For each outcome, we fitted modified Poisson regression models with robust standard errors[9], using person-years as the offset term to address different follow-up times among participants, and clustering by family identification number to account for non-independence of repeated observations within families.

Compared to offspring of unaffected parents, individuals with one affected parent had a significantly increased risk of disability pension receipt, when accounting for demographic characteristics (IRR=1.88, 95% CI: 1.84-1.91, p<0.001; in 332,357 offspring of single-affected pairs vs. 1,641,244 offspring of unaffected pairs). The risk was doubled in offspring of dual-affected parents (IRR=2.84, 95% CI: 2.73-2.95, p<0.001; in 36,986 offspring of dual-affected pairs vs. 1,973,601 offspring of unaffected pairs). While all parental psychiatric disorders showed a significant association with offspring disability pension risk, the highest risk was observed in the offspring of parents affected with neurodevelopmental disorders (single-affected: IRR=3.36, 95% CI: 3.20-3.54, p<0.001; dual-affected: IRR=7.25, 95% CI: 5.68-9.26, p<0.001) and psychotic disorders (single-affected: IRR=2.11, 95% CI: 2.03-2.19, p<0.001; dual-affected: IRR=5.31, 95% CI: 4.33-6.52, p<0.001). Results were robust to further adjustment for offspring somatic disorders and education (single-affected with any disorders: IRR=1.73, 95% CI: 1.69-1.76, p<0.001; dual-affected with any disorders: IRR=2.38, 95% CI: 2.28-2.47, p<0.001) and for parental socioeconomic characteristics (IRR=1.40, 95% CI: 1.38-1.43, p<0.001; and IRR=1.60, 95% CI: 1.54-1.67, p<0.001, respectively). Results by parental disorder groups were also robust across models.

Offspring with one affected parent had a significantly increased risk of unemployment, compared to offspring of unaffected parents (IRR=1.46, 95% CI: 1.45-1.48, p<0.001). This risk was markedly raised among offspring of dual-affected pairs (IRR=1.92, 95% CI: 1.87-1.96, p<0.001). Offspring of parents single- and dual-affected by neurodevelopmental and substance use disorders showed the highest unemployment burden across both the base model and the model controlling for offspring somatic disorders and education. The fully-adjusted model resulted in significant, but attenuated, risks among offspring: IRR=1.21, 95% CI: 1.20-1.23, p<0.001 (single-affected with any disorders) and IRR=1.34, 95% CI: 1.30-1.38, p<0.001 (dual-affected with any disorders). Corresponding results by parental disorder groups were also attenuated, though the majority of them retained significance.

Repetition of analyses in a sub-cohort of offspring free from the diagnosis of interest produced comparable results for both outcomes. Likewise, the use of the "cleaned" comparison group in a sensitivity analysis did not alter the results.

Taken together, these results indicate a consistent and profound association between psychiatric history of parents and labour market marginalization in their offspring, which is particularly striking in dual-affected families. Though our primary finding is one of global, relative occupational adversity among the children of all affected parents, variation was further observed by parental diagnosis, with children of families impacted by neurodevelopmental, psychotic and substance use disorders having increased risk for adverse occupational outcomes.

Further work will be needed to gain nuanced insight into the mechanisms impeding labour market prospects in these populations, particularly given the limited impact of suspected determinant factors (e.g., child's own psychiatric health) on this association. Our findings suggest that such work should continue to extend consideration of differential risk dynamics by parent diagnosis and, particularly, parental diagnostic structure (e.g., single- vs. dual-affected families), in order to identify subgroups with particular need for preventive and early intervention strategies aimed to increase their chances of labour market participation.

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1. Stuart H. Curr Opin Psychiatry 2006;19:522-6.
2. Engels M, Wahrendorf M, Dragano N et al. Adv Life Course Res 2021;50:100432.
3. Jami ES, Hammerschlag AR, Bartels M et al. Transl Psychiatry 2021;11:197.
4. Harter SL. Clin Psychol Rev 2000;20:311-37.
5. Nordsletten AE, Larsson H, Crowley JJ et al. JAMA Psychiatry 2016;73:354-61.
6. Maes HH, Neale MC, Kendler KS et al. Psychol Med 1998;28:1389-401.
7. Sidorchuk A, Brander G, Pérez-Vigil A et al. Psychol Med 2022; doi: 10.1017/S0033291722003506.
8. Gottesman II, Laursen TM, Bertelsen A et al. Arch Gen Psychiatry 2010;67:252-7.
9. Zou G. Am J Epidemiol 2004;159:702-6.

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Is it possible to differentiate ICD-11 complex PTSD from symptoms of borderline personality disorder?

The introduction of complex post-traumatic stress disorder (CPTSD) and the revised descriptions of personality disorders in the ICD-11[1] is being accompanied by some uncertainty in clinical practice regarding the differentiation between the diagnostic profiles of CPTSD and borderline personality disorder (BPD).

