



Papeles del Psicólogo

ISSN: 0214-7823

ISSN: 1886-1415

papeles@correo.cop.es

Consejo General de Colegios Oficiales de Psicólogos
España

Fonseca-Pedrero, Eduardo; Inchausti, Felix
ACTUALIZACIÓN EN LA PREVENCIÓN DE LOS TRASTORNOS DEL ESPECTRO PSICÓTICO
Papeles del Psicólogo, vol. 39, no. 2, 2018, May-August, pp. 127-139
Consejo General de Colegios Oficiales de Psicólogos
España

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UPDATE ON THE PREVENTION OF PSYCHOTIC SPECTRUM DISORDERS

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El objetivo de este trabajo fue realizar una actualización en el campo de la prevención de los trastornos del espectro psicótico, concretamente en detección precoz e intervención temprana. En primer lugar, se aborda la conceptualización del síndrome de psicosis y su prevención. A continuación, se comentan los diferentes procedimientos e instrumentos de medida para la evaluación de la supuesta condición de riesgo. Seguidamente, se revisan las intervenciones tempranas disponibles en psicosis, se expone el modelo de estadificación, se examina la eficacia de tales intervenciones y se comentan algunas limitaciones y propuestas de modificación. Finalmente, se dibujan algunas debilidades y fortalezas en este campo así como sus perspectivas futuras. Finalmente, a modo de conclusión, se realiza una breve recapitulación.

Palabras clave: Psicosis, Detección, Intervención, Riesgo, Evaluación, Intervención, Prevención.

The objective of this work is to carry out an update in the field of the prevention of psychotic spectrum disorders, specifically in early detection and intervention. First, the conceptualization of the psychosis syndrome and its prevention are addressed. Second, the different procedures and measurement instruments for the evaluation of the risk condition are discussed. Then, the early interventions available for psychosis are reviewed; the staging model is presented; the effectiveness of such interventions is examined and some limitations and proposals for modification are discussed. Finally, a number of strengths and weaknesses in this field are highlighted as well as its future perspectives. Finally, by way of conclusion, a brief recapitulation is made.

Key words: Psychosis, Detection, Intervention, Risk, Evaluation, Intervention, Prevention.

The possibility of preventing the appearance of a first episode of psychosis (FEP) is most likely one of the chimeras of psychology. Obviously, the idea of preventing psychosis syndrome is not new. Almost a century ago, Emil Kraepelin (1919) observed that many of his patients, between 50-70% of them, had psychic peculiarities since childhood, such as, for example, a shy, withdrawn, and solitary character. Back then, in his writings he hinted at the possibility of detecting behaviors –prior to developing the disorder– that could be seen as “the doorway” to schizophrenia. Well, at the dawn of the 21st century, it seems that the prevention of psychotic spectrum disorders has become a somewhat more real possibility. The advances that have taken place in recent years have been astonishing. The optimism associated with the eventual prevention of a FEP has caused an explosion in the number of scientific studies, books, research projects, associations (e.g., IEPA Early Intervention in Mental Health) and screening and early intervention programs around the world (e.g., PRONIA, P3, PSYCAN). The huge amount of research published to date requires a review and

synthesis that will allow us, on the one hand, to summarize the current state of the question and, on the other, to reflect deeply, highlighting the limitations and obstacles but also the strengths and benefits.

Within this context, the objective of this paper is to produce an update in the field of the prevention of psychotic disorders, specifically in early detection and intervention. The structure of this exposition is as follows. First, the conceptualization of the psychosis syndrome and its prevention is addressed. Next, the different procedures and measurement instruments (preferably tests) for the evaluation of the supposed risk condition are discussed. Subsequently, the results of the early interventions carried out are exposed, the staging models are introduced and the effectiveness of these interventions is examined. Possible difficulties are discussed and a number of improvement proposals are considered in response. Some future research perspectives are also outlined. Finally, by way of conclusion, a brief recapitulation is made. Obviously, it is not possible to develop here extensively and in depth each and every one of the questions dealt with, so the reader is referred to excellent previous works (Fonseca-Pedrero, 2018; Fonseca Pedrero & Debbané, 2017; Fusar-Poli, Carpenter, Woods, & McGlashan, 2014; Fusar-Poli, McGorry, & Kane, 2017; Millan et al., 2016; Obiols & Barrantes-Vidal, 2014; Riecher-Rössler & McGorry, 2016).

Received: 15 de enero 2018 - Accepted: 23 febrero 2018

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THE PSYCHOTIC SYNDROME AND ITS PREVENTION

It seems logical to think that in order to prevent “something” it is necessary to define conceptually what one wishes to prevent; nevertheless, it can be affirmed that there still does not exist an operative and consensual definition of “psychosis” (Guloksuz & van Os, 2018). In this sense, and considering the current state of the field, reaching a consensus on what “psychosis” is (and what it is not) or any of its related disorders for that matter seems to be a difficult undertaking (Fonseca-Pedrero, 2018). Moreover, as more evidence about this syndrome is accumulated and collected, there is less certainty and more confusion about its true nature and conceptual delimitation (Maj, 2011; Pérez-Álvarez, 2012). Furthermore, and as the reader will know, for the time being and no matter how much it is promulgated otherwise, no pathognomonic marker or etiological mechanism has been found to explain the origin of this syndrome, i.e., no necessary and sufficient cause has been found (Keshavan, Tandon, Boutros, & Nasrallah, 2008; Lemos Giráldez, Fonseca-Pedrero, Paino, & Vallina, 2015). Now even in the 21st century, definitive answers are lacking to some of the most basic questions about the nature and conceptualization of the psychosis syndrome (Keshavan, Nasrallah, & Tandon, 2011), which is rather paradoxical.

