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Research paper

Efficacy of the unified protocol for transdiagnostic treatment of comorbid emotional disorders in patients with ultra high risk for psychosis: Results of a randomized controlled trial

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ABSTRACT

Background: The most common reason for help-seeking in ultra-high risk (UHR) for psychosis patients is comorbid symptoms, mainly anxiety and depression. However, psychological interventions are mainly focused on subthreshold psychotic symptoms. There is a growing push to include transdiagnostic therapies in specialized intervention teams for psychosis in young people. The Unified Protocol for the Transdiagnostic Treatment of Emotional Disorders (UP) has demonstrated efficacy in emotional disorders, and its application has recently expanded to other pathologies such as borderline personality disorder (BPD) and bipolar disorder (BD).

Methods: This pilot study was conducted with 36 patients with UHR for psychosis and symptoms of comorbid emotional disorders who were receiving treatment in an early intervention programme for psychosis. This is a randomised control trial (RCT) with two conditions: treatment as usual (TAU) with the group and online application of the UP (UP+TAU) (n = 18) and TAU (n = 18). Evaluations were conducted at baseline, after treatment, and at the three-month follow-up.

Results: Comorbid anxiety and depression symptoms improved significantly in patients in the UP+TAU group compared to those in the TAU. Significant improvements in negative affect, emotional dysregulation, neuroticism, extraversion, functioning, and quality of life were also observed, and satisfaction with the intervention was high.

Conclusions: UP may be an acceptable and effective intervention for the treatment of symptoms of comorbid emotional disorders in patients with UHR for psychosis.

Limitations: The sample size was small, and further studies are needed to test this intervention with larger samples of patients with UHR for psychosis with emotional comorbidities.

1. Introduction

Young adults aged 18–25 have a higher prevalence of severe mental illness (11.4 %) compared to adults aged 26–49 years (7.1 %) and those aged 50 and older (2.5 %) (Substance Abuse and Mental Health Services Administration, 2021). Furthermore, once young people with early psychosis begin receiving treatment in a specialized service, disengagement rates are high (12–53 %) (Mascayano et al., 2021). One of the mental disorders in young people that has received the most attention in the last two decades is ultra-high risk (UHR) for psychosis. UHR has been conceptualised as a group of subclinical manifestations of psychosis and categorised into three different groups: 1) 'Attenuated psychotic symptoms', i.e. individuals who have experienced attenuated forms of positive psychotic symptoms in the past year; 2) 'Brief limited

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intermittent psychotic symptoms', i.e. Individuals who had episodes of overt psychotic symptoms that lasted less than one week and spontaneously self-limited; and 3) 'Trait Group': Individuals with schizotypal personality disorder or a first-degree relative with a psychotic disorder who also have a deterioration in Global Assessment of Functioning (GAF) of 30 points or have had a GAF of <50 in the last year (Yung et al., 2005). There is evidence that approximately 36 % of patients who fulfil the UHR criteria will develop a first psychotic episode within 3 years (Fusar-Poli, 2012). The average age of these patients is 20.6 years old, the majority are male (58 %), and they present with at least 1 year of attenuated psychotic symptoms before seeking help from specialized health services (Thompson et al., 2015).

Comorbidity rates with other disorders in people with UHR are high (66.7 % for depressive disorders, 50.9 % for anxiety disorders; 12.3 % for obsessive-compulsive disorder; 8.7 % for bipolar disorder; 4 % for eating disorder) (Albert et al., 2018). The most common reason for help-seeking in these patients is comorbid symptoms, with depression being the greatest predictor of poorer functioning in the long term (Barajas et al., 2019; Falkenberg et al., 2015; Fusar-Poli et al., 2020). These findings have made an important contribution to contemporary psychopathological models, which assume that the early stages of mental illness consist of diffuse and fluctuating anxiety and depression states, often accompanied by psychosis-like disturbances in cognition or emotional dysregulation, leading to a variety of disorders and clinical presentations (McGorry et al., 2018).

Recent studies have shown that people at high risk of developing psychosis are less likely to use emotion regulation techniques than controls (Strakeljahn et al., 2023). These differences may be present even before the onset of symptoms (Kimhy et al., 2016). Difficulties with emotion regulation have been identified as mediating factors between psychosis-like symptoms in the general population and the onset of attenuated psychotic symptoms with clinical relevance (Laloyaux et al., 2016). Difficulties in emotion regulation have been associated with some temperament variables such as high neuroticism and low extraversion (Barlow et al., 2014). The triple vulnerability model (Barlow, 2000; Brown and Naragon-Gainey, 2013) considers these personality dimensions as a general biological vulnerability factor contributing to the etiology and maintenance of emotional disorders (i.e., anxiety, depression, and related disorders; Bullis et al., 2019). Individuals with high neuroticism also show difficulties in emotion regulation (Aldao et al., 2010) and previous studies have shown that difficulties in emotion regulation moderate efficacy outcomes related to anxiety symptoms and quality of life (Peris-Baquero et al., 2023).

This personality profile has also been found in psychotic patients compared to their relatives and to healthy controls, suggesting that these personality traits have predictive value for subclinical psychotic symptoms (Boyette et al., 2013). In addition, high neuroticism in patients with psychosis has been found to be associated with higher levels of positive symptoms, distress, and emotional symptoms, as well as a tendency towards avoidance, inactivity, and emotion-focused coping strategies (Scholte-Stalenhoef et al., 2023). All of this work suggests that emotion regulation training should be included in the treatment of patients with emotional disorders, psychosis and UHR.

Cognitive behavioural therapy (CBT) is one of the treatments of choice for early psychosis, according to the main clinical guidelines (Early Psychosis Guidelines Writing Group and EPPIC National Support Program, 2016; NHS England, 2016). Although its efficacy in reducing subthreshold positive symptoms and at least delaying the onset of a full-blown first episode of psychosis has been demonstrated (McGorry et al., 2021), its effectiveness in treating comorbid mood and anxiety disorders remains unknown (Rutigliano et al., 2016). Most treatments developed in UHR samples target transition to psychosis as the unique outcome (Valmaggia et al., 2013). The need to address comorbid symptoms in patients with UHR is therefore a priority that has not yet been translated into changes in psychological treatments applied in early intervention teams for psychosis (Falkenberg et al., 2015).

