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The case for including Attenuated Psychotic Symptoms Syndrome in DSM-5 as a psychosis risk syndrome

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Abstract

The American Psychiatric Association Task Force on DSM-5 has recently proposed consideration of Attenuated Psychotic Symptoms Syndrome as a new diagnosis, based on nearly 15 years of prospective research in centers across the globe. The condition is also known as “psychosis risk syndrome,” “at-risk mental state,” “ultra-high risk,” and “putative prodrome.” We review evidence favoring its inclusion as a new diagnosis in DSM-5 and report new preliminary findings on DSM-IV diagnoses in current clinical use for these patients and on results of diagnostic interviews in unselected volunteers.

The main evidence supporting inclusion is: (1) the patients are currently ill, (2) the patients are at high risk for getting worse, (3) no DSM-IV diagnosis accurately captures their current illness or future risk, (4) the diagnosis has been made with reliability and validity in the research setting, and (5) placement in DSM-5 would help promote the needed treatment and prevention research to enable articulation of a standard of care to benefit these patients and their families. Potential harms can be minimized by patient, family, and provider education. It will be important to demonstrate through well-designed field trials whether the diagnostic criteria can be used with reliability in everyday clinical practice.

Keywords

Risk syndrome; APS syndrome; Psychosis; Early detection; Prevention; DSM-5

1. Attenuated Psychotic Symptoms Syndrome

The Psychosis Workgroup of the American Psychiatric Association (APA) DSM-5 Task Force has been considering a proposal for a psychosis risk syndrome as a new diagnosis (Carpenter, 2009; Heckers, 2009). In February, 2010, APA posted draft criteria invited comment. In May–August the draft criteria were revised based on comments (DSM-5 Task Force, 2010a). The revised draft criteria are shown in the Panel. The new Attenuated Psychotic Symptoms Syndrome, or APS syndrome, nomenclature focuses on the current clinical state and parallels the preferred terminology for the dementia risk syndrome: mild

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Contributors
Author SWW designed the new data collection and wrote the first draft of the manuscript. All authors contributed to and have approved the final report.

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Drs. Woods and McGlashan are advisors to the Psychosis Work Group of the American Psychiatric Association DSM-5 Task Force. All authors declare that they have no other conflicts of interest.

cognitive impairment (Petersen et al., 1999) or minor neurocognitive disorder (DSM-5 Task Force, 2010b).

The primary purpose of this paper is to review published evidence in favor of inclusion of APS syndrome in DSM-5. New preliminary data on DSM-IV diagnoses in current clinical use for these patients and on results of diagnostic interviews in unselected community volunteers are also presented.

2. The proposed DSM-5 criteria

The proposed criteria are more restrictive than both related research criteria sets in current use (Table 1). Specifically, the proposed DSM-5 criteria require that the characteristic attenuated positive symptoms must be associated with distress, disability, and help-seeking (Panel). The requirement for distress arises from studies suggesting that recruited patients whose distress arises not from attenuated positive symptoms but from other complaints may be at low risk of conversion (Section 4). The requirement for disability arises from a comparison of 6 large studies (Addington et al., 2010;Cannon et al., 2008;Mason et al., 2004;Ruhrmann et al., 2010b;Yung et al., 2004b;Yung et al., 2006b), all of which found that low functioning is associated with higher conversion rates. The requirement for help-seeking is derived from epidemiologic studies suggesting high prevalence of psychotic-like symptoms (Eaton et al., 1991;Hanssen et al., 2005;Rossler et al., 2007;Tien, 1991;van Os et al., 2000;van Os et al., 2009;Yung et al., 2006a) and a low rate of conversion to psychosis (Hanssen et al., 2005;Rossler et al., 2007) among persons with no need for care.

