## cambridge.org/psm

# **Review Article**

Cite this article: Zachar P, First MB, Kendler KS (2020). The DSM-5 proposal for attenuated psychosis syndrome: a history. *Psychological Medicine* **50**, 920–926. https://doi.org/10.1017/S0033291720000653

Received: 25 November 2019 Revised: 29 February 2020 Accepted: 3 March 2020 First published online: 1 April 2020

#### Key words:

At-risk mental state; basic symptoms; prodrome; psychosis; schizophrenia; ultra-high

#### Author for correspondence:

Kenneth S. Kendler, E-mail: kendler@vcu.edu

# The DSM-5 proposal for attenuated psychosis syndrome: a history

Peter Zachar<sup>1</sup>, Michael B. First<sup>2</sup> and Kenneth S. Kendler<sup>3</sup>

<sup>1</sup>Department of Psychology, Auburn University Montgomery, Montgomery, AL, USA; <sup>2</sup>Department of Psychiatry, Columbia University, New York, NY, USA and <sup>3</sup>Virginia Institute for Psychiatry and Behavioral Genetics and Departments of Psychiatry, and Human Genetics, Medical College of Virginia of Virginia Commonwealth University, Richmond, VA, USA

#### **Abstract**

This article narrates a consensus history of the proposal to include diagnostic criteria for a psychosis risk syndrome in the DSM-5, in part, to document what happened, but also to potentially help focus future efforts at clinically useful early detection. The purpose of diagnosing a risk state would be to slow and ideally prevent the development of the full disorder. Concerns about diagnosing a psychosis risk state included a high false positive rate, potentially harmful use of anti-psychotic medication with people who would not transition to psychosis, and stigmatization. Others argued that educating professionals about what 'risk' entails could reduce inappropriate treatments. During the revision, the proposal shifted from diagnosing risk to emphasizing current clinical need associated with attenuated psychotic symptoms. Within the community of researchers who studied psychosis risk, people disagreed about whether risk and/or attenuated symptoms should be an official DSM-5 diagnosis. Once it became clear that the DSM-5 field trials did not include enough cases to establish the reliability of the proposed criteria, everyone agreed that the criteria should be put in a section on conditions for further study rather the main section of the DSM-5. We close with recommendations about some practical benchmarks that should be met for including criteria for early detection in the classification system.

#### Introduction

When the most recent revision of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) commenced, some researchers and clinicians interested in the prospect of identifying individuals in the early stages of psychosis hoped that diagnostic criteria for a *psychosis risk syndrome* would be placed in the main section of the manual. Despite a transition from a psychosis risk syndrome to a reconceptualized *attenuated psychosis syndrome* during the revision process, the proposed diagnostic criteria were not included in the main section of the DSM-5 but placed in the Conditions for Further Study section.

A primary reason for narrating this history is that the main issues driving the proposal, the clinical importance of being able to identify people in the early stages of psychosis, remains as crucial as ever. Documenting a consensus view of what happened with the DSM-5 proposal could help focus future efforts to develop widely used diagnostic criteria to aid in clinically useful early detection.

Our approach to this project mirrored that taken in four previous narrative histories on the development of the DSMs (Zachar & Kendler, 2014; Zachar, First, & Kendler, 2017; Zachar, Krueger, & Kendler, 2016; Zachar, Regier, & Kendler, 2019). First, we compiled a list of people both inside and outside the revision process who were knowledgeable about the issues and conducted phone interviews with the goal of narrating a history of the attenuated psychosis syndrome proposal. Second, we conducted a review of the published literature on the main issues prior to and during the revision. The interviews and the literature were the basis for composing the first draft. The third and very important feature of the consensus history approach was that we distributed the first draft of the article to all those interviewed and used their feedback to compose a final draft. A list of those interviewed can be found in the Acknowledgements section.

### Prior to the DSM-5 revision: 1990-2007

From the inception of modern psychiatric classification, researchers and clinicians knew that less severe symptoms are correlated with, precede, or follow the severe distress and dysfunction of psychosis. The notion of *formes frustres* (or attenuated forms) of insanity in the early 20<sup>th</sup> century represented one attempt to classify less severe presentations. Labels for attenuated forms include latent schizophrenia, pseudo-neurotic schizophrenia, ambulatory schizophrenia, borderline schizophrenia, and incipient schizophrenia.

© The Author(s), 2020. Published by Cambridge University Press



Despite the long-standing interest in attenuated forms, the impetus for the DSM-5 proposal was a renewed interest in the psychosis prodrome that began in the 1990s about the time DSM-IV was published. In contrast to a premorbid stage, the prodrome refers to the early stages of the actual illness in which there is a change in functioning, but full-blown psychotic symptoms have not yet emerged.

Why the renewed interest in detecting the prodrome? McGlashan and Johannessen (1996) argued that by the time someone makes the transition to psychosis and is diagnosed, significant deterioration in functioning has already occurred, with most of the deterioration taking place in the first year after transition. If interventions could be made earlier, perhaps the progression of the disorder could be slowed and even prevented. If so, negative long-term outcomes might be avoided. Yung and McGorry (1996a) concurred, arguing that minimizing the duration of untreated psychosis, or the period of time from the onset of the disorder to the initiation of treatment, would result in better outcomes.

