Huijun Li · Daniel I. Shapiro · Larry J. Seidman
Editors

Handbook of Attenuated Psychosis Syndrome Across Cultures

International Perspectives on Early Identification and Intervention

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Dedication

Dr. Larry Seidman unexpectedly passed away in September 2017, when this book was roughly two thirds complete. This volume is dedicated in loving memory to Larry, as well as to his wife, children, and grandchildren, and to the extended family of people spread around the world who have been touched by his kindness, welcoming generativity, intellectual curiosity, and sage foresight. The book is a tribute to Larry's tireless efforts to better understand and improve the lives of all those touched by psychosis, ADHD, and other conditions affecting neurocognition. But even more broadly, and fitting as a last book, it is a homage to a man who at his core valued people most and relished the opportunity to experience something new—some new ideological horizon or perspective to be pondered or hashed out with others, some shared food or event or sight enjoyable for its novelty and pleasure, or some new tradition or culture experienced together with somebody from somewhere else. He was a man who valued diversity of thought and experience and, among all the things he was good at, had an uncanny sense of how things fit into their larger contexts and a vision for how this might guide the future of his field. Dr. Seidman has been mentor, friend, or colleague to both coeditors and many of the authors who contributed to this book. True to his nature, he was proud of this project and of the collaborations across all conceivable geographical, political, and cultural lines that it represents. This was not as new an endeavor to Larry as it is to our field. In more ways than one, this book would not exist without his influence. And in more ways than one, it is a tribute to him.

Daniel I. Shapiro and Huijun Li
October 2018

Foreword

Prevention and early intervention in psychotic disorders was regarded for many decades as a pipe dream. Those who held that dream were accused by their senior colleagues of the cardinal sin of offering false hope and indulging in "rescue fantasies." How much the world has changed over the past three decades! Schizophrenia and psychotic disorders, imbued with pessimism and the "soft bigotry of low expectations," seemed to be the least promising arena for the development of a preventively oriented psychiatry, but a global wave of dynamic translational research has transformed our field. We have finally realized that every other branch of medicine values the power of hope, and to strip hope away from patients and families at the onset of any treatable illness, however potentially disabling, deprives clinicians of one of their most powerful therapeutic tools. However, hope is not enough. We have also learned from cancer and other major noncommunicable diseases that if we diagnose early, treat intensively, and guarantee a secure tenure of expert care for as long as needed, especially in the early years post diagnosis, then outcomes can be dramatically improved, even with existing treatments. The evidence base for psychosis confirms the same is true for these disorders, provided that once we have got people well, we endeavor to *keep* them well. This approach however is still in mental health care, more honored in the breach than the observance. Despite the progress we have made, only a minority of patients worldwide benefit from implementation of this knowledge. We can do so much more for our patients, and the early intervention paradigm powered by implementation science and advocacy is the key.

The origins of what in North America is now increasingly referred to as the "Attenuated Psychosis Syndrome" goes back a long way. Kraepelin and Bleuler both described how dementia praecox and schizophrenia all too often developed imperceptibly and gradually with subtle changes and precursor signs and symptoms which eventually evolved into more florid and acute phases of frank psychosis. Harry Stack Sullivan in the 1920s described carefully the onset of schizophrenia and imagined the day when interventions might forestall the full expression of the illness. More recently, Ainsley Meares and Heinz Hafner described the prodromal stage of illness, and an operational definition of this prodromal stage was even included in the *DSM III-R*. Ironically, it was dropped from DSM IV because it was regarded as non-specific and unreliable. Yet, non-specificity is an essential feature of the concept of prodrome as adapted from infectious disease. Inspired by the

knowledge that over 70% of first episode cases manifested a prodromal stage, our early psychosis research group, from 1991, initially Henry Jackson and I, and, then from 1993, Alison Yung, decided to study this stage of illness, initially retrospectively and then prospectively, using an operational definition that combined known risk factors, such as family history, functional decline, and attenuated or subthreshold symptoms as "warning signs" of fully fledged and sustained psychotic disorder. This later became known as "indicated prevention." We established a satellite (PACE) clinic of the recently established EPPIC program in Melbourne and studied a prospective cohort of patients who manifested what we termed an "at-risk mental state." We observed a 40% rate of progression to first episode psychosis within 1 year, despite providing needs-based clinical care to these patients. This led us to coin the term "ultrahigh risk" state to underline the huge elevation of risk that was present. In the USA, Barbara Cornblatt amended this term to "clinical high-risk" state to contrast the approach with the genetic high-risk paradigm that had been pursued to that point. The at-risk or ultrahigh risk approach was an example of the "close-in" research strategy that studied risk factors, including subthreshold symptoms, close to onset of disorder. It was able to enrich the sample for risk and collapse follow-up periods, offering huge advantages.