In addition, criteria B and C (Panel) are absent in one set of research criteria (Table 1). Epidemiologic evidence suggests that psychotic-like experiences that do not persist (present in past month) are unlikely to lead to frank psychosis (Dominguez et al., 2009). The help-seeking control group in the NAPLS validity study demonstrates that, among nonschizotypal patients, attenuated positive symptoms that have been longstanding and stable rather than recently progressive (criterion C) are also unlikely to lead to frank psychosis (Woods et al., 2009).

Since the proposed DSM-5 criteria are more restrictive than currently employed research criteria, the DSM-5 criteria are likely to identify patients at higher risk of conversion to psychosis and to exclude more false positive patients than the research criteria.

3. APS syndrome patients are currently ill

Individuals meeting the more restrictive DSM-5 criteria may still be true positives or false positives for conversion to psychosis, but no person meeting APS syndrome criteria is a false positive for current illness. APS patients are symptomatic, functionally impaired, and treatment-seeking. These features alone seem sufficient for a new diagnosis.

3.1. APS syndrome patients are symptomatic

APS patients have positive symptoms, negative symptoms, disorganization symptoms, and nonspecific general symptoms such as depressed and anxious mood (Hawkins et al., 2004b; Woods et al., 2009). Two early studies demonstrated that untreated APS patients had more severe positive symptoms than treated first episode psychosis patients (Miller et al., 2003b; Yung et al., 1996). Depressive and manic symptoms were less severe than in adolescent depression and mania samples (Miller et al., 2003b).

3.2. APS syndrome patients are functionally impaired

Representative early studies found baseline current Global Assessment of Functioning (GAF) scores for APS patients in the 40s (serious impairment) (Miller et al., 2003b) and 50s (moderate impairment) (Mason et al., 2004; Yung et al., 1998). Recent studies using more specific measures confirm current impairments of social and/or role functioning (Addington et al., 2008; Ballon et al., 2007; Shim et al., 2008).

3.3. APS syndrome patients as a group are cognitively impaired

Most studies find that at-risk patients are more cognitively impaired than controls (Table 2).

3.4. Many APS syndrome patients are help-seeking

Although epidemiologic studies are lacking, several reports document that at least some at-risk patients are help-seeking (Amminger et al., 2010; McGlashan et al., 2007; McGlashan et al., 2006; McGorry et al., 2002a; Morrison et al., 2004; Preda et al., 2002; Walker et al., 2009; Woods et al., 2003; Woods et al., 2007). As noted above, the proposed DSM-5 criteria require help-seeking.

4. APS syndrome patients are at high risk for getting worse

In the large NAPLS cohort (at-risk *n*=303), Kaplan–Meier analyses show that 40% of at-risk patients converted to fully psychotic illness during 2.5 years of follow-up (Woods et al., 2009). Many patients who do not convert continue to be symptomatic (Woods, 2010).

In the next largest cohort, the recent European Prediction of Psychosis (EPOS) study, conversion rates among APS disorder-type patients were lower: around 20% at 1.5 years (Ruhrmann et al., 2010b). In both NAPLS and EPOS, the conversion rates may have been reduced by treatment received during naturalistic follow-up. In NAPLS, among subjects not enrolled in clinical trials, 25% received antipsychotics (Walker et al., 2009), and at least 13% in EPOS (Ruhrmann et al., 2010b). Since both studies report that subjects prescribed antipsychotics were more symptomatic at baseline, the possibility exists that the highest-risk subjects in the cohorts were selected for antipsychotic treatment, which then had a beneficial effect (McGlashan et al., 2006; McGorry et al., 2002b; Ruhrmann et al., 2007; Woods et al., 2003; Woods et al., 2007) that lowered their risk.

Although in both NAPLS and EPOS cohorts the conversion rate decelerated across the follow-up interval, the possibility still exists that more patients would have converted with longer follow-up. With an alternate conception of the at-risk syndrome that overlaps considerably with the APS-like conception in the EPOS sample (Ruhrmann et al., 2010b), the conversion rate was 70% over a mean 9.6 year follow-up (Klosterkotter et al., 2001).

