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Cost-effectiveness evaluation of the individual vs. group transdiagnostic psychological treatment for emotional disorders in Primary Care (PsicAP-COSTS)

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ABSTRACT

The **aim** of this multicenter, single-blinded, randomized controlled trial is to compare, in cost-effectiveness terms, a brief transdiagnostic, cognitive-behavioural therapy in two different modes, individual and group, with the pharmacological treatment usually administered in Primary Care.

Participants between 18 and 65 years old and with, according to pretreatment evaluation, mild or moderate emotional disorders will be randomly allocated to the three experimental groups. After treatment phase and 6 and 12 months later they will be assessed again.

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KEYWORDS

emotional disorders, depression, anxiety disorders, somatoform disorders, transdiagnostic, Primary Care, cost-effectiveness evaluation, brief psychological treatments, randomized controlled trial

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MATERIALS TEXT

Primary outcome measures

- *Patient Health Questionnaire 9 items (PHQ-9)*

The PHQ-9 (Kroenke et al., 2001) is the depression module of the PHQ (Spitzer et al., 1999), which scores the 9 DSM-IV criteria present in the last two weeks from 0 ("not at all") to 3 ("nearly every day"). A score of 10-14 indicates minor depression, moderate major depression, or dysthymia; 15-19, moderately severe major depression; and 20-27, severe major depression. It has been added a tenth item that assess de dysfunction level.

This tool has been tested in Spanish PC centers (Muñoz-Navarro, Cano-Vindel, Medrano, et al., 2017), finding that a score greater than or equal to 12 (sensitivity of 84% and specificity of 78%), or a score of 2 or 3 in at least five of the nine items, being al least one of them the item 1 or 2 (sensitivity 88% and specificity of 80%), are the best criteria for diagnosing major depression disorder. Furthermore, according to McMillan et al. (2010), the best therapeutic success criterion is a score less than or equal to 9, with a standard deviation of 5 points.

- *General Anxiety Disorder Assessment (GAD-7)*

The GAD-7 (Spitzer et al., 2006) assesses common anxiety symptoms in the last two weeks, scoring from 0 ("not at all") to 3 ("nearly every day"). Scores of 5, 10, and 15 are taken as the cut-off points for mild, moderate and severe anxiety, respectively. Generally, a score of 2 in at least four of the seven items, being one of them the item 1, is the cut-off point for anxiety disorders. In Spanish population, a score of 10 is the best diagnostic criterion, with a sensitivity of 87% and a specificity of 78% (Muñoz-Navarro, Cano-Vindel, Moriana, et al., 2017).

- *Patient Health Questionnaire - Panic Disorder (PHQ-PD)*

The PHQ-PD is the panic disorder module of the PHQ and scores each DSM-IV criteria as "yes" or "no". According to Muñoz-Navarro et al. (2016), the best diagnostic criterion in Spanish population is a "yes" answer in the first item and in any of the subsequent three items, plus four or more somatic symptoms (sensitivity of 77% and specificity of 72%).

- *Patient Health Questionnaire 15 items (PHQ-15)*

The PHQ-15 (Kroenke et al., 2002) is the somatization module of the PHQ and scores each DSM-IV criteria as 0 ("not bothered at all") to 2 ("bothered a lot"). For the somatoform disorder diagnosis is necessary a score of 2 in three out of the thirteen first symptoms, plus in two PHQ-9 items (sleeping problems and fatigue), and the absence of a biological cause. Sensitivity of 78% and specificity of 71% (Kroenke et al., 2010; van Ravesteijn et al., 2009).

Secondary outcome measures

- *Sheehan Disability Inventory (SDI)*

The SDI (Sheehan et al., 1996) is a 5-item self-administered test that measures the subjective impairment in three areas in the past month: work, family and social functioning. It has two additional items to assess the stress level and the perceived social support in the last week. The Spanish version (Bobes et al., 1999) has shown good properties.

- *World Health Organization Quality of Life Instrument-Short Form (WHOQOL-BREF)*

It is a brief adaptation of the WHOQOL-100. It measures the quality of life through 26 questions about four relevant, life domains: psychological, physical, social and environmental. It has been validated with Spanish population and has shown good psychometric properties (Lucas-Carrasco, 2012).