In retrospect, these features, which seem simple and obvious, underpinned a real breakthrough in research strategy and methodology and paved the way for a global wave of research effort in many countries. Tom McGlashan and Barbara Cornblatt introduced these ideas and strategies into the USA, and others followed their lead. The leadership mantle was later taken up by Ty Cannon and, crucially, by Bob Heinssen at the National Institute of Mental Health, who brought the US leaders in this field, including Larry Seidman, together under the North American Prodrome Longitudinal Study (NAPLS) banner. This extension of early intervention added an extra edge to the momentum building around the first episode research and has produced new evidence confirming biological changes around the onset phase of illness and of the efficacy of intervention during the subthreshold stage. It is now possible to at least delay the onset of psychosis in some people who are starring down the barrel of risk. There is now Cochrane level 1 evidence for this, and I have seen countless examples of bullets which appeared to have been dodged (at least temporarily) in my clinical practice. Even if psychosis becomes sustained, duration of untreated psychosis is minimized, and outcomes can be improved. From follow-up studies, we now know so much more about the natural history of these at-risk mental states, which have not only a heightened valence for psychotic disorders but also a heightened risk for a range of other syndromes. In general, they connote risk for poorer functional outcomes, suicidal behavior, and a range of exit syndromes, often comorbidly.

This paradigm shift has created controversy, and, while genuine concerns have been raised appropriately, the issue has been exploited by scaremongers of various hues to promote their particular causes. Fortunately, the evidence that has accumulated now speaks for itself. People who meet these

UHR/APS criteria have an undeniable need for care, without which their prognosis is more guarded. Engagement in care at this stage of illness gives people the best chance of recovery. Treatment must be carefully staged, sequenced, and guided exquisitely by risk-benefit considerations. And now that we know, unequivocally, the importance and demonstrated benefits of such early intervention in those with an APS, the mantle can be taken up by clinicians and researchers around the world to investigate how this engagement, sequencing, and implementation of care are affected by differences in culture and variations in global systems of care. This comprehensive and scholarly edited volume captures the state of play of research in this dynamic field, not only in North America and Europe but, admirably, in other parts of the world too, and even other hemispheres! It is a tour de force, and the editors, with Larry as the generative, modest, and inspiring "coach," would be so proud of the final product.

The next phase of research and reform will likely proceed along three parallel trajectories. Firstly, researchers will seek to enrich samples and enhance prediction of transition not only to psychosis but to other outcomes, notably poor functioning, using sophisticated statistical approaches such as machine learning. Doing so will also require a study of diverse peoples to ensure that such approaches can be appropriately applied across differing places and peoples. Secondly, the clinical staging model reveals that the earliest stages of illness where a need for care exists are not linked purely to one of the traditional syndromal silos. Operational definitions of this stage may have a variable level of valence for different late syndromes like psychosis or mania, but there is overlap. We need to consider transdiagnostic definitions of early stages of illness. Biomarkers may be helpful in refining prediction and guiding treatment; however, it is unlikely they will validate the current DSM/ICD nosology. The APS or UHR syndromes may come to be seen as a prototype concept on a pathway to a new nosology, one with greater utility and validity and one which may be moderated by culturally linked factors. Larry Seidman would have been 100% behind such an exciting venture. Lastly, understanding how differences in cultural context might affect all of this work represents a different kind of frontier, one that has been seriously underrepresented in the history of psychiatry. The paradigm shift toward early intervention in those with UHR/APS syndromes was catalyzed in primarily Australian, European, and North American centers with primarily Western populations. Much of the precipitous expansion from these hubs has been to translate, validate, and replicate approaches into new cultures and systems, each with differing pathways to care, valued outcomes, and ways of conceptualizing mental constructs, health, and healing. It may be that extant approaches can be modified, but it may also be that homologous interventions, built from unique cultural vantage points, need to be included in our models. This work has only just begun—the volume that follows is an exciting and significant step in this endeavor.

It is a huge honor to have been asked to write the foreword for this book, an honor tinged with deep sadness, because the senior editor, Dr. Larry Seidman, a dear friend and one of my most admired and inspiring colleagues, is no

longer with us. Larry is not only one of the international pioneers of the paradigm shift to which I have already referred but truly one of the most generative and collegial of the array of international leaders in psychiatry research that I have ever known. I am extremely pleased to see this book come to fruition as part of a lasting tribute to his contribution to early intervention in psychosis.

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Acknowledgments

We thank all the patients and their families who passionately seek change for them and us by engaging in clinical treatment and participating in research. Their drive, curiosity, and willingness to channel and challenge difficult experiences are inspiring and have led to improvements in quality of life for countless families around the world. We appreciate our family members, friends, supportive institutions, and graduate students for their incredible support and understanding during the writing and publication process. Finally, we owe so much to wonderful mentors past and future, who make endeavors like this imaginable.

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About the Editors

Huijun Li received her Ph.D. in School Psychology from the University of Arizona in 2003. She is a Nationally Certified School Psychologist and Nationally Certified Youth Mental Health First Aid Trainer and an Associate Professor in the Department of Psychology, College of Social Sciences, Arts, and Humanities, Florida A&M University. She is also a Research Collaborator of Psychiatry and served as the Director of Multicultural Research of the Commonwealth Research Center, prior to joining Florida A & M University, at Beth Israel Deaconess Medical Center, Harvard Medical School. She has received federal and foundation grants to study psychosocial factors such as culture-specific beliefs about causes of mental illness, stigma, and barriers to services related to help-seeking behaviors among individuals from diverse backgrounds and actively contributes to local community services by providing presentations and workshops on youth mental health. In addition, she served as Expert Professional on youth mental health on the local *ABC News* after the Newtown, Connecticut, school shooting incident and is the author or coauthor of peer-reviewed journal articles, book, book chapters, translated books, and conference presentations.