In the past few years, the site that originally described the at-risk syndrome (Yung et al., 1996) has reported a declining rate of conversion to psychosis (Yung et al., 2008; Yung et al., 2007). Interpretation has emphasized the possible role of sample dilution via referral of subjects whose attenuated positive symptoms were not associated with help seeking but were only incidental to help seeking behavior associated with other psychiatric syndromes. This experience contributed to the inclusion of criterion D (Panel), where the attenuated positive symptoms themselves must be associated with distress, disability, and help-seeking, so that the proposed DSM-5 criteria should not permit the low risk patients diluting the samples in these reports to receive the diagnosis.

One concern about proposing an APS syndrome diagnosis is that it will be abused by using the criteria to screen general populations. Without criterion D, this practice would be likely

to yield low rates of conversion among the screened cases and thus should probably be conducted only very cautiously (Woods et al., 2010). We agree, however, with McGorry that potential for misuse is an insufficient argument against inclusion of a new diagnosis (McGorry, 2010).

Another concern about the APS syndrome is that the most common risk outcome is said to be persistence or emergence of nonpsychotic affective or anxiety disorders (McGorry, 2010). Our field has still not clarified this issue, but it seems that the large majority of nonpsychotic affective or anxiety disorders outcomes are not newly emergent incident outcomes but rather are cases of persistence of comorbid symptoms previously present at baseline (e.g. being “at risk” for something that was already there). Assuming that future data presentations bear out this impression, then among the newly emergent disorders psychosis should be quite specific (Woods et al., 2010). Baseline anxiety and affective disorders are very common not only among patients meeting APS criteria, but also among patients who seek an at-risk structured interview but do not meet criteria (Woods et al., 2009). This last group of anxious and depressed young people who do not have qualifying attenuated positive symptoms do not convert to psychosis at appreciable rates (Woods et al., 2009).

5. No DSM-IV diagnosis accurately captures these patients

APS syndrome patients currently seek help in our health care systems, and they are given a variety of DSM-IV diagnoses clinically. As there is little or no specific evidence on this point available in the literature, we conducted a survey on 14 consecutive patients meeting SIPS criteria referred to our research clinic February through March 2010 from providers who had billed third party payers for their clinical evaluation. We asked about the provider’s background, the specific DSM-IV diagnoses used for billing purposes, and whether the provider was satisfied with the DSM-IV diagnoses.

Table 3 shows the results. Ten different diagnoses were given; the more frequent included psychotic disorder NOS (n=4) and attention-deficit/hyperactivity disorder (n=2). Of the 14 surveyed providers, 13 indicated that they were not satisfied with these diagnoses. Edited provider comments are shown.

These data do demonstrate that clinicians can select DSM-IV diagnoses for APS syndrome patients when required do so for reimbursement. However, the data also show that clinicians are not satisfied that DSM-IV accurately captures the clinical picture with these patients. Consistent with this dissatisfaction, review of DSM-IV indicates that attenuated positive symptoms are not mentioned in the text describing any disorder in Table 3.

6. Reliability and validity

6.1. APS syndrome may be diagnosed with validity in research settings

Two large studies have demonstrated statistically significant predictive validity of an at-risk diagnosis compared to help-seeking controls (Woods et al., 2009; Yung et al., 2008). Since help-seeking controls are patients referred for at-risk research evaluation who did not meet criteria, they constitute the optimal ecologically valid control group. In one study, 88 of 303 SIPS-diagnosed patients (29%, 40% using Kaplan Meier methods that adjust for loss to follow-up) developed frank psychosis over up to 2.5 years, while only 3 of 135 (2%, 4% by Kaplan–Meier) help-seeking controls converted ($p < 0.001$). In the other study, 19 of 119 CAARMS-diagnosed patients (12%) developed frank psychosis over 6 months, while only 2 of 173 (1%) help-seeking controls converted ($p < 0.001$).