In contrast to disorder-specific CBT, i.e. CBT interventions delivered to treat a specific disorder (e.g. panic disorder or major depression), transdiagnostic CBT interventions have emerged as a new therapeutic approach that targets common underlying mechanisms associated with the etiology and maintenance of groups of disorders, such as anxiety disorders and depression (Sandín et al., 1999; Sauer-Zavala et al., 2017a, 2017b), but also psychosis (McGorry et al., 2018). The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP; Barlow et al., 2018a; Barlow et al., 2018b) is one of the most consolidated evidence-based psychological treatments to target common mechanisms associated with the etiology and maintenance of emotional disorders (anxiety, depressive and related disorders; Bullis et al., 2019), such as neuroticism, rumination, and avoidance, leading to emotion dysregulation (Barlow et al., 2014). Thus, UP targets core dysfunction (i.e., emotional dysregulation and maladaptive cognitive beliefs and behaviours) and applies traditional CBT techniques (e.g., cognitive flexibility, emotional exposures), as well as motivational enhancement and mindfulness-based techniques, typically resulting in increasing the tolerance to intense and uncomfortable emotions and improving functioning (Barlow et al., 2018a; Barlow et al., 2018b). The efficacy of UP in reducing anxiety and depressive symptoms and improving the quality of life, the use of regulation skills, and the functional status of patients with emotional disorders has been demonstrated in recent systematic reviews and meta-analyses (Carlucci et al., 2021; Cassiello-Robbins et al., 2020; Sakiris and Berle, 2019). UP has shown similar and even slightly greater efficacy compared to disorder-specific CBT (Eustis et al., 2020; Longley and Gleiser, 2023) including in a group format (Reinholt et al., 2022; Peris-Baquero and Osma, 2023). Regarding online formats, different studies have applied the UP with promising results (Celleri et al., 2022; Schaeuffele et al., 2022).

In recent years, clinicians and researchers have become increasingly interested in whether UP could be used to treat emotional disorders and/or symptoms in individuals with a primary diagnosis other than emotional disturbance, such as borderline personality disorders (Sauer-Zavala et al., 2016) or bipolar disorder (Ellard et al., 2017). In terms of personality, UP has shown efficacy in decreasing neuroticism compared to TAU and also to symptom-focused CBT (Sauer-Zavala et al., 2017a, 2017b). An increase in extraversion has also been observed with group application (Peris-Baquero and Osma, 2023).

Although there is previous evidence of interventions targeting emotions in psychosis with promising results (Lawlor et al., 2020; Spidel et al., 2018), individuals with UHR have not been included in studies examining the efficacy of UP. To our knowledge, there are only two published single-case studies applying the UP, one in an individual with treatment-resistant schizophrenia (Grasa et al., 2023) and the other in an individual with UHR (Peláez et al., 2023), both with promising results. Thus, it seems necessary to intervene in these processes to improve comorbid emotional symptomatology and emotional regulation in these types of patients.

We hypothesise that emotional comorbid symptoms will improve in both groups, but patients who additionally receive the group intervention with the UP will improve more significantly, particularly in anxiety and depressive comorbid symptoms, and will have specific positive effects on emotional regulation.

2. Method

2.1. Design

This is a randomised control trial (RCT) with two conditions: Treatment as usual (TAU) with the group and online application of the UP (UP+TAU) ($n = 18$) and TAU (n = 18). Participants were randomly assigned to either the UP group (experimental intervention) or TAU group by a computerised algorithm independent of the investigators (no stratification factors) in blocks of 4 subjects (maximum number of each group) and assessor (JDLM)-patient blind. This study was registered at

https://clinicaltrials.gov (NCT04929938).

2.2. Sample size calculation

A priori sample size determination was performed to detect effect sizes of 1 with a statistical power of 80 % in a bilateral *t*-test, using a significance level of 0.05 and an expected loss rate of 20 % at follow-up. It was estimated that a total of 21 patients were required for each condition. For this calculation, we have used Barlow's 2017 article as a reference (Barlow et al., 2017).

2.3. Participants

The inclusion criteria were: (1) age between 18 and 35 years old, (2) a diagnosis of UHR for psychosis with the CAARMS in the last 3 years and inclusion in our early intervention program, (3) a diagnosis of a comorbid emotional disorder with the MINI, in this study we included the following disorders: Anxiety disorders, depressive disorders, bipolar and related disorders, obsessive-compulsive and related disorders, trauma and stress-related disorders, somatic symptoms and related disorders and substance-related and addictive disorders, or scores above the clinical cut-off points on the BDI and/or BAI as a measure of depressive and anxiety symptoms, (4) fluent in Spanish or Catalan, and (5) signing the informed consent (IC). The exclusion criteria were (1) meeting the criteria for a full-blown psychotic disorder according to the DSM in the past or in the present, (2) intellectual disability, and (3) an organic disorder that explains current symptomatology. The sample for this study consists of 36 patients with a UHR diagnosis and symptoms of a DSM-5 comorbid emotional disorder who were receiving treatment in a community early intervention program for psychosis in Parc Sanitari Sant Joan de Déu and who agreed to participate in our study (Peláez et al., 2022). Eighteen patients were randomised to the UP condition and another eighteen patients were randomised on the TAU condition. A flowchart of participant enrollment is shown in Fig. 1.

2.4. Instruments

Sociodemographic data. We used an ad hoc questionnaire to collect information regarding participants' age, sex, level of education, ethnicity, and marital status.

Mini-International Neuropsychiatric Interview 7.0.2 for DSM-5 (MINI; Sheehan et al., 1998). We used the MINI to diagnose comorbid emotional disorders. This evaluates 17 diagnostic categories according to the Diagnostic and Statistical Manual of Mental Disorders Five Edition (DSM-5; American Psychiatric Association [APA], 2013). Questions about the presence or absence of the symptom were closed and had to be asked by the interviewer.

The Comprehensive Assessment of At Risk Mental States (CAARMS; Yung et al., 2005) is a semi-structured assessment interview to identify help-seeking young people who are at UHR of psychosis. We used the abbreviated version of the CAARMS, which contains four subscales regarding subthreshold positive psychotic symptoms (unusual thought content, non-bizarre ideas, perceptual abnormalities, disorganized speech). It is assessed on the basis of the severity, frequency and level of distress caused by the symptoms.