Work in the 1980s by Ian Falloon (1992); Falloon, Kydd, Coverdale, & Laidlaw (1996) suggested that 'secondary prevention,' or interventions in the early stages of the disorder could succeed in delaying or preventing the onset of psychosis. As McGlashan and Johanssen wrote:

Currently, the most common strategy with early and tentative cases is to 'wait and see' in order to avoid unnecessary treatment and iatrogenic stigmatization of false positive cases. Falloon's study strongly suggests that such caution and delay may be deleterious and actively pathogenic (p. 216).

A critical event occurred in April 1995, when McGlashan and Johannessen sponsored an international conference in Norway on early detection and intervention in schizophrenia. They invited leading researchers from across the world and in 1996 published a series of papers in *Schizophrenia Bulletin* that captured the attention of the research community. Two more special issues on the prodrome followed in 2003 and 2007 (Cannon, Cornblatt, & McGorry, 2007; Cornblatt, Heinssen, Cannon, & Lencz, 2003). In 1998 what became the International Early Psychosis Association (IEPA) was founded. The IEPA current hosts conferences on early intervention biennially.

Afterwards, there was a sizeable increase in published research on the prodrome. The quantity of research annually increased from about 10 articles in 1996 to about 90 articles in 2008, the year that the DSM-5 Psychotic Disorders Work Group first met (Fusar-Poli et al., 2013).

Prior to the first international conference, in 1992 McGorry and his group in Australia set up a program for treating first episode psychosis, but they also encountered patients who were not yet psychotic (McGorry, Edwards, Mihalopoulos, Harrigan, & Jackson, 1996). They began working with the DSM-III-R criteria for the schizophrenia prodrome (which were the same as the symptoms occurring during the residual phase of the illness), but in an initial study found that the criteria lacked predictive validity. In 1993, one of McGorry's students, Alison Yung, completed a review of the previous literature on the prodrome and proposed that they develop new diagnostic criteria, resulting in the description of an at-risk mental state (ARMS) (Yung & McGorry, 1996a). An ARMS is one in which a person is currently experiencing symptoms that commonly precede psychosis, but do not portend its onset with certainty. The semi-structured

interview they developed was then used to select patients for a new clinical service for at-risk youth in 1994 under the direction of Yung (Yung et al., 1996b). The at-risk concept encompasses three subgroups: (1) presentations of attenuated psychotic symptoms, (2) presentations of a recent decline in functioning for someone with a family history of psychosis, and (3) presentations with full-blown but transient psychotic episodes.

About a decade later, informed by their experience working with at-risk youth, Yung et al. (2005) published the semi-structured interview as the *Comprehensive Assessment of At-Risk Mental State* (CAARMS). Aware of the work being done at Yung and McGorry's clinic, Thomas McGlashan with his colleagues at Yale began a similar program for people at risk in the U.S. In an attempt to improve on the CAARMS' assessment of symptoms in the subpsychotic range, they developed a rating scale now called the *Scale of Psychosis-risk Symptoms*. This became the basis for their own semi-structured interview for detecting the schizophrenia prodrome, named the *Structured Interview for Psychosis-risk Syndromes* (Miller et al., 2003; Woods, Walsh, Powers, & McGlashan, 2019). In 2007 Riecher-Rössler et al. (2007) started publishing research on the early detection of psychosis using the *Basel Screening Instrument for Psychosis*.

A different strategy based on the work of Huber and Gross (1989), Huber, Gross, Schüttler, & Linz (1980) is called the basic symptom approach. The basic symptom approach focuses on a cluster of subjectively experienced changes from one's normal functioning. They include being overly literal, repeated intrusion of irrelevant thoughts, and hypersensitivity to sounds. Although subtle, advocates of the basic symptom approach believe that these changes represent the most direct psychological manifestations of the diseases process, with characteristic psychotic symptoms being secondary manifestations (Schultze-Lutter et al., 2016). Basic symptoms are assessed by several instruments developed by Joachim Klosterkötter, Frauke Schultze-Lutter and colleagues, including The Bonn Scale for the Assessment of Basic Symptoms and the Schizophrenia Proneness Instruments (Schultze-Lutter, Ruhrmann, Picker, & Klosterkötter, 2006). This work is associated with The Cologne Early Recognition and Intervention Center established in 1997 (Schultze-Lutter, Picker, Ruhrmann, & Klosterkotter, 2008).

The symptom clusters measured by all of the various instruments described above are often grouped under the umbrella term of ultra-high risk (UHR). An exciting feature of this work was that, previously, the prodrome was identified only retrospectively, after a person became psychotic. The new measures raised the possibility of prospective identification. McGorry, Hickie, Yung, Pantelis, and Jackson (2006) in particular advocated for a staging model which uses different interventions for earlier and later 'stages' of a disease process.

# The DSM-5 psychosis risk proposal and early controversy: 2007

No member of the DSM-5 Psychotic Disorders Workgroup was conducting prodromal/UHR research. In their interviews, Psychotic Disorders Workgroup members Stephan Heckers and Deanna Barch both reported that there was unanimous agreement in the workgroup that mental health professionals were making a diagnosis of schizophrenia only after psychosis manifested, which is far too late in the active diseases process. Researchers and clinicians needed a way to identify people at the beginning of the disease process. The members of the work group who we

922 Peter Zachar *et al.* 

interviewed reported that the chair of the work group, Will Carpenter, felt strongly that psychiatry was failing its patients and advocated including what the workgroup was calling 'the prodrome' in the main section DSM-5, but the majority of the members began the revision thinking it would be better to place the prodrome in the Conditions for Further Study section (aka section III).