6.2. APS syndrome may be diagnosed and rated with reliability in research settings

One structured interview has shown excellent diagnostic interrater reliability across eleven sites (Addington et al., 2007; Miller et al., 2003a Miller et al., 2002). Reliability for severity of the characteristic positive symptoms has also been excellent (Lencz et al., 2003; Miller et al., 2003a; Yung et al., 2005).

Before APS syndrome could be accepted as a DSM-5 diagnosis, well-designed field trials would need to demonstrate that the diagnosis is reliable not just in the research setting but also under ordinary clinical conditions.

6.3. Prevalence of APS syndrome among community-dwelling young people

One concern about the proposed DSM-5 APS syndrome diagnosis is the perception that large numbers of seemingly healthy young people would qualify (First, 2010; Shorter, 2010). This concern would seem valid given the frequent endorsement of psychotic-like experiences on self-report (Section 2). On closer inspection, however, the proportion of community-dwelling young people whose psychotic-like experiences would actually qualify for an APS syndrome diagnosis on psychiatric interview constitutes an unaddressed empirical question. We thus conducted a preliminary study in February–March 2010.

An on-line advertisement was placed in the “volunteers” section of a popular website (Craig’s List New Haven). The advertisement invited young people to participate in a paid study, but by design did not stipulate that subjects needed to be healthy. The only exclusion criteria were psychiatric medication or a family history of schizophrenia. Thirty young people aged 25±3 years responded to the advertisement and underwent SIPS interview without any further screening.

One subject met SIPS criteria (3.3%, 95% confidence interval 0.1 to 17.2%). This subject was actually seeking help for his symptoms, but didn’t know how to find it. Seventeen other subjects scored nonzero scores on one or more positive symptoms; however, in all these cases the scores were below APS syndrome range (Fig. 1).

The sample size is small and the confidence intervals are wide, but the data do suggest both that psychotic-like symptoms are common in young people and that they usually are not sufficiently severe to meet diagnostic criteria on interview. Thus a deluge of misdiagnosis with the APS syndrome seems unlikely, even based on consideration of attenuated positive symptoms alone. Moreover, as articulated above, the proposed criteria require distress, disability, and treatment seeking as well.

As Carpenter has pointed out (Carpenter, 2009), the APS syndrome is not unique among psychiatric disorders in being based on behaviors that are on a continuum of human experience. Anxiety, depression, and attention and memory disturbances are similar in this regard. The general requirement in DSM that such disorders be characterized by distress or disability (American Psychiatric Association, 1994), is specifically emphasized in the APS syndrome criteria (Panel).

7. Stigma can be managed and minimized

The possibility that patients diagnosed with an APS syndrome will be stigmatized constitutes an important risk that we do not mean to underestimate. Stigma, either internalized “self-stigma” or social stigma from peers, family, or others, can occur with any psychiatric disorder in adults. Less empirical data is available for young patients, but adolescents receiving intensive care at one service have been reported to experience some stigma associated with their mental illnesses, psychiatric treatment, or psychiatric diagnosis

(Moses, 2009a, b, 2010). We have as yet no similar reports in APS syndrome youth, with the exception of a small study showing that family members of at-risk patients endorsed feeling little stigma themselves as a consequence of being related to an at-risk patient (Wong et al., 2009). Despite the current dearth of empirical data, it is likely that future research will show that risk syndrome patients do experience some stigma (Yang et al., 2010). However, there are several reasons to believe the likelihood of stigma does not outweigh the potential benefit of the diagnosis.

First, harm from stigma that does occur for false positives can potentially be reversed. If no APS syndrome diagnosis is made, and patients develop chronic psychosis, stigma is potentially lifelong.