The current, more or less consensual, form of what is understood as “schizophrenia” (to be specified in one of the possible multiple expressions of the psychotic phenotype) basically picks up the Schneiderian, Bleulerian and Kraepelinian traditions (Tandon, Nasrallah, & Keshavan, 2009). The DSM / ICD models represent a simplified and incomplete view of the syndrome that leads to the (mistaken) assumption that it is a simple, clear and discrete phenomenon (Cuesta & Peralta, 2016; Guloksuz & van Os, 2018). In addition, among other things, it continues to be a descriptive approach, which does not incorporate possible etiopathogenic mechanisms, which lacks validity (Lemos Giráldez et al., 2015) and which does not consider the phenomenological structure of the signs and symptoms (Parnas, 2015). Bearing these issues in mind, it could be considered that the psychosis syndrome brings together a set of mental health problems that have a functional and occupational impact on people and their families (Bobes & Saiz, 2013). It seems to be a complex construct composed of several symptomatic dimensions (e.g., hallucinations, delusions, negative symptoms, disorganized language and abnormal psychomotor behavior) (van Os & Reininghaus, 2016), which may result in different nosological entities (notion of spectrum). Perhaps, the psychosis syndrome is rather the final common path of phenotypic expression of a heterogeneous set of disorders of diverse etiologies, physiopathological mechanisms and different forms of clinical presentation (course and prognosis) that are modulated by environmental variables and that are circumscribed to a specific social and cultural context,

and are experienced (subjectively, phenomenologically) by a person (Keshavan et al., 2011; Lemos Giráldez et al., 2015; Segarra, 2013; Tandon, Keshavan, & Nasrallah, 2008; Tandon et al., 2009).

Prevention strategies (universal, selective, and indicated), and specifically the detection and early identification of psychosis, have been improving over the years (Fusar-Poli et al., 2014), to such an extent that the prediction rates show values similar to and even superior to those of other branches of medicine (Fusar-Poli et al., 2015). These strategies are based on the premise that a longer prolonged period of untreated psychosis or duration of untreated psychosis (DUP) will be associated with a worse short, medium-, and long-term prognosis as well as a poorer response to treatment. The working hypothesis is that early detection and identification with a subsequent effective early intervention could alter the natural course of the disorder, either delaying its onset, diminishing its severity or, perhaps, aborting its appearance. In this sense, previous studies have shown that a delay in both detection and identification and in beginning treatment is associated with significant negative consequences, such as an increase in comorbidity, a greater deterioration of cognitive, personal, occupational, family, and social function, in addition to a slower and more incomplete later recovery (Fusar-Poli et al., 2014; Larsen et al., 2011).

Retrospective and prospective studies highlight the existence of a period of progression before and immediately after the presentation of a FEP (Fusar-Poli, Bonoldi, et al., 2012; Häfner & An Der Heiden, 1999). The first symptoms and signs of psychotic spectrum disorders are usually preceded by a prodromal stage of three to five years. In addition, different meta-analyses indicate that people who end up developing a FEP already present various deficits at the psychophysiological, motor, neurocognitive and behavioral levels, as well as structural and functional brain alterations, and furthermore functional impact, disability and poorer quality of life prior to its onset (Dickson, Laurens, Cullen, & Hodgins, 2012; Fusar-Poli et al., 2015; Fusar-Poli et al., 2012; Fusar-Poli, Radua, McGuire, & Borgwardt, 2012). Moreover, certain risk factors and markers of vulnerability (e.g., healthy children of patients with psychosis, cannabis use, traumatic experiences, and attenuated psychotic experiences), seem to be associated with a higher probability of developing a psychotic spectrum disorder. in the future (Davis et al., 2016; Debbané et al., 2015; Fusar-Poli, Tantardini, et al., 2017; Kaymaz et al., 2012; Keshavan, Delisi, & Seidman, 2011; Linscott & van Os, 2013; van Os & Kapur, 2009; van Os, Kenis, & Rutten, 2010). For example, psychotic-like experiences and schizotypal features represent the behavioral expression of latent vulnerability to psychotic disorders (Debbané et al., 2015; Fonseca Pedrero & Debbané, 2017). People in the general population who report psychotic-like experiences end up transitioning to psychosis at a rate of 0.6%.



On the other hand, approximately 10% of patients with anxiety or depression and subclinical psychotic symptoms end up presenting psychosis, while in samples of individuals at clinical high risk for psychosis the transition values oscillate between 20-30% (van Os & Linscott, 2012).

In short, if the door to the possibility of prevention is opened, it is necessary to have adequate tools to identify this supposed risk or vulnerability condition and, additionally, to have effective preventive interventions. These prevention strategies must collect the different levels of analysis involved (from the genetic to the cultural) in the phenotypic expression of the disorder, in addition to placing at the center of the equation the person experiencing the disorder (see Figure 1). This implies a holistic, comprehensive and integrated, multidisciplinary and intersectoral vision where individuals and families have a nuclear role, and it must be conveyed by a consensual national mental health strategy.