Daniel I. Shapiro recently joined the University of California-Davis, Department of Psychiatry, where he serves as Director of Operations of the EDAPT/SacEDAPT Early Psychosis Programs. He is also a Co-Director of the Atlanta Center for Cognitive Therapy certification and training program. Prior to this move, Dr. Shapiro was on the faculty at Harvard Medical School, Department of Psychiatry, where the majority of the work on this volume was completed. There he served as Project Director of Clinical High-Risk Research and a Project Scientist at the Commonwealth Research Center of the Beth Israel Deaconess Medical Center, as well as a Clinical Psychologist and Supervisor at the Massachusetts Mental Health Center. He is an expert in the identification and treatment of early stages of psychotic illness and has directed the operations of both community-based clinical programs and federally- and privately-funded clinical research grants aimed at better understanding the developmental trajectory, treatment of, and barriers to care in early stages of psychosis and other serious mental illness. Within this work, he is particularly interested in: (1) the role stress, neurocognition, and individual factors play in the development and recovery from mental illness, and (2) development and dissemination of targeted and specialized interventions for individuals and families affected by psychotic illness. Dr. Shapiro is a

practicing Clinical Psychologist with a secondary specialization in the practice and teaching of Cognitive Behavioral Therapy, which began during his fellowship at the University of Pennsylvania. He is active as a clinician and clinical supervisor and is passionate about the training of developing clinicians.

Larry J. Seidman was Professor of Psychology in the Department of Psychiatry at Harvard Medical School, at the Beth Israel Deaconess Medical Center (BIDMC), and at Massachusetts General Hospital, where he conducted neuroimaging research since 1992. He was Director of the Massachusetts Department of Mental Health sponsored "Center of Excellence in Clinical Neuroscience and Psychopharmacological Research" at BIDMC beginning in 2002 and Vice Chair for Research at BIDMC Public Psychiatry Division at Massachusetts Mental Health Center beginning in 2005. He spent more than 30 years studying the causes of psychotic disorders and mapping the components of neurodevelopmental disorders of prefrontal cortex and executive control in schizophrenia and ADHD. He focused primarily on cognition in schizophrenia and ADHD and studies of youth "at risk" for psychosis. He was a Licensed Clinical Psychologist who had long worked with teenagers. He published more than 380 peer-reviewed papers and was Principal Investigator of 31 grants, participating in 80-funded grants since 1978. His focus over the past 10 years was investigating the phase of clinical high risk for psychotic illnesses and treatment of psychosis in the early phases. He was involved in teaching and mentoring and mentored more than 50 individuals with faculty appointments around the world in addition to scores of clinicians and many others. In recognition of these efforts, he was awarded the prestigious William Silen Lifetime Achievement Excellence in Mentoring Award in 2016. He also served as Director of Neuropsychological Training and Services at Massachusetts Mental Health Center and President of The Massachusetts Neuropsychological Society. He was recognized in August 2014 by Thomson Reuters Science Watch as one of the "The World's Most Influential Scientific Minds of 2014" based on his highly cited papers.

Part I

Introduction and Overview of Assessment and Intervention in Attenuated Psychosis Syndromes

1 Attenuated Psychosis Syndromes Seen Through the Cultural Prism: Relevance, Terminology, and Book Structure

Daniel I. Shapiro, Huijun Li, and Larry J. Seidman

1 Introduction

Psychotic disorders, including schizophrenia, appear to affect a significant proportion of the world's population. No culture seems to be immune, even though presentation and interpretation of the causes of the illnesses and intervention strategies may vary. The latest meta-analysis reports the pooled median global prevalence of psychotic disorders at 4.6 per 1000 persons; the median point and 12-month prevalence at 3.89 and 4.03 per 1000 persons, respectively; and the median lifetime prevalence at 7.49 per 1000 persons (Moreno-Kustner, Martin, & Pastor, 2018). Conditions involving threshold symptoms of psychosis vary in their severity and range from single episode, or easily manageable symptoms, to more chronic and debilitating disorders. However, in all cases psychosis has the potential to disrupt the lives of those who experience it—to disrupt social, cognitive, vocational, and psychological functioning; to impact caregivers, family members, and other supports; and to affect society via need for clinical resources and lost productivity (Vigo, Thornicroft, & Atun, 2016). These disorders typically reach diagnosable threshold in adolescence or young adulthood but are often preceded by nonspecific premorbid cognitive, social, motor, and academic/vocational functioning difficulties that frequently date from early childhood (Tandon, Nasrallah, & Keshavan, 2010). More proximal to the onset of threshold clinical symptoms, most individuals who develop a psychotic disorder experience a prodromal period of worsening symptoms and increasing impact on functioning that can last from a few months to a few years (McGorry & Singh, 1995). This means not only that illness-related mechanisms may begin to exert their effects long before they can currently be identified but that they do so at critical periods of development. They can cause disruptions at times during which people typically build foundational knowledge and critical thinking skills, build social skills and use them to begin navigating relationships with others, start to develop interest in a trade and transition into independent life, learn how to manage emotion and cope with distress, and build important psychological