Second, stigma associated with an APS syndrome diagnosis is manageable. We do not consider it ethically unacceptable to enroll subjects in at-risk research clinics. That is because our research clinics intervene to reduce stigma in every case (Yung et al., 2010), by empathically counseling patients and their families on what it means to be at-risk and how being at-risk differs from actually being psychotic. Psychiatric clinicians can do the same.

Lastly, APS syndrome patients are already receiving DSM-IV diagnoses in the community (Table 3), and it is not immediately apparent that an APS syndrome diagnosis is more stigmatizing than psychotic disorder NOS or the other DSM-IV diagnoses currently being given to these patients.

8. Promoting needed treatment and prevention research

Patients who qualify for an APS syndrome diagnosis are in need both of evidence-based treatment for their current symptoms and of evidence-based preventive interventions for their risk of further decline (Ruhrmann et al., 2010a; Woods et al., 2001). However, current practice guidelines are relatively sparse on specific suggestions (Table 4).

The reason that guidelines are relatively sparse in this area is that the evidence itself is sparse. Since 1996, only four modest randomized studies have been published: three of them evaluating medications and two of them cognitive-behavioral therapy (Amminger et al., 2010 McGlashan et al., 2006; McGorry et al., 2002a Morrison et al., 2004).

It might be argued that that APS syndrome is premature to include in DSM-5 if the treatment evidence base is still so thin. However, the DSM is not a therapeutic manual, and the availability of effective treatment is not ordinarily required for a disorder to be included. Moreover, we believe that inclusion in DSM-5 would help to stimulate the conduct of the informative trials that we need, both for psychosocial therapies and for medications.

8.1. The process for large, informative medication treatment studies

In the U.S., large, informative studies of medication treatments are usually funded by pharmaceutical companies. These companies are generally reluctant to fund large studies unless they can legally use the results to promote their products. Medications may not be promoted legally in the U.S. without FDA approval that the medication is reasonably safe and effective for the indication being promoted. Thus the rate-limiting step to generate large, informative treatment studies in the U.S. is an FDA indication. The absence of an FDA indication is one reason why we have so few trials for APS disorder and why the sample sizes are so modest. Although there is no requirement for a disorder to be recorded in the DSM to receive an FDA indication, in our view placement in DSM-5 is likely to facilitate the process.

8.2. The process for development of new, specific medication treatments

The optimal medication treatment for APS would have few or no adverse effects and would be effective, specifically so for this early stage of the disorder and perhaps less so for later stages. A recent trial offers preliminary proof of this concept, reporting that 12 weeks of fish oil treatment might by itself, without any antipsychotic medication, protect APS syndrome patients from becoming psychotic for at least 12 months (Amminger et al., 2010), when findings in chronic patients are inconclusive (Irving et al., 2006). This treatment was studied without a goal of an FDA indication; however, such a pathway to wide use of a new treatment is unusual. Our concern is that without a DSM diagnosis supporting an FDA indication, Phase II programs for other promising new medications specifically for the APS syndrome may never to be launched.

8.3. An APS syndrome diagnosis should reduce inappropriate prescribing

An important concern about the APS syndrome proposal is that it will lead to unnecessary exposure to (Corcoran et al., 2010), and commonplace prescription of (Yung et al., 2010), antipsychotic medications. We agree with Carpenter (Carpenter, 2009) that such practice would not be evidence-based and would do harm. Broadened use of antipsychotics medication has occurred among children and adolescents in recent years (Crystal et al., 2009) across a wide variety of diagnostic classes; thus this concern is not unique to APS syndrome. Moreover, our own view is that inclusion of an APS syndrome diagnosis in DSM-5 should reduce inappropriate prescribing.

First, including an APS syndrome diagnosis in DSM-5 enriches the differential diagnosis, which should help prescribing be more appropriate. The patient with attenuated positive symptoms who receives a DSM-5 APS syndrome diagnosis may be less likely to be prescribed antipsychotics than if that same patient receives a DSM-IV diagnosis of psychotic disorder NOS.