Those who advocated for including psychosis risk in the main section were well represented among the advisors to the DSM-5 Psychotic Disorders workgroup. A snapshot of their thinking was articulated by Carpenter (2009) in an editorial in Schizophrenia Bulletin. Carpenter noted that the views expressed in the editorial were his personal views, not those of the workgroup. He also identified Ming Tsuang (workgroup member), and Thomas McGlashan and Scott Woods (advisors) as having informed his view.

According to Carpenter, there was a clear clinical need and also some preliminary evidence that interventions can help, but whether the prodromal stage of psychotic disorders is better thought of as a specific schizophrenia prodrome or a more general psychosis prodrome was an open question. Although progress had been made in identifying participants for research, whether the research criteria could be used reliably in general psychiatric settings needed to be evaluated in field trials.

As issues of concern, Carpenter listed the risk of false positive diagnoses, the use of potentially harmful treatments such as antipsychotic medication, and stigmatization. With respect to false positives, he claimed that no one should be diagnosed unless they are demonstrating clinically significant distress and dysfunction – which suggests that they are also already seeking help. With respect to the initiation of potentially harmful treatments, he argued that presently there is no scientific basis for using antipsychotic medication as a standard of care for treating individuals with only prodromal symptoms. With respect to stigmatization, Carpenter suggested that to name this new diagnostic class 'the prodrome' would not be a good choice. His alternative, based on a suggestion from Heckers, was 'risk syndrome for psychosis.' It would be somewhat analogous to hypertension or abnormal glucose indices – risk syndromes with multiple possible disease outcomes.

Published online in July 2009, the editorial was, in part, a response to an eventful encounter, at the annual meeting of the American Psychiatric Association in May, between Carpenter and Allen Frances, the chair of the DSM-IV Task Force. In that brief encounter, Carpenter told Frances that they were hoping to put a risk syndrome for psychosis in the DSM-5. Carpenter remembers Frances being opposed to the idea and Frances remembers Carpenter not being responsive to the concerns he articulated.

In his interview, Frances offered some insight into his opposition to adding a psychosis risk syndrome to the DSM. In the early 1970s, Frances completed his residency at the New York State Psychiatric Institute (NYSPI). Under the director, Phillip Polatin, he was taught to diagnose patients with pseudoneurotic schizophrenia, prescribe medication, and keep them in the hospital for up to a year to prevent the development of psychosis. A few years after Frances' residency ended, Otto Kernberg took over as the NYSPI Clinical Director, at which time these same patients were re-diagnosed as borderline personality disorder, for which intensive psychotherapy was recommended. Two years later Donald Klein became the NYSPI Clinical Director and the diagnosis switched again to hysteroid dysphoria (a type of atypical depression treated with MAOI anti-depressants).

Frances was suspicious of the changing diagnostic fads and treatment recommendations that had been applied to this class of patients over a short 4-year period and so was alarmed about the plans for the DSM-5. In Frances' view, the patient's problems were real, but diagnostic constructs are utilitarian conventions used to suggest appropriate treatment strategies. He had seen how the pharmaceutical industry deployed DSM-IV diagnoses such as bipolar II disorder to expand the market for drugs to new groups of patients, and anticipated the same thing occurring with 'psychosis risk.'

In his view, those advocating for the risk syndrome needed to worry more about harmful unintended consequences. As a low base-rate phenomenon, the prodrome could be expected to incur a high false positive rate – meaning that anti-psychotic medication could be prescribed to youth who were not in fact prodromal. Alison Yung agreed with these arguments but in her interview stated that they were more pertinent to the U.S. where antipsychotics are more liberally prescribed.

The DSM-5 revision process was designed to be driven by the workgroups who had a great deal of latitude to develop proposals with minimal direction from the leadership. The workgroups were encouraged to not be bound by the past and to propose new and exciting ideas (Zachar et al., 2019). Carpenter was clearly excited about the possibilities. Looking back, we can see that even though he was the chair of the workgroup, he was at that time in the minority with respect to his views about the advisability of adding a psychosis risk syndrome to DSM-5. As articulated in the editorial, he recognized the problems but hoped that they could be worked out.

# During the DSM-5 revision – from psychosis risk to attenuated psychosis syndrome: 2008–2010

The first draft of the criteria for the DSM-5 was made public on the 'DSM-5: The Future of Psychiatric Diagnosis' web site (http://www. dsm5.org) in February 2010, including a proposal for a psychosis risk syndrome (DSM-5 Psychosis Work Group, 2010). For Frances, although the psychosis risk syndrome was the most alarming DSM-5 proposal, it only affected a small number of people. In contrast, other proposals to add subthreshold presentations to DSM-5 would affect many more people. In a Psychiatric Times essay, Frances (2009) grouped the psychosis risk criteria with two other subthreshold conditions: minor depression and mild cognitive disorder. By linking these proposals together and writing about the shared risks of false positive diagnoses, Frances called the psychosis risk proposal to the attention of a larger audience. He wrote this essay for the print edition of the paper, not even considering that it would also be published online in a form that could be easily forwarded to others. The online version took off - and thus began Frances' widely followed critique of the DSM-5 revision.