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foundations for one's sense of self and how one fits into the world. Much of the foundation for all aspects of adult functioning is laid during the very times that psychosis typically begins to unfold. Disruptions during such critical periods can have long-lasting effects, suggesting that efforts to identify individuals before psychosis develops may provide opportunities to intervene and avoid or mitigate these effects (Woodberry, Shapiro, Bryant, & Seidman, 2016), potentially prevent or delay psychosis, or reduce the morbidity associated with developing a full-blown psychotic episode.

With this aim, the last few decades have seen a groundswell of efforts to develop and refine reliable methods for prospectively identifying those "at elevated risk" for later manifestation of a psychotic disorder. A major focus has been on identifying those who might be in the prodromal phase of illness, a key period for intervention, and methods for identifying possible prodromal syndromes have been developed that have reasonable predictive power (Keith & Matthews, 1991; Loebel et al., 1992; Yung & McGorry, 1996). This has opened up exciting possibilities for early intervention and to better understand the predictors and the mechanisms of psychosis onset. Indeed, the promise represented by the notion of early intervention has led to a quickening in the pace with which this movement is spreading from the primarily Australian, Western European, and North American contexts in which they were developed into new international sociocultural contexts. New efforts to identify and intervene in those who are "at risk" are now underway in many countries around the world, typically put forth by importing models developed elsewhere and exploring whether they function similarly in new cultures. The approaches and interventions are often modified and tailored to these new contexts, with variations among cultural lines typically examined as secondary outcomes or concerns. These efforts thrust into the spotlight the importance of understanding how differences in culture may impact risk assessment and intervention paradigms as they transport out of the cultural contexts in which they were developed into new ones.

The purpose of this book is to present international perspectives on the identification of those at risk for psychosis, with a particular focus on efforts to intervene in those who may be in the prodromal phase of illness.

The goal is to examine how culturally linked factors may affect this endeavor, a topic that has to date been vastly understudied. It is of critical importance as the early intervention paradigm revolutionizes traditional models in psychiatry and catches new roots.

This volume gathers the broadest set of authors on this topic to date in order to broaden the scope of the field at a key time in its growth. A second goal is to summarize international research and clinical endeavors that facilitate culturally informed assessment and intervention approaches. Terminology and structure of this edited book are discussed below.

2 Terminology Conventions in the Present Volume

A number of paradigms have been developed for identifying individuals thought to be at incipient risk of psychosis (e.g., in the prodromal phase), each with corresponding terminology and syndrome names, typically attached to the measure or method used for identification. In preparing the current volume, it has become evident that different conventions, terminologies, and names predominate in different areas of the world. Sometimes, similar terms are applied according to different conventions or operationalized in unique ways, due to linguistic differences, necessity, structural limitation, or culturally linked differences in how psychosis and mental health are conceptualized. Sociocontextual systems shape how models developed in one place and time are understood and implemented in another. Sometimes culturally linked factors, including community and healthcare structures that have developed within specific cultural contexts, affect when individuals come to clinical attention, for what concerns, and to whom, all of which may constrain how the same models of high psychosis risk are implemented. However, all systems for operationalizing putative incipient risk tend to share one major overlap in core phenomenology, which is that they involve the presence of certain characteristic signs and symptoms that manifest

in attenuated forms during the risk phase, relative to the acute phase of psychosis. Major terms that have been used in the field include prodromal (e.g., Keith & Matthews, 1991), ultrahigh risk (Yung 2003), at risk mental state (McGorry & Singh, 1995; McGorry et al., 2005), clinical high risk (CHR) (Correll, Hauser, Auther, & Cornblatt, 2010), psychosis risk syndrome (PRS) (Correll et al., 2010; McGlashan, Walsh, & Woods, 2010), outpost syndrome (Huber, Gross, Schiittler, & Linz, 1980), "prepsychotic," and basic symptom syndrome or COGDIS (Klosterkötter, Ebel, Schultze-Lutter, & Steinmeyer, 1996; Schultze-Lutter et al., 2012), among others discussed throughout this volume. In an attempt to capture this diversity, we use in this volume the term Attenuated Psychosis Syndromes (APS) to collectively refer to the class of putative prodromal or high-risk syndromes that have been empirically validated. Additional specificity (e.g., CHR, PRS) is used when warranted or in reviewing a particular study or methodology that uses a particular term. We acknowledge that this is not a universally accepted convention but use it here as a general umbrella term that can allow for a discussion and comparison of both similar and different operationalizations from writers around the world.