Second, prescribers may now give antipsychotics in the mistaken belief that they are prescribing for APS syndrome patients when the patients do not meet APS syndrome criteria, because clinicians do not have the ready access to the criteria and accompanying text that publication in DSM provides.

Third, inappropriate prescribing is enabled by the paucity of the treatment evidence base. Providers are forced to make decisions based almost solely on clinical judgment.

Lastly, if a DSM-5 diagnosis helps promote specific new therapies for APS syndrome patients, these developments ought to reduce overprescription of antipsychotics.

8.4. The APS syndrome diagnosis as a stage of schizophrenia and related disorders

Clinical staging, akin to staging of neoplastic conditions, has been advocated for psychiatric disorders (McGorry, 2007; Tandon et al., 2009). An evidence-based system of clinical staging would clearly provide a conceptual framework for pathophysiologic studies of progression of disease and therapeutic studies of prevention of progression. In order to reduce a proposed system of staging to practice, operational criteria for each stage of each disorder must be articulated, refined, and tested prospectively for reliability and validity. The current paper argues that these necessary steps have been achieved for the APS syndrome over the past 15 years. APS syndrome then fits into the proposed staging model (McGorry, 2007) as stage 1b of schizophrenia and related psychotic disorders.

9. DSM-5 or DSM-IV?

The alternatives about inclusion of an APS syndrome diagnosis in DSM-5 should not be posed as yes vs no. The question should be posed thus: Which is better for patients and their families—an APS syndrome diagnosis in DSM-5 or sticking with DSM-IV? As we have outlined above, APS syndrome patients are symptomatic and functionally impaired, and no DSM-IV diagnosis accurately captures their suffering. DSM-IV diagnoses are no less stigmatizing and no less in need of empathic management to reduce stigma. DSM-IV has not served to facilitate the generation of treatment research evidence in this area or to prevent inappropriate prescribing. DSM-IV is simply outdated and deficient for this diagnosis, and research documenting the reliability and validity of the APS syndrome over the last decade should enable us to redress this deficiency to the benefit of our patients and their families.

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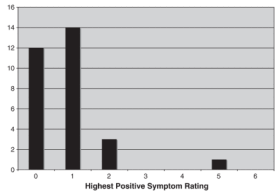

Fig. 1.

Highest SIPS positive symptom score among 30 community volunteers. On the positive symptom scales, the normal range is 0–2, the APS syndrome range 3–5, and frank psychosis 6.

All six of the following:

a) 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;
   (i) delusions
   (ii) hallucinations
   (iii) disordered communication

b) Frequency/Currency: symptom or symptoms meeting criteria A must be present in the past month and occur at an average frequency of at least once per week in the past month;

c) Progression: symptoms meeting criteria A must have begun or worsened in the past year;

d) 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;

e) Symptoms meeting criterion A are not better explained by any other DSM-5 diagnosis, including substance-related disorder.

f) Clinical criteria for any DSM-5 frank psychotic disorder have never been met.

Panel.
Revised proposed DSM-5 criteria for APS syndrome.

Table 1

Comparison of proposed DSM-5 for APS syndrome and research criteria.

Criteria items	DSM-5	SIPS	CAARMS
A. Characteristic symptoms	X	X	X
B. Present in past month	X	X	
C. Worsened in past year	X	X	
D. Distress/disability/help seeking	X		
E. Not better explained by Axis I/II	X	x	x
F. Never psychotic	X	X	X

X—explicit.

x—implicit.

SIPS—Structured Interview for Psychosis-risk Syndromes (McGlashan et al., 2010).

CAARMS—Comprehensive Assessment of At Risk Mental States (Yung et al., 2004a).

Table 2

Studies of cognitive functioning in APS syndrome patients vs controls.

