Identification and Characterization of Prodromal Risk Syndromes in Young Adolescents in the Community: A Population-Based Clinical Interview Study

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While a great deal of research has been conducted on prodromal risk syndromes in relation to help-seeking individuals who present to the clinic, there is a lack of research on prodromal risk syndromes in the general population. The current study aimed first to establish whether prodromal risk syndromes could be detected in non-help-seeking community-based adolescents and secondly to characterize this group in terms of Axis-1 psychopathology and general functioning. We conducted in-depth clinical interviews with a population sample of 212 school-going adolescents in order to assess for prodromal risk syndromes, Axis-1 psychopathology, and global (social/occupational) functioning. Between 0.9% and 8% of the community sample met criteria for a risk syndrome, depending on varying disability criteria. The risk syndrome group had a higher prevalence of co-occurring nonpsychotic Axis-1 psychiatric disorders (OR = 4.77, 95% CI = 1.81–12.52; P < .01) and poorer global functioning (F = 24.5, df = 1, P < .0001) compared with controls. Individuals in the community who fulfill criteria for prodromal risk syndromes demonstrate strong similarities with clinically presenting risk syndrome patients not just in terms of psychotic symptom criteria but also in terms of co-occurring psychopathology and global functioning.

Key words: at risk mental states/epidemiology/ultra-high risk/clinical high risk

Introduction

The onset of psychosis is usually preceded by a prodromal period prior to full-blown illness. Intervention at this early stage offers the hope of disease prevention. The concept of prodromal intervention as currently conceived emerged from research at the University of Melbourne in the 1990s. Yung, McGorry and colleagues developed a set of “ultra high risk” (UHR) criteria for help-seeking individuals who presented to the clinic, which they demonstrated could predict a very high transition rate to psychosis (approximately 40%) over a 12-month period. Individuals meeting UHR criteria are said to have an “at risk mental state” (ARMS). These criteria were used to formulate the Comprehensive Assessment of At Risk Mental States (CAARMS), a clinical instrument for the assessment of ARMS based upon defined criteria involving (1) attenuated psychotic symptoms, (2) frank psychotic symptoms of brief duration, or (3) genetic risk combined with functional deterioration.1–3 Researchers at Yale University developed the Structured Interview for Prodromal Syndromes (SIPS) with a similar goal and demonstrated that, in line with Australian findings, individuals who met criteria for these “prodromal risk syndromes” were at very high risk for psychosis.4–6 In Europe, a set of “basic symptoms,” such as problems in dividing attention, thought blockages and disturbances in receptive and expressive language, have been used to successfully predict high risk for psychosis, either alone or in combination with UHR criteria.7–10 The largest study to date examining transition from prodromal risk syndrome to psychosis has been the collaborative North American Prodrome Longitudinal Study, which reported that up to 40% of individuals who met risk syndrome criteria converted to psychosis over 2.5 years.6,11

Such has been the impact of risk syndrome research that a new diagnosis—“Attenuated Psychosis Syndrome”—has been proposed for the next version of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) (see table 1). The goal of a new diagnosis is to provide a diagnostic category that facilitates identification, treatment, and research. This proposal, however, has sparked a great deal of debate...
among leading researchers in the field. One important issue is the lack of population studies—while a great deal of research has been conducted on psychotic symptoms in the general population to date, population researchers have not conducted the in-depth clinical assessments that have characterized the work of researchers at UHR clinics. On the other hand, UHR researchers have, to date, focused almost exclusively on help-seeking (ie, self-presenting) individuals, without venturing into the community. A more complete understanding of prodromal risk syndromes requires that the detailed work carried out in UHR clinics be combined with a community-based epidemiological approach. One preliminary report that has begun to address this issue involved telephone SIPS interviews with a sample of 16–35 year olds from the general population. The researchers reported that just one participant fulfilled criteria for a prodromal risk syndrome. However, this study was limited by the small sample size \( n = 58 \) and the lack of information on the validity of telephone interviews compared with face-to-face assessment. In order to (1) test whether prodromal risk syndromes at risk mental states could be identified among young adolescents in the general population and (2) characterize these individuals in terms of psychopathology and general functioning, we conducted in-depth assessments of psychotic symptomatology among 212 school-going adolescents aged 11–13 years.