Much of the early discussion about the proposal among the UHR research community occurred at debates during conferences. Cheryl Corcoran and Alison Yung reported that the opposing sides met and debated several times – and that the debates were conducted in a congenial manner.

People also articulated their views in the special issues of the journals *Schizophrenia Research* and *Psychosis*, both posted online in April 2010. Let us now summarize some (not all) competing perspectives on the proposal.

### Competing arguments

Morrison, Byrne, and Bentall (2010) addressed the potential for false positives, which could lead to the harmful use of

antipsychotics with those not at risk for psychosis. For instance, a recent estimate of the 3-year rate of the psychosis onset for those considered at risk across studies is 23%, making the false positive rate 77% (Salazar de Pablo, Catalan, & Fusar-Poli, forthcoming). Yung, Nelson, Thompson, and Wood (2010a) and Ross (2010) argued that general practitioners could interpret psychosis risk as a quasi-schizophrenia diagnosis and use it as an off label indication to prevent the development of full-blown schizophrenia in at-risk individuals. According to Corcoran, First, and Cornblatt (2010), fear of malpractice liability related to not aggressively treating a person at risk for schizophrenia may motivate practitioners to prescribe anti-psychotics for those diagnosed with psychosis risk syndrome.

Woods, Walsh, Saksa, and McGlashan (2010b) responded by re-asserting Carpenter's (2009) point that the concern about false positives leading to overmedicating was misplaced because the evidence for the efficacy of antipsychotics with this group was so limited. Psychotherapeutic interventions are more appropriate for the risk stage. The danger of inappropriate treatment may even be reduced because professionals could be better educated about the appropriate treatments for these kinds of symptoms. Woods, Carlson, and McGlashn (2010a) also claimed that when using the DSM-IV, many of those at risk for psychosis were being diagnosed with psychotic disorder NOS, which is a more likely target for antipsychotic medication than would be a risk syndrome that was defined by the absence of full-blown psychotic symptoms. As Woods, Calrson, and McGlashan (2010a) argued, the DSM-5 proposal was better than the options available with the DSM-IV.

McGorry (2010) expanded on the staging model by proposing an earlier stage called the *common risk syndrome* which is pluripotential, meaning it is not yet fixed as to the type of end-stage disorder it will eventually evolve into (i.e. a psychotic or a non-psychotic syndrome). A psychosis risk syndrome would be a stage in between the earlier pluripotential stage and the development of a full-blown psychotic disorder. McGorry acknowledged the perspective of those who would set a high diagnostic threshold in order to avoid false positive diagnoses, but argued instead that the threshold should be set lower. Rather than waiting until one sees the first signs of schizophrenic or bipolar pathology, the threshold for care should be set wherever the benefits of an intervention outweigh the risks – even for problems that are self-limiting.

Another issue of concern was the risk of social stigma and self-stigma, especially if a negative label is imposed on young people who are still developing their identities (Corcoran et al., 2010; Larkin & Marshall, 2010; Yang, Wonpat-Borja, Opler, & Corcoran, 2010). In response, Woods, Walsh, Saksa, and McGlashan stated that stigma can be sensitively managed by educating patients and families that this is not a diagnosis of psychosis, but of distressing symptoms that indicate risk. Woods *et al.* (2010b) also argued that if someone is at risk and converts to chronic psychosis, they would potentially incur lifelong stigma which could potentially have been prevented by the early interventions that the diagnosis would initiate.

An additional area of concern was that the diagnostic criteria may be less predictive than they looked like when the UHR research program began. In fact, the conversion rate from being at risk of developing psychosis had significantly declined (Salazar de Pablo et al., forthcoming). In one of their initial reports of this change, Yung et al. (2007) stated that the conversion rate may have declined because clinical interventions delayed

or prevented conversion. Sampling issues may also have played a role. When the Australian research program began, those diagnosed as UHR were referred by mental health practitioners who already suspected that they may be prodromal, but later on, the UHR research criteria were applied to a much larger sample drawn from the general psychiatric population, thus likely raising the false positive rate.

A final concern about the proposal turned on disagreements about viewing psychotic disorders as diagnostic entities  $\nu$ . viewing them in terms of a broader psychosis spectrum. Kaymaz and van Os (2010) claimed that if schizophrenia and bipolar disorder are not valid entities in the first place, there cannot be syndrome that represents risk for them. Indeed, for those who are actually at risk, the most appropriate diagnosis is already available – psychotic disorder NOS – the purpose of which is to describe the early stages of psychotic disorder.

#### From at-risk to current clinical need

In her interview, Alison Yung reported being alarmed when Scott Woods mailed her the proposed DSM-5 criteria for psychosis risk syndrome. Indeed most of the concerns people had about diagnosing a psychosis risk syndrome were articulated in the 1993 literature review that led to the development of the ARMS concept (Yung & McGorry, 1996a). Yung voiced her opposition in the early debates at conferences and research meetings beginning in 2009. In the 2010 special issue in *Schizophrenia Research*, she and her colleagues opined that it would be premature to include psychosis risk syndrome in the DSM-5 because current knowledge about its validity and reliability contained too many gaps (Yung, Nelson, Thompson, & Wood, 2010b). Even when the diagnostic class was narrowed by the requirement that those diagnosed were already help-seeking, too many of them will not convert to psychosis to consider it a prodrome.

