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# Schizophrenia: Analysis and psychological treatment according to the clinical staging

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The present paper provides an overview of the recent contributions to the study of the course of schizophrenia. This is not a disorder as chronic and as acute at its start as traditionally thought. Beyond the positive and negative symptoms and different subtypes of illness, it is important to call attention to the development and course of schizophrenia. According to this approach, the aim of this paper is to review the most recent studies on schizophrenia according to clinical stages. With this aim, we review the research carried out by leading research teams and recently published clinical practice guidelines (Birmingham Group, Melbourne Group, GPCNS, NICE) in relation to the course, the main features, and more adjusted treatment alternatives, aimed to improve the characteristic symptoms of each stage of the disease. Finally, we point out the necessity to integrate this approach with the proposed changes for the upcoming DSM-V. This review identifies effective treatment options for each of the phases of the disease defined by the clinical stage approach.

**Key words:** Schizophrenia, Clinical staging, Diagnosis, Psychological treatment

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## Análisis y tratamiento psicológico de la esquizofrenia en función de los estadios clínicos

En este texto se presenta una síntesis de las aportaciones recientes en el estudio del curso de la esquizofrenia. Este trastorno no es tan crónico ni su inicio tan agudo como tradicionalmente se pensaba. Más allá de los síntomas positivos y negativos y de los diferentes subtipos, es importante prestar atención a la evolución y al curso de la esquizofrenia. En consonancia con este enfoque, el objetivo de este trabajo es realizar una revisión de las investigaciones más recientes sobre la esquizofrenia en función de los estadios clínicos.

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Para ello, se ha realizado un estudio de las aportaciones de los principales grupos de investigación y de las Guías de Práctica Clínica editadas recientemente (Grupo de Birmingham, Grupo de Melbourne, GPCNS, NICE) en relación con el curso, las características principales y las alternativas de tratamiento más orientadas a mejorar la sintomatología propia de cada una de las fases de la enfermedad. En esta revisión se señalan las alternativas de tratamiento eficaces para cada una de las fases de la enfermedad definidas mediante el enfoque de los estadios clínicos. Por último, se señala la integración de esta perspectiva con los cambios propuestos para la próxima publicación del DSM-V.

**Palabras clave:** Esquizofrenia, Estadios clínicos, Diagnóstico, Tratamiento psicológico

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## INTRODUCTION

Schizophrenia is a serious mental illness that leads to alteration in perception, thinking, affects and behavior.<sup>1</sup> The combination of positive and negative symptoms has given rise to different clinical subtypes of the diagnostic classification. However, the diagnosis based on the subtypes is not generally revised with the course of the disorder, as schizophrenia is considered a chronic and deteriorating disease.<sup>2</sup>

Due to longitudinal research on the course of schizophrenia, a new diagnostic system has become necessary. This system should focus more on the evolution of the disease and different stages.<sup>3-5</sup> In fact, a recoverability rate of 14% to 20% of the first episodes has been demonstrated. However, 80% of the patients would have a deteriorating course of the disorder, 20% of whom would not achieve complete remission of the disorder.<sup>1</sup>

As data has been becoming available from research on what occurs prior to the first acute episode and on the course of the disorder, different diagnostic models have been proposed based on the disease phases and their

Table 1		Course of schizophrenia				
AUTHORS		PHASES				
DSM-III (APA, 1980)	Stage 1 Prodromic	Stage 2 Acute	Stage 3 Residual	Stage 4 Subchronic (>6 months < 2 years)	Stage 5 Chronic > 2 years	
Fava, 1993	Prodromes	Acute	Residual			
Birchwood, 1999	Prodromes	Acute	Critical period 3 years			
Singh, 2005	Prodromes	First episode	Chronic phase			
McGorry, 2006	Stage 0, 1a, 1b	Stage 2	Stage 3a, 3b	Stage 3c	Stage 4	
Klosterkotter, 2008	Ultra risk	First episode	Critical period 2-5 years		Chronicity > 5 years	
Clinical practice guidelines, 2009	High risk mental state	First episode	Critical period Recovery phase Stabilization phase		Chronification phase	
Agius et al, 2010	High risk period	First episode	Critical period		Chronic phase	

prognosis. One model is, for example, the clinical stages model of the McGorry group.<sup>3-7</sup>

In accordance with this approach, this work has aimed to make a review of the most recent contributions on schizophrenia based in its course. To do so, a study has been made on the findings of the most relevant research groups and on the most recent clinical practice guidelines (Birmingham Group, Melbourne Group, GCO-NHS, NICE) in relation to course, principal characteristics and more adapted treatment alternatives to improve the symptoms per se of each phase of schizophrenia.