PSYCHOSIS RISK ASSESSMENT

The prevention of the psychosis syndrome requires having, on the one hand, a standardized evaluation protocol that allows us to identify and detect unequivocally the potential risk or vulnerability condition, and on the other, effective (evidence based) prophylactic treatments. Therefore, in order to prevent, you have to detect, identify and intervene, and do it early, the sooner the better. Without correct identification and detection, it may be pointless to apply a prophylactic intervention.

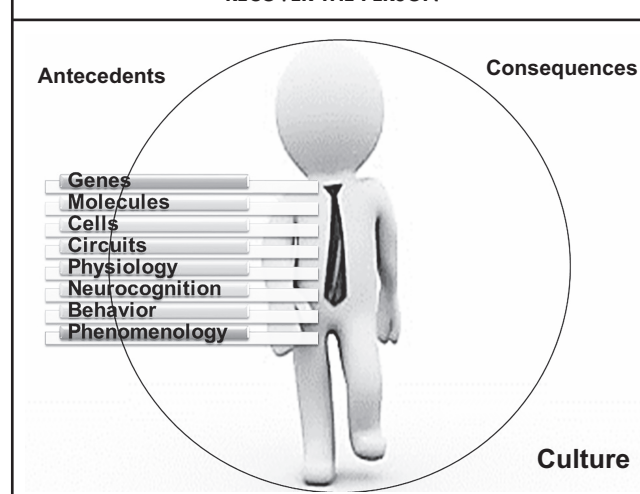
The assessment of the risk condition of psychosis involves detection and identification. Detect and identify should not be used as interchangeable terms, since, as indicated by the dictionary of the Spanish Royal Academy, the former refers to using a method to show what cannot be observed directly, while the latter refers to recognizing whether a person (or thing) is the same as what is supposed or sought (Fonseca-Pedrero & Debbané, 2018).

Needless to say, before continuing, the very concept of "risk" (sometimes confused with vulnerability) and specifically "risk" of psychotic syndrome is certainly a complex issue (Carpenter, 2018; Fonseca-Pedrero & Debbané, 2018; van Os & Guloksuz, 2017). In this area of research, we start from several premises, sometimes not scientifically proven, namely: a) that this risk condition exists; b) that it can be captured or prevented; c) that in addition it can be measured with different instruments and procedures (not only psychometric tests) in a reliable and valid way; and d) that once a rapid intervention has been detected and identified, it could abort (or reduce the probability of) the potential transition or it could improve the prognosis. Moreover, it is currently suggested that there may even be a diagnosable mental disorder called "attenuated psychosis syndrome" (Fonseca-Pedrero, Paino, & Fraguas, 2013; Fusar-Poli & Yung, 2012; Tsuang et al., 2013). The evaluation of the risk condition

is a complex topic which, moreover, is not exempt from dilemmas and difficulties (e.g., stigmatization, possible economic interests, psychopathologization of "normality", treatment with medication, false positives, etc.) and which presents innumerable intricacies. As the reader can see, from the study of the risk of psychosis, rather delicate matters arise, with chiaroscuros, and with great social and scientific impact.

Let's be clear, no system of evaluation and early diagnosis is perfect. The errors of evaluation and diagnosis are translated into false positives and negatives with clear practical implications (Fonseca-Pedrero, 2018). However, as a whole and depending on the prism through which you look at it, the results seem to indicate that it is possible to detect and identify a risk condition that predisposes to disorders of the psychotic spectrum, specifically, and to other forms of psychopathology in general (Bernardini et al., 2017; Schultze-Lutter et al., 2015; Stafford, Jackson, Mayo-Wilson, Morrison, & Kendall, 2013). The findings also seem to point out that the nature of this risk condition (reflected in the literature in different concepts such as clinical high risk or schizotypy) is pleiotropic, that is, the aforementioned susceptibility can lead to different psychopathological entities (e.g., depression, bipolar disorder), beyond the traumas of the psychotic spectrum. It is also variable/fluctuating, being able to remain stable or remit over time, and it is heterogeneous, i.e., it is not a homogenous set of psychopathological symptoms (at least three groupings can be found: attenuated psychotic symptoms, brief, limited and intermittent psychotic symptoms, and genetic risk/schizotypal personality disorders plus functional impact) (Fusar-Poli et al., 2014; Schmidt et al., 2016; Schultze-Lutter et al., 2015).

FIGURE 1
MODEL IN THE STUDY OF THE PSYCHOSIS SYNDROME:
"RECOVER THE PERSON"



Here we will briefly expose what are known as the high risk paradigms. The leitmotiv of this methodology is based on the ability to detect and identify early those people with a higher theoretical risk of developing psychosis in the future. The high risk paradigms are three: genetic, psychometric, and clinical. To simplify, the high genetic risk analyzes healthy children of patients with psychosis. The high psychometric risk examines schizotypal traits or psychotic-like experiences in samples of the general population, preferably young people. The paradigm of "clinical high risk" is aimed at identifying people who present attenuated psychotic symptoms (with associated distress) and who seek treatment or psychological help.

Within the paradigm of psychosis, high-risk state basically encompasses two approaches: "ultra-high risk" for psychosis and basic symptoms. Conceptually, the "ultra-high risk" approach come from the *Structured Interview for Prodromal Syndromes* (SIPS) (Miller et al., 2003), while the "at-risk mental state" (ARMS)", derive from the *Comprehensive Assessment of At Risk Mental States* (CAARMS) (Yung et al., 2005). On the other hand, the basic symptoms refer to subjectively experienced

disturbances of different domains including perception, thought processing, language, and attention, experienced subjectively by the person and not necessarily observable by others (Huber, 1983; Miret, Fatjó-Vilas, Peralta, & Fañanás, 2016). Two criteria of basic symptoms have been developed called COGDIS (Cognitive Disturbances) and COPER (Cognitive-Perceptive), as well as different assessment tools (see Table 1). Far from being seen as independent approaches, they are two complementary approaches that are often used in combination to improve prediction rates (Schultze-Lutter, Klosterkötter, & Ruhrmann, 2014).