Methods

Recruitment

A sample of 212 adolescents from the general population aged 11–13 years took part in the current study. They were drawn from a sample of 1131 pupils from 16 schools in Counties Dublin and Kildare, Ireland, who took part in a survey of psychopathology, using the Strengths and Difficulties Questionnaire (SDQ). which is a validated measure of global functioning adapted from the Irish Social Class Scale from the Irish Central Statistics Office. We divided the sample into 2 major groups according to social class: the first group contained SES groups 1 and 2 (professional/managerial) and the second group contained SES groups 3 to 7 (non-manual skilled; skilled manual; semiskilled manual; unskilled manual; and unemployed). The SES of participants approximated national figures: 34.6% of participants were categorized as SES groups 1–2 (compared with 32.1% of the national population) and 65.4% as SES groups 3–7 (compared with 67.9% of the national population). Participants were also representative of the overall national ethnic profile from the 2006 national census, including 88.9% Irish-born participants (compared with 90.3% of 0 to 14 year olds nationally). In addition, adolescents who attended for interview did not differ from the larger surveyed sample in the proportion of abnormal or borderline-abnormal scores on the SDQ measure of general psychopathology \( \chi^2 = 1.22 \text{ (df} = 1\text{, } P = .27) \) or on their score on the APSS measure of psychotic symptoms (interviewed group mean = 1.8 [SE = 0.12]; noninterviewed group mean = 1.9 [SE = 0.19]; \( t = 0.26, df = 1130, P = .79 \)).

Interview Assessment

The principal interview instrument used to assess psychopathology in this study was the Schedule for Affective Disorders and Schizophrenia for School-aged Children, Present and Lifetime Versions (K-SADS). The K-SADS is a well-validated semistructured diagnostic interview for the assessment of Axis-1 psychiatric disorders in children and adolescents. Adolescents and parents were interviewed separately, both answering the same questions about the adolescent. The K-SADS includes a psychosis section where participants are assessed for psychotic symptomatology. This section of the interview was altered to include questions covering the 5 positive symptom sections of the SIPS (P1–P5) in order to provide additional information necessary to diagnose prodromal risk syndromes. Questions were also added about the onset and frequency of and attributions for symptoms, as well as questions about whether or not symptoms caused distress to the interviewee. The K-SADS interview finished with an assessment of the young person’s functioning using the Children’s Global Assessment Scale, which is a validated measure of global functioning adapted from the Global Assessment Scale for adults. Interviews were conducted by 2 psychiatrists and 4 psychologists with extensive training in the assessment of psychotic symptomatology and involved assessments of between 2 and larger surveyed sample. A frequency weight was applied in STATA for the statistical analyses to account for enrichment at a rate of 2:1 in the first 20% of interviewed participants.

Socioeconomic status (SES) of each study participant was determined using parental occupation assessed according to the Irish Social Class Scale.
Prodromal Risk Syndromes in the Community

Ethical approval for this study was granted by the Beaumont Hospital Medical Ethics Committee.

Results

Prodromal Risk Syndromes/At Risk Mental States
A total of 22.6% (n = 53) of the sample reported psychotic symptoms, primarily auditory hallucinations. Applying SIPS criteria, 8.1% (n = 19) of the total sample met criteria for a current prodromal risk syndrome. Specifically, 7.7% met criteria for an APSP and 3.5% met criteria for a BIPS. One additional participant met criteria for APSP in remission. Three participants had a first-degree relative with a psychotic disorder but none of these participants had experienced a significant decline in functioning within the past year and so no participant met criteria for GRD. There was no significant effect of age or SES on risk syndrome status. However, significantly more males than females fulfilled criteria for a risk syndrome ($\chi^2 = 4.17, P = .04$).

