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## **Publicación 1ª**

Conejo-Cerón S, Moreno-Peral P, Rodríguez-Morejón A, Motrico E, Navas-Campaña D, Rigabert A, Martín-Pérez C, Rodríguez-Bayón A, Ballesta-Rodríguez MI, Luna JD, García-Campayo J, Roca M, Bellón JÁ. Effectiveness of psychological and educational interventions to prevent depression in primary care: a systematic review and meta-analysis. *Annals of Family Medicine*. 2017 May;15(3):262-271.

### **Purpose:**

Although evidence exists for the efficacy of psychosocial interventions to prevent the onset of depression, little is known about its prevention in primary care. We aimed to evaluate the effectiveness of psychological and educational interventions to prevent depression in primary care.

### **Methods:**

We conducted a systematic review and meta-analysis of relevant randomized controlled trials (RCTs) examining the effect of psychological and educational interventions to prevent depression in nondepressed primary care attendees. We searched MEDLINE, PsycINFO, Web of Science, OpenGrey Repository, Cochrane Central Register of Controlled Trials, and other sources up to May 2016. At least 2 reviewers independently evaluated the eligibility criteria, extracted data, and assessed the risk of bias. We calculated standardized mean differences (SMD) using random-effects models.

### **Results:**

We selected 14 studies (7,365 patients) that met the inclusion criteria, 13 of which were valid to perform a meta-analysis. Most of the interventions had a cognitive-behavioral orientation, and in only 4 RCTs were the intervention clinicians primary care staff. The pooled SMD was -0.163 (95%CI, -0.256 to -0.070;  $P = .001$ ). The risk of bias and the heterogeneity ( $I^2 = 20.6\%$ ) were low, and there was no evidence of publication bias. Meta-regression detected no association between SMD and follow-up times or SMD and risk of bias. Subgroup analysis suggested greater effectiveness when the RCTs used care as usual as the comparator compared with those using placebo.

### **Conclusions:**

Psychological and educational interventions to prevent depression had a modest though statistically significant preventive effect in primary care. Further RCTs using placebo or active comparators are needed.

## **Publicación 2ª**

Bellón JÁ, Conejo-Cerón S, Moreno-Peral P, King M, Nazareth I, Martín-Pérez C, Fernández-Alonso C, Ballesta-Rodríguez MI, Fernández A, Aiarzaguena JM, Montón-Franco C, Ibanez-Casas I, Rodríguez-Sánchez E, Rodríguez-Bayón A, Serrano-Blanco A, Gómez MC, LaFuente P, Del Mar Muñoz-García M, Mínguez-Gonzalo P, Araujo L, Palao D, Espinosa-Cifuentes M, Zubiaga F, Navas-Campaