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To the Editors: A novel algorithm to detect early risk of psychosis: results from the Prevention Program for Psychosis (P3) in a representative sample of Spanish adolescents

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Article Type:	Correspondence
Corresponding Author:	Mercedes Paino, Ph.D. University of Oviedo: Universidad de Oviedo SPAIN
First Author:	Mercedes Paino, Ph.D.
Order of Authors:	Mercedes Paino, Ph.D.
	Ana María González-Menéndez, Ph.D.
	Óscar Vallina-Fernández, Ph.D.
	Mar Rus-Calafell, Ph.D.

TO THE EDITORS: A novel algorithm to detect early risk of psychosis: results from the Prevention Program for Psychosis (P3) in a representative sample of Spanish adolescents

Dear Editor,

We know that the implementation of detection and prevention programs of psychosis in teens offers the most cost-effective choice by providing life-long benefits to affected people and their families (Campion et al., 2019). The availability of a rapid, rigorous, and updated screening procedure aiming to detect young individuals considered to be at risk of psychosis is undoubtedly essential.

But, *what to look for in adolescents at risk for developing psychosis?* Within the wide variety of existing risk approaches, attempts have been made to describe the Clinical High-Risk of psychosis (CHRp) or "at-risk mental state of psychosis" syndrome, with special focus on detecting the so-called "psychotic-like experiences" by means of self-reporting scales. And, *what prepsychotic experiences should we look for*? There is no single answer. The delimitation of the CHRp is characterized by a variety of symptoms assessed from different approaches to early detection (Ramella Carvaro & Raballo, 2014; Sanfelici et al., 2020), highlighting: a) the ultra-high risk criteria (UHR), focusing on the so-called attenuated psychotic symptoms or "positive" symptoms or anomalous experiences, such as depersonalization, suspicious or magical thinking below the psychosis threshold; b) the basic symptoms perspective (BS), consisting of perceived subjective alterations of different cognitive domains; and, more recently c) the non-psychotic anomalies in the subjective self-experience (ASE) approach, grouping symptoms such as hyperreflexivity or exaggerated self-awareness. Additionally, a recent meta-analysis of factors associated with the onset of psychosis in

individuals at CHRp (Oliver et al., 2020) underlines the key predictive role of global functioning.

These different approaches to CHRp result in great disparity of percentages of individuals detected to be at risk (ranging from 0.9% to 80%), depending on the chosen criteria, screening tool used, and the sample setting. A preliminary literature review conducted by our team and limited to studies from 2015 onwards confirmed this big window with the lowest rates being around 10-15% (Dolphin et al., 2015; Fonseca-Pedrero et al., 2016). Note also that studies that report high-risk percentages are not usually conducted with samples of only adolescents, but often include young adults, which increases the probability of transition rates.

In this updated study we aimed to create a new and systematic procedure for an effective and rapid early detection of CHRp in educational settings (set up within our *Psychosis Prevention Program* (P3; http://www.p3-info.es). Although other attempts have been conducted in similar contexts, (i.e., Fonseca-Pedrero et al., 2016), we have developed an advanced algorithm encompassing the operational criteria of the three main CHRp approaches (i.e., 3 tracks) mentioned above and in combination with assessment of functional deficits.

In line with this objective, we hypothesized that: i) the proposed algorithm would identify and distinguish different groups of CHRp individuals according to combined risk levels of the three tracks; ii) the detected percentage of adolescents at CHRp would be lower than the lowest rates of 10-15% reported in recent studies, considering the accuracy of the proposed methodology and given the age of the sample.

Using an online platform to deliver the symptom screening and following stratification and probability procedures in a two-stage sampling, a representative sample of 1,824 adolescents was recruited. A selection of valid and brief instruments

specifically developed for the evaluation of UHR, BS and ASE were used: 1) UHR symptoms: *The Oviedo Schizotypy Assessment* (ESQUIZO-Q-A; Fonseca-Pedrero et al., 2010) and the *Prodromal Questionnaire-Brief Version* (PQ-B; Loewy et al., 2011); 2) BS: the *Frankfurt-Pamplona Subjective Experience Scale* (EEFP; Cuesta et al., 1995); and 3) ASE assessment: *Self-Experience Lifetime Frequency Scale* (SELF; Heering et al., 2016). Complementarily, the *Global Functioning: Social* and *Role* (GF: Social & GF: Role; Cornblatt et al., 2007) and the *Oviedo Infrequency Response Scale-Revised* (INF-OV; Fonseca-Pedrero et al., 2011) were also included.