Applying the CAARMS criteria, 7.7% of the sample met criteria for an at risk mental state without applying a criterion of a 30% decrease in functioning in the last year. Just 0.9% (n = 2) of participants would have met criteria for an at risk mental state, however, were a 30% decrease in functioning used as an obligate criterion (using the Children’s Global Assessment Scale as the measure of functioning).

Attenuated Psychosis Syndrome
The proposed DSM-V diagnosis of attenuated psychosis syndrome (see table 1) differs from APSP in Criterion D, that is, the requirement that, in addition to attenuated psychotic symptoms, there is also distress and disability. The majority of adolescents who fulfilled criteria for APSP, in fact, did report being distressed by their symptoms (89%). Similarly, in terms of disability, adolescents who fulfilled criteria for APSP also demonstrated significantly impaired functioning compared with controls, as measured by the Children’s Global Assessment Scale ($F = 24.5, df = 1, P < .0001$).

Prodromal Risk Syndromes and Psychiatric Comorbidity

A total of 63% of the adolescents who met criteria for a prodromal risk syndrome also met criteria for at least one lifetime Axis-I diagnosis (OR = 4.77, 95% CI = 1.81–12.52; $P < .01$) (see table 2). The most common lifetime Axis I diagnosis was major depressive disorder (MDD) (26%). Thirty seven percent of adolescents with risk syndromes met criteria for a depressive disorder, 32% met criteria for an anxiety disorder, and 21% met criteria for a behavioral disorder.

Discussion
In a general population sample of 212 school-going adolescents, we found that up to 8% fulfilled criteria for...
diagnosis of a current prodromal risk syndrome. The findings of the current work suggest that there are many prospectively identifiable individuals with risk syndromes in the community who have not presented to clinical services. What proportion of these individuals would ultimately present to services is unknown. However, while the overwhelming majority of cases of new onset psychosis have been established to be preceded by a prodromal period, only a minority of the population-wide incidence of psychosis emerge in patients from prodrome risk syndrome clinics, which suggests that many such individuals will not clinically present prior to illness onset.

APSP, as described, differs from the proposed DSM-V diagnosis of attenuated psychosis syndrome in Criterion D ("distress/disability/treatment seeking," see Table 1). However, the majority of adolescents meeting criteria for APSP reported distress as a result of their symptoms, and this group demonstrated significantly poorer functioning on the Children’s Global Assessment Scale. BIPS diagnoses, which usually constitute a relatively small proportion of patients seen in prodromal risk syndrome clinics, were present in 40% of all risk syndromes in the current study. Interestingly, in the clinic, risk for psychosis has been demonstrated to be particularly high for patients with BIPS, with a faster onset of psychosis compared with young people with APSP. It is possible that fewer BIPS patients will present clinically during the prodrome and are more likely to present for the first time during first-episode psychosis due to what appears to be a shorter prodromal period. It is also possible, because the symptoms are “brief” and “intermittent,” that patients believe their symptoms have resolved and are, as a result, less likely to seek help. Further research will be necessary to understand this difference between the clinic and the community.

Nonpsychotic psychiatric disorders were present in a large majority of adolescents with prodromal risk syndromes, consistent with research on clinically presenting individuals. For example, reported that in a sample of clinically presenting individuals who met criteria for a prodromal risk syndrome, 76% had at least one diagnosable lifetime Axis I disorder. Similarly, reported that over 90% of help-seeking individuals who met criteria for a prodromal risk syndrome had at least one comorbid disorder. Depressive disorders were the most common diagnosis in both studies, as in the current report. Lenz et al. using the same diagnostic instrument as the current study to assess for Axis-I psychopathology in a sample of putatively prodromal help seekers, found MDD to be the most common

