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# Early psychotic experiences: Interventions, problems and perspectives

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**P**sychotic or psychotic-like experiences and symptoms may precede and be indicative of later psychosis emergence. DSM-5 has introduced Attenuated Psychosis Syndrome (APS) as a condition for further study, arguing for its clinical validity and the need for identifying sub-threshold psychotic states. Early psychosis intervention has an already established role in reducing the Duration of Untreated Psychosis (DUP), delaying psychosis onset and relieving Ultra High Risk (UHR) individuals from their presenting symptoms. Pharmacological and mainly psychotherapeutical approaches are suggested for this purpose. Cognitive Behavior Therapy (CBT) seems to have clear evidence of favorable outcome concerning transition to psychosis rates, omega-3 fatty acids lower but promising evidence, while low-dose antipsychotic medication or antidepressant treatment may seem beneficial, but it remains unclear if the reported favorable effects persist in the long term and how long intervention in UHR subjects should be given for. Case management and close monitoring based on principles of social psychiatry are considered key elements for the management of UHR individuals. However, the blazing case about early psychosis concerns the accurate specification of the prodromal stage of psychosis, which may set the basis for meaningful and effective early intervention. Although psychometric tools have been developed and provide a common criteria-based recognition method, debate is alive and well regarding “false positive” cases, since most UHR subjects will not finally develop psychosis. Moreover, transition rates to psychosis have been declining over the years, leading to fierce criticism over the validity of the UHR/APS state and legitimacy of its treatment. On this framework, ethical issues of stigmatizing through unnecessary diagnosing and antipsychotics’ prescribing are matters of serious questioning. Clinical heterogeneity and high comorbidity are further implications of the UHR state. Current research emphasizes on improving validity of inclusion criteria and formulating personalised and clinical stage-based intervention strategies. In order to do that, early psychosis recognition and intervention ser-

vices are established throughout the world, trying to contribute in research by applying clinical, cognitive or neuropsychological criteria. Nevertheless, in the majority of so far conducted studies, samples sizes are considered small and duration of follow-up short, which are limitations yet to overcome. Other scientific voices argue that the UHR state might represent a non-specific risk factor for psychiatric disorders in general and not necessarily for psychosis and tend to examine the UHR and early intervention idea under the prism of subthreshold or early mental distress state. Either way, recognizing and intervening early in emerging psychiatric states, especially in those with psychotic or psychotic-like symptomatology, share indisputable benefits under the broader concept of prevention, setting a strong scientific-clinical rationale for service provision to help-seeking people and the possibility of changing the course for those with vulnerability to psychotic illnesses.

**Key words:** Early psychosis, Attenuated Psychosis Syndrome, psychosis prodrome, preventive psychiatry.

## Introduction

Early detection and care are as critical in potentially serious mental illness as they are in physical illnesses such as cancer, diabetes and cardiovascular disease. According to the World Health Organization's World Health Report 2001, schizophrenia and other forms of psychoses, which affect at most young people, represent a major public health problem. Worldwide, schizophrenia ranks among the top 10 causes of disability.<sup>1</sup> Schizophrenia is related with poor physical health and premature death, with a reduction in life expectancy of 10–25 years compared to general population, mainly due to higher risk for cardiovascular, metabolic, respiratory diseases and suicide.<sup>2</sup> Moreover, there are major social and financial consequences, though it is hard to estimate precisely the direct and indirect impact.<sup>3,4</sup> Thus, schizophrenia and psychosis in general pose an enormous burden, both in terms of economic cost and of human suffering. Beside the importance of this serious mental illness and the need for research regarding its nature, it is common knowledge that prevention is the best therapy. Although therapeutic options are improving, the illness course for patients with psychotic disorders is often disappointing with multiple hospitalizations and a lifetime of antipsychotic medication prescriptions.<sup>5</sup> As the field is far from a "cure" for psychotic disorders, advancing prevention and early intervention is vital to improving functional deficits and later outcome. Identification of those most at risk for developing a psychotic disorder is a crucial step. The onset of psychosis may be preceded by

weeks, months or years of psychological and behavioral abnormalities, including disturbances in cognition, speech, emotion, perception, motivation and sleep. The emergence of these symptoms provides researchers with an opportunity to identify those at heightened risk for psychosis conversion and to conduct research on early treatment. Over the last 20 years, a focus on early intervention in psychotic disorders has emerged. Initially, the early psychosis movement focused on timely recognition, phase-specific treatment of first-episode psychosis and the crucial time period coming up.<sup>6</sup> However, early psychosis researchers suspected that pushing the point of intervention even further, back to the prodromal phase of psychotic disorders, may result in even better outcomes.