As shown in Table 1, a wide range of instruments is currently available for the evaluation of the psychosis risk condition. The construction and validation, in recent years, of tools for this purpose has been overwhelming. The psychometric properties of the tools are supported empirically, although it is true that new studies are needed in representative samples of the general population. In Spain, in one way or another, there are numerous instruments validated for use depending on the interest of the practitioner. It is true that we must continue to make progress in this line. A more exhaustive review of the different assessment instruments, both nationally and internationally, can be found in previous works (Addington, Stowkowy, & Weiser, 2015; Fonseca-Pedrero & Debbané, 2018; Fonseca-Pedrero, Gooding, Debbané, & Muñiz, 2016). However, it must be mentioned that genetic markers, neuroimaging techniques, psychophysiological records and/or neurocognitive tasks are also being used in the detection and prediction of the psychosis syndrome (e.g., Carrión, Correll, Auther, & Cornblatt, 2017; Schmidt et al., 2016).

When assessing the risk status of psychosis or the diagnosis of psychosis high-risk state, the professional should follow guidelines or indications similar to those of any psychological or psychiatric evaluation process (see the *National Institute for Health and Care Excellence*, *European Psychiatric Association*, *American Psychological Association*, *International Test Commission*, etc.). For more details, the reader can consult previous works (e.g., Fonseca-Pedrero, 2018; Schultze-Lutter et al., 2015). Some of the most relevant recommendations are briefly mentioned here:

- The use of self-report and/or clinical interview implies benefits and limitations, the practitioner must weigh appropriately the method to be used.
- The instruments must be properly adapted to the specific context of evaluation and their psychometric properties duly guaranteed for that population, use, and context.
- The evaluation instruments must be used in an appropriate manner by the practitioner, following the deontological code and the international guidelines regarding the use, safety, and quality control of the tests (Muñiz, Hernández, & Ponsoda, 2015).

TABLE 1
DESCRIPTION OF SCREENING INSTRUMENTS FOR
HIGH RISK FOR PSYCHOSIS

Measuring instrument	Acronym	Nº items	Response format
Clinical High risk			
Structured Interview for Prodromal Syndromes	SIPS	N/A	Likert interview
Comprehensive Assessment of At Risk Mental State	CAARMS	N/A	Likert interview
Prodromal Questionnaire	PQ	92	T/F
Youth Psychosis at Risk Questionnaire	Y-PARQ	92	Likert 3
Prime Screen Revised	PS-R	12	Likert 7
Early Recognition Inventory based on IRAOS	ERIraos	65	Likert 3
Basic symptoms			
Bonn Scale for the Assessment of Basic Symptoms	BSABS	66	Likert interview
Schizophrenia Proneness Instrument adult version	SPI-A	34	Likert interview
Schizophrenia Proneness Instrument child and youth version	SPI-CY	49	Likert interview
Psychometric high risk			
Perceptual Aberration Scale	PAS	35	T/F
Revised Physical Anhedonia Scale	RPhA	65	T/F
Revised Social Anhedonia Scale	RSAS	40	T/F
Magical Ideation Scale	MIS	30	T/F
Oxford-Liverpool Inventory of Feelings and Experiences	O-LIFE	159	Yes/No
Schizotypal Personality Questionnaire	SPQ	74	Yes/No
Structured Interview for Schizotypy-Revised	SIS-R	19	Likert 4
Community Assessment Psychic Experiences-42	CAPE-42	42	Likert 4
Peters et al. Delusions Inventory-21 (PDI-21)	PDI-21	21	Yes/no; Likert 5
Oviedo Questionnaire for the Evaluation of Schizotypy	ESQUIZO-Q	51	Likert 5
Multidimensional Schizotypy Scale	MMS	77	T/F



- d) The communication of a psychosis high-risk state to the family or the person may be associated with stigma (including self-stigma).
- e) In minors, greater care and attention is needed when evaluating, diagnosing and monitoring the possible risk condition due to various difficulties (for example, the absence of criteria and specific instruments for children and adolescents, the changing nature and dynamics of this stage of development, possible somatic problems, etc.).
- f) A trained specialist (clinical psychologist or psychiatrist) with sufficient experience in the detection of the risk of psychosis should carry out the evaluation.
- g) For the diagnosis of a psychosis high-risk state, the criteria of the SIPS or CAARMS interviews must be met, in addition to collecting information on the search for help and the need for treatment by the individual and analyzing the possible functional impact or significant decrease in the social and/or occupational functioning.
- h) The history of past or present psychosis, the presence of other mental disorders or somatic illness should be ruled out.