### Table 1. Criteria for the Proposed Attenuated Psychosis Syndrome for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V)

| Characteristic symptoms: at least one of the following in attenuated form with intact reality testing but of sufficient severity and/or frequency that it is not discounted or ignored | Delusions |
| Frequency/Currency: symptoms meeting criterion A must be present in the past month and occur at an average frequency of at least once per week in past month | Hallucinations |
| Progression: symptoms meeting criterion A must have begun in or significantly worsened in the past year | Disorganized speech |
| Distress/Disability/Treatment Seeking: symptoms meeting criterion A are sufficiently distressing and disabling to the patient and/or parent/guardian to lead them to seek help | Symptoms meeting criterion A are not better explained by any DSM-5 diagnosis, including substance-related disorder |
| Clinical criteria for any DSM-V psychotic disorder have never been met | |

### Table 2. Lifetime Axis I Diagnoses in Patients with Prodromal Risk Syndromes and in Controls

<table>
<thead>
<tr>
<th>Lifetime Axis I Diagnosis</th>
<th>Prodromal Risk Syndrome, (n = 19)</th>
<th>Controls, (n = 193)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any diagnosis</td>
<td>63%</td>
<td>28%</td>
</tr>
<tr>
<td>Affective disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major depressive Disorder</td>
<td>37%</td>
<td>13%</td>
</tr>
<tr>
<td>Dysthymic disorder</td>
<td>26%</td>
<td>5%</td>
</tr>
<tr>
<td>Adjustment disorder with depressed mood</td>
<td>16%</td>
<td>8.4%</td>
</tr>
<tr>
<td>Behavioral disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attention deficit/hyperactivity disorder</td>
<td>21%</td>
<td>7%</td>
</tr>
<tr>
<td>Oppositional defiant disorder</td>
<td>16%</td>
<td>4%</td>
</tr>
<tr>
<td>Conduct disorder</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>16%</td>
<td>6%</td>
</tr>
<tr>
<td>Separation anxiety disorder</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Avoidant disorder</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Obsessive compulsive disorder</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>Social phobia</td>
<td>5%</td>
<td>2%</td>
</tr>
</tbody>
</table>

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diagnosis, followed by attention deficit/hyperactivity disorder, in keeping with our own community findings. There are a number of implications of this research in relation to the proposed DSM-V diagnosis of attenuated psychosis syndrome. Findings from the current study that might support this diagnosis include that (1) a large majority of the individuals identified are distressed by their symptoms; (2) this group demonstrates significantly poorer global functioning; and (3) the majority of these adolescents have other diagnosable psychopathology that suggests that they as a population are truly in need of care. On the other hand, the findings of the current study also raise a number of concerns or limitations with regard to creation of an attenuated psychosis syndrome diagnosis, including that (1) the proposed diagnostic criteria are applicable to a relatively large proportion of adolescents, meaning that, following publication of DSM-V, many young people could suddenly be imposed with a stigmatizing diagnosis that they did not previously have; (2) we do not know the relative risk for psychosis among this group since longitudinal community research has not been conducted. Given the high prevalence of the syndrome, however, it is unlikely to approach the level of risk observed in help-seeking samples reported on to date; thus, we risk greatly increasing the rate of false positives; (3) since the majority of these individuals already have psychiatric disorders, there would not, in most cases, appear to be a major financial barrier to receiving psychiatric treatment in healthcare systems that require a formal diagnosis for insurance purposes; (4) the proportion of adolescents who fulfill criteria for a risk syndrome varies greatly depending on how “disability” is interpreted in terms of the degree of functional decline, something that is not currently specified in the proposed criteria; and (5) attenuated psychosis syndrome may be a misnomer for a syndrome that is, in fact, associated with a wide range of (nonpsychotic) disorders.