## The early (prodromal) phase

The "prodromal phase" is characterized by non-specific or subtle psychotic symptoms and functioning impairment.<sup>7</sup> People with such symptoms are considered Ultra High Risk (UHR) for developing psychosis. People UHR of psychosis are associated with an approximately 30% risk of developing psychosis in the following two years, 400 times greater risk than normal people, three- to four-fold higher risk than people with family history of psychosis alone.<sup>8,9</sup> We can conclude that most UHR subjects will not develop psychosis. Hence the term "Ultra High Risk" is preferred rather than "prodromal", as the last one refers to the period of subclinical signs and symptoms that usually precedes the onset of psychosis.

Intervening early and effectively in the course of psychosis can limit initial problems and improve long-term prospects for recovery. This is further reinforced by the emerging role of the Duration of Untreated Psychosis (DUP). Recent research indicates that longer DUP is associated with worse functional outcomes in addition to persistent symptoms, poorer quality of life and lower treatment response.<sup>10,11</sup> This is one additional reason for early recognition and intervention for UHR people. Moreover, effective treatment of first psychotic episode improves prediction and determines more or less further outcome with an emphasis given in the first five years of the psychotic disease.<sup>12</sup>

### **Early recognition (Psychometric tools and Criteria)**

The clinical assessment of UHR people is considered rather challenging, since these people have a difficult, subtle psychopathology and are usually guarded. As a result, two or three sessions may be required for safe clinical evaluation. The small percentage of individuals that will finally develop full-blown psychosis in comparison with the total number of those diagnosed as UHR raises the question of "false positive" diagnoses and stigmatization. In order to limit false positive cases, efforts for accurate diagnostic tools and better screening methods are made.

For this purpose, established psychometric tools are being used, specifically CAARMS (Comprehensive Assessment of At Risk Mental States) and SPI-A (Schizophrenia Proneness Instrument). These tools display the patient's emerging symptoms and combined with psychiatric examination, genetic predisposition, family history, young age, presence of risk factors (such as cannabis abuse or immigration) and recent functioning impairment, contribute in the formulation of Ultra High Risk criteria<sup>13</sup> in order to compose a Close-in Strategy.<sup>14</sup> The most prevalent classification of UHR people has been suggested from PACE (Personal Assessment and Crisis Evaluation) clinic in Australia. According to this suggestion,<sup>15</sup> UHR people are classified in three groups: (a) group of Attenuated Psychotic Symptoms (APS) in which subjects have experienced subthreshold, attenuated positive symptoms during the past year, (b) group

of Brief Limited Intermittent Psychotic Symptoms (BLIPS) in which subjects have experienced episodes of frank psychotic symptoms that have not lasted longer than a week and have spontaneously abated, (c) group of Trait and State Risk Factor (TSRF) in which subjects have either a first-degree relative with psychotic disorder or a schizotypal personality disorder and have experienced a significant decrease in functioning during the last year.