Beck Depression Scale- II (BDI-II) (Beck et al., 1996; Sanz et al., 2005). This measures the presence and severity of depressive symptoms using a 4-point Likert scale ranging from 0 ("absence") to 3 ("maximum

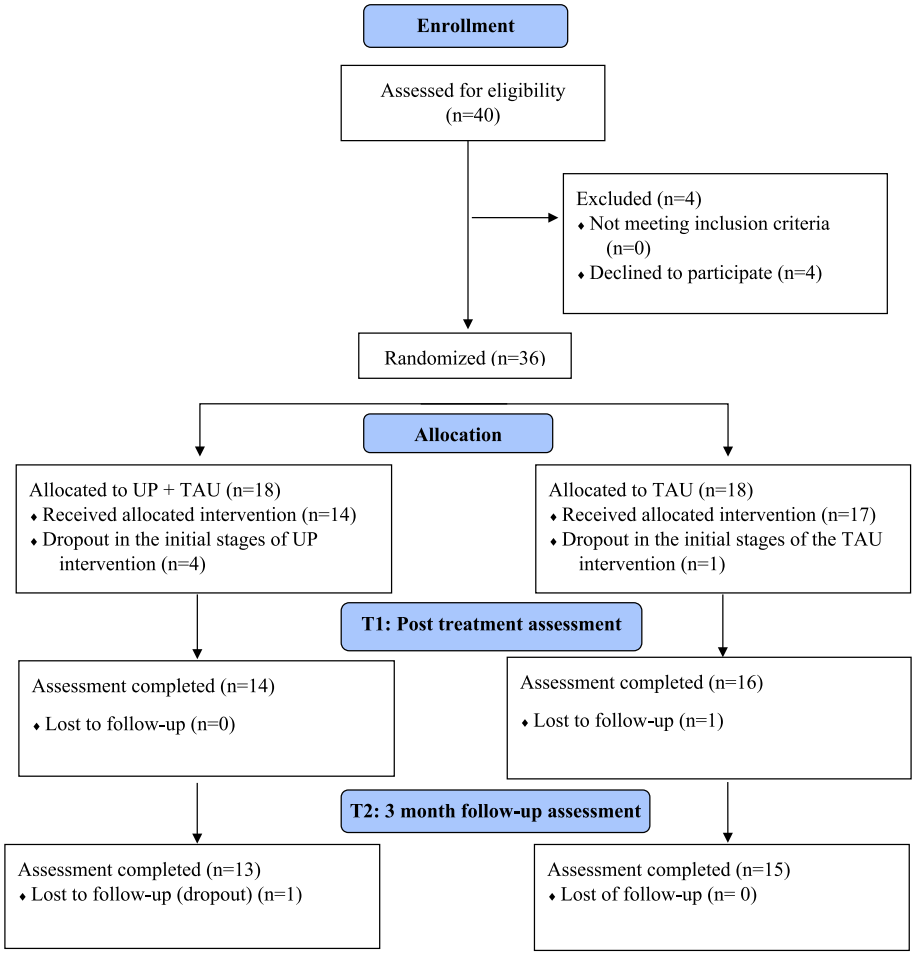

Fig. 1. CONSORT study flowchart showing the number of participants at each time point.

severity"). Higher values mean more severe depressive symptoms. A Cronbach's alpha of 0.87 was obtained in the present sample.

Beck Anxiety Inventory (BAI; Beck et al., 1988; Sanz et al., 2012): This scale measures the presence and severity of anxiety symptoms using a 4-point Likert scale ranging from 0 ("Not at all") to 3 ("It bothered me a lot"). Higher values mean more severe anxiety symptoms. In our sample, an internal consistency of Cronbach's alpha 0.90 was obtained.

NEO Five-Factor Inventory (NEO-FFI; Costa and McCrae, 1992). The neuroticism and extraversion scales were used with a Likert scale ranging from 0 ("strongly disagree") to 4 ("strongly agree"). Higher values mean a stronger expression of the respective trait. An adequate internal consistency was obtained with a Cronbach's alpha value of 0.64 (neuroticism) and 0.92 (extraversion) in our sample.

Difficulties in Emotion Regulation Scale (DERS; Gratz and Roemer, 2004; Hervás and Jódar, 2008). This contains 28 items with 5-point Likert items rated from 1 ("Never") to 5 ("Always") that estimate emotional dysregulation severity. Total scores range from 28 to 140. Higher scores indicate more difficulties in emotion regulation. An internal consistency of Cronbach's alpha 0.93 was obtained in our sample.

Positive and Negative Affect Schedule (PANAS; Watson et al., 1988; López-Gómez et al., 2015). This instrument measures positive and negative affect and consists of 20 items that describe positive and negative emotions that are rated on a 5-point Likert scale from 0 ("Not at all") to 5 ("Extremely"). Higher scores indicate a stronger presence of positive and negative affect. A Cronbach's alpha of 0.88 for negative affect and 0.92 for positive affect were obtained in our sample.

Maladjustment scale (EI; Echeburúa et al., 2000). This measure consists of 6 items that assess the impact of subjects' current problems on different areas of daily life (work, social life, leisure, relationships, family life, and overall). Higher scores indicate greater maladjustment. In our sample, an internal consistency of 0.94 was obtained.

Quality of life Index, Spanish version (QLI-sp; Ferrans and Powers, 1985; Mezzich et al., 2000). This is a 10-item questionnaire that assesses various aspects of quality of life related to health (physical disability, emotional well-being, self-healing and independent functioning, occupational functioning, interpersonal functioning, etc.). It is scored on a scale of 1–10 points, with higher scores corresponding to a better quality of life. A Cronbach's alpha of 0.89 was obtained in our sample.

Participant's satisfaction. An ad hoc satisfaction with intervention scale was developed to obtain more detailed information about the opinion of patients who completed the intervention with UP. It had four domains: online format, emotional regulation, general satisfaction with the program, and specific satisfaction with each component of the intervention. Each question was rated from 0 ("Not satisfied/not important at all/technological issues/therapeutic alliance maintained/not helpful") to 10 ("Completely satisfied/very important/serious technological issues/therapeutic alliance not maintained/completely helpful").

