberman) helped to show that treatment delay was substantial even for clear-cut first-episode psychosis [7, 8].

Clinical services based on early intervention principles began to develop in the 1990s, beginning with the EPPIC program in 1992, which not only aimed to reduce the duration of untreated psychosis, but also to engage and treat prodromal patients and to ensure that all early psychosis patients had the best chance of recovery in the early ‘critical’ period after diagnosis. In 1994, McGorry, Yung and colleagues [9, 10] established the PACE Clinic as part of EPPIC, the first clinical and research program for potentially prodromal individuals in Australia. They began to investigate the predictive validity of prospectively defined risk criteria, developing the ultra-high-risk (UHR) criteria and the first psychometric instrument [11]. Similar services and instruments were later developed in the United States, e.g. by Miller et al. [12] and in Switzerland by Riecher-Rössler and colleagues [13–15].

In Germany, Klosterkötter et al. [16] have especially pursued the predictive power of basic symptoms as very early risk indicators. Other major contributions to the field have come from the United Kingdom and Scandinavia, and similar clinical services for early detection and intervention have been established worldwide, often accompanied by research projects. So far, it has been shown quite clearly that (1) the disease, even in these very early stages, can – if untreated – have very severe consequences for the patient, (2) early detection of the disease, even in its prodromal phase, is possible, and (3) early treatment not only ameliorates presenting symptoms, but also improves illness course and psychosocial outcome [for reviews, see 17–24].
However, despite significant advances in the field, early detection of psychosis still faces some problems and obstacles. Thus, the accuracy of identifying those at risk for psychosis could certainly be improved. Existing risk-prediction approaches have achieved only modest predictive accuracy with 3-year transition rates of 30–43% of those originally identified as being ‘at risk’ [19]. These have even been falling in recent times. This means that many ‘false positives’ are identified who will in fact not develop frank psychosis. It was argued by critics that these individuals are not only exposed to the unnecessary stress of being confronted with such a diagnosis and the potential stigma associated with it, but potentially also to unnecessary treatment [18].

On the other hand, we now know that even the patients without later transition to psychosis often suffer from severe symptoms and functional impairment, are seeking help and treatment, and have a longer-term need for care [25–27]. It was suggested that the stigma associated with being identified as having a risk for psychosis was more related to the behavior associated with the illness rather than the diagnosis. Educating patients and clinicians and providing care in stigma-free settings might actually reduce stigma and unnecessary treatment [25]. In any case, it would be of utmost importance to improve the accuracy of the risk assessment. This should involve a ‘staging’ of the emerging disease and profiling of the patients, which would allow interventions tailored to the respective stage and personalized for the individual patient.

At the same time, there is a clear need for better evidence regarding therapeutic approaches in the different stages, which has prompted several questions. How shall we treat patients with suspected early prodromal symptoms and low risk, and how should we treat those with subthreshold psychotic symptoms and high risk? How should we treat patients with predominantly negative symptoms or cognitive deficits? An initial wave of intervention trials have indicated that certain psychological, pharmacological and other intervention strategies may be of value in terms of symptom reduction and delay or prevention of transition to frank psychosis. However, clear guidelines for clinicians as to which treatment to offer to which patient with which symptoms and impairments and in which sequence have not yet been established. This volume will give the reader a state-of-the-art overview on the current knowledge, developments, questions and discussions in the area of early detection and intervention for psychosis. It will also provide perspectives on how to improve early detection as well as early intervention.

In this context, the reader will learn how to recognize the very first signs of emerging psychosis. The significance and correlates of the high-risk state in adolescence and early adulthood will be outlined. Some debates and controversies will be captured, such as whether the ‘high risk for a psychosis state’ is really a valid entity, a question which stirred huge controversy when DSM-5 was being finalized [18]. Furthermore, the question of whether being informed about the risk for psychosis in fact is a negative, stigmatizing experience for patients – or rather a helpful one – will be considered.
Several authors will discuss in different chapters the possibilities to improve the accuracy of early detection by using different domains in addition to the clinical assessments such as neurocognition, fine motor functioning and neurophysiology. Also, structural and functional MRI, including the use of new methods such as pattern recognition methods or the analysis of connectivity abnormalities will be discussed regarding their values for improving the prediction of psychosis. Finally, different methods for early intervention will be presented – psychological methods as well as other nonpharmacological interventions including potentially neuroprotective substances for early intervention in the at-risk mental state, as well as pharmacological, psychosocial and other interventions in first-episode psychosis.

This volume will hopefully stimulate clinicians as well as researchers to further develop the field, which, in our opinion, is one of the most promising areas of current psychiatry. If performed correctly and wisely, early detection and intervention should extend to a transdiagnostic focus and could prevent enormous suffering in patients and their families.

This early intervention focus and spreading the concept of staging and stepwise intervention across the current diagnostic silos may well help to modernize psychiatry to become a 21st-century medical discipline with a truly preventative approach, and in the process further reduce the stigma that still holds the field back. Last but not least, intensive research in this relatively new field of emerging illness will hopefully contribute to a better understanding of the pathogenetic mechanisms leading to psychosis.

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References