### **Early management**

The experience of early intervention services has indicated that UHR subjects are 'help-seeking', clinically unwell, functionally impaired and usually in distress. They ask for some form of treatment and are mostly concerned about their presenting problems and less about their risk of developing a psychotic disorder.<sup>16</sup> It is important to notice that in UHR patients insight is less impaired than in psychotic patients. This is a key difference in the appraisal of symptoms, as UHR subjects attribute abnormal experiences to their personal being unwell, while psychotic patients display bizarre or externalizing explanations for their symptoms.<sup>17</sup> Since an UHR patient is presented or referred in an early intervention service, there are short and long term objectives regarding his clinical management. Short term objectives concern relieving of presenting symptoms and functional disability and providing information (psychoeducation), while long term focuses on prevention of psychosis and outcome improvement, if psychosis eventually develops. The efficacy of clinical management is related to engagement maximization and rapid response to referral, flexibility with time and place of assessments, psychoeducation, targeted case management (help with occupational and social problems), psychological intervention (Cognitive Behavioural Therapy at most), low dose antipsychotic medication or antidepressant treatment. Both pharmacological and psychological interventions appear to be effective in reducing the severity of presenting symptoms in UHR subjects. Monitoring of UHR subjects for the first signs of frank psychosis has shown promise in reducing the delay of untreated psychosis. Follow-up studies are required to test whether the reduction of DUP leads to an improved long term outcome and thus prognostic value.

## Early treatment-intervention

### **Antipsychotics**

Antipsychotic medication has been established as a standard of care for persons diagnosed with a psychotic disorder. According to this rationale, several trials of antipsychotic agents' administration have been conducted in UHR individuals.

Two randomized clinical trials (RCT) have tested antipsychotic medication in early psychosis. In the first study, risperidone (1–2 mg/day) or CBT added to needs-based intervention was compared to needs-based intervention alone for six months and was found superior regarding transition to psychosis rates. However, the study groups were not blinded to the treatment and the effects of treatment did not persist at either 12 months or 3 years of follow-up.<sup>18</sup> Another study compared the effects of olanzapine versus placebo with a double-blind randomization, with no significant differentiation in transition to psychosis after 12 months.<sup>19</sup> while high drop-out rates did not allow analysis for two-year outcome. In two additional open-label studies, researchers have examined the effect of atypical antipsychotics on symptom severity in prodromal individuals. A small, non randomized study examined UHR participants after 8 weeks of receiving aripiprazole. Results indicated moderate reductions in positive, disorganization and general symptoms and a significant functional improvement.<sup>20</sup> Another randomized parallel-group study compared amisulpride plus needs-based treatment to needs-based treatment alone. At the 12-week outcome, amisulpride plus needs-based treatment was associated with a reduction in positive, basic, negative and depressive symptoms, as well as an improvement in functional deficits.<sup>21</sup> Both aripiprazole and amisulpride were associated with less weight gain than has been observed with olanzapine or risperidone.

In summary, results of antipsychotic medication studies in UHR studies suggest that intervention may delay conversion to psychosis and improve symptoms during the active phase of treatment, but there is no evidence of lasting effects after treatment cessation. Meanwhile, there is skepticism over sensitization of dopamine receptors in the brain, as it has been suggested that possibly leads to supersensitiv-

ity psychosis or rapid-onset psychosis following cessation of antipsychotic medication.<sup>22</sup>

### **Antidepressants**

Since administration of antipsychotic agents is accompanied by social stigmatizing, low adherence and small tolerance due to side effects, antidepressant studies in UHR population are conducted. Moreover, up to 50% of UHR subjects present with low mood and anxiety in addition to their attenuated psychotic symptoms.<sup>23</sup> Antidepressants may have an effect on the development of psychosis, as emotional dysregulation processes, anxiety and depressive symptoms have impact on ongoing psychopathology and isolated psychotic experiences are more likely to develop into delusional mood and frank psychosis, if they occur in the context of depression. Antidepressants could improve mood, thereby reducing faulty attributions and appraisals of prodromal symptoms. Similarly, antidepressants may also minimize the risk of psychosis by modulating how individuals respond to environmental stressors.

Studies comparing antidepressant to antipsychotic treatment for UHR, found that both improved clinical symptoms, but conversion rates in antidepressant treatment groups were much lower than those of antipsychotic treatment.<sup>24–26</sup> Issues regarding studies' methodology question the results, as UHR individuals with more severe attenuated symptoms or higher level of disorganized thinking tended to be administered with antipsychotics, while UHR individuals with less severe symptoms were treated with antidepressants.