It is important to note that none of the participants in the current study, despite meeting criteria for prodromal risk syndromes, had presented to a prodrome or other healthcare clinic and so none of the participants can be considered “help seekers” in the same way as individuals who have been reported on to date in clinic-based research. Why some individuals who meet risk syndrome criteria present to clinics while others do not is unclear and will require further research. There are many possible reasons for this. As already speculated, given the high proportion of BIPS in the current community study compared with the proportion of BIPS in clinic-based studies, it is possible that young people with BIPS are less likely to present to the clinic. The young age of participants in the current study may also be a contributing factor. Although, in our experience, even at this age, young people are very aware that these experiences are unusual, it is possible that younger individuals are less likely to attend their doctor or other health professional compared with older teenagers and young adults. Education around psychotic symptoms and psychosis risk syndromes may also be a factor. Additiong et al, for example, showed that, following an extensive community education program, referrals to prodrome services increased. Thus, a lack of community education and confusion about “where to turn for help” with these unusual experiences may play a role in nonpresentation. There may be multiple other differences between help-seeking and nonhelp-seeking individuals with prodromal risk syndromes. Further cross-sectional and longitudinal research comparing clinical and community samples will be necessary to address this question.

Strengths and Limitations

The general population sampling method used in the current study is the major strength, which allowed us to estimate the population prevalence of prodromal risk syndromes at risk mental states. In addition, the approach used in the current study allowed us to investigate psychopathology and global functioning in very early stages of psychosis risk—earlier even than clinically presenting risk syndrome cases. A limitation is that the standard SIPS interview instrument was not used; rather the K-SADS instrument was altered to include SIPS questions on positive symptoms from sections P1 to P5. Thus, it might be argued that this could result in underestimation of the true prevalence of prodromal risk syndromes. While we surveyed a relatively large number of adolescents, a relatively small proportion was brought to interview, introducing the risk of ascertainment bias, whereby individuals with a personal or family history of disorder may be more likely to agree to participate, thus self-selecting for increased rates of the disorder under study. However, we do not believe this to be the case in the current study for a number of reasons: (1) adolescents who attended the full interview study did not differ from the larger surveyed school sample from which they were drawn in terms of symptoms of general psychopathology, as measured by the SDQ, or in terms of psychotic symptoms, as measured by the APSS; (2) only 1.3% of participants had a first-degree relative with a history of psychotic illness, suggesting that families with psychosis were not more likely to participate; and (3) the prevalence of mental disorders was very similar to previous epidemiological work both nationally and internationally.

Participants were also representative of the general population in terms of ethnicity and SES. Nonetheless, further work to confirm our findings will be valuable.

It is important to note that research to date suggests that psychotic symptoms are more prevalent in early compared with later childhood. In a meta-analysis of population-based studies on the prevalence of psychotic symptoms in child and adolescent populations, we found...
that psychotic symptoms were more common in younger (ages 9 to 12 years) compared with older (ages 13 to 18 years) children. Thus, research in later adolescence, when psychosis risk is highest, might not find an equally high prevalence of prodromal risk syndromes compared with the younger population assessed in the current study. Further research among different age groups is necessary to address this question.

Conclusions

Up to 8% of a community sample of 11- to 13-year-olds met criteria for a prodromal risk syndrome in the current study. Adolescents with risk syndromes demonstrated poorer global functioning and high rates of nonpsychotic psychopathology, consistent with findings on clinically presenting risk syndrome patients. The long-term outcomes for these “community risk syndromes” has yet to be determined and will require further research. However, the decline in rates of conversion to psychosis at risk syndrome clinics over the past number of years highlights the fact that, even in clinically presenting individuals, outcomes are not clear cut. Follow up research will be necessary to determine the degree of risk for clinical psychosis associated with prodromal risk syndromes in the community.

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Appendix

Structured Interview for Prodromal Syndromes (SIPS) Criteria

Prodromal syndrome diagnostic categories include: (1) brief intermittent psychotic symptoms prodromal syndrome (BIPS), (2) attenuated positive symptoms prodromal syndrome (APSP), and (3) genetic risk and deterioration prodromal syndrome (GRD).