3 Book Structure

This edited book includes research and clinical findings on APS and the role culture plays in its symptom presentation, assessment, and treatment in various cultures around the world. It includes contributions from prominent researchers from six continents, each using a similar structure to identify their context and elaborate on their region of focus, composite racial and ethnic groups, health systems, typical APS presentations, help-seeking behaviors, barriers to services, and assessment and intervention strategies in their unique sociocultural contexts. There are six major sections in the book, following a forward by Dr. Patrick McGorry. Section I is comprised of summaries of the theoretical framework that has guided scientific and clinical attempts to identify those likely to develop psychosis later in life and how different paradigms for identifying those at high risk do at prospectively predicting illness (Chap. 2). In Chap. 3, we summarize the rationale for early intervention and provide a brief review of extant treatments and their effects in those at putative risk for psychosis. Section II addresses the conceptual and measurement foundations of APS, with chapters written by key figures in the development of each of the currently predominant APS paradigms. Specifically, Chap. 4 summarizes early identification and intervention programs for APS in Australian youth and the role that the originators of the UHR paradigm have played in shaping early intervention throughout the world. The development and utility of the Structured Interview for Psychosis-Risk Syndromes and the Scale of Psychosis Risk Symptoms is discussed in Chap. 5. In Chap. 6 the basic symptoms approach is presented in the context of a discussion about disorders of the self. This model of psychosis risk is demonstrated via discussion of its application among Swiss and German youth. There are two chapters in Sect. III Borderlands of Cultural and Medical Conceptualizations of APS: Chap. 7 on early psychotic experiences from an anthropological perspective, illustrated via an Indonesian cultural viewpoint, and Chap. 8 on medical causes of APS. Section IV includes contributions from a diverse collection of international authors, summarizing research and clinical practice on APS in their specific regions and cultures. Each set of authors also provides an overview of their specific cultural and structural context and then some discussion of how culture may affect presentation, pathways and barriers to care, the validity and reliability of methods of identifying APS, and suggestions or guidelines for providing culturally competent care. Furthermore, using a case illustration approach, the authors in Sect. IV provide readers an opportunity to understand the illness and its assessment and intervention within their specific cultural landscape, giving an in-depth view of individuals, families, and the mental health systems they interact with. There are 12 chapters in this section, presenting work from North America (Canada, African Americans,

Asian Americans, Latino Americans, Mexico), South America (Brazil), Africa (Nigeria), Asia (China, India), and Europe (Denmark, Spain). A summary and directions for the future are presented in Sect. V. Dr. Barbara Cornblatt concludes the book with an epilogue, highlighting where the next horizon in APS research and clinical practice may be amidst a future of increasing globalization.

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Assessment of Risk for Psychosis

2

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Editors' Note A number of paradigms exist for prospectively identifying individuals who have elevated risk for developing psychosis due to the presence of syndromes comprised of identifiable risk factors and risk indicators. Conventions for which models are used, how individuals are identified, and which terminologies predominate vary throughout the world, sometimes related to culturally linked factors. In order to capture this diversity within one volume, the term Attenuated Psychosis Syndromes (APS) is used here to collectively refer to the class of putative prodromal or psychosis-risk syndromes that have been empirically validated. We acknowledge that this is not a universally accepted convention but use it as an umbrella term due to its heuristic value.

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1 Introduction and Orientation to the Chapter

This chapter aims to summarize methods for assessing risk for psychosis, presented with an eye to how the history of this endeavor has shaped its methodologies. While efforts to identify individual markers of risk for psychosis predate the development of psychosis-risk syndromes, we will start this chapter by introducing the concept of risk in psychiatry, then identify Attenuated Psychosis Syndromes (APS), and briefly discuss the methods and major measures for identifying them (Part I). We also include vignettes that illustrate prototypal presentations of a number of APS. In the second part of the chapter, we attempt to broaden our lens by presenting the theoretical framework that underlies efforts to assess risk for psychosis, both via specific markers

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and via methods that attempt to prospectively quantify risk at the individual level. In total, we aim to give a brief overview of approaches to the identification of risk factors and risk indicators and then summarize research devoted to their elucidation. We will close with remarks on how these different sources of knowledge, clinical observations, epidemiology, research on biomarkers, and a newer focus on prediction of psychosis, can be used jointly to maximize the predictive power of available tools to aid in real-time clinical decision-making regarding the possible course of unfolding illness.

2 Part I

2.1 Approaches to Psychosis-Risk Identification: An Introduction

From a public health perspective, approaches to preventing psychiatric illness can be characterized as falling into universal, selective, and indicated (Mrazek & Haggerty, 1994) strategies. Universal approaches are applied at the population level and do not relate to any specific person or markers of risk. They are meant to target risk factors thought to affect a whole population. Anti-stigma campaigns that place billboards in busy thoroughfares are a good example. Because lack of understanding and negative beliefs about mental illness are associated with decreased and later utilization of mental health care, these risk factors are thought to affect everybody. Putting fluoride in the common water supply to prevent tooth decay is another. Selective approaches are applied to members of a subgroup because membership in that subgroup conveys risk. A good example is a special education and treatment group for children of substance using parents because membership in this group is known to be associated with higher incidence of substance abuse later in life. In the indicated prevention framework, early signs of illness or risk "indicators" that imply one is in the early stages of illness are identified and lead to intervention (McGorry, 1998).