Based on the data from the most used clinical approaches to psychosis risk, the algorithm consists of a combination of the original scales' cut-off points or, alternatively, weighted scores based on extreme values. The algorithm also allows to establish 6 high-risk groups by combining the different risk levels (high/moderate) of the three tracks. The algorithm could be synthesized in the following formula *(Table 1):*

----------Insert Table 1 around here----------

Sixty-eight participants (3.7%) were identified as high-risk, having scored 2 on one (or more) of the three risk tracks. Analyses by tracks also showed that 44 of those 68 high-risk participants (2.4% of the total sample) were detected by Track 1 based in UHR symptoms. Furthermore, all cases classified as high-risk (2 score) by Track 1 (UHR) were of high or moderate risk on the other two tracks (BS and ASE). But not vice versa: most of the cases categorized as high risk (point 2) on Track 2 (BS, n=37; 2.0%) or Track 3 (ASE; n=26; 1.4%) obtained a 0 (low risk) for Track 1 (UHR) *(for a more detailed explanation of tracks' combinations see Table 1).*

The second hypothesis has also been confirmed, as a low percentage of high-risk adolescents (3.7%) was detected, similar to the low prevalence rates of meta-analytical studies focusing on psychotic-like experiences (PLEs) in adolescents (reported to average around 7-9%) (Healy et al., 2019).

The emerging question then is to propose an explanatory model for the process of psychosis risk, considering the algorithm measures and its results. It appears that the combination of UHR symptoms with global functional deficit (Track 1) could be more restrictive and accurate in identifying high-risk cases than the use of indicators based only on BS or ASE. Following the parallelism between the present results and the clinical staging model (McGorry et al. 2006), and in line with recent reviews (Nelson et al., 2017; Oliver et al., 2020), one plausible explanation could be a dynamic process of increased risk of psychosis rather than a hierarchical one.

A longitudinal design is proposed to follow up those participants identified as being at high risk, and invite them to participate in early prevention programs, with preventive measures adapted to their risk profile.

Yours sincerely,

M. Paíno

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References

Campion, J., Taylor, M.J., McDaid, D., Park, A.L., Shiers, D., 2019. Applying economic models to estimate local economic benefits of improved coverage of early intervention for psychosis. Early Interv. Psychiatry. 13(6), 1424-1430. https://doi.org/10.1111/eip.12787

Cornblatt, B.A., Auther, A.M., Niendam, T., Smith, C.W., Zinberg, J., Bearden, C.E. Cannon, T.D., 2007. Preliminary findings for two new measures of social and role functioning in the prodromal phase of schizophrenia. Schizophr. Bull. 33(3), 688–702. https://doi.org/10.1093/schbul/sbm029.

Cuesta, M.J., Peralta, V. Irigoyen, I., 1995. Escala de Experiencias Subjetivas Frankfurt-Pamplona. Actas Luso-Esp. Neurol. Psiquiatr. 23(4), 193-199.

Dolphin, L., Dooley, B., Fitzgerald, A., 2015. Prevalence and correlates of psychotic like experiences in a nationally representative community sample of adolescents in Ireland. Schizophr. Res. 169, 241-217. https://doi.org/10.1016/j.schres.2015.09.005.

Fonseca-Pedrero, E., Gooding, D.C., Ortuño-Sierra, J., Pflum, M., Paino, M., Muñiz, J., 2016. Classifying risk status of non-clinical adolescents using psychometric indicators for psychosis spectrum disorders. Psychiatry Res. 243, 246–254. https://doi.org/10.1016/j.psychres.2016.06.049.

Fonseca-Pedrero, E, Lemos-Giráldez, S, Paino, M, Muñiz, J., 2011. Schizotypy, emotional-behavioural problems and personality disorder traits in a non-clinical adolescent population. Psychiatry Res. 190, 316-321. https://doi.org/10.1016/j.psychres.2011.07.007

Fonseca-Pedrero, E., Muñiz, J., Lemos-Giráldez, S., Paino, M., Villazón-García, U., 2010. ESQUIZO-Q: Oviedo Schizotypy Assessment Questionnaire. TEA Ediciones S.A., Madrid.

Healy, C., Brannigan, R., Dooley, N., Coughlan, H., Clarke, M., Kelleher, I., Cannon, M., 2019. Childhood and adolescent psychotic experiences and risk of mental disorder: a systematic review and meta-analysis. Psychol. Med. 49(10), 1589–1599. https://doi.org/10.1017/S0033291719000485.