### DIAGNOSIS BASED ON DISEASE COURSE

Table 1 shows the course of schizophrenia according to different authors. The diagnosis based on the course of the disease is derived from the pioneer ideas of Fava. He contributed a diagnostic system focused on the longitudinal study of prodromes, acute phases of the disease and residual states.<sup>8</sup> The development of this model requires implementing a psychometric scales system that measures the patient's state at each moment and the establishment of clear criteria to identify the comorbidity of the disorders and the treatment response predictors.<sup>8</sup>

Birchwood<sup>9,10</sup> established a critical period after the disease debut that covers the three years after the episode and that is decisive, according to personal, social and biological factors involved in the future balance between disease and well-being. In general, the greatest degree of incapacity associated to psychotic disease develops during the first years. However, after this time, it tends to stabilize. The recovery level achieved in the first two years can be used

as a predictor of functioning 15 years later. Interventions in the critical period should focus on the symptoms, but also should be aimed at the psychological and psychosocial features.<sup>8-11</sup>

Years later, the Singh group described three stages in the development of schizophrenia, these being a prodromic phase, a first episode and a chronic phase, all of them preceded by a premorbid phase.<sup>12</sup> After, and considering the presence of prodromic symptoms and high risk mental states, they indicated three differentiated stages with different implications for diagnosis and treatment.<sup>13</sup> These were ultra-risk stage, first episode, and the critical period following the first episode with a duration of 2 to 5 years.

The McGorry group provided empirical support to the previous proposals. The stages proposed correspond to structural and functional changes in the brain. They affect the functioning of the individuals and can be measured with psychometric tests.<sup>4</sup> In this way, an 8-stage system has been established. This system summarizes the disease course, principal characteristics of each phase, therapeutic objectives and the most adequate intervention strategies in each one of them (Figure 1 and Table 2).

Recently, Agius et al.<sup>3</sup> reduced the McGorry model, comparing it to that of Klosterklötter<sup>13</sup> and establishing a high risk period of development of psychosis, a first episode, a critical period and a chronic phase. In turn, the clinical practice guidelines published in Spain take into account the early phases of the psychoses (high risk mental state, first psychotic episode, recover and critical period) and the stable phase of schizophrenia (relapse, stabilization and chronification).<sup>14</sup>

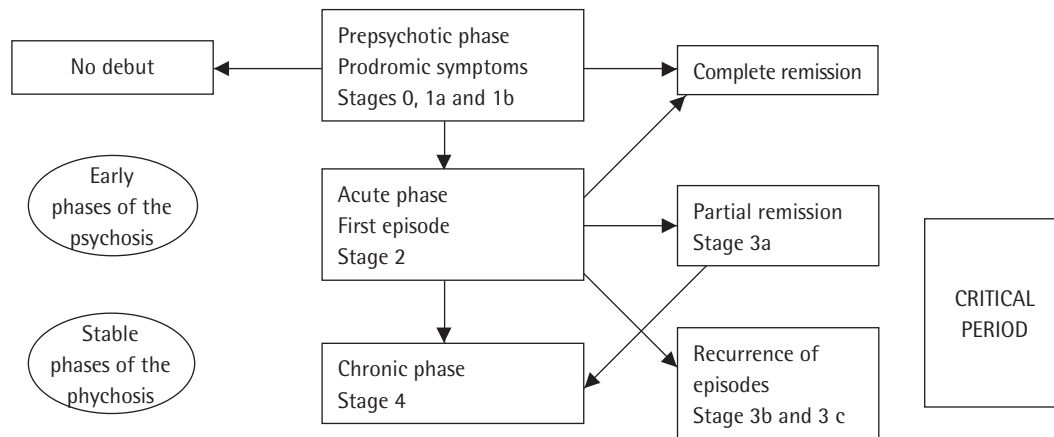


Figure 1 Scheme of the stages of schizophrenia

### EMPIRICAL BASES OF THE CLINICAL STAGES MODEL

The clinical stages model especially analyzes the prepsychotic and high risk stages, the psychotic endophenotypes as vulnerability markers and the initial phases of the disorder.

#### Endophenotypic markers of schizophrenia

Endophenotypes can be defined as objective and hereditary traits that represent the genetic risk of developing a mental illness<sup>16</sup> and that they are present in all the clinical stages and even in the high risk or subsyndromic ones.<sup>13</sup> A series of endophenotypic brain traits high risk individuals and first grade relatives have been found.<sup>17,20</sup> Among them are alterations that cause structural and functional abnormalities in the prefrontal cortex, reflected in temporal working memory and in verbal declarative memory deficits.<sup>17-19</sup>

The Pantelis group has studied the structural changes occurring in the early phases of psychoses and in the transition phases using neuroimaging techniques. In each stage proposed by McGorry, there are changes corresponding to them in cerebral plasticity,<sup>6,4,22</sup> and in progressive cognitive and functional decline.

Another line within endophenotypic research refers to the presence of psychological symptoms. The Cunningham group<sup>21</sup> wanted to know if the presence of certain symptoms are vulnerability markers regarding the transition from a prepsychotic to the acute phase. Thus, individuals who make the transition to the first episode had greater levels of nonspecific and affective symptoms prior to the debut, it

being possible to consider the presence of this type of symptoms as a vulnerability marker.<sup>23</sup>

#### Study of the initial phases of psychoses

This setting includes two principal lines of work: research on the high risk states and study of the duration of untreated psychoses and their relation with the disease prognoses.

Normally, there is a period of prodromic symptoms (principally negative and affective) prior to the appearance of the disease in the development of schizophrenia. Mean duration of this period, which generally remains untreated, is 1 to 2 years.<sup>24</sup> Thus, according to the Häfner and An der Heiden study,<sup>25</sup> 73% of the first episodes initiate with nonspecific or negative symptoms, 20% with negative, positive and nonspecific symptoms, and only 7% with positive symptoms. In most of the cases studied (82%), there was a form of chronic initiation, with a five-year long prodromic period and with a clearly psychotic period of more than one year prior to the first admission. Only 18% showed a form of acute initiation, with approximately one month of evolution of the symptoms.

Another aspect studied is the effect of the duration of the untreated psychoses. According to the data obtained, this exerts an ataxic biological effect, affecting the daily functioning and causing important cerebral deterioration.<sup>26-28</sup>

### THERAPEUTIC IMPLICATIONS OF THE STAGES MODEL

If the symptoms associated to each stage are taken into account, they can be more accurately targeted (table 2). In

Table 2		Therapeutic implications of the model of stages			
Phase (CPG-NHS <sup>a</sup> )	Premorbid-prepsychotic phase	Acute phase	Remission phase	Stable phase	
Term (NICE)	HRMS (high risk mental stage) UHR (Ultra-High risk of psychosis)	First episode	Critical period	Subchronic phase	Chronic phase
Stages (McGorry)	0, 1a, 1b	2	3a, 3b	3c-	4
Symptoms	Prodromes (attenuated negative or positive). Affective or nonspecific symptoms. Thought disorder. Deterioration of social functioning.	Positives. Delusions, hallucinations, disorganized speech, behavior alterations.	Cognitive symptoms. Negative symptoms. Brief or limited positive symptoms.	Recurrence of episodes Negative and residual symptoms Reactivity or emotional lability	Predominance of negative symptoms. Predominance of emotional reactivity and lability.
Treatment	Psychoeducation Healthy habits and use of toxics Social skills Work with distorted ideas	Psychodrugs Psychoeducation Cognitive therapy for delusions and hallucinations	Adherence to drug treatment. Treatment of positive symptoms. Toxic consumption. Prevention of relapses.	Adherence to drug treatment. Treatment of positive, negative symptoms and cognitive deficits. Toxic consumption. Prevention of relapses.	Treatment of cognitive and social-relational deficits. Integrated treatment programs.
Treatment programs	COPE	COPE; Fowler cognitive-behavioral therapy; Yusufoff coping treatment, Bentall's focalization T; Kingdon and Turkington cognitive-behavioral T.	STOPP; Kingdon and Turkington cognitive-behavioral T	IPT <sup>b</sup> ; Kingdon and Turkington cognitive-behavioral T	IPT

<sup>a</sup>CPG-NHS: Clinical Practice Guidelines - National Health Service; <sup>b</sup>IPT: Integrated Psychological Therapy

the following, a description is made of the symptoms, therapeutic objectives, treatment and possible evolution of each one of the disease phases.