Ruhrmann, Schultze-Lutter, and Klosterkötter (2010) argued that the cluster of symptoms identified by the at-risk criteria should not be thought of as a risk syndrome at all but as an independent disorder in its own right on the psychosis spectrum. Some whose symptoms meet at-risk criteria will develop more severe disorders, but many will not. Indeed, the focus of treatment should not be on potential future conversion, but on improvement of current symptoms. Ruhrmann and colleagues even proposed dropping the impairment criterion to encourage interventions as soon as symptoms become manifest. The people classified as at-risk have a collection of symptoms that are not captured by any other DSM-IV construct and if they lack co-morbid symptoms such as depression and anxiety, they will fall through the cracks of current healthcare systems. To say that they have a psychotic disorder NOS, or ADHD, or a mood disorder, or an anxiety disorder or oppositional defiant disorder would be inaccurate and clinicians need a better option. Echoing this view, in her interview Cheryl Corcoran observed that the content of symptoms such as compulsivity are very different with attenuated psychosis presentations than they are with typical obsessive-compulsive disorder.

In his interview, Will Carpenter reported that when he first heard Schultze-Lutter argue that the UHR symptoms themselves represent a valid disorder, he had an 'aha moment' because it eliminated the false positive problem which had deeply concerned him. Thus, psychosis risk syndrome became attenuated psychosis syndrome. The analogy for the risk syndrome was hypertension, which was problematic because hypertension is often

924 Peter Zachar *et al.* 

asymptomatic. For attenuated psychosis syndrome, the analogy (used earlier by Yung and McGorry) was chest pain – a symptom that is distressing, leads to help-seeking, and can be benign and self-limiting or be an early sign of a variety of possible disorders. Woods et al. (2010b) stated that the new naming convention was analogous to calling a 'dementia risk syndrome' *mild cognitive impairment*, a diagnosis which was added to the main section of the DSM-5 (as mild neurocognitive disorder).

## Awaiting the field trial results: 2011-spring 2012

Reflecting a cooperative spirit in the UHR research community overall, the participants in the debate agreed that if the diagnosis could not be reliably made, it would be placed in the Conditions for Further Study section. While waiting for the field trial results, various stakeholders published articles that outlined the main points on different sides of the debate, for instance, Carpenter and van Os (2011) in American Journal of Psychiatry, Fusar-Poli and Yung (2012) in The Lancet, and Tandon and Carpenter (2012) in Schizophrenia Bulletin. Generally, those who favored a psychosis spectrum approach were less inclined to place attenuated psychosis syndrome in the main section of the manual.

Although the workgroup made the conceptual shift from at-risk to attenuated symptoms, they did not make any substantive changes to the criteria and Allen Frances continued to publicly raise concerns about adding this condition to DSM-5. Frances (2011) had a small victory when he reported that Patrick McGorry had withdrawn his support for including attenuated psychosis syndrome in DSM-5.

The most enthusiastic advocate for the proposal was Scott Woods in his role as an advisor to the workgroup. In his interview, Woods noted that he contacted Darrel Regier soon after Regier was named vice chair of the DSM-5 Task Force to advocate for a psychosis risk syndrome. Woods and McGlashan wrote the first draft of the criteria. They chose only the attenuated symptoms from the UHR concept because they were the most prevalent.

The most vociferous opponent of the proposal within the workgroup was Jim van Os. A proponent of the psychosis spectrum notion, van Os does not believe that schizophrenia is a valid nosological entity. In his interview, van Os said that there is even less evidence in support of attenuated psychosis syndrome. He supports efforts at early intervention but argues that it would be a mistake to take a group of people who are beginning to experience psychotic symptoms, anoint them a diagnostic class, and then look for that class in the general population. According to van Os and Murray (2013), hallucinations and delusions are transdiagnostic symptoms that occur in about 25% of those with non-psychotic mental disorders. The base rate of the 'prodrome' is so low that most diagnosed cases will be false positives, largely composed of people with a depressive disorder, anxiety disorder, and substance abuse issues who are also experiencing some incidental psychotic symptoms. In van Os' view, the interventions that would be most useful would be at the public health level, - not at the level of individual treatment.

The result of the field trials became available in early 2012. Unfortunately for the advocates of adding attenuated psychosis syndrome to the DSM-5, an inadequate number of diagnosed cases were evaluated as part of the field trial. While the diagnostic reliability of those cases appeared to be good, because of the small

number of cases assessed, it was not possible to determine diagnostic reliability with any kind of precision.

From the beginning of the DSM revision, demonstrating some degree of reliability was a necessary condition for including the diagnosis in the main section of the manual. When the workgroup met in April to decide the issue, the inconclusive field trial results circumvented any final debate about where the criteria should be placed because the majority of members favored putting it in the Conditions for Further Study section at that point (Tsuang et al., 2013). Carpenter was ill and could not attend that meeting. In an interview conducted shortly after the decision was announced, he reported that had he been there, he would have pushed for obtaining more data on reliability before a final decision was made (Maxmen, 2010). As he told us, the debate could have been more intense if reliability had been established as it would have meant that one of the significant roadblocks to its inclusion has been lifted, but without the evidence, there was never any chance for acrimony to develop within the group.