EARLY INTERVENTION IN PSYCHOSIS (EIP)

The proliferation of programs and centers specialized in early intervention in psychosis (EIP) has been very significant in the last twenty years (Fusar-Poli, McGorry, et al., 2017; McGorry et al., 2010). This type of services, generally socio-health and supra-specialized, are based on at least two fundamental premises in the field of psychosis: on the one hand, they assume a modern approach to predictive, preventive and personalized medicine, which not only takes into account the intervention in people with a FEP but also those individuals vulnerable to suffer one; and on the other hand, they assume a dimensional model or clinical stages of psychosis that extends the focus of intervention to a wide spectrum of clinical phenomena that seem to be relevant for the prevention of the onset of psychosis, such as neurocognitive symptoms (Juuhl-Langseth, Holmén, Thormodsen, Øie, & Rund, 2014), negative symptoms (Lyne et al., 2017) or attenuated psychotic symptoms (Mongan, Shannon, Hanna, Boyd, & Mulholland, 2017), to name a few.

If current EIP programs are examined, several common characteristics and objectives can be detected: a) early detection of new cases; b) reducing the period of time from when the patient presents a clearly psychotic symptomatology until they receive appropriate treatment, that is, reducing the DUP; and c) providing better and more intensive treatment in the "critical period" of the disorder. The first two characteristics extend the target population to individuals at risk who have prodromal symptoms or ARMSs but not a FEP (Humiston et al., 2004) as well as people with a FEP who are not being adequately treated (Wyatt & Henter, 2001). The third transversal characteristic highlights the importance of these services being formed by

multidisciplinary teams oriented towards assertive community monitoring (Alameda et al., 2016) and with care burdens lower than those of conventional community mental health teams (Csillag et al., 2017).

The models of clinical stages in psychosis

Until relatively recently, the focus had essentially been on the mere diagnosis and subsequent intervention. However, the enormous intra- and inter-individual variability reported by the patients, together with the inherent dimensional nature of psychopathology and the interest to move towards a preventive approach, has meant that the clinical stage models have been gradually incorporated into the field of psychosis. (McGorry & van Os, 2013; Yung & McGorry, 2007). In essence, the staging models propose interventions based on the chronological development, the degree of progression and the discomfort of the symptoms/signs declared by the person. These models of clinical stages are an essential piece in the understanding of the current EIP programs. Table 2 presents a model of clinical stages for the psychotic syndrome that includes possible interventions that have been shown to be effective in improving remission and clinical recovery after a FEP (Fusar-Poli, McGorry, et al., 2017). This type of model provides a very useful conceptual framework for the development and testing of interventions specifically aimed at preventing and/or improving the remission and recovery of a FEP as well as other forms of psychopathology.

Effectiveness of the EIP

Numerous clinical trials have examined the effectiveness of different types of EIP. Fundamentally, those that have been studied the most have included atypical neuroleptics, mainly risperidone (A.Yung et al., 2011), olanzapine (McGlashan et al., 2006), and amisulpride (Ruhrmann et al., 2007); psychotherapy, mainly cognitive-behavioral therapy (CBT) (Addington et al., 2011; Morrison et al., 2012; van der Gaag et al., 2012; A.Yung et al., 2011); and food supplements, such as omega-3 fatty acids (Amminger et al., 2010). For an in-depth review of this issue, previous works (Fusar-Poli, McGorry, et al., 2017; Marshall & Rathbone, 2011; Stafford et al., 2013) can be consulted. Table 3 presents some prominent clinical trials that have examined the effectiveness of prophylactic interventions in populations detected as being at high clinical risk for psychosis (HCR-P).

Based on the results, it appears that individual CBT, with or without family CBT, could be the first-line intervention in people with HCR-P (Stafford et al., 2013; van der Gaag et al., 2013). However, although in the short term CBT seems to reduce by half the risk of the appearance of a FEP (that is, between 6 and 12 months after the intervention), its effect seems to disappear in longer periods, specifically from 24 months onwards (van der Gaag et al., 2013).



To date, no trial has examined the long-term effects of existing preventive interventions, which is a genuine handicap when establishing more conclusive intervention protocols (Fusar-Poli, McGorry, et al., 2017). Despite this, it seems that intervening in people with HCR-P is effective in improving their perception of self-efficacy and ability to engage in social activities. The EIP services also allow us to treat other comorbid subclinical disorders that would otherwise go unnoticed in conventional

mental health centers, providing vocational support and reducing family stress (Fusar-Poli, Byrne, Badger, Valmaggia, & McGuire, 2013). Finally, people who have been treated in these services and who subsequently suffer a FEP, received adequate treatment earlier (average DUP = 11 days) than those who have not received such treatment (average DUP = 1 year) (Valmaggia et al., 2015).

Difficulties and proposals for improvement in EIP

When implementing and developing EIP programs and services in our context, there are a number of difficulties that should be taken into account. Table 4 summarizes some of the strengths and weaknesses related to EIP in Spain.

As mentioned before, one of the most significant difficulties is the detection of the population at risk. A priori, schools seem to be the best environment for the early detection of vulnerable adolescents and young adults. However, this usually occurs late in primary care, mental health, or emergency services. There is also a lack of coordination between educational and mental health institutions, both acting as storage compartments where the information does not flow between the various actors involved in the intervention with the young person. For example, it can happen that schools do not know which students are children of parents with schizophrenia (genetic risk) or that teachers have relevant information at the level of the social, academic, or family functioning of the child that mental health services cannot access. It should also be mentioned that although mental health centers for children and adolescents (which usually cater for children between 0 and 16 years old) seem to be more aware of the importance of coordinating with schools, this does not happen in such a widespread way in adult mental health centers (serving the population over 17). However, it is just at this moment—from the age of 16—that the risk of changes in the psychotic spectrum seems to increase. This division by age of the child and youth centers and those of adults in Spain is a clear limitation due to the fact that in this transition a great amount of information about the adolescents and their families is lost. A possible solution could be to create intermediate mental health centers to serve adolescents and young adults between the ages of 12 and 25 years, as has been done in other countries such as Australia. Another possibility would be to create the figure of the “case manager” that would serve the young person both on an outpatient basis and in any hospital admissions that may be required over time.