2.5. Procedure

The assessments that required clinical interviews took place in person, with the exception of a few cases that were conducted online via the Premium Zoom platform due to some patients' travel issues. The redcap platform was used for data support. Evaluators had been trained in psychological evaluation and specifically in administration of the CAARMS (Yung et al., 2005). They also were blind to the condition of the study to which the participants were assigned. CAARMS scores were also collected at the time patients began treatment in our early psychosis program, prior to entering the baseline assessment for the present study. The evaluation was carried out at 3 time points: baseline (T0), post-treatment (T1), and 3 months of follow-up (T2). Patients were randomly assigned to the treatment group with UP (UP condition) or to a waiting list. Both groups continued to receive treatment as usual (TAU) during the study. This type of methodology has been used previously in similar studies (Farchione et al., 2012; Sauer-Zavala et al., 2012).

2.6. Interventions

In the UP condition 15 online group sessions were conducted following the 2nd edition of the UP manuals (Barlow et al., 2018a; Barlow et al., 2018b) and using the Zoom Premium platform. Groups were composed of up to 8 participants and were conducted by a therapist and co-therapist both trained in the UP and supervised in the first group by a certified UP expert. All the UP group sessions were conducted online due to the context of the SARS-CoV-2 pandemic at the beginning of the study. Patients were allowed to switch off the camera if they felt uncomfortable and were also encouraged to participate via chat if they could not switch on the computer sound for any reason. The 8 original modules of the UP were applied in weekly 2-h sessions over a period of about 4 months. The objectives of the UP modules are detailed in the supplementary material (Table 6). Two further follow-up sessions were carried out one month and three months after the end of the group intervention. TAU consisted of a multidisciplinary intervention within an early intervention program for psychosis. It includes the following interventions: psychological therapy (about 20–40 sessions of CBT weekly or fortnightly), psychiatric treatment (with antidepressants, benzodiazepines and antipsychotic medication only when needed), social work (vocational orientation and support), nursing care (monitoring of side effects and healthy habits), individual cognitive remediation (if needed) and family therapy. The content and duration of the TAU sessions were individualised for each patient.

2.7. Data analysis

All statistical analyses were performed with the intention-to-treat sample ($n = 36$). A descriptive analysis of the data was carried out. Frequency tables were created for categorical variables, which are described with frequencies and the corresponding percentages. Descriptive statistics were calculated for numerical variables and these variables are described with their mean values and standard deviations. Linear mixed models were used to analyse the temporal evolution for both groups studied. These models included time, group, and the interaction between these two factors as fixed effects. A random effect was included in the models for each subject. The homoedasticity and normality of the residuals were checked to determine whether the models were appropriate. In cases where the residuals did not show a good fit, we used robust scoring equation estimators as an alternative method to generate the linear mixed effects. We used a significance level of 0.05. The analysis was performed using R 4.3.1, which works with RStudio 2022.02.0 + 443. Linear and logistic mixed models were generated using the R packages lme4 (v. 1.1–34) and lmerTest (v. 3.1–3). Robust linear mixed models were created using the robustlmm package (v. 0.99–0). The partial R^2 was calculated as a measure of effect size for the mixed model fixed effects. The R package r2glmm was used to calculate the partial R^2 (Cohen, 1988; Jaeger, 2017).

3. Results

3.1. Sample characteristics at baseline

The socio-demographic data are listed in Table 1. The average age of our sample was 23 years (SD = 4.4) and 63.9 % had completed secondary school. There was a slight majority of women (51.4 %), a larger majority of Caucasian ethnicity (69.4 %), and almost all were single (94.1 %). There were no statistical differences in socio-demographic variables in either group at baseline.

With regard to comorbid diagnoses at baseline, depressive disorders (25.7 %), agoraphobia (25.7 %), and social anxiety (31.4 %) were the most common diagnoses (see Table 2). In our sample, the majority of patients met criteria for at least one comorbid emotional disorder as measured by the MINI (94.3 %). As shown in Table 2, more than half of the sample had 2 or 3 comorbid emotional disorders (31.4 % and 25.7 %,

Table 1
Sociodemographic characteristics of the sample.

		Mean (SD), range	
		UP + TAU	TAU
Age		21.7 (3.37)	24.8 (4.81)
		N (%)	
Gender	Female	11 (61.1 %)	7 (38.9 %)
	Male	6 (33.3 %)	11 (61.1 %)
	Others	1 (5.6 %)	0 (0 %)
Educational level	Primary	1 (5.6 %)	0 (0 %)
	Secondary incomplete	2 (11.1 %)	4 (22.2 %)
	Secondary complete	8 (44.4 %)	4 (22.2 %)
	University incomplete	6 (33.3 %)	5 (27.8 %)
	University complete	1 (5.6 %)	5 (27.8 %)
Marital status	Single	17 (94.4 %)	17 (94.4 %)
	Married/living with partner	1 (5.6 %)	0 (0 %)
	Divorced	0 (0 %)	1 (5.6 %)
Ethnicity	Caucasian	13 (72.2 %)	12 (66.7 %)
	Hispanic	3 (16.7 %)	2 (11.1 %)
	North African	2 (11.1 %)	1 (5.6 %)
	Mixed or others	0 (0 %)	3 (16.7 %)

Note: SD: Standard deviation.

Table 2
Comorbid diagnosis at baseline.

	UP + TAU N (%)	TAU N (%)
Depressive episode	4 (22.2 %)	5 (29.4 %)
Major depressive disorder	2 (11.1 %)	4 (23.5 %)
Hypomanic episode	3 (16.7 %)	1 (5.9 %)
Bipolar II disorder	2 (11.1 %)	1 (5.9 %)
Non-specified bipolar disorder	0 (0 %)	1 (5.9 %)
Panic disorder	3 (16.7 %)	1 (5.9 %)
Agoraphobia	5 (27.8 %)	3 (17.6 %)
Social anxiety disorder	7 (38.9 %)	4 (23.5 %)
Obsessive-compulsive disorder	3 (16.7 %)	5 (29.4 %)
Posttraumatic stress disorder	3 (16.7 %)	4 (23.5 %)
Bulimia nervosa	2 (11.1 %)	0 (0 %)
Binge eating disorder	4 (22.2 %)	0 (0 %)
Anorexia nervosa	1 (5.6 %)	0 (0 %)
Generalized anxiety disorder	9 (50 %)	7 (41.2 %)
Alcohol abuse disorder	1 (5.6 %)	2 (11.8 %)
Substance use disorder (non-alcohol)	4 (22.2 %)	8 (31.2 %)

respectively). There were no differences at baseline between the patients of the UP condition (3.22; SD = 2.13) and the TAU condition (2.88; SD = 1.73) or in the number of diagnoses at baseline ($p = 0.60$).