- *Ruminative Responses Scale (RRS)*

The RRS (Nolen-Hoeksema & Morrow, 1991) has 22 items that measure the ruminative responses to depressed mood. It has been validated with Spanish population (Hervás, 2008). In this study, only the brooding subscale (RRS-B; 5 items) will be used (Muñoz-Navarro et al., 2020).

- *Penn State Worry Questionnaire (PSWQ)*

The PSWQ (Meyer et al., 1990) has 16 items and measures the pathological worry as an uncontrollable and general state (i.e. as a GAD feature). It has been validated in Spain (Sandín et al., 2009) and, in this study, it will be used the abbreviated version (PSWQ-A) (Crittendon & Hopko, 2006; Muñoz-Navarro et al., 2020).

- *Inventory of Cognitive Activity in Anxiety Disorders (IACTA)*

An abbreviated version (5 items) of the IACTA (Panic Brief version; IACTA-PB) (Cano-Vindel, 2001; Muñoz-Navarro et al., 2020) will be used for measuring attentional and interpretative biases.

- *Cognitive Emotion Regulation Questionnaire (CERQ)*

The CERQ was developed for measuring the specific cognitive emotion regulation strategies (Garnefski & Kraaij, 2006) and it has been validated with Spanish population (Domínguez-Sánchez et al., 2013). In this study, the shortened version (18 items) will be used.

- *Metacognitions Questionnaire 30 items (MCQ-30)*

The MCQ-30 (Wells & Cartwright-Hatton, 2004) is a short form of the MCQ, which measures the beliefs about the own thinking processes. It has been validated with Spanish population by Ramos-Cejudo et al. (2013). In this study, only the negative beliefs subscale (6 items; MCQ-NB) will be used (Muñoz-Navarro et al., 2020).

- *EuroQol 5D-5L (EQ-5D-5L)*

The Spanish version of the EQ-5D-5L (Badia et al., 1999; van Reenen et al., 2019) will be used for measuring the quality of life, for the cost-utility assessment.

- *Ad-hoc questionnaire*

In order to collect information about previous therapy experiences, satisfaction with the treatment, complaints, etc.

- *Medical records*

In order to collect information about health service utilization: medication, check-ups, consultations, etc.

Other pre-specified outcome measures

- *Patient Health Questionnaire 4 items (PHQ-4)*

The PHQ-4 (Kroenke et al., 2009) gathers both items from the PHQ-2 (depression symptoms) and two items from the GAD-7 (anxiety). It has been studied with Spanish population (Cano-Vindel et al., 2018) and it helps to accelerate the screening process: a score greater than or equal to 3 (PHQ-2: sensitivity of 90%, specificity of 61%; GAD-2: sensitivity of 88%, specificity of 61%) would indicate a need of additional assessment. A fifth item from the PHQ-PD has been added to measure panic disorder.

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RECRUITMENT AND FIRST ASSESSMENT

1 The recruitment will be accomplished in three different **primary care settings** of the province of Cordoba: the "Carlos Castilla del Pino" Health Centre, the "Levante Sur Dr. Manuel Barragán Solís" Health Centre, and the Community Mental Health Unit of Montilla. General practitioners (GPs) will invite the patients in whom they suspect a diagnosis of emotional disorder (ED) to participate in the study. Participants will be informed and asked for the written consent, and an assessor-investigator (the blinded party) will administer the instruments (see Materials).

Participants will be only adult (18-65 year-old) men and women who have mild or moderate EDs (i.e. depressive, anxiety and/or somatoform disorders) according to the PHQ subscales: the PHQ-4 for the screening, and the PHQ-9, the GAD-7, the PHQ-PD, and the PHQ-15 to determine the kind of disorder and the severity level. Those who do not have an ED and/or do have a severe mental illness, will be returned to their GPs. Participants with a recent, severe suicide attempt, or with a high level of impairment (according to the SDI) will be excluded as well.

The **sample size** needed would be 150.