The CPTSD diagnosis requires "exposure to an event or series of events of an extremely threatening or horrific nature, most commonly prolonged or repetitive events from which escape is difficult or impossible"[1]. Such events include, but are not limited to, torture, slavery, genocide campaigns and other forms of

organized violence, prolonged domestic violence, and repeated childhood sexual or physical abuse. At a symptom level, CPTSD includes the core PTSD symptoms of re-experiencing the traumatic event in the present, avoidance of traumatic reminders, and persistent perception of heightened current threat, along with the three symptom clusters of pervasive problems in affect regulation, negative self-concept, and relationship difficulties.

BPD has been reformulated in the ICD-11, due to the introduction of a fundamentally different approach to the classification of personality disorders[1]. Instead of diagnosing these disorders according to categorical types, the ICD-11 now requires impairments of the self (e.g., identity, self-worth, accuracy of self-view, self-direction) and interpersonal functioning as core features. A borderline pattern qualifier has been included, based on the nine DSM-5 diagnostic criteria for BPD, where the salient diagnostic features are instability in sense of self, relationships and affects, and the marked presence of impulsivity (e.g., unsafe sex, excessive drinking, reckless driving, uncontrollable eating). These diagnostic features represent some problems in the same general symptom domains as CPTSD, i.e. those related to affect dysregulation, identity, and relational capacities.

For several decades, the overlap between symptoms of BPD and various forms of CPTSD has been a subject of debate. There have been several studies exploring the association between these conditions using disorder-specific measures. These studies have been conducted in general population samples as well as in clinical samples of traumatized individuals, and they include factor analysis, latent class analysis and network analysis designs. All these studies concluded that there is a group of individuals who fulfil criteria for both disorders, but CPTSD and BPD were generally found to be distinguishable at the symptom and individual level.

There are several differences in the diagnostic criteria for the two disorders that are clinically informative in this respect.

While exposure to traumatic life events can precipitate both conditions, a history of trauma is not required for a diagnosis of BPD, while it is for CPTSD. Nevertheless, it is also important to highlight that a significant number of people with BPD report exposure to traumatic life events such as sexual abuse[2].

Diagnostic items related to affect dysregulation are often equally endorsed across the disorders, and in network analyses these symptoms appear to be common in both CPTSD and BPD[3]. However, BPD is associated with high rates of impulsivity and suicidal and self-injurious behaviours, while in CPTSD these characteristics may be present, but do not occur as frequently as other CPTSD symptoms, nor as often as in BPD[4]. Indeed, addressing suicidal and self-injurious behaviours has been viewed as the defining concern and primary treatment target in BPD.

Our clinical observations of people with CPTSD suggest that difficulties in affect regulation are ego-dystonic, stressor-specific and variable over time. In BPD, affect dysregulation and unstable mood seem to be ego-syntonic and persistent over time[5]. In BPD, self-concept difficulties reflect an unstable sense of self which includes changing goals and beliefs, whereas individuals with CPTSD have a consistent and stable negative sense of self. While it is frequently the case that individuals with CPTSD and BPD will both report feelings of low self-esteem, the additional presence of a changing view of self supports a BPD diagnosis.

Relational difficulties in BPD are characterized by unstable or volatile patterns of interactions, whereas in CPTSD they are defined by consistent difficulties in trusting others and avoidance of intimacy or closeness.

An important consideration in diagnosis is to avoid over-pathologizing the individual. For example, a symptom that is common to both disorders, such as emotional volatility, should be considered as part of each disorder when summing the totality of symptoms to determine whether the person meets criteria for a specific disorder. However, once a primary diagnosis has been made, the symptom should not be counted twice. The symptom should be counted once and designated to the diagnosis that been identified as primary, applying a "hierarchical" approach to diagnosis.

The clinical utility of formulating two diagnoses is primarily to guide treatment decisions and provide an intervention that optimizes outcomes by addressing the most impairing features associated with each disorder. Usually, BPD is likely the more severe disorder, with the greater impairment due to the presence of suicidality and self-injurious behaviours. We recommend that future research survey practitioners about what they find are the benefits and drawbacks of the current classification of these two conditions. In addition, the development of reliable and valid clinical interviews will further enable diagnostic accuracy.

There is a need to develop tailored treatments informed by the phenomenology and severity of the two conditions. A number of treatments with proven efficacy for PTSD, such as cognitive behavioural therapy or eye movement desensitization and reprocessing, might also be helpful for CPTSD[6]. It is also worth noting that dialectical behavioural therapy, a treatment that has been extensively used for people with BPD, has been modified and found effective for PTSD and comorbid BPD symptoms, BPD with comorbid PTSD, and BPD alone[7].

A trauma-informed modular approach has also been suggested for the treatment of CPTSD[8]. The modular approach proposes that symptom clusters of CPTSD should be targeted using a formulation-based model and based on a client's treatment goals and the severity of his/her symptoms. Modular approaches, such as skills training in affective and interpersonal regulation narrative therapy, have been found useful for those who have experienced PTSD related to childhood trauma[9] and have been adapted for CPTSD.

For those who meet the criteria for both conditions, a trauma-informed approach might still be the best treatment option. There is, however, an urgent need to explore the effectiveness of existing and new interventions for ICD-11 CPTSD, and for the new construct of personality disorder (including the new pattern qualifier for BPD).