1. BIPS criteria
   1a) At least one of the P1 to P5 scales scored a 6 (that is, psychotic)
   1b) The symptom(s) have reached a psychotic level of intensity within the past 3 months
   1c) The symptom(s) have been present for at least several minutes per day at a frequency of at least once per month

2. APSP criteria
   2a) At least one of the P1 to P5 scales (which relate to positive psychotic symptoms) is scored 3 (moderate), 4 (moderately severe), or 5 (severe but not psychotic)
   2b) Symptom(s) have begun, or worsened by one or more scale points, within the past 12 months
   2c) Symptom(s) have occurred at an average frequency of at least once per week in the past month

3. GRD criteria
   3a) The participant meets criteria for current schizotypal personality disorder or has a first-degree relative with a psychotic disorder
   3b) A drop of at least 30% in the Global Assessment of Functioning score over the past month as compared with 12 months ago.

Note, in the current study, given the complex issues around diagnosing young people (aged 11–13 years) with personality disorders, a diagnosis of GRD could only be given if, in addition to the stipulated functional decline, the individual had a first-degree relative with a psychotic disorder.

Clinical Assessment of At Risk Mental States (CAARMS) criteria

Prodromal syndrome diagnostic categories include (1) vulnerability group, (2) attenuated psychosis group, and (3) brief limited intermittent psychotic symptoms (BLIPS group)

1. Vulnerability Group criteria
   1a) Family history of psychosis in a first-degree relative or schizotypal personality disorder in the identified patient
   Plus
   1b) 30% drop in social/occupational functioning (measured on the Social and Occupational Functioning Assessment Scale—SOFAS) compared with premorbid level, sustained for a month, occurred within past 12 months or a SOFAS score of 50 or less for past 12 months or longer
2. Attenuated Psychosis Group criteria
2a) Psychotic symptoms of subthreshold intensity, specifically a global rating scale score of 3–5 on Unusual Thought Content subscale, 3–5 on Non-Bizarre Ideas subscale, 3–4 on Perceptual Abnormalities subscale, and/or 4–5 on Disorganized Speech subscales of the CAARMS
Plus
2b) Frequency Scale Score of 3–6 on Unusual Thought Content, Non-Bizarre Ideas, Perceptual Abnormalities, and/or Disorganized Speech subscales of the CAARMS for at least a week
2c) Subthreshold frequency: Global Rating Scale score of 6 on Unusual Thought Content, 6 on Non-Bizarre Ideas, 5–6 on Perceptual Abnormalities, and/or 6 on Disorganized Speech subscales of the CAARMS
Plus
2d) Frequency scale score of 3 on Unusual Thought Content, Non-Bizarre Ideas, Perceptual Abnormalities, and/or Disorganized Speech subscales of CAARMS
Plus (for both categories)
2e) Symptoms present in past year
Plus (for both categories)
2f) 30% drop in SOFAS score from premorbid level, sustained for a whole month, occurred within past 12 months or SOFAS score of 50 or less for past 12 months or longer
3. BLIPS Group criteria
3a) a Global Rating Scale score of 6 on Unusual Thought Content subscale, 6 on Non-Bizarre Ideas, 5 or 6 on Perceptual Abnormalities subscale, and/or 6 on Disorganized Speech subscales of the CAARMS
Plus
3b) Frequency Scale score of 4–6 on Unusual Thought Content, Non-Bizarre Ideas, Perceptual Abnormalities, and/or Disorganized Speech subscales
Plus
3c) Each episode of symptoms is present for less than 1 week and symptoms spontaneously remit on every occasion
Plus
3d) Symptoms occurred during last year
Plus
3e) 30% drop in SOFAS score from premorbid level, sustained for a month, occurred within past 12 months, or SOFAS score of 50 or less for past 12 months or longer

Note: In the current study, the social/occupational functioning measure was the Children’s Global Assessment Scale and not Social and Occupational Functioning Assessment Scale. The criterion of a 30% decline in social/occupational functioning was added to the most recent edition of the CAARMS but was not a criterion for prodromal syndromes in previously published research. We report prevalences for CAARMS prodromal syndromes (1) without and (2) with this new criterion.

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