Start date of the recruitment: May 2021.

INTERVENTION

2 Participants will be **allocated, by a non-assessor investigator with a computer-generated randomization**, to the **three experimental groups**:

- **Group psychotherapy**

Brief transdiagnostic, cognitive-behavioural therapy focused on the emotion regulation strategies that maintain the emotional symptoms. It is an adaptation of the Unified Protocol for the Transdiagnostic Treatment of Emotional Disorders (Barlow et al., 2011) and the "Improving Access to Psychological Therapies (IAPT)" program (Clark, 2011). It consists on seven 90-minute sessions, provided by a non-assessor clinical psychologist in 12-16 weeks, with 8-10

participants per group (more information in Cano-Vindel et al., 2016):

Sessions 1 and 2 (weeks 1 and 2): Psychoeducation and relaxation tecniques.
Sessions 3 and 4 (weeks 3 and 5): Cogntive restructuring and emotion regulation training.
Sessions 5 and 6 (weeks 7 and 9): Behaviour modification tecniques.
Session 7 (week 12): Review and relapse prevention.

- **Individual psychotherapy**

An adaptation to individual format of the group intervention. From 2 to 8 sessions of 30-60 minutes. Provided by a non-assessor clinical psychologist.

- **Treatment as usual** (TAU)

Mainly pharmacological treatment prescribed by the GP. If they recommended psychotherapy as part of the TAU, the participant would be excluded to avoid bias.

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SECOND ASSESSMENT AND FOLLOW-UPS

3 Instruments will be administered again after each intervention is finished. They will be administered again 6 and 12 months later in order to assess if the potential changes remain over time.

ANALYSES

4 STATISTICAL ANALYSES

Data will be analyzed both intention-to-treat and per protocol approaches. After homogeneity intra and intergroups has been checked, changes over time (baseline, postintervention, and follow-ups) in primary and secondary outcomes will be analyzed through linear mixed models. Likewise, effect size (Cohen's *d*) will be calculated, as well as its accuracy taking into account the number of sessions received. Additionally, it will be estimated the percentage of patients in each group who experience a 50% decrease in the number of clinical symptoms and scores by one standard deviation, as well as the percentage of cases with a probable ED before and after receiving treatment (according to cut-off criteria). Therapeutic success criteria will be the obtaining of postintervention means significantly lower ($p \leq .05$) and medium/large effect sizes significantly greater than the control's, specially in the ED scores. Furthermore, groups will be compared regarding impairment, quality of life, satisfaction with the treatment, and cost-effectiveness and cost-utility results.

COST-EFECTIVENESS ANALYSES

Data will be collected through medical records and assessments 3 months before the inclusion, immediately before and after the intervention, and 6 and 12 months later. Direct costs will be calculated by adding the costs due to drugs use (antidepressants, anxiolytics, hypnotics, and sedatives), checkups and other health services, and health personnel.

Since group psychotherapy has not a specific tariff, it will be considered as a GP consultation without medical tests (as GPs and clinical psychologists have similar salaries in Spain). Indirect costs will be calculated by multiplying the days of sick leave from work by the daily minimum salary at the moment. It will be also taken into account if it is necessary a replacement worker. Total costs will be obtained by adding the previous ones.

Cost-effectiveness analysis will be accomplished by calculating the incremental cost-effectiveness ratios (ICER). Furthermore, the EQ-5D-5L will be used to calculate the intervention utility as quality-adjusted life years (QALYs), and these to obtain the incremental cost-utility ratios (ICUR). The bootstrapping method will be used in order to obtain more accurate ICUR. Lost data will be analyzed through Student's *t* and χ^2 tests regarding ED severity level, sex and age. Finally a sensitivity analysis will be done to test the cost-effectiveness results.

Hypothesis 1: The individual treatment will be generally more effective than the group one.
Hypothesis 2: The group therapy will be more effective than the individual with mild disorders and it will get better results in terms of cost-effectiveness.
Hypothesis 3: The usual pharmacological treatment will get the worst cost-effectiveness results.
Hypothesis 4: The same results will be found across the follow-up assessments.