### **Psychotherapy**

Psychological interventions have been explored as cost-effective, well-tolerated and more preferable as treatment options by consumers. In patients with schizophrenia, research indicates that social skills, cognition and interaction training programs lead to improvements in measures of social functioning. Psychoeducational family interventions also improve social adjustment as well as quality of life, family burden and treatment adherence.

Moreover CBT is widely used in UHR subjects. For example, in the OASIS (Outreach And Support In South London) Early Psychosis service, when pa-

tients are offered the choice of treatment, the majority (70%) of UHR subjects choose to have CBT. In a recent meta-analysis,<sup>27</sup> five trials of CBT were found to have moderate effect on transition to psychosis at both 12 and 18 months. There has also been evidence that complex psychosocial interventions (integrated psychotherapy, psychotherapy plus pharmacological treatment) could reduce transition or delay onset of psychosis, relative to supportive counselling or treatment as usual.

In conclusion, CBT has shown clear evidence of moderate quality on reducing transition to psychosis at 12 months.

### Emerging treatments

There is evidence on neurodevelopmental disorders suggesting that fatty acid deficiencies or imbalances may be a contributing factor. Researchers have begun to examine the effects of fatty acids, such as omega-3 fish oils [eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)], on neuropsychiatric disorders such as schizophrenia, depression, bipolar disorder, autism, attention-deficit/hyperactivity disorder, dyslexia and dyspraxia.<sup>28,29</sup> A 12-week trial was conducted comparing EPA with placebo in UHR subjects. At 12 months of follow-up, only 5% of UHR individuals in the EPA group had developed psychosis, compared to 29% in the placebo group. There were also improvements in the levels of attenuated positive and negative symptoms in the active EPA treatment group.<sup>30</sup> This robust finding is being questioned due to small number of events,<sup>27</sup> however, replication, large multi-center study is currently ongoing.

Other ongoing trials, such as PREVENT, are multi-centered, with larger samples and aim in comparing psychotherapeutic interventions, omega-3 fish oils, antipsychotic agents (ziprasidone, quetiapine, aripiprazole) with placebo.<sup>31</sup> Moreover, other neuroprotective agents, as lithium or glycine, have been tested in small open label studies<sup>32</sup> in UHR individuals. Finally, two other studies investigate the influence of glutamatergic agents as D-serine and sarcosine compared to placebo.

The upcoming results of these studies will substantially expand the literature on the use of pharmaco-

logical or psychological treatments among individuals meeting prodromal or UHR criteria.

### Limitations of trials to date

Though it is suggested that both pharmacological and psychological interventions at the UHR stage can ameliorate presenting symptoms reporting positive results, it remains unclear whether each or any intervention can prevent psychosis onset. To date trials are underpowered, because of small sample sizes. UHR individuals are difficult to identify and engage, unless they are help-seeking and significantly distressed. Another important feature yet to be determined is how long treatment in the UHR stage should last. Trials conducted so far do not answer this question, as both the duration of the interventions and the follow-up periods have been relatively short. It also remains unclear if benefits persist after cessation of treatment.<sup>6</sup> Finally, neither heterogeneity in UHR population nor phase-specific intervention approaches are adequately considered.

### The DSM-5 "Attenuated Psychosis Syndrome" and current attitudes

Attenuated psychosis syndrome (APS) was not included in DSM-5 as an official psychiatric disorder, but introduced as a "condition for further study". In section 3 of DSM-5, APS is described as a subthreshold (in duration and/or severity) psychotic syndrome. In comparison with psychotic disorders, the APS psychotic-like symptoms are less severe and more transient, are accompanied with distress and impaired function, while insight is relatively maintained. The need of defining APS has emerged, since research indicate that APS individuals are at higher risk of developing a full-blown psychotic disorder within the next two years.