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1. World Health Organization. International classification of diseases, 11th revision. Geneva: World Health Organization, 2022.
2. de Aquino Ferreira LF, Pereira FH, Benevides AM et al. Psychiatry Res 2018; 262:70-7.
3. Owczarek M, Karatzias T, McElroy E et al. J Pers Disord 2023;37:112-29.
4. Cloitre M, Garvert DW, Weiss B et al. Eur J Psychotraumatol 2014;5:25097.
5. Biskin RS, Paris J. CMAJ 2012;184:1789-94.
6. Voorendonk EM, De Jongh A, Rozendaal L et al. Eur J Psychotraumatol 2020; 11:1783955.
7. Bohus M, Kleindienst N, Hahn C et al. JAMA Psychiatry 2020;77:1235-45.
8. Karatzias T, Cloitre M. J Trauma Stress 2019;32:870-6.
9. Cloitre M, Stovall-McClough KC, Nooner K et al. Am J Psychiatry 2010;167: 915-24.

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Promoting schizophrenia research in Europe: the contribution of the European Group for Research in Schizophrenia

The European Group for Research in Schizophrenia (EGRIS) was founded in the late 1990s to develop strategies for the promotion and coordination of schizophrenia research in Europe.

The founding members were W. Fleischhacker (Austria), J. Peuskens (Belgium), D. Naber (Germany), I. Bitter (Hungary), J. Gerlach (Denmark), J.-J. Lopez-Ibor (Spain), S. Galderisi (Italy), J. Libiger (Czech Republic), M. Paes de Sousa (Portugal) and T. Burns (UK). W. Fleischhacker was the chairperson of the group, and J. Peuskens the co-chair.

The primary aim of the group was to encourage independent collaboration in schizophrenia research across Europe, by identifying research gaps, exploring innovative approaches, and favoring "technology transfer" across centers joining the research projects designed by the group.

The group met two times per year. Open as well as in-depth scientific discussions, together with a friendly and pleasant atmosphere, characterized the meetings. The group discussed drafts of research protocols prepared and presented by one or more members, sometimes enriching them or, more often, after an in-depth discussion, either tabling them until the next meeting, with some suggestions for revision, or rejecting them.

Of the many protocols drafted and discussed during the meetings, very few survived the criticisms of the group members and were proposed to external bodies for funding. The first very successful initiative was the European First Episode Schizophrenia Trial (EUFEST), the largest randomized trial comparing the clinical effectiveness of second- vs. first-generation (haloperidol below 5 mg/day) antipsychotics in first-episode schizophrenia-spectrum patients[1].

This has been the first trial in a relatively unselected group of first-episode schizophrenia patients performed across a large number of European countries. Its focus was effectiveness of antipsychotic treatment, measured as retention of patients on treatment (non-retention can be the result of insufficient clinical efficacy and/or poor tolerability/acceptability). The primary outcome was the 1-year retention rate in first-episode patients treated with haloperidol, olanzapine, quetiapine, amisulpride or ziprasidone. Secondary objectives included the comparison of changes in various dimensions of psychopathology, social needs and quality of life, substance abuse and cognitive functions in response to treatment with the above antipsychotics, as well as the assessment of their side effects. The main paper was published in the Lancet[2]. The group discussed many proposals for secondary analyses and, for the approved ones, invited contributions by other group members, in addition to those who had presented the proposal.

The large database generated by the study resulted in over 40 papers, many by the EUFEST study group, and some by researchers who had not participated in the study, but later had shown interest in the study findings and conducted *post-hoc* analyses.

Through the EUFEST study, we learnt a lot about challenges and opportunities in running multicenter, multinational trials, and the EGRIS grew in terms of cohesion, skills and enthusiasm.

Over time, the composition of the group changed, with the admission of new members (based on the recommendations of existing ones), adopting a one country/one member policy. By 2009, for instance, the group had included five more members/countries, i.e., S. Dollfus (France), M. Davidson (Israel), R. Kahn (The Netherlands), W. Rössler (Switzerland) and J. Rybakowski (Poland); in addition, B. Glenthoj (Denmark) had joined the group, as J. Gerlach had retired.

While searching for innovative ideas, drafting new research protocols, and applying for funds, the group joined the European College of Neuropsychopharmacology (ECNP) Network Initiative, and created the ECNP Schizophrenia Network. However, after a couple of years, the EGRIS decided to return to its previous autonomy and working style. Part of the group also remained in the ECNP Schizophrenia Network, and, under my leadership, the Network included new members, who had never been EGRIS members, and focused on research on negative symptoms of schizophrenia[3,4].

In 2012, the EGRIS approved another large multicenter, multinational study, the European Long-acting Antipsychotics in Schizophrenia Trial (EULAST). The group moved from the evidence that discontinuation of antipsychotic medication is by far the most important reason for relapse, and concluded that a study comparing long-acting injectable antipsychotic drugs (LAIs) to corresponding oral formulations could shed some light on the ongoing discussion concerning the effectiveness of different formulations in reducing relapses[5].