Currently, the predominant approaches to early, putatively preventive intervention for psychosis use a risk factor and/or indicated prevention framework. Specifically, the broad theory is that all individuals carry some level of risk, or probability, for developing psychosis based on the accumulation of dynamic and interactive biological (e.g., genetic impacting brain structure and function), environmental, and psychological contributants (Woodberry, Shapiro, Bryant, & Seidman, 2016). This risk for psychosis is not dichotomous but rather exists on a continuum; we are all vulnerable to developing psychosis under the right conditions, but some people are more vulnerable than others, and certain stressors or circumstances are more likely to activate this vulnerability or protect against its expression (e.g., Rosenthal, 1970). This degree of risk, however, is difficult to unambiguously and prospectively measure because there are no sufficiently sensitive predictors of psychosis that can portend every case and because none of the risk indicators that have been identified are specific at an individual level—the same risk marker may lead to different end points for different individuals (multifinality). In the absence of such markers, clinicians are left to estimate latent risk by measuring risk/protective factors and indicators and making inferences about the probability of illness. Risk and protective factors are phenomena that have been shown to be associated with a higher or lower likelihood of a specific outcome—here, the development (or not) of psychosis—e.g., having a first-degree relative with psychosis confers a greater risk of psychosis development, while a host of mitigating factors confers protection (Kendler & Diehl, 1993). In a clinical suicide assessment, the presence of a previous suicide attempt is a risk factor for a subsequent attempt. With respect to psychosis, risk indicators are signs and symptoms that, while manifest, signal an increased likelihood of developing psychosis.

Insights on risk indicators for psychosis have come from retrospective reports about individuals who already have psychosis (Yung & McGorry, 1996a, 1996b), from studies of family members of those with psychosis who presum-

ably share some of the same (epi)genetic risk factors (e.g., Kendler, Neale, & Walsh, 1981), and more recently from prospective research on those with syndromes shown to predict psychosis in a significant proportion of cases (e.g., ultra/clinical high-risk or basic symptom Attenuated Psychosis Syndromes (APS)). Indices that discriminate those with an APS who develop psychosis from those who do not are indicators of risk, when present. Examples of risk indicators are specific syndromes of signs (observable phenomena) and symptoms (subjectively experienced phenomena). With APS, these include decline in social and vocational functioning, subthreshold positive and disorganized symptoms of psychosis, and new or worsening cognitive symptoms (see next section). As discussed in Part II of this chapter, other risk indicators include characteristic cognitive function changes like difficulties with memory and executive functions (Seidman et al., 2016), disruptions of function like impaired tolerance or experience of stress (e.g., Walker et al., 2013), early social difficulties (Tarbox & Pogue-Geile, 2008), changes in brain structure and function (Pantelis et al., 2009), and neuroinflammation (Flatow, Buckley, & Miller, 2013) or environmental factors that indicate chronic stress or adversity (Bentall et al., 2014; Longden & Read, 2016). Detailed review of each of these areas is beyond the scope of this chapter, but we summarize the major areas after discussing Attenuated Psychosis Syndromes (APS). We present APS here because in recent decades they have played a major role in efforts to identify markers of risk.

3 Attenuated Psychosis Syndromes

The question of how to identify individuals who might be at highest risk for developing psychosis or who may already be experiencing its prodromal stages has guided efforts to balance the benefits of intervening at the earliest possible moment with the potential risks or costs of undertaking clinical interventions where they are not warranted. To this end, a number of paradigms have been developed over roughly the past half century to identify individuals with clinical syndromes that (1) resemble what retrospective research has identified as common prodromal presentations or (2) presumably indicate high levels of biological risk. Most typically these syndromes involve the presence of subthreshold forms of psychotic or thought disorder symptoms or decline in functioning in those with a known family history, presumably due to early aspects of illness processes. Because different systems for identifying such syndromes have developed and are utilized around the world, all sharing in common some of these features, we collectively refer to them as Attenuated Psychosis Syndromes (APS). The most prominent examples, discussed separately, are the ultra/clinical high-risk syndromes, basic symptoms syndromes, and syndromes that assess schizotypy or "milder" ends of a psychosis spectrum. Each of these will be briefly discussed, key measurement tools will be presented, and a vignette depicting a prototypical case will be presented.

3.1 Ultra-High-Risk and Clinical High-Risk Syndromes

In the 1990s Alison Yung, Pat McGorry, and colleagues at the University of Melbourne (and the PACE clinic) utilized a "close-in" strategy to develop the concept of "ultra-high-risk" syndromes (see Chap. 4 for thorough discussion by Nelson and McGorry). Building on research on biological relatives of those with schizophrenia or other psychotic disorders, as well as retrospective research in those with extent illness, these authors developed three different syndromes comprised of the most commonly described clinical features and presentations observed during the prodrome (McGorry, Yung, & Phillips, 2003; Yung & McGorry, 1996a, 1996b). These so-called "ultra-high-risk" syndromes, characterized by specific attenuated positive symptoms of particular duration and intensity (attenuated psychosis symptoms syndrome/group), outpost syndromes characterized by brief periods of threshold psychotic symptoms (Brief Limited or Intermittent Psychosis Symptoms Syndrome/

group) and a trait and state risk factor group comprised of individuals with a recent decrease in functioning plus either a first-degree relative with a psychotic disorder or who meet criteria for schizotypal personality disorder (vulnerability syndrome). While these syndromes are meant to identify individuals who are putatively in the prodrome, these authors collectively refer to the period categorized by these three syndromes as the "at-risk mental state" (ARMS), given that a prodrome can only be defined as such once an endpoint is known.