No differences were detected in any of the clinical measures between the two groups of patients at baseline (see TAU coefficients at mixed models in Table 4). Boxplots of the individual measurements can be found in the supplementary material (Fig. 2).

3.2. Depression

The model estimated a significant decrease in depression scores in the treatment group at post-treatment (T0-T1: estimate = −11.78, SE = 2.70, $p < 0.001$) and at the three-month follow-up (T0-T2: estimate = −11.77, SE = 2.70, $p < 0.001$) (see Table 4). The scores in the control group showed no significant differences either at post-treatment or at the 3-month follow-up. The evolution in the scores in the two groups was significantly different (T0-T1$_{(\text{interaction with TAU}}$: estimate = 13.01, SE = 3.61, $p < 0.001$; T0-T2$_{(\text{interaction with TAU}}$: estimate = 9.52, SE = 3.58, $p = 0.01$). The values of R^2 showed medium effect sizes for the interaction at post-treatment ($R^2 = 0.047$) (Table 3).

3.3. Anxiety

With regard to anxiety (see Table 4), a significant decrease in scores for the treatment group was observed at post-treatment (T0-T1: estimate = −10.91, SE = 2.65, $p < 0.001$) and at 3 month of follow-up (T0-T2: estimate = −11.03, SE = 2.65, $p < 0.001$). Although the control group also decreased the anxiety scores, the interaction between time and group showed that the decrease in the treatment group was significantly higher both in the post-treatment (T0-T1$_{(\text{interaction with TAU}}$: estimate = 9.51, SE = 3.54, $p = 0.009$) and at the three month of follow-up (T0-T2$_{(\text{interaction with TAU}}$: estimate = 9.02, SE = 3.54, $p = 0.013$).

Table 3
Descriptive statistics of the variables for the two groups at the three evaluation points.

Measures	Timepoint	UP + TAU		TAU	
		M	SD	M	SD
BDI	Baseline	31.9	14.1	24	13.9
	Post	19.3	18.2	25.7	14.2
	3M	19.1	15.4	21.1	13.4
BAI	Baseline	28.1	14.8	24.4	12.7
	Post	18.8	11.8	22.8	12.3
	3M	17.3	15.0	22.3	13.7
PANAS_N	Baseline	34.4	8.63	32	7.32
	Post	28.6	12.1	31.9	8.84
	3M	24.5	10.6	32.1	7.27
PANAS_P	Baseline	29.2	9.50	28.4	8.18
	Post	29.7	8.04	27.3	7.51
	3M	28.8	7.91	28.9	8.79
DERS	Baseline	94.6	24.3	85	19.4
	Post	66.2	26.8	88.4	16.3
	3M	72.1	25.6	80.9	18.5
NEO-FFI_N	Baseline	34.7	7.88	32.3	7.33
	Post	27.4	12.2	32.3	8.46
	3M	30.5	11.4	29.8	9.14
NEO-FFI_E	Baseline	21.4	8.01	23	10.6
	Post	23.9	11.2	29.4	11.3
	3M	25.4	6.87	23.5	9.96
EI	Baseline	19.4	5.69	14.9	7.93
	Post	16.1	9.92	16.3	8.21
	3M	12.5	8.61	13.9	6.37
QLI	Baseline	4.46	1.45	5.33	1.77
	Post	5.17	2.38	5.39	1.89
	3M	6.03	1.51	5.64	1.83
MINI_D	Baseline	3.22	2.13	2.88	1.73
	3M	2.43	2.65	2.19	1.64
CAARMS	Baseline	10		12	
	3M	3		10	

Note: UP+TAU: UP plus Treatment as Usual; TAU: Treatment As Usual; M: Mean; SD: Standard deviation; SE: Standard error; Baseline: Baseline evaluation; Post: Post-treatment evaluation; 3 M: 3 month follow-up evaluation; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; PANAS_N; Positive and Negative Affect Schedule (Negative Affect); PANAS_P: Positive and Negative Affect Schedule (Positive Affect); DERS: Difficulties in Emotion Regulation Scale; NEO-FFI_N: NEO Five-Factor Inventory (Neuroticism); NEO-FFI_E: NEO Five-Factor Inventory (Extraversion); EI: Maladjustment scale; QLI-SP; Quality of life Index, Spanish version; MINI_D: Number of MINI (Mini International Neuropsychiatric Interview) diagnosis; CAARMS_p: Number of patients with UHR diagnoses with CAARMS (Comprehensive Assessment of At Risk Mental States).

3.4. Positive and negative affect

With regard to negative affect (Table 4), the model showed a significant reduction in PANAS_N scores in the treatment group at post treatment and at 3 month follow-up compared to baseline (T0-T1: estimate = −6.71, SE = 1.88, p < 0.001; T0-T2: estimate = −8.71, SE = 1.80, p < 0.001). The control group showed no significant changes either after treatment or at the 3-month follow-up, being the evolutions of the two groups significantly different (T0-T1$_{(\text{interaction with TAU}}$: estimate = 6.85, SE = 2.49, $p = 0.008$; T0-T2$_{(\text{interaction with TAU}}$: estimate = 9.23, SE = 2.40, $p < 0.001$). Moderate effect sizes were detected for the interaction at three-month follow-up ($R^2 = 0.062$). As far as positive affect is concerned, none of the effects were significant and we could not find any changes in either group during post-treatment or at the 3-month

Table 4
Results of mixed effect models for all the variables.