### A. Prepsychotic or prodromic phase

This is a period in which the subject has nonspecific symptoms that are prior to the acute phase or has a family background with risk of developing schizophrenia.

**Symptoms:** According to the Melbourne team,<sup>29</sup> the indicators in this phase are the following: existence of first degree relatives with schizophrenia, possible presence of attenuated positive symptoms or in brief and limited periods, and a decrease in functioning level of the patient, even if the diagnostic criteria for a disorder on axis I of DSM IV-TR<sup>30</sup> are not fulfilled.

**Therapeutic objectives:** The therapeutic objective is to avoid, delay, or minimize risk of transition to psychosis. The interventions will be aimed at treating the symptoms present and at reducing the risk of deterioration and manifestation of a first episode.<sup>14,30</sup>

**Treatment:** On the pharmacological level, different studies have tested the effectiveness of the use of low dose antipsychotic medication, although accompanied by psychological therapy to reduce the likelihood of transition to psychoses.<sup>14,29,28,31,32,35</sup>

The objectives of the psychotherapeutic intervention are to increase understanding of the disease, promote adaptation of the patient, increase self-esteem, coping strategies and adaptive functioning, reduce emotional alteration and comorbidity of other disorders, control the stress associated to the presence of positive symptoms and to prevent relapse.<sup>33,34</sup>

*Evolution:* In the first studied conducted with this type of sample,<sup>32</sup> a 40% transition rate to psychosis in high risk stages in the period of one year was found.

## B. Acute phase

This is the disease phase in which clear and positive symptoms appear. It is when the patients generally have their first contact with the Mental Health Services and receive their first pharmacological treatment.

*Symptoms:* This phase is defined by the presence of positive symptoms as delusions, hallucinations, disorganized speech and behavior that appear in severe form.

*Therapeutic objectives:* The objectives of the intervention in this phase of the disorder are recruitment of the patient and pharmacological treatment compliance; analysis of the disease adaptation processes; and clinical evaluation of the disease and different treatment alternatives as well as intervention on the affective and mood state symptoms.

*Treatment:* The recommendations of this phase are the use of atypical antipsychotics at optimum doses, with the additional objective of reducing the presence of side effects from the medication.

On the psychotherapeutic level, the most effective treatments are based on the cognitive-behavioral therapy to control positive symptoms, using both the group and individual format.<sup>36</sup> Thus, there are empirically validated treatment programs, among them the COPE (Cognitively-oriented psychotherapy for early psychosis).<sup>37</sup> This program is designed to improve knowledge about the disease and the patient's adaptation to it. Regarding the treatment of delusions, some programs that have been shown to be effective are STOPP (Systematic Treatment of Persistent Psychosis),<sup>38</sup> and Fowler's<sup>39</sup> cognitive-behavioral therapy for psychoses and the Yusupoff<sup>40</sup> coping therapy for hallucinations and delusions. There are also other effective therapeutic programs for the treatment of the content of hallucinations, among them cognitive therapy of Chadwick, Birchwood and Towler<sup>41</sup> or focalizations therapy of Bentall, Haddock and Slade.<sup>42</sup>

Other additional objectives are the early identification of prodrome symptoms and their management and reducing the use of toxics or another type of addictive behaviors, such as gambling,<sup>43</sup> and teaching of healthy habits.

*Evolution:* Once the acute symptoms are controlled, the patients enter into the so-called critical period.<sup>10</sup>

However, approximately 20% of patients will derive into the chronic forms of the disease.

## C. Critical period

This is a period subsequent to the disease debut, with an estimated duration of 3 to 5 years.

*Symptoms:* In this phase, moderate to severe positive symptoms, moderate cognitive deterioration, social isolation and disruptive behaviors may appear. Symptoms that are moderate negative symptoms, but not sufficient to cause another hospital admission and cognitive and social functioning deficits that prevent the subject from reaching the premorbid stage level, may also appear.

*Therapeutic objectives:* The proposed goals are related with pharmacological treatment compliance, in order to achieve symptomatic stability of the patients and progressive readaptation to the workforce.