No.	Studies reporting impairment	Studies reporting no impairment
1	Hambrecht et al. (2002)	Brewer et al. (2003)
2	Wood et al. (2003)	Silverstein et al. (2006)
3	Gschwandtner et al. (2003)	Broome et al. (2009)
4	Hawkins et al. (2004a)	
5	Bartok et al. (2005)	
6	Brewer et al. (2005)	
7	Francey et al. (2005)	
8	Gschwandtner et al. (2006)	
9	Keefe et al. (2006)	
10	Lencz et al. (2006)	
11	Niendam et al. (2006)	
12	Pukrop et al. (2006)	
13	Smith et al. (2006)	
14	Eastvold et al. (2007)	
15	Myles-Worsley et al. (2007)	
16	Pflueger et al. (2007)	
17	Pukrop et al. (2007)	
18	Simon et al. (2007)	
19	Becker et al. (2010)	
20	Seidman et al. (2010)	

Table 3

DSM-IV billing diagnoses prior to APS syndrome research referral.

Case	Practitioner	DSM-IV diagnoses used	Satisfaction comments
1	APRN	299.80 PDD	Didn't capture clinical picture
2	APRN	313.81 ODD	Not satisfied, thus the referral
3	Psychologist	296.90 Mood disorder NOS	Not totally satisfied
4	Child psychiatrist	314.0 ADHD 311 Depressive disorder NOS 300.02 Generalized anxiety disorder	With GAD, yes; with other two, no
5	Psychologist	300.9 Unspecified mental disorder	Not satisfied. Former PRS intern
6	Social worker	309 Adjustment disorder	Not satisfied, thus the referral
7	Social worker	298.9 Psychotic disorder NOS	Wasn't confident it was accurate
8	Social worker	300.9 Unspecified mental disorder	Not satisfied, thus the referral
9	Psychiatrist	298.9 Psychotic disorder NOS 311 Depressive disorder NOS 296.90 Mood disorder NOS	Would love a PRS rule out
10	Psychiatrist	298.9 Psychotic disorder NOS	Not satisfied, thus the referral
11	Psychologist	314.0 ADHD 313.81 ODD	Satisfied with both
12	Social worker	301.22 Schizotypal PD	Not satisfied, thus the referral
13	Psychologist	298.9 Psychotic disorder NOS	Not satisfied. A PRS diagnosis would be wonderful in the DSM
14	Psychologist	296.90 Mood disorder NOS	Not satisfied

Abbreviations: APRN—advanced practice registered nurse; PDD—pervasive developmental disorder; ODD—oppositional defiant disorder; NOS—not otherwise specified; ADHD—attention-deficit/hyperactivity disorder; GAD—generalized anxiety disorder; PRS—psychosis risk syndrome; PD—personality disorder.

Table 4

Published practice guideline recommendations for APS syndrome patients.

Organization	Citation	Recommendations
American Psychiatric Association	Lehman et al. (2004)	"Careful assessment and frequent monitoring"
Canadian Psychiatric Association	Addington et al. (2005a)	"Should be offered monitoring" "May be offered supportive therapy and symptomatic treatment"
International Early Psychosis Association	Addington et al. (2005b)	"Offered regular monitoring and support" "Provided with psychoeducation" "Offered family education and support" "Antipsychotic medications not usually indicated" unless "rapid deterioration" or "severe suicidal risk and treatment of depression has proved ineffective" or "aggression and hostility are increasing and pose a risk to others" "If antipsychotics are considered, ideally used in low doses," "may be continued" up to 2 years, and then "a gradual attempt to withdraw the medication should be made"
Royal Australian and New Zealand College of Psychiatrists	McGorry et al. (2005)	"Monitored in a context of ongoing support" "Antipsychotic medication not normally prescribed" unless "symptoms are directly associated with risk of self-harm or aggression"
Italian National Institute of Health	De Masi et al. (2008)	"Use of antipsychotic medication" "is doubtful" "Behavioural-cognitive therapy is recommended" for treating current state