Measures	Fixed effects	Estimate	SE	df	t value **	*P* value	Effect size R^2
BDI	Intercept	30.95	3.51	45.28	8.81	<0.001	
	T1	−11.78	2.70	57.33	−4.35	<0.001	0.070
	T2	−11.77	2.70	57.33	−4.35	<0.001	0.070
	TAU	−6.95	4.95	44.59	−1.40	0.17	0.030
	T1*TAU	13.01	3.61	56.11	3.60	<0.001	0.047
	T2* TAU	9.52	3.58	56.06	2.66	0.01	0.026
BAI	Intercept	27.32	3.21	46.85	8.50	<0.001	
	T1	−10.91	2.65	56.66	−4.12	<0.001	0.069
	T2	−11.03	2.65	56.66	−4.17	<0.001	0.070
	TAU	−2.87	4.52	46.06	−0.64	0.52	0.006
	T1* TAU	9.51	3.54	55.46	2.68	0.009	0.029
	T2* TAU	9.02	3.54	55.46	2.55	0.013	0.026
PANAS_N	Intercept	33.70	2.12	47.58	15.87	<0.001	
	T1	−6.71	1.88	53.64	−3.58	<0.001	0.056
	T2	−8.70	1.80	54.75	−4.84	<0.001	0.100
	TAU	−1.70	2.98	46.69	−0.57	0.57	0.005
	T1* TAU	6.85	2.49	52.74	2.75	0.008	0.033
	T2* TAU	9.23	2.40	53.25	3.84	<0.001	0.062
PANAS_P*	Intercept	28.45	2.13	58.88	13.37	<0.001	
	T1	1.52	1.83	56.34	0.83	0.40	0.001
	T2	1.36	1.76	57.67	0.77	0.45	0.000
	TAU	0.17	2.99	57.80	0.06	0.96	0.001
	T1* TAU	−2.19	2.42	54.94	−0.91	0.37	0.003
	T2* TAU	−0.37	2.34	55.44	−0.16	0.87	0.001
DERS	Intercept	92.78	6.21	44.91	14.94	<0.001	
	T1	−27.52	6.15	40.10	−4.48	<0.001	0.132
	T2	−21.72	6.07	41.45	−3.58	<0.001	0.091
	TAU	−7.46	8.53	46.69	−0.87	0.39	0.013
	T1* TAU	28.29	8.50	40.04	3.33	0.001	0.077
	T2* TAU	16.69	8.34	42.30	2.00	0.051	0.031
NEO-FFI_N	Intercept	34.67	2.07	42.39	16.72	<0.001	
	T1	−8.06	1.73	46.41	−4.67	<0.001	0.091
	T2	−5.37	1.73	46.41	−3.11	0.003	0.042
	TAU	−2.33	2.93	42.39	−0.80	0.43	0.012
	T1* TAU	7.99	2.36	45.61	3.38	0.001	0.048
	T2* TAU	3.35	2.24	45.49	1.49	0.14	0.010
NEO-FFI_E*	Intercept	21.44	2.40	42.51	8.94	<0.001	
	T1	2.63	2.00	46.33	1.32	0.19	0.004
	T2	4.69	2.00	46.33	2.35	0.02	0.026
	TAU	1.06	3.40	42.51	0.31	0.76	0.004
	T1* TAU	−0.41	2.74	45.49	−0.15	0.88	0.000
	T2* TAU	−5.45	2.60	45.36	−2.10	0.042	0.019
EI*	Intercept	18.91	2.02	51.77	9.36	<0.001	
	T1	−4.11	1.63	53.56	−2.52	0.014	0.036
	T2	−7.15	1.57	54.88	−4.56	<0.001	0.077
	TAU	−3.97	2.84	50.71	−1.40	0.170	0.031
	T1* TAU	5.21	2.16	52.37	2.42	0.020	0.025
	T2* TAU	5.68	2.09	52.92	2.72	0.009	0.028
QLI*	Intercept	4.44	0.44	50.40	10.12	<0.001	
	T1	0.80	0.38	55.94	2.14	0.037	0.029
	T2	1.59	0.35	55.47	4.51	<0.001	0.078
	TAU	0.98	0.62	50.40	1.57	0.12	0.031
	T1* TAU	−0.53	0.50	54.80	−1.06	0.30	0.010
	T2* TAU	−1.08	0.48	54.36	−2.26	0.028	0.022
MINI_D*	Intercept	3.06	0.43	60.33	7.15	<0.001	
	T2	−1.17	0.65	33.51	−1.80	0.08	0.020
	TAU	−0.32	0.62	60.33	−0.52	0.60	0.004
	T2* TAU	0.51	0.90	32.02	0.57	0.57	0.000
CAARMS	Intercept	2.17	1.43		1.52	0.13	
	T2	- 4.35	2.22		−1.96	0.05	
	TAU	0.27	1.56		0.17	0.86	
	T2* TAU	3.15	2.22		1.42	0.16	

Note: BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; PANAS_N; Positive and Negative Affect Schedule (Negative Affect); PANAS_P: Positive and Negative Affect Schedule (Positive Affect); DERS: Difficulties in Emotion Regulation Scale; NEO-FFI_N: NEO Five-Factor Inventory (Neuroticism); NEO-FFI_E: NEO Five-Factor Inventory (Extraversion); EI: Maladjustment scale; QLI-SP; Quality of life Index, Spanish version; MINI_D: Number of MINI (Mini International Neuropsychiatric Interview) diagnosis. (*): Robust analyses were applied. (**): z value for CAARMS scores.

follow-up.

3.5. Emotion regulation

The model showed a significant decrease in DERS scores (see Table 4) for the treatment group at post-treatment (T0-T1: estimate = −27.52, SE = 6.15, $p < 0.001$) and at 3-month follow-up (T0-T2: estimate = −21.72, SE = 6.07, $p < 0.001$). The scores of the patients in the control group did not change significantly at the different time points. The interaction between time and group showed significant differences between the two conditions ($T0\text{-}T1_{(\text{interaction with TAU})}$: estimate = 28.29, SE = 8.50, $p = 0.001$; $T0\text{-}T2_{(\text{interaction with TAU})}$: estimate = 16.69, SE =

8.34, $p < 0.051$). Moderate effect sizes were detected for the interaction at post-treatment ($R^2 = 0.077$).

3.6. Personality

With regard to neuroticism, the model showed a significant decrease in the treatment group at the post-treatment assessment (T0-T1: estimate = −8.06, SE = 1.73, $p < 0.001$), which was maintained at the 3-month follow-up (T0-T2: estimate = −5.37, SE = 1.73, $p = 0.003$). No significant differences were found in patients in the control group at either post-treatment or 3-month follow-up. Significant differences between the groups were observed only at post-treatment assessment (T0-$T1_{(interaction\ with\ TAU)}$: estimate = 7.99, SE = 2.36, $p = 0.001$; T0-$T2_{(interaction\ with\ TAU)}$: estimate = 3.35, SE = 2.24, $p = 0.14$).