*Treatment:* This is the phase that shows the greatest risk of abandoning the medication, of relapse and of suicide.<sup>4</sup> Therefore, these three aspects represent the principal intervention focal points. Presence of affective symptoms should also be evaluated, in order to minimize the presence of risk of suicide. Intervention should also be made on the presence of the positive symptoms through the application of specific programs, among them the cognitive therapy of Kingdon and Turkington,<sup>43</sup> whose objective is both residual psychotic symptoms and negative symptoms, affective disorders and prevention of relapses.<sup>44</sup>

*Evolution:* In this phase, the patients may improve and be maintained in the same phase of the disorder, and even have a remission, or they may evolve to chronic forms of the disease.

## D. Subchronic phase

This phase is characterized by patients having many relapses, many of which lead to re-hospitalizations. This means a step backwards in the course of the disorder.

*Symptoms:* Attenuated positive symptoms and moderate residual or negative symptoms appear. There is progressive clinical deterioration and the impact of the disease is clear, both physically and psychologically.

*Therapeutic objectives:* As in the previous phase, the principal objective of this phase is long-term stabilization of the patients and their progressive social readaptation using the available psychosocial resources (workshops or protected employments).

*Treatment:* For the treatment of subchronic and chronic phases, the clinical practice guidelines recommend the application of multimodal treatment programs, since the disease has severely affected all of the life spheres of the patient in these phases. These programs intervene on the presence of the cognitive symptoms as well as on the social deficits and

problem solving. If the patients have a predominance of positive symptoms, a specific treatment program could be used, such as those described previously. Another one of the therapeutic targets is progressive independence of the patients, using psychosocial resources and decrease of emotional burden in the families as well as the reduction of toxic consumption, which may be predictors of recurrence.

*Evolution:* The patients may experience a relapse, above all if they do not comply with the treatment, and evolved to chronic forms of the disease.

**E. Chronic phase**

Even though there is no unified definition regarding chronic schizophrenia, this can be established when the patients have passed more than five years since debut, with poor disease evolution, several relapses and show problems in re-initiating activities that they performed before the initiation of the disease.

*Symptoms:* The presence of negative symptoms and severe residual symptoms is observed: impoverishment of expression of emotions and feelings; thought and speech limitations; lack of energy; difficulty to experience interest or pleasure for things that they previously liked or activities

normally considered pleasurable; incapacity to create appropriate close relationships for their age, gender and familial condition; and concentration and attention problems that are manifested, above all, within the social context.

*Therapeutic objectives:* The goal of the clinicians for these patients focuses on improving quality of life as well as achieving a certain degree of independence.

*Treatment:* The use of antipsychotics such as clozapine is recommended on the pharmacological level since they reduce extrapyramidal symptoms and facilitate therapeutic compliance. Efficacy of integrated treatment programs has been verified on the psychotherapeutic level. This is especially found for the Integrated Psychological Therapy (IPT) of the Roder group.<sup>45,46</sup> IPT consists in a group therapy program that integrates cognitive and social rehabilitation.

Its principal objective is to reduce deficits in cognitive functions of attention and perception (Figure 2) so that said improvement is reflected in better social and interpersonal functioning.

**CONCLUSIONS**

This work presents a synthesis of the current knowledge on the course and evolution of schizophrenia based on