Nevertheless, concerns regarding its validity as a clinical entity, ethical issues related to the stigma of a given diagnosis and unnecessary antipsychotic medication to a probable self-limited psychopathology, raise skepticism and serious objections in determining whether APS should be accepted as an official diagnosis in later editions of DSM.<sup>33</sup>

In order to avoid stigmatization, authors have proposed the term "Subthreshold Prodromal State",

"Subthreshold" because of the decreased severity of psychotic symptoms, "Prodromal" both because the term has been associated with psychosis and because the subjects could manifest major psychopathology in the future, and "State" because diagnosis may change with time.<sup>34</sup>

At the same time, the majority of APS individuals has one or more other current psychiatric comorbid conditions<sup>35</sup> (usually mood or anxiety disorders) and does not (as could initially be hypothesized) exhibit conversion to psychosis, but other psychiatric outcomes (most of them either fully recovery or development of some other psychiatric disorder and only a small proportion develops psychotic disorder). As a consequence, the UHR state might not necessarily be indicative of future psychosis. Moreover, the transition risk varies among studies with the age of the patient, the type of treatment provided and the way the syndrome and transition to psychosis are defined.<sup>36</sup> Recent studies have echoed this with the observed decline in transition rates<sup>36</sup> and presume that the UHR state might represent a non-specific risk factor for psychiatric disorders<sup>37</sup> and not specific for psychosis.

Besides, subthreshold psychotic experiences are commonly met in general population and the majority of them are transitory and disappear over time.<sup>38</sup> Nevertheless, it may become abnormally persistent –and subsequently impairing and clinically relevant– depending on the degree of environmental risk the person is additionally exposed to, according to the psychosis continuum hypothesis.<sup>38</sup>

Therefore, other key researchers tend to abandon the UHR idea and focus early, specific-phase intervention concept on the broad syndrome of early mental distress.<sup>39</sup>

### **Outstanding issues**

Early psychosis services worldwide have adopted certain intervention strategies and face common problems. It is debated whether duration of early intervention should last for one, two years or more. The most popular approach in early intervention services worldwide is to provide care for two years, as during this period the risk of transition to psychosis is considered to be maximal.

Clinical staging has been proposed as an intervention model in UHR subjects. This model<sup>40</sup> is suggested in correspondence to somatic diseases (e.g. staging in cancer), examines the course of prepsychotic phase and the quantitative and qualitative features of psychopathology in terms of phenomenology and respective severity. This suggests that the nature of the intervention should depend on the stage of illness, progressing from low intensity/frequency attenuated psychotic symptoms and low-risk treatments towards more intensive interventions for those who do not show a response and who may be more at risk. It is suggested that through clinical staging, it is possible to provide acceptable and less stigmatizing interventions to patients.<sup>41</sup> Up to date, there have been efforts in formulating evolving phases of clinical model in the prodromal states according to severity of positive symptoms at baseline. For example, the Hillside-RAP (Recognition and Prevention programme) suggested a modified version of the PACE criteria<sup>15</sup> using the term of CRH (Clinical High Risk) based on presence of positive or negative symptoms,<sup>42</sup> the PRIME (Prevention through Risk Identification, Management and Education) programme suggested another early recognition method with modified criteria (COPS, Criteria of Prodromal Syndromes) and psychometric tool (SIPS, Structured Interview for Prodromal Syndromes),<sup>43</sup> while the GRNS (German Research Network for Schizophrenia) programme focused on a risk classification model (Initial Prodromal State, EIPS and Late Initial Prodromal State, LIPS)<sup>44</sup> based on basic symptoms criteria.<sup>45</sup>

Need for targeted intervention has been emphasized, since validity of current UHR criteria are debated, as only a minority of UHR subjects will later develop psychosis. Researchers focus on determining factors or features that could identify the subgroup of subjects who will later become psychotic, so that preventative treatment could be given to those who need it most. This would permit a more efficient use of clinical resources and would be more acceptable from an ethical perspective. A number of clinical measures have been identified that are associated with the later onset of psychosis within UHR samples. The multi-center NAPLS study (North American Prodrome Longitudinal Study) reported

that the combination of a family history of schizophrenia, recent functional deterioration, unusual thought content and suspiciousness/paranoia, and social functioning deficits provided a positive predictive power for later psychosis of up to 80%.<sup>46</sup> The EPOS (European Prediction of Psychosis Study) multicenter study found that SIPS (Structured Interview for Prodromal Syndromes) positive score, bizarre thinking, sleep disturbances, schizotypal personality disorder, global functioning score in the past year, and years of education were the best predictor variables.<sup>47</sup> Neuropsychological studies of UHR subjects at clinical presentation have suggested that certain deficits, particularly impairments in episodic memory, are more marked in subjects who later develop psychosis.<sup>48</sup> Recent studies indicate that Basic Symptom Criteria<sup>49</sup> or combining UHR and cognitive Basic Symptom Criteria may have greater predictive value,<sup>50</sup> improving sensitivity and risk estimation.