As with extraversion, the model showed significant differences between the two groups only at the three-month follow-up (T0-$T2_{(interaction\ with\ TAU)}$: estimate = −5.45, SE = 2.60, $p = 0.042$), with a significant increase in NEO-FFI-E scores in the UP condition (T0-T2: estimate = 4.69, SE = 2.00, $p = 0.02$). The values of R^2 showed medium effect sizes for the interaction at post-treatment ($R^2 = 0.048$). These results can be seen in Table 4.

3.7. Maladjustment and quality of life

As can be seen in Table 4, the model estimated a decrease in maladjustment scores in the treatment group after treatment and at the three-month follow-up (T0-T1: estimate = −4.11, SE = 1.63, $p < 0.014$; T0-T2: estimate = −7.15, SE = 1.57, $p < 0.001$). The interaction between time and group showed that this decrease in the treatment group was not observed in the control group (T0-$T1_{(interaction\ with\ TAU)}$: estimate = 5.21, SE = 2.16, $p = 0.020$; T0-$T2_{(interaction\ with\ TAU)}$: estimate = 5.68, SE = 2.09, $p = 0.009$).In terms of quality of life, the model only showed significant differences between the two groups only at the three-month follow-up (T0-$T2_{(interaction\ with\ TAU)}$: estimate = −1.08, SE = 0.48, $p = 0.028$), with a significant increase in QLI-sp scores in the UP condition (T0-T2: estimate = 1.59, SE = 0.35, $p < 0.001$).

3.8. Comorbid diagnoses

We analysed the average number of comorbid diagnoses at baseline and at three-months' follow-up in both groups. A non-significant trend towards a decrease in the number of diagnoses was observed in both groups (−1.17; SE = 0.65; $p = 0.08$), as we had a non-significant interaction between time trend and study condition (0.51; SE = 0.91; $p = 0.574$).

3.9. Ultra-high risk for psychosis criteria

A significant reduction in UHR criteria fulfilment with the CAARMS was observed at the three-month follow-up in both conditions compared to baseline. Although the results are not statistically significant, patients who participated in the UP intervention appear to have a stronger tendency to remission of subthreshold psychotic symptoms compared to TAU patients.

3.10. Satisfaction and retention rates

As shown in Table 5, overall satisfaction with the UP intervention was high. The perceived effectiveness in emotion regulation was rated at 8.13 and general satisfaction with the program was 9.06. The dropout rate of the UP therapy in our study was 22 %. Fourteen patients out of eighteen allocated in the UP intervention dropped out of the UP therapy before the post-treatment assessment. The four patients who discontinued the UP sessions did so in the first sessions and for clinical reasons "(intense paranoid thoughts, social anxiety and/or suicidal thoughts) that disturbed the group dynamics and had to be prioritised in the individual TAU sessions. One patient was excluded from the trial between the baseline and the post-treatment evaluation because of transition to a full-blown psychotic episode. He was in the TAU group.

Table 5
Satisfaction with unified protocol.

UP Satisfaction	Mean	SD
Satisfaction online group format		
To what extent do you feel that you could participate actively in the online group sessions?	8.81	1.56
To what extent were you able to interact with the other participants in the group during the online sessions?	8.44	1.67
To what extent do you feel you have been listened to during the online group sessions?	9.81	0.40
To what extent were you able to maintain your attention focused on the online sessions?	7.25	1.24
To what extent do you feel that the online format affected the therapeutic alliance?	5.50	3.67
General satisfaction in emotional regulation skills		
To what extent do you feel that the UP intervention has helped you to regulate your emotions more adaptively?	8.13	1.20
Satisfaction with specific content of the UP		
Identifying the three components of emotions: thoughts, physical sensations, and behaviour	8.50	1.16
Analyzing the ARC of emotions: Antecedents, emotional Response, and Consequences	8.06	1.57
Emotional Consciousness in the present without judgement	8.27	1.39
Identifying automatic thoughts	8.56	1.63
Cognitive flexibility	8.60	1.64
Identifying emotionally driven behaviours	8.56	1.46
Opposed behaviours technique	7.67	1.72
Problem-solving skills	8.44	1.75
General UP satisfaction		
In general, how would you rate the quality of the program you participated in?	9.06	1.06
In general, how would you rate the utility of the program you participated in?	9.38	0.71
Would you recommend this program to a friend or family member in your situation?	9.19	1.47
To what extent do you feel that the content you have learnt has helped you to deal with your problems more efficiently?	9.06	1.12
Overall, how satisfied are you with the program?	8.81	1.10
To what extent did this program cause you any discomfort?	2.25	2.27

4. Discussion

Our results show that UP was effective in reducing comorbid symptoms of anxiety and depression in our sample of patients with UHR for psychosis. The significant reductions in anxiety and depressive symptoms in our study are similar to those previously found in patients with emotional disorder diagnoses in both international (Carlucci et al., 2021; Longley and Gleiser, 2023; Sakiris and Berle, 2019) and national studies (Peris-Baquero and Osma, 2023). These results are particularly relevant when considering that the TAU condition included individualised CBT for subthreshold psychotic symptoms, an intervention that has demonstrated its efficacy (Van der Gaag et al., 2013; Morrison et al., 2004; Morrison et al., 2012).

We found a decrease in the number of comorbid emotional disorders (MINI) in both groups, but this change was not significant. However, in the UP group, the tendency towards reduction of the number of comorbid diagnoses was greater than in the TAU condition.

There is a need for further studies investigating the potential impact of positive and negative affect on the development or maintenance of subthreshold psychotic symptoms, or on emotional comorbidity in samples of individuals with UHR for psychosis. There is some evidence that patients with chronic schizophrenia have higher levels of negative affect and lower levels of positive affect than controls, and that this

condition may be related to anhedonia and depressive symptoms (Cho et al., 2017). The improvement in negative affect observed in patients participating in the UP intervention was consistent with improvements in other outcomes measured in our study such as depressive symptoms comorbidity. Given the importance of negative affect in the development of emotional disorders (Barlow et al., 2014; Sandín et al., 2021), the effectiveness of UP in reducing this transdiagnostic factor may be a very important finding of this research. The observed improvement in the use of emotion regulation skills appears to have an effect in reducing negative affect and neuroticism. For the latter, the significant differences in the UP condition did not persist after 3 months of follow-up. This could be due to the small sample size.