Shortly after these developments in Australia, Tandy Miller, Tom McGlashan, and colleagues in the United States picked up this framework and developed a measurement tool called the SIPS, originally the Structured Interview for Prodromal Syndromes (Miller et al., 2002, 2003) (see Chap. 5 for discussion from the developing group). They referred to syndromes in the ARMS as psychosis-risk syndromes and operationalized nearly the same three specific syndromes as Attenuated Psychosis Symptom Syndrome, Brief Intermittent Psychosis Syndrome, and Genetic Risk and Deterioration Syndrome, which they refer to as "clinical high-risk" syndromes.

3.1.1 Assessment of Ultra-High-Risk and Clinical High-Risk Syndromes

Two clinician-administered assessment tools have been developed and widely disseminated for assessment of clinical/ultra-high-risk syndrome APS and are the most utilized methods for identifying an APS worldwide: the Comprehensive Assessment of At-Risk Mental States (CAARMS) and the Structured Interview for Prodromal/Psychosis-Risk Syndromes (SIPS). These measures are discussed in depth by the authors involved in their respective development in Chaps. 4 and 5, so they are covered only briefly here. In short, both are semi-structured assessment instruments containing questions for interviewers, rating anchors for symptom severity, and diagnostic criteria and scales for identifying psychosis-risk syndromes. In the SIPS, the scale for identifying clinical high-risk syndromes is called the Summary of SIPS Syndrome Criteria (SOPS). A seminal meta-analysis including predictive validity studies of these two tools indicates that approximately 29–36% of those identified with a CHR/UHR syndrome transition to full psychosis within 2–3 years (Fusar-Poli et al., 2012).

The Comprehensive Assessment of At-Risk Mental States (CAARMS; Yung et al., 2005) is a semi-structured interview and assessment tool initially developed at the Personal Assistance and Crisis Evaluation (PACE) clinic in Australia to identify vulnerability, attenuated psychosis, and brief limited intermittent psychosis "ultra-high-risk" (UHR) syndromes, and criteria for psychosis is called "psychosis threshold." The scale is comprised of 28 items organized into seven symptom subscales and rated separately for severity and frequency. On several of the subscales, both subjective and objective observation is rated. The subscales cover the following domains: positive symptoms (unusual thought content, non-bizarre ideas, perceptual abnormalities, disorganized speech), cognitive change (subjective experience, observed cognitive change), emotional disturbance (subjective emotional disturbance, observed blunted affect, observed inappropriate affect), negative symptoms (alogia, avolition/apathy, anhedonia), behavioral change (social isolation, impaired role functioning, disorganizing/odd/stigmatizing behavior, aggression/dangerous behavior), motor/physical change (subjective complaints of impaired motor functioning, informant reported or observed changes in motor functioning, subjective complaints of impaired bodily sensation, subjective complaints of impaired autonomic functioning), and general psychopathology (mania, depression, suicidality and self-harm, mood swings/lability, anxiety, obsessive-compulsive disorder symptoms, dissociative symptoms, impaired tolerance to normal stress). Only the positive symptom domain is used to identify UHR syndromes. This instrument has been translated into four languages, and the Youth Psychosis At-Risk Questionnaire (YPARQ; Ord, Myles-Worsely, Blailes, & Ngirlmau, 2004) has been constructed as a screening questionnaire based on the CAARMS.

The CAARMS has demonstrated good discriminant validity and excellent inter-rater reliability (ICC in the range of 0.62–0.93 with only one subscale below 0.7). Sensitivity, or the ability to predict psychosis in all tested individuals, was 83% at 6 months, and specificity, or the percentage of all tested individuals who did not meet criteria and did not develop illness, was 74% at 6 months. Construct validity is high since high CAARMS scores in a UHR groups are significantly associated with onset of psychotic disorder (Yung et al., 2005).

The Structured Interview of Psychosis-Risk (née Prodromal) Syndromes (SIPS; Miller et al., 2003) is a semi-structured diagnostic interview designed for trained clinicians to identify clinical high-risk syndromes. The SIPS includes five components: a 19-item Scale of Prodromal Syndromes (SOPS), a checklist for the Criteria of Prodromal Symptoms (COPS), Global Assessment of Functioning, DSM-IV Schizotypal Personality Disorder checklist, and a family history of mental illness. The SIPS is used to identify the attenuated positive symptom syndrome, the Brief Intermittent Psychosis Syndrome, the Genetic Risk and Deterioration Syndrome, and criteria for transition to psychosis called the presence of psychosis syndrome (POPS). The SIPS has been translated into 15 different languages and is the basis of the screening instrument, the PRIME screen (Miller, 2004), which has also been translated into at least two other languages (Kobayashi et al., 2008; Mamah et al., 2012).