Finally, neuroimaging studies of UHR subjects at presentation have found that the subsequent onset of psychosis is associated with smaller prefrontal and medial temporal volumes, increased prefrontal, medial temporal, lateral temporal and midbrain activation increased subcortical dopamine function and an alteration in the relationship between subcortical dopamine function and medial temporal glutamate levels.<sup>51,52</sup>

## Conclusion

Till now, early psychosis intervention trials have indicated that both pharmacological and psychological intervention strategies may be of value in terms of symptom reduction and onset delay of threshold psychotic disorder. Reducing DUP and severity of first episode is an indisputable benefit and very important for the first critical period of psychosis. On the other hand, it remains unsure whether these interventions have preventive value. UHR criteria lack convincing validity and sensitivity, since the majority of at risk individuals will not develop psychosis and “false positive” cases consist an issue of strong debate. Small cohort samples and limited duration of follow-up are limitations of so far conducted studies and are yet to overcome. It also remains unclear if the reported beneficial effects persist in the long term and how long intervention in UHR subjects should be given for. Clinical heterogeneity and high comorbidity in UHR subjects impose different methodological research conceptualization and individualized intervention. Clinical staging is proposed as an effective model in order to make early intervention meaningful. Ethical matters and stigmatizing in terms of unnecessary diagnosing and treating should always be considered. DSM-5 has introduced APS as an under consideration psychiatric condition, but all the above issues should be addressed in the field of research.

# Πρώιμες ψυχωσικές εμπειρίες: Παρεμβάσεις, προβληματισμοί και προοπτικές

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Οι ψυχωσικού τύπου εμπειρίες και συμπτώματα μπορεί να προηγούνται και να προειδοποιούν για μετέπειτα εμφάνιση ψύχωσης. Το DSM-5 εισήγαγε την έννοια του «Συνδρόμου Εξασθενημένης Ψύχωσης» (Attenuated Psychosis Syndrome, APS) ως «κατάσταση για περαιτέρω διερεύνηση», υποστηρίζοντας την κλινική της εγκυρότητα και την ανάγκη για έγκαιρη ανίχνευση των υποουδικών ψυχωσικών εκδηλώσεων. Η πρώιμη παρέμβαση στην ψύχωση έχει ήδη καθιερωμένο ρόλο στη μείωση του χρόνου μη θεραπευόμενης ψύχωσης, στην καθυστέρηση της έναρξης της ψύχωσης και στην