Heering, H.D., Goedhart, S., Bruggeman, R., Cahn, W., de Haan, L, Kahn, R.S., Meijer, C. J., Myin-Germeys, I., van Os, J., Wiersma, D., 2016. Disturbed Experience of Self: Psychometric Analysis of the Self-Experience Lifetime Frequency Scale (SELF). Psychopathology. 49, 69-76. https://doi.org/10.1159/000441952.

Loewy, R.L., Pearson, R., Vinogradov, S., Bearden, C.E., Cannon, T.D., 2011. Psychosis risk screening with the prodromal questionnaire–brief version (PQ-B). Schizophr. Res. 129, 42-46. https://doi.org/10.1016/j.schres.2011.03.029.

McGorry, P.D., Hickie, I.B., Yung, A.R., Pantelis, C., Jackson, H.J., 2006. Clinical staging of psychiatric disorders: a heuristic framework for choosing earlier, safer and more effective interventions. Aust. N. Z. J. Psych. 40(8), 616–622. https://doi.org/10.1080/j.1440-1614.2006.01860.x.

Nelson, B., McGorry, P.D., Wichers, M., Wigman, J., Hartmann, J.A., 2017. Moving from static to dynamic models of the onset of mental disorder: A review. JAMA Psychiatry. 74(5), 528–534. https://doi.org/10.1001/jamapsychiatry.2017.0001.

Oliver, D., Reilly, T.J., Baccaredda Boy, O., Petros, N., Davies, C., Borgwardt, S., McGuire, P., Fusar-Poli, P., 2020. What causes the onset of psychosis in individuals at clinical high risk? A meta-analysis of risk and protective factors. Schizophr. Bull. 46(1), 110-120. https://doi.org/10.1093/schbul/sbz039.

Ramella Carvaro, V., Raballo, A., 2014. Early detection of schizophrenia: a clinical-psychopathological revision of the ultra-high risk approach**.** J. Psychopathol. 20, 442-450.

Sanfelici, R., Dwyer, D.B., Antonucci, L.A., Koutsouleris, N., 2020. Individualized diagnostic and prognostic models for patients with psychosis risk syndromes: a meta-analytic view on the state of the art. Biol. Psychiatry. 88, 349-360. https://doi.org/10.1016/j.biopsych.2020.02.009.

Mercedes Paino

Department of Psychology, University of Oviedo, Spain

E-mail address: mpaino@uniovi.es

Ana María González-Menéndez

Department of Psychology, University of Oviedo, Spain

E-mail address: anagon@uniovi.es

Óscar Vallina-Fernández

Sierrallana Hospital, Cantabria Health Service, Torrelavega, Cantabria, Spain

E-mail address: osvallina@gmail.com

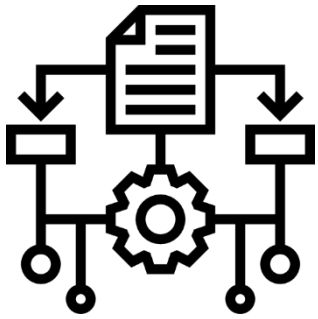
Mar Rus-Calafell

Mental Health Research and Treatment Center, Faculty of Psychology, Ruhr-University of Bochum, Bochum, Germany

E-mail address: mar.rus-calafell@rub.de

Table 1: CHRp algorithm formula.

(T^1 ≈ UHR + low GF) OR (T^2 ≈ BS + low GF) OR (T^3 ≈ ASE + low GF) = AT RISK MENTAL STATE (points 2/1/0)



Note: T^1 = Track 1 ≈ UHR + low GF (Global Functioning) (Risk levels: 2= above the cut-off point in the three included scales; 1= above the cut-off point in [Schizotypy AND low GF] OR [Schizotypy AND Prodromes] OR [Prodromes AND low GF]; 0= below the cut-off point in all the scales OR exceeding the cut-off point in just one of them-;
T^2 = Track 2 ≈ BS + low GF (Risk levels: 2= above the cut-off point in [Basic Symptoms Scale AND GF Social AND GF Role]; 1= above the cut-off point in one of the three included scales; 0= below the cut-off point in all the scales):
T^3 = Track 3 ≈ ASE + low GF (Risk levels: 2= above the cut-off point in [SELF scale "anomalous self-experience" AND GF Social AND GF Role]; 1= above the cut-off point in one of the three included scales; 0= no alteration in any of them).
At-risk mental state (levels): Points: 2= high risk; 1= moderate risk; 0= low or no risk