A second problematic issue, although not new or exclusive to mental health (Riley, Patterson, Lane, Won, & Ranalli, 2018), is whether the socio-health environments (mental healthcare units and hospitals), as they are conceived at present, are the best physical space for attending to adolescents and young adults at risk of or presenting a FEP. It would be beneficial to rethink the configuration of these spaces to make them truly youth friendly

TABLE 2
MODEL OF CLINICAL STAGES FOR PSYCHOTIC SYNDROME AND INTERVENTIONS RECOMMENDED BY STAGE

Stage	Clinical definition	Characteristics	Recommended interventions
0	Premorbid	Asymptomatic with genetic risk	<i>Selective primary prevention</i> General psychoeducation Family psychoeducation
1a	HCR-P	Negative and neurocognitive symptoms	<i>Indicated primary prevention</i> Specific psychoeducation Family psychoeducation Active reduction of substance abuse
1b	HCR-P	Attenuated psychotic symptoms	<i>Indicated primary prevention</i> Individual and family psychoeducation
1c	HCR-P	Short psychotic episodes with remission	<i>Indicated primary prevention</i> Same as in 1b Regular follow-up
2	Early complete recovery	First complete psychotic episode	<i>Early intervention and secondary prevention</i> Individual and family psychoeducation Psychological therapy Active reduction of substance abuse Atypical antipsychotics and other psychotropic drugs Vocational rehabilitation
3a	Late/incomplete recovery	Relapse of psychotic recovery	<i>Early intervention and tertiary prevention</i> Same as in 2, but emphasizing relapse prevention and early identification of warning signs
3b	Late/incomplete recovery	Multiple relapses recovery	<i>Early intervention and tertiary prevention</i> Same as in 2, but emphasizing long-term stabilization
3c	Late/incomplete recovery HCR-P: high clinical risk of psychosis	Incomplete recovery from the first episode	<i>Early intervention and tertiary prevention</i> Same as in 3a; clozapine in case of resistance to treatment
4	Chronicity	Severe or persistent mental disorder	<i>Maintenance intervention</i> Same as in 3a-c, but emphasizing the social functioning and participation

HCR P: high clinical risk of psychosis



for this target population, for example, locating them in attractive areas, free of potential stigmas, and with programs that are very focused on being playful (Fraser, Berger, & McGorry, 2006) and virtual (Laine, Anttila, & Valimäki, 2016). For example, Niendam et al. (2018) have successfully used mobile applications to monitor vulnerable youths.

Thirdly, although the current dimensional models in psychosis, such as, for example, the stages of Fusar Poli et al. (2017), are very useful, at a theoretical and practical level they must deal with many obstacles. Although staging models have been widely used in other branches of medicine, such as in oncology, in order to determine issues related to prognosis and treatment based on stable pathophysiological limits, their use in psychosis is not comparable (Dietsche, Kircher, & Falkenberg, 2017). In this sense, the high heterogeneity and clinical variations within the same stage make it difficult to be able to relate them to a specific pathophysiology (Fusar-Poli et al., 2016). Therefore, it is necessary to continue investigating their clinical justification (Duffy, Malhi, & Grof, 2017). On a practical level, moreover, these models are not widely known or shared by all of the professionals involved, which can make both intercommunication and the design of multidisciplinary prophylactic interventions difficult. Compared with dimensional models, traditional categorical models suffer from a bias towards the premature diagnosis of schizophrenia (stage 2) in vulnerable adolescents in crisis who may present, for example, brief psychotic symptoms (stage 1c). This early diagnosis can lead to an overuse of antipsychotic drugs or to these drugs being seen as the only possible treatment. The perception on the part of youths and adolescents of a lack of non-pharmacological preventive interventions may also hinder adherence to later psychological treatments that have been shown to be effective in schizophrenia (Morrison et al., 2014). For example, a teenager prematurely diagnosed with schizophrenia and treated with

antipsychotics in an acute care unit may perceive mental health institutions as coercive, counterproductive or even stigmatizing.

Therefore, a change is necessary in the healthcare model of practitioners, from paternalistic models to others that are more collaborative, dialectical and adapted to young people today, where the use of medication is consensual or even optional, as a second line of intervention if others of a psychoeducational or psychotherapeutic nature fail (Klosterkötter, 2014). This also requires greater training for practitioners to understand an increasingly complex clinical and social reality. For example, a teenager with negative and cognitive symptoms (stage 1a) with attentional difficulties, poor academic performance and cannabis use may be diagnosed with ADHD and may receive treatment with methylphenidate. This treatment could induce or accelerate the presentation of a FEP in a teenager that is vulnerable to psychosis (Mosholder, Gelperin, Hammad, Phelan, & Johann-Liang, 2009).