ανακούφιση των ατόμων λίαν υψηλού κινδύνου (Ultra High Risk, UHR) από τα συμπτώματά τους. Έχουν προταθεί τόσο φαρμακολογικές όσο και ψυχοθεραπευτικές προσεγγίσεις για τον σκοπό αυτόν. Η Γνωσιακή-Συμπεριφορική Ψυχοθεραπεία φαίνεται να έχει σαφείς ενδείξεις και ευνοϊκό αποτέλεσμα όσον αφορά στα ποσοστά μετάβασης σε ψύχωση, τα ωμέγα-3 λιπαρά οξέα χαμηλότερα αλλά υποσχόμενα αποτελέσματα, ενώ η χρήση αντιψυχωσικών (σε χαμηλές δόσεις) ή αντικαταθλιπτικών φαρμάκων μπορεί να φανεί ευεργετική, ωστόσο παραμένει ασαφές, εάν τα ευνοϊκά αποτελέσματα της όποιας παρέμβασης διαρκούν και για πόσον καιρό θα πρέπει να εφαρμόζεται στους UHR. Η διαχείριση περιπτώσεων και η στενή παρακολούθηση σε επίπεδο οργανωμένης δομής με βάση αρχές της κοινοτικής ψυχιατρικής αποτελούν βασικά στοιχεία για τον χειρισμό των ατόμων υψηλού κινδύνου. Ωστόσο, το φλέγον ζήτημα σχετικά με την πρώιμη ψύχωση αφορά στον ακριβή και έγκυρο προσδιορισμό του προδρομικού σταδίου της ψύχωσης, που μπορεί να θέσει τις βάσεις για ουσιαστική και αποτελεσματική έγκαιρη παρέμβαση. Αν και έχουν αναπτυχθεί ψυχομετρικά εργαλεία που παρέχουν μια κοινή, βάσει κριτηρίων, μέθοδο αναγνώρισης των UHR ατόμων, η διαμάχη μεταξύ ερευνητών καλά κρατεί όσον αφορά στις «ψευδώς θετικές» περιπτώσεις, δεδομένου ότι τα ποσοστά μετάβασης σε ψύχωση έχουν μειωθεί με την πάροδο των ετών, οδηγώντας σε έντονη κριτική για την κλινική εγκυρότητα των UHR/APS καταστάσεων και τη δεοντολογία ως προς την όποια παρέμβαση σε αυτές. Σε αυτό το πλαίσιο, τα ηθικά ζητήματα, που προκύπτουν από τον στιγματισμό μέσω των περιττών διαγνώσεων και της συνταγογράφησης αντιψυχωσικών, συνιστούν σημεία σοβαρής συζήτησης. Η κλινική ετερογένεια και η υψηλή συννοσηρότητα των UHR ατόμων αποτελούν στοιχεία περαιτέρω προβληματισμού. Η τρέχουσα έρευνα δίνει έμφαση στη βελτίωση της εγκυρότητας των κριτηρίων ένταξης και τη διαμόρφωση εξατομικευμένων στρατηγικών παρέμβασης με βάση το μοντέλο κλινικών σταδίων. Προς τον σκοπό αυτόν, δομές πρώιμης αναγνώρισης και παρέμβασης στην ψύχωση, που έχουν αναπτυχθεί ανά τον κόσμο, προσπαθούν να συμβάλουν στην έρευνα με την εφαρμογή κλινικών, γνωστικών ή νευροψυχολογικών κριτηρίων. Παρόλ' αυτά, στην πλειονότητα των μέχρι τώρα δημοσιευμένων μελετών, υπάρχουν αρκετοί περιορισμοί που δεν έχουν ακόμα αρθεί, καθώς τα μεγέθη των προς έρευνα πληθυσμών θεωρούνται μικρά και η διάρκεια της παρακολούθησης σύντομη. Άλλες επιστημονικές φωνές υποστηρίζουν ότι η κατάσταση UHR μπορεί να αντιπροσωπεύει έναν μη ειδικό παράγοντα κινδύνου για ψυχιατρικές διαταραχές γενικά και όχι απαραίτητα για ψύχωση, ενώ υπάρχει η τάση να εξετάζεται η ιδέα της έγκαιρης παρέμβασης υπό το πρίσμα της υποουδικής ή πρώιμης ψυχικής κατάστασης δυσφορίας. Είτε έτσι είτε αλλιώς, η αναγνώριση και η έγκαιρη παρέμβαση σε αναδυόμενες ψυχιατρικές καταστάσεις, ιδιαίτερα σε εκείνες με ψυχωσική ή ψυχωσικού τύπου συμπτωματολογία, συνεπάγονται αδιαμφισβήτητα οφέλη υπό την ευρύτερη έννοια της πρόληψης, θέτοντας ένα ισχυρό επιστημονικο-κλινικό πλαίσιο για πρόσβαση σε παροχή υπηρεσιών σε όσους έχουν ανάγκη από βοήθεια και τη δυνατότητα αλλαγής πορείας της ψυχικής νόσου για εκείνους που έχουν ευαλωτότητα για ανάπτυξη ψυχωσικών διαταραχών.

**Λέξεις ευρητηρίου:** Πρώιμη ψύχωση, Σύνδρομο Εξασθενημένης Ψύχωσης, προδρομική ψυχωσική συνδρομή, προληπτική ψυχιατρική.

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