In addition to identifying the presence of clinical high-risk syndromes, newer versions of the SIPS also evaluate progression or remission of these syndromes over time. It is comprised of four subscales—positive, negative, disorganization, and general symptoms scales. The positive subscale is made up of five items: unusual thought content/delusional ideas, suspiciousness/persecutory ideas, grandiose ideas, perceptual abnormalities/hallucination, and disorganized communication. Like the CAARMS, only the positive symptoms subscale is used to identify CHR syndromes, and the other three subscales measure the severity of symptoms once the "diagnosis" is established.

Reliability and validity data indicate excellent inter-rater reliability and predictive validity. Specifically, the developers of the SIPS found inter-rater agreement in making diagnostic judgments regarding the presence of psychosis-risk syndromes of 93% (Miller et al., 2003). The SOPS rating scale has shown high reliability (ICC values at 0.95 for the total score and above 0.75 for all four subscales—positive, negative, disorganized, and general symptoms subscales). Sensitivity (percentage of all tested individuals who have developed this illness) was 100% at 6, 12, and 24 months; and specificity (percentage of all tested individuals who did not meet criteria and have not developed illness) was assessed at 71%, 74%, and 73% at 6, 12, and 24 months.

3.1.2 Attenuated Psychosis Vignette

The following vignette illustrates a typical APS presentation in North America.

Mark: Attenuated Psychosis Syndrome

"Mark" is a 16 year old who lives with his mother and stepfather in a poor urban neighborhood in Canada. He is in 9th grade and was diagnosed with ADHD at age 11 in the context of academic difficulties. He had typically gotten As, Bs, and Cs in school and had a good group of friends. However, over the past school year, his grades have been trending downward, and he has become a C average student, stating that he has had a lot of difficulty paying attention in class. He enjoys riding his bike and creating art and videos that he posts online. According to Mark's mother, there is no known family history of mental illness in either her or Mark's father's families. He was referred to a specialized early psychosis clinic by his general practitioner where the SIPS was administered in the context of a specialized psychodiagnostic assessment.

About 6 months ago, Mark began to feel that he could predict events in the future. For example, he recently entered the cafeteria at lunchtime and felt strongly that there would be a fight, and then a fight did take place. At other times, he feels he is predicting odd details of daily life, such as random body movements of his classmates, his mother's car pulling into the driveway, or that an object will fall off a table or wall. Over time, his predictions have become more specific and frequent. He finds this phenomenon weird rather than scary, and his friends generally believe and get excited about his predictions rather than finding them odd. He states that he does not behave any differently due to these predictions but finds them absorbing, and they occupy his attention.

Mark also states that "I can never let my guard down. That's just my opinion." His mother describes him as "vigilant" without any particular focused concern about his safety. She also stated that she feels their neighborhood is somewhat dangerous, and at times she wishes he was more (rather than less) vigilant. He feels that his peers are not trustworthy because everyone at school gossips. He denies feeling that anyone in particular is talking about him or trying to make things harder for him. He denies feeling watched or singled out. His feelings of mistrustfulness began last year when he was bullied by some classmates.

Mark reports hearing three voices that occur on and off every day. He hears them outside his head as actual sounds but is aware that no one else can hear them. They are sometimes helpful and sometimes have violent or sexual content. He is not sure where the voices are coming from; it could be his mind playing tricks on him or maybe spirits. He has noticed that he tends to hear the voices more when he is stressed out or upset and that he rarely hears them when he is relaxed and hanging out with friends.

Based on these experiences and a drop in his functioning at school (but not with friends), Mark met criteria for an attenuated positive symptom CHR syndrome on the SIPS.

A few details about "Mark" make this case a good example of a CHR/UHR APS. First, he has prominent attenuated positive symptoms (auditory hallucinations, a vague sense of paranoia or foreboding, an odd experience of predicting the future). Second, these positive symptoms are new and worsening rather than long-standing or viewed by Mark as part of his typical personality. Third, Mark has experienced some difficulties maintaining attention and follow-through in his schoolwork over the last year which has led to a decline in his academic functioning but in general was functioning fairly well socially and academically before his positive symptoms began. Frequency of experiences was not discussed in the vignette, but as assessed with either the SIPS or the CAARMS, attenuated positive symptoms would need to occur at least once per week over the past month (SIPS) or at least once per month if they persisted for more than an hour and three to six times per week if shorter (CAARMS).

3.2 Basic Symptoms Syndrome

The basic symptoms concept developed prior to and independently of the UHR/CHR model that focuses primarily on attenuated positive symptoms (Huber & Gross, 1989). The "basic symptoms syndrome" has a number of similarities to the attenuated symptoms model of a clinical high-risk state. Like APS, the basic symptoms concept was first described by clinician scientists examining retrospectively the emergence of psychosis among patients prodromal to schizophrenia (Schultze-Lutter & Theodoridou, 2017). These careful retrospective observations were then operationalized in order to study the predictive validity of a psychosis-risk category focus-