Finally, it must be emphasized that the clinician is often required to evaluate and contextualize a young person, usually in a critical situation of crisis, in 45-60 minutes in the worst case (the average time a consultation lasts in mental health) or, at best, over a hospital stay in an acute care unit of about 2 weeks. Even in the best of cases, 2 weeks are often not enough to gather all the information of other variables relevant to the diagnosis, beyond the signs and symptoms present in the adolescent, such as family context, social, academic, and occupational functioning, cognitive functioning and personality structure. As a result of this lack of time and information, false diagnoses of schizophrenia can occur in young people with psychotic symptoms in contexts of personality traits of clusters A (e.g., schizotypal disorder) and B (e.g., emotional dysregulation), with intellectual disability or borderline intelligence, on the autistic spectrum or with substance use. In these cases, the main diagnosis and treatments should not be the usual ones in

TABLE 3
CLINICAL TRIALS ON PREVENTION IN PSYCHOSIS

Study	Country	N	Detection instrument	Average age (range)	Comparison	Duration (weeks)	Follow-up (weeks)
Addington et al. (2011)	Canada	51	SIPS	20.9 (NR)	CBT vs. support advice	26	52 and 78
Amminger et al. (2010)	Austria	81	PANSS	16.4 (NR)	Omega 3 fatty acids (1200 mg / day) vs. placebo	12	52
McGlashan et al. (2006)	USA	60	SIPS	17.8 (12-36)	Olanzapine (8 mg/day) vs. placebo	52	104
Yung et al. (2011)	Australia	115	CAARMS	17.9 (NR)	Risperidone (2 mg/ day) + CBT vs. CBT + placebo vs. support advice + placebo	52	104
Morrison et al. (2012)	UK	288	CAARMS	20.7 (14-34)	CBT + support advice vs. support advice	26	104
Ruhrmann et al. (2007)	Germany	124	ERtraos	25.6 (NR)	Amisulpride (118.7 mg/day) + NBI vs. NBI	12	NR
van der Gaag et al. (2012)	Netherlands	201	CAARMS	22.7 (NR)	CBT vs. support advice	26	52 and 78

NR=not reported; CBT=cognitive behavioral therapy; NBI=needs based intervention



schizophrenia, but should focus instead on working on other therapeutic targets. Another of the main advantages of the dimensional models of prevention compared with traditional categories is that they allow intervention (prevention) without the need to label (without diagnosing).

NEW VIGOR IN THE STUDY OF PSYCHOSIS PREVENTION

The field of psychosis prevention is the subject of continuous analysis, and progress is occurring with great speed. Here we will discuss some of the advances that, in our opinion, deserve special attention (for more details see Fonseca-Pedrero, 2018):

New psychopathological models. Especially interesting are the contributions of the network model (Borsboom, 2017; Fonseca-Pedrero, 2017, 2018), dynamic systems theories or chaos theory (Nelson, McGorry, Wichers, Wigman, & Hartmann, 2017). In addition, new ways of conceptualizing and classifying mental problems such as Research Domain Criteria (RDoC) (Insel et al., 2010), are coming into use in response to

the limitations of the DSM/ICD model. These aspects undoubtedly favor the analysis of mental disorders from a new perspective that drives, among other things, the search for etiological mechanisms and multidisciplinary.

Risk equations. Regarding studies of prediction of the risk of psychosis, algorithms are being implemented that attempt to give a psychosis “risk probability” score for healthy relatives of patients based on certain variables (e.g., cannabis use, obstetrics complications, trauma experiences, month of birth, etc.) (<https://kesh-lab.shinyapps.io/PERS-calc/>) or calculating the probability of transitioning to a psychotic disorder in healthcare contexts (Fusar-Poli, Rutigliano, et al., 2017) (<http://www.psychosis-risk.net/step1.asp>).

Improve prediction levels. The combination of different risk markers from different levels of analysis (e.g., genetic, cerebral, psychophysiological, cognitive, behavioral) and considering the role of the environment, seems to be one of the best options when predicting the transition to psychosis (Schmidt et al., 2016; Zarogianni, Storkey, Johnstone, Owens, & Lawrie, 2017). The combination of multiple indicators of different levels of analysis in sequential phases may substantially improve psychosis prediction (Schmidt et al., 2016). In addition, current works are attempting to design a finer evaluation of the high risk groups, generating more homogeneous subgroups, stratified by some variable (e.g., neurocognitive performance or positive psychotic symptoms) (Carrión et al., 2017; Cornblatt & Carrión, 2016).

Incorporation of new information technologies. Information technologies are having a clear impact in the field of evaluation and diagnosis of psychotic spectrum disorders and mental health (Insel, 2017). Artificial intelligence (learning machine), virtual reality, ambulatory assessment via mobile devices (e.g., experience sampling method, ESM), digital phenotyping, are just some examples. For example, the incorporation of ESM enables us to avoid some of the limitations of self-reports, to analyze the patient in their real context, in a personalized way, in interaction with the context and to look for possible underlying causal mechanisms (Myin-Germeys et al., 2009; van Os, Delespaul, Wigman, Myin-Germeys, & Wichers, 2013; van Os, Reininghaus, & Meyer-Lindenberg, 2017).

From the patient to the person. Different movements (e.g., *Hearing voices*) and research show that the most current model is one that talks about patients in “third person”. A new vision of this syndrome should try to put the emphasis on the “first person”, i.e., listen to the people –from a phenomenological perspective– (Kendler, 2014; Nelson, Parnas, & Sass, 2014; Parnas, 2015; Pérez-Álvarez, 2012). In addition, and related to the previous point, other studies should focus on the “p” of the person and not on the “p” of statistical significance. The functional impact on the person is much more relevant –due to its impact on day to day life– than statistical significance. Research studies must have an echo in the real world of people.