In his interview Rajiv Tandon summarized why the workgroup believed it was important that the diagnostic criteria be in the DSM-5, even if not in the main section of the manual. After someone converts to psychosis, it is hard to reverse changes that may have already occurred – especially if treatment is delayed, so earlier interventions are necessary. The prodromal period has an early and a later phase, with the attenuated psychosis symptoms being more common in the late phase, but even if those who can be diagnosed do not convert to psychosis, they are still experiencing significant distress and dysfunction (Tandon, Shah, Keshavan, & Tandon, 2012).

# After the revision: 2013 and beyond

Being able to identify people at risk for psychosis who can be helped with early interventions is an important goal, but debates about the chances for success continue (Ajnakina, David, & Murray, 2019; Moritz, Gawęda, Heinz, & Gallinat, 2019; van Os & Guloksuz, 2017; Yung et al., 2019). The problem is that the signs and symptoms that appear to be features of an emerging psychosis are not specific to psychosis and thus produce false positives. Whether biomarkers related to underlying etiology and pathophysiology can provide the required diagnostic specificity to reduce false positives have not yet been determined.

Subsequently, researchers have introduced the idea of attenuated psychosis syndrome as a *placeholder diagnosis* (Carpenter & Schiffman, 2015; Fusar-Poli, Carpenter, Woods, & McGlashan, 2014). As Barch said in her interview, part of the idea is that people with this diagnosis are in transit to something else. With placeholder presentations, early developing symptoms are less severe and may be heterogeneous, drawn from across the domain of psychopathology. As symptoms become more severe, they can start to become causally linked together syndromally, but are still *pluripotent* in McGorry's sense. Some of the presentations will continue to increase in severity and transition to recognized syndromes, including psychosis.

The concept of a pluripotent placeholder diagnosis is a potentially useful addition to our understanding of developmental psychopathology. In the minds of those who opposed placing attenuated psychosis syndrome in the main section of the manual, however, the current clinical need associated with the placeholder diagnosis was not sufficiently demarcated from a more specific psychosis risk diagnosis.

Research on early detection of psychosis is continuing apace and does not seem to have been hampered by the diagnostic criteria not being placed in the main section of the manual. Addition of risk criteria for psychosis to the main section of manual therefore, should probably not be based on promissory reasons, but contingent on empirically demonstrated improvements in treatment specificity that are sensitive to different positions on the severity continuum, in combination with the diagnostic validity indicators that are required for the criteria to be placed into the main section of the DSM.

**Acknowledgements.** This article greatly benefited from interviews and feedback from Deanna Barch, Will Carpenter, Tyrone Cannon, Cheryl Corcoran, Allen Frances, Stephen Heckers, Paolo Fusar-Poli, Rajiv Tandon, Jim van Os, Scott Woods, Alison Yung, and three anonymous reviewers

Conflict of interest. None.

#### References

- Ajnakina, O., David, A. S., & Murray, R. M. (2019). 'At risk mental state' clinics for psychosis an idea whose time has come and gone!. *Psychological Medicine*, 49(4), 529–534.
- Cannon, T. D., Cornblatt, B., & McGorry, P. (2007). Editor's introduction: The empirical status of the ultra high-risk (prodromal) research paradigm. *Schizophrenia Bulletin*, 33(3), 661–664.
- Carpenter, W. T. (2009). Anticipating DSM-V: Should psychosis risk become a diagnostic class? Schizophrenia Bulletin, 35(5), 841–843.
- Carpenter, W. T., & Schiffman, J. (2015). Diagnostic concepts in the context of clinical high risk/attenuated psychosis syndrome. Schizophrenia Bulletin, 41 (5), 1001–1002.
- Carpenter, W. T., & van Os, J. (2011). Should attenuated psychosis syndrome be a DSM-5 diagnosis? *American Journal of Psychiatry*, 168(5), 460–463.
- Corcoran, C. M., First, M. B., & Cornblatt, B. (2010). The psychosis risk syndrome and its proposed inclusion in the DSM-V: A risk-benefit analysis. Schizophrenia Research, 120(1), 16–22.
- Cornblatt, B. A., Heinssen, R. K., Cannon, T. D., & Lencz, T. (2003). Editors' introduction: New frontiers in prodromal research. *Schizophrenia Bulletin*, 29(4), 621–624.
- DSM-5 Psychosis Work Group. (2010). Psychosis risk syndrome. Retrieved from https://web.archive.org/web/20100215023016/; http://www.dsm5.org/ProposedRevisions/Pages/proposedrevision.aspx?rid=412.
- Falloon, I. R. H. (1992). Early intervention for first episodes of schizophrenia: A preliminary exploration. *Psychiatry*, 55(1), 4–15.
- Falloon, I. R. H., Kydd, R. R., Coverdale, J. H., & Laidlaw, T. M. (1996). Early detection and intervention for initial episodes of schizophrenia. Schizophrenia Bulletin, 22(2), 271–282.
- Frances, A. (2009). A warning sign on the road to DSM-V: Beware of its unintended consequences. *Psychiatric Times*. Retrieved from http://www.psychiatrictimes.com/display/article/10168/1425378.
- Frances, A. (2011). Seven questions for Professor Patrick McGorry. *Psychiatric Times*. Retrieved from https://www.psychiatrictimes.com/couch-crisis/seven-questions-professor-patrick-mcgorry.
- Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rössler, A., Schultze-Lutter, F., ... Yung, A. (2013). The psychosis high-risk state: A comprehensive state-of-the-art review. *JAMA Psychiatry*, 70(1), 107–120.
- Fusar-Poli, P., Carpenter, W. T., Woods, S. W., & McGlashan, T. H. (2014). Attenuated psychosis syndrome: Ready for DSM-51? Annual Review of Clinical Psychology, 10, 155–192.
- Fusar-Poli, P., & Yung, A. R. (2012). Should attenuated psychosis syndrome by included in DSM-5. The Lancet, 379, 591–592.
- Huber, G., & Gross, G. (1989). The concept of basic symptoms in schizophrenic and schizoaffective psychoses. *Recenti Progressi in Medicina*, 80 (12), 646–652.
- Huber, G., Gross, G., Schüttler, R., & Linz, M. (1980). Longitudinal studies of schizophrenic patients. Schizophrenia Bulletin, 6(4), 592–605.