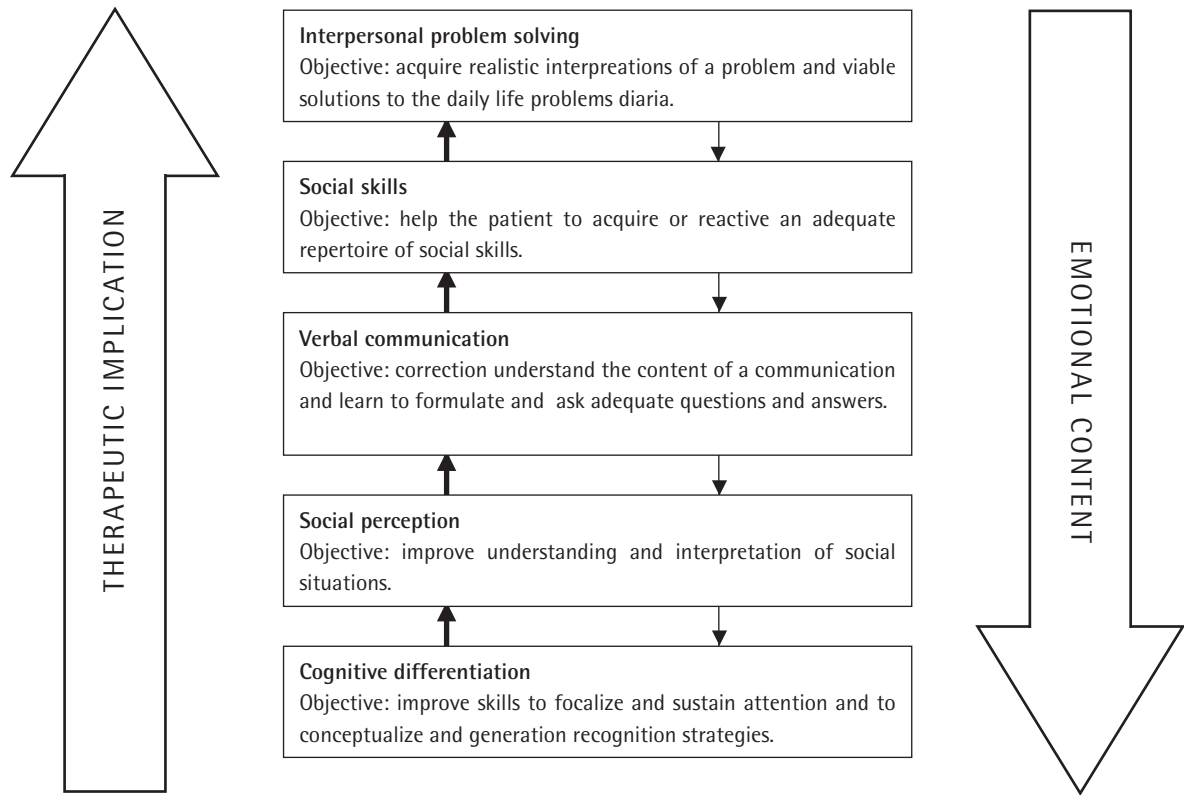


Figure 2 Intervention areas of the Integrated Psychological Therapy Program - IPT (Roder et al., 1996, 2007).

medical, neurological and psychosocial research. Based on the data provided, it can be established that the mere description of the symptoms is not sufficient for the current categorizing of schizophrenia. It is also necessary to take the disease course and progression into account. That is why, in our opinion, the clinical stages model is so effective. This model provides a more refined way of diagnoses<sup>3-6,8</sup> and contributes specific information for the treatments to be effective based on the disorder phase.<sup>13</sup> This model provides an efficient summary of the knowledge on biological, social, personal and familial factors of vulnerability.<sup>3-5</sup> From our point of view, this approach is a complete diagnostic and treatment model of schizophrenia, even though the limits between one stage and other in relation to the symptoms are not always clearly defined

The objective of this model is to design specific and effective treatments that reduce or prevent progression to more advanced phases of the disease. This requires extensive knowledge on the social, biological factors and personal risk factors and protection of the individuals who intervene in the progression from one phase to another.

In addition, refined evaluation instruments that make it possible to locate the corresponding stages of the patients in accordance with the disorder course are needed. Furthermore, in the clinical sense, defining the mental disorders in discrete stages in accordance with the disease progress may create an adequate frame for the evaluation of interventions aimed at prevention.<sup>4</sup>

Finally, the changes proposed in the current draft of the DSM-V by the American Psychiatric Association in relation to the diagnostic criteria of schizophrenia<sup>47</sup> are coherent with the model proposed in this article. In the first place, the creation of a *high risk psychotic syndrome* is suggested. This would include adolescents with symptoms related to thought disorders who do not meet criteria for the diagnosis of psychotic disorder, but who, however, have high vulnerability to develop it. In the second place, the creation of an *attenuated psychotic symptoms syndrome* is proposed. This syndrome is characterized by the presence of at least one of the symptoms of criterion A for a period of one month, with a minimum occurrence of at least once a week and that may negatively affect the patients' functioning.<sup>48</sup> All of this suggests that the course of the disorder, and not only the symptoms, must be taken into account in the new diagnostic classifications.

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