TABLE 4
FACILITATORS AND OBSTACLES FOR THE IMPLEMENTATION OF EIP SERVICES

Sector	Facilitators	Obstacles
Scientific	EIP experts promote and develop rigorous research investigations The social, clinical, and economic benefits of prevention in psychosis are demonstrated	It is essential to expand the focus from the clinical and healthcare fields to the educational and social fields
Political	Greater sensitivity of the population for mental health and prevention Opt for the creation of EIP services in many Autonomous Communities	Lack of political interest Little recognition of the specific needs of young people with early psychosis
Communication and involved parties	High involvement of families and users of services from the beginning Patient and family associations can contribute funds and initiatives Successful experiences of users and their families can create an awareness of the importance of prevention in psychosis and EIP services	Lack of disclosure of studies and prevention models in psychosis Lack of specific training in prevention in psychosis Lack of effective communication with family members, health practitioners and other professionals such as teachers and professors Lack of effective communication with politicians and administrators
Economic, structural and administrative	Incorporation or creation of new EIP programs and services in public healthcare and social services Evolution of mental health practitioners and structures from paternalistic models to other more collaborative and dialectical ones Reduction of stigma Establishment of alliances and synergies between practitioners and public and private organizations	Cuts in healthcare and social policies Excessive emphasis on medicalization or institutionalization Poor coordination between specialists in mental health and primary care units Reluctance to share information relevant to EIP Poor access to EIP services Facilities not adapted to the needs of young people

EIP=early intervention in psychosis



Focusing on positive aspects and strengths. We must gradually transition towards a positive and optimistic, non-stigmatizing, view of the psychotic disorder (Jeste, Palmer, & Saks, 2017). There must be a transition from focusing on the limitations of patients to their strengths. Until recently, the idea that psychosis was “a chronic mental disorder of cerebral origin” (Guloksuz & van Os, 2018) predominated, however, there has been a gradual change in the conceptualization of psychotic disorders, increasing the interest in other aspects and areas, such as the phenomenological perspective or the process of personal recovery.

Beyond the schizo-prism and the concepts of “transition” and “risk of psychosis”. Additionally, it would be more beneficial to move into a broad syndrome of early mental distress. From this point of view, the focus of action would no longer be solely psychosis, but a risk condition that could predispose towards different psychopathological conditions. We are moving towards a prevention model that goes beyond the schizo-prism, the concepts of “transition” or “risk of psychosis” and move towards an approach based on stages (levels of severity), personalized, dynamic (longitudinal and developmental) and multidimensional. It is a more global mental health prevention model that is not limited to the conglomerate of psychotic disorders and that is creating interesting initiatives such as Headspace (<https://headspace.org.au/>).

RECAPITULATION

The essence of the present work has been to produce an update in the field of the prevention of psychotic disorders, specifically in early detection and intervention. Our aim has been to synthesize the state of the question and reflect on this fascinating topic that has been the object of research and debate in recent years.

First of all, the conceptualization of the syndrome of psychosis and its prevention has been addressed, highlighting the current limitations in its definition, understanding, measurement, diagnosis, and intervention. As has been mentioned, the prevention of the psychosis syndrome requires, on the one hand, a rigorous evaluation protocol to identify and detect unequivocally the potential condition of risk or liability, and on the other hand, effective prophylactic treatment. To prevent, we must detect, identify and intervene, and do it early, the sooner the better.

Secondly, the different procedures and measurement instruments for the evaluation of the psychosis risk liability have been mentioned. The reliable identification of people with latent vulnerability to psychosis seems to be a valid and useful strategy, which allows us to advance in: a) the understanding of the etiological mechanisms involved, b) the analysis of risk and protection markers involved in the transition, and c) improving the prediction rates of the clinical condition.

Third, early interventions in psychoses available to the mental health professional have been discussed. The staging models, the effectiveness of EIPs and the difficulties associated with them have been addressed, an aspect that enables us to formulate proposals for future improvement in EIP. Fourth, some future perspectives of research in this area of study have been outlined, which in essence, go beyond the mere study of psychosis, and are cross-sectional to different areas of psychology.

In short, even though vast progress has been made in the last five decades, we are still in the early stages. In the absence of new results, moderation and prudence must prevail. Be that as it may, these advances in prevention have made it possible to improve our understanding of the psychosis syndrome, both in terms of understanding the etiological mechanisms and in improving the negative, stigmatizing, deteriorating and brain-centrist vision associated with this clinical condition in previous historical stages.

Future studies will clarify which is the best approach and prevention, and which is the best algorithm to identify, detect, and predict the risk not only of psychosis, but of any mental disorder. In this way, it is possible to prevent, reduce or even abort the possible transition to the clinical condition, thus improving the quality of life of individuals and families, the management of social and healthcare resources and reducing its impact at multiple levels.

ACKNOWLEDGMENTS

This research has been funded by the Ministry of Science and Innovation of Spain (MICINN) (reference PSI2014-56114-P), by the Instituto Carlos III, Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM) [Carlos III Institute, Center for Biomedical Research in Mental Health Network], by the 2015 Call for Proposals “Ayudas Fundación BBVA a Investigadores y Creadores Culturales” [“BBVA Foundation support for researchers and cultural creators” and for the “Ayudas Fundación BBVA a equipos de investigación científica 2017” [“BBVA Foundation support to scientific research teams 2017”].

CONFLICT OF INTERESTS

There is no conflict of interest.

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