Kaymaz, N., & van Os, J. (2010). DSM-5 and the 'Psychosis Risk Syndrome': Babylonic confusion. Psychosis: Psychological, Social and Integrative Approaches, 2(2), 100–103.

- Larkin, W., & Marshall, M. (2010). DSM-5 and the 'psychosis risk syndrome': No different than any other diagnostic test. *Psychosis: Psychological, Social and Integrative Approaches*, 2(3), 191–195.
- Maxmen, A. (2010). Psychosis risk syndrome excluded from DSM-5. *Nature News*.
- McGlashan, T. H., & Johannessen, J. O. (1996). Early detection and intervention with schizophrenia: Rationale. Schizophrenia Bulletin, 22(2), 201–222.
- McGorry, P. D. (2010). Risk syndromes, clinical staging and DSM V: New diagnostic infrastructure for early intervention in psychiatry. Schizophrenia Research, 120(1), 49–53.
- McGorry, P. D., Edwards, J., Mihalopoulos, C., Harrigan, S. M., & Jackson, H. J. (1996). EPPIC: An evolving system of early detection and optimal management. Schizophrenia Bulletin, 22(2), 305–326.
- McGorry, P. D., Hickie, I. B., Yung, A. R., Pantelis, C., & Jackson, H. J. (2006). Clinical staging of psychiatric disorders: A heuristic framework for choosing earlier, safer and more effective interventions. Australian & New Zealand Journal of Psychiatry, 40(8), 616–622.
- Miller, T. J., McGlashan, T. H., Rosen, J. L., Cadenhead, K., Ventura, J., McFarlane, W., ... Woods, S. W. (2003). Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: Predictive validity, interrater reliability, and training to reliability. Schizophrenia Bulletin, 29(4), 703–715.
- Moritz, S., Gawęda, Ł, Heinz, A., & Gallinat, J. (2019). Four reasons why early detection centers for psychosis should be renamed and their treatment targets reconsidered: We should not catastrophize a future we can neither reliably predict nor change. *Psychological Medicine*, 49(13), 2134–2140.
- Morrison, A. P., Byrne, R., & Bentall, R. P. (2010). DSM-5 and the 'Psychosis Risk Syndrome': Whose best interests would it serve? *Psychosis*, *2*(2), 96–99.
- Riecher-Rössler, A., Gschwandtner, U., Aston, J., Borgwardt, S., Drewe, M., Fuhr, P., ... Stieglitz, R. D. (2007). The basel early-detection-of-psychosis (FEPSY)-study – design and preliminary results. *Acta Psychiatrica Scandinavica*, 115(2), 114–125.
- Ross, C. A. (2010). DSM-5 and the 'Psychosis Risk Syndrome': Eight reasons to reject it. *Psychosis: Psychological. Social and Integrative Approaches*, 2(2), 107–110.
- Ruhrmann, S., Schultze-Lutter, F., & Klosterkötter, J. (2010). Probably at-risk, but certainly ill – Advocating the introduction of a psychosis spectrum disorder in DSM-V. Schizophrenia Research, 120(1), 23–37.
- Salazar de Pablo, G., Catalan, A., & Fusar-Poli, P. (forthcoming). DSM-5 attenuated psychosis syndrome: A systematic review and meta-analysis of the evidence. *JAMA Psychiatry*.
- Schultze-Lutter, F., Debbané, M., Theodoridou, A., Wood, S. J., Raballo, A., Michel, C., ... Uhlhaas, P. J. (2016). Revisiting the basic symptom concept: Toward translating risk symptoms for psychosis into neurobiological targets. Frontiers in Psychiatry, 7, 9–9.
- Schultze-Lutter, F., Picker, H., Ruhrmann, S., & Klosterkotter, J. (2008). The cologne early recognition and intervention center for mental crises (FETZ). evaluation of service use. *Medizinische Klinik*, 103(2), 81–89.
- Schultze-Lutter, F., Ruhrmann, S., Picker, H., & Klosterkötter, J. (2006). WC1C Development and evaluation of the schizophrenia proneness instrument, adult version (SPI-A). Schizophrenia Research, 86, S4–S5.
- Tandon, R., & Carpenter, W. T., Jr. (2012). DSM-5 status of psychotic disorders: 1 year prepublication. Schizophrenia Bulletin, 38(3), 369–370.
- Tandon, N., Shah, J., Keshavan, M. S., & Tandon, R. (2012). Attenuated psychosis and the schizophrenia prodrome: Current status of risk identification and psychosis prevention. *Neuropsychiatry (London)*, 2(4), 345– 353.
- Tsuang, M. T., Van Os, J., Tandon, R., Barch, D. M., Bustillo, J., Gaebel, W., ... Carpenter, W. (2013). Attenuated psychosis syndrome in DSM-5. *Schizophrenia Research*, 150(1), 31–35.
- van Os, J., & Guloksuz, S. (2017). A critique of the "ultra-high risk" and "transition" paradigm. *World Psychiatry*, 16(2), 200–206.
- van Os, J., & Murray, R. M. (2013). Can we identify and treat "schizophrenia light" to prevent true psychotic illness? *Bmj*, 346, f304.