In our study, significant differences were found in extraversion at the 3-month follow-up in patients who were in the UP condition compared to those who were in the TAU. These results are very similar to others previously obtained applying the UP in patients with emotional disorders (Peris-Baquero and Osma, 2023). We believe that the group format, as discussed in previous studies (e.g., Peris-Baquero and Osma, 2023), could promote the use of social skills and improve the subjective perception of social relationships. Higher extraversion has been associated with an active coping style and greater self-esteem in previous studies with psychotic patients (Scholte-Stalenhoef et al., 2023). However, we found no changes in positive affect in patients from either condition. In an RCT conducted recently in Spain ($N = 533$) with patients with emotional disorders, statistically significant changes were found in positive affect in the UP condition with medium effect sizes (Cohen's d − 0.77 at 12 months follow-up) (Peris-Baquero and Osma, 2023). Further studies are needed to clarify whether the addition of specific content to work on positive affect might be necessary to optimise its improvement. Although the results observed for personality and affect measurements point in different directions, we believe that these are promising findings, as there have been no studies to date measuring the effects of psychotherapy in these transdiagnostic variables in young people with UHR for psychosis.

We also believe it important to emphasize the significant improvements obtained in emotion regulation, as this is a transdiagnostic variable that has only shown significant improvements in response to transdiagnostic interventions so far, as opposed to interventions targeting specific disorders (Sakiris and Berle, 2019). Given the clinical correlates that emotional dysregulation has been shown to have in patients with psychotic disorders (Laloyaux et al., 2016), it seems very important to integrate the use of transdiagnostic interventions such as UP into the usual clinical practise of early intervention services for psychosis and other psychiatric disorders (Sloan et al., 2017). Significant improvements in maladjustment and quality of life are of particular relevance, given the importance of functionality and subjective perception of quality of life in this type of patients.

Regarding the significant results in reducing the number of patients meeting UHR criteria at three-month follow-up, our results support previous evidence that individual CBT is an effective therapy for reducing subthreshold psychotic symptoms. The fact that patients in the UP group showed a tendency towards greater improvement in these symptoms may suggest that the additional use of UP in a group format could increase its efficacy.

The dropout rate in the UP condition in our study (22 %) was slightly lower than in other studies in which UP was previously used, both in the face-to-face format (36 %; Peris-Baquero and Osma, 2023) and in the Internet self-help format (26.6 %; Schaeuffele et al., 2022). The online intervention format could promote engagement in therapy in young patients with attenuated psychotic spectrum symptoms and emotional comorbidity. In our study, the main reason for patients discontinuing participation was clinical destabilisation. In the cases in which the study was discontinued during the UP sessions, this occurred during the first three UP sessions. Patients who completed the intervention with the UP reported high levels of satisfaction with the treatment and with the online and group format. We believe that the online format of the intervention, which allowed the intervention to be conducted from home, with the option of not connecting the camera and intervening via audio or chat, facilitated adherence in these participants. In addition, the clinical improvements we observed in a relatively short period of time (15 weeks) and the non-stigmatising nature of the intervention (working on emotion regulation) could have contributed to improving the lack of adherence to treatment in this type of young patient (Mascayano et al., 2021).

We believe that our results are encouraging, not only because of the improvement in comorbid emotional symptoms such as anxiety, depression, and negative affect, but also in relation to the improvement in transdiagnostic variables such as extraversion, neuroticism, emotional regulation, maladjustment, and quality of life, as these variables have been identified as relevant targets for transdiagnostic interventions (e.g., Boettcher et al., 2019). Despite these results, further studies with larger patient samples and a longer follow-up period need to be conducted to investigate the effects of UP temperament, affect, and number of comorbid diagnoses in patients with psychotic spectrum disorders. To our knowledge, this is the first study to investigate the efficacy of UP on emotional comorbid symptoms of anxiety or depression in a sample of UHR patients. These results could have important implications for clinical practice, as the addition of UP to TAU could be a valuable addition to individualised CBT for subthreshold psychotic symptoms. These findings support the potential benefits of integrating the use of transdiagnostic interventions based on emotion regulation training, such as UP, into the usual clinical practice of early intervention services for psychosis and other psychiatric disorders (Sloan et al., 2017).

5. Limitations

In this article, we presented the results of our RCT in relation to the main hypothesis, namely that UP would improve comorbid symptoms of anxiety and depression in patients with UHR for psychosis, as well as other variables related to subthreshold psychotic symptoms, emotion regulation, temperament, and broader measures of functionality. Although we used semi-structured interviews to assess patients' clinical diagnoses, we used a large number of self-reports for the outcome variables. This could also be considered a limitation given the influence that patients' subjective perceptions may have.

The short follow-up period of 3 months should also be considered. For this reason, it might be difficult to detect changes in the diagnostic criteria measured with the MINI and CAARMS. On the other hand, we have no information on the maintenance of changes in the analysed variables beyond 3 months after the end of the intervention. The follow-up assessment does not cover the 3-year period during which the highest percentages of transition to psychosis most frequently occur (Fusar-Poli, 2012). Therefore, we cannot determine whether the efficacy of UP in delaying the onset of full-blown psychotic disorder is similar to that of CBT or whether UP might even improve clinical outcomes. In addition, it is recommended that emotion regulation skills be practised independently by the patients after completing the UP treatment sessions so that these become established in their daily lives. With a three-month follow-up period, we cannot determine whether new emotional regulation skills have really been integrated and what impact it has on the other clinical and functional variables. On the other hand, the small sample size may not be sufficient to detect significant changes in some variables that are not very sensitive to change, such as the diagnostic criteria of UHR or comorbid emotional disorders.

Although the results obtained are promising, we believe it is important to interpret them with caution as they are preliminary. To our knowledge, this is the first RCT to examine the efficacy of UP in a sample of UHR treated in public mental health early intervention programmes. Further studies with larger samples and a longer follow-up period need to be conducted to replicate these results.

CRediT authorship contribution statement

Trinidad Peláez: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Raquel López-Carrilero:** Writing – review & editing, Software, Investigation, Data curation. **Victoria Espinosa:** Writing – review & editing, Writing – original draft, Software, Investigation, Data curation. **Sol Balsells:** Writing – review & editing, Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Susana Ochoa:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Investigation, Funding acquisition, Conceptualization. **Jorge Osma:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

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