926 Peter Zachar *et al.* 

Woods, S. W., Carlson, J. P., & McGlashan, T. H. (2010a). DSM-5 and the 'psychosis risk syndrome': The DSM-5 proposal is better than DSM-IV. *Psychosis: Psychological, Social and Integrative Approaches*, 2(3), 187–198.

- Woods, S. W., Walsh, B. C., Powers III, A. R., & McGlashan, T. H. (2019). Reliability, validity, epidemiology, and cultural variation of the Structured Interview for Psychosis Risk Syndrome (SIPS) and the Scale of Psychosis Risk Symptoms (SOPS). In L. Huijun, D. I. Shapiro & L. J. Seidman (Eds.), *Handbook of attenuated psychosis syndrome across cultures* (pp. 85–113). Cham, Switzerland: Springer Nature.
- Woods, S. W., Walsh, B. C., Saksa, J. R., & McGlashan, T. H. (2010b). The case for including attenuated psychotic symptoms syndrome in DSM-5 as a psychosis risk syndrome. Schizophrenia Research, 123(2-3), 199-207.
- Yang, L. H., Wonpat-Borja, A. J., Opler, M. G., & Corcoran, C. M. (2010). Potential stigma associated with inclusion of the psychosis risk syndrome in the DSM-V: An empirical question. Schizophrenia Research, 120(1), 42–48.
- Yung, A. R., & McGorry, P. D. (1996a). The prodromal phase of first-episode psychosis: Past and current conceptualizations. *Schizophrenia Bulletin*, 22 (2), 353–370.
- Yung, A. R., McGorry, P. D., McFarlane, C. A., Jackson, H. J., Patton, G. C., & Rakkar, A. (1996b). Monitoring and care of young people at incipient risk of psychosis. *Schizophrenia Bulletin*, 22(2), 283–303.
- Yung, A. R., Nelson, B., Thompson, A. D., & Wood, S. J. (2010a). The psychosis threshold in ultra high risk (prodromal) research: Is it valid? Schizophrenia Research, 120(1), 1–6.

- Yung, A. R., Nelson, B., Thompson, A. D., & Wood, S. J. (2010b). Should a "risk syndrome for psychosis" be included in the DSMV? Schizophrenia Research, 120(1), 7–15.
- Yung, A. R., Wood, S. J., Malla, A., Nelson, B., McGorry, P., & Shah, J. (2019) The reality of at risk mental state services: A response to recent criticisms. *Psychological Medicine*, 1–7. doi: 10.1017/S003329171900299X [Epub ahead of print].
- Yung, A. R., Yuen, H. P., Berger, G., Francey, S., Hung, T.-C., Nelson, B., ... McGorry, P. (2007). Declining transition rate in ultra high risk (prodromal) services: Dilution or reduction of risk? *Schizophrenia Bulletin*, 33(3), 673–681
- Yung, A. R., Yuen, H. P., McGorry, P. D., Phillips, L. J., Kelly, D., Dell'Olio, M., ... Buckby, J. (2005). Mapping the onset of psychosis: The comprehensive assessment of at-risk mental states. Australian and New Zealand Journal of Psychiatry, 39(11–12), 964–971.
- Zachar, P., First, M. B., & Kendler, K. S. (2017). The bereavement exclusion debate in the DSM-5: A history. Clinical Psychological Science, 5(5), 890–906.
- Zachar, P., & Kendler, K. S. (2014). A diagnostic and statistical manual of mental disorders history of premenstrual dysphoric disorder. *Journal of Nervous & Mental Disease*, 202(4), 346–352.
- Zachar, P., Krueger, R. F., & Kendler, K. S. (2016). Personality disorder in the DSM-5: An oral history. *Psychological Medicine*, 46(1), 1–10.
- Zachar, P., Regier, D. A., & Kendler, K. S. (2019). The aspirations for a paradigm shift in DSM-5: An oral history. *Journal of Nervous & Mental Disease*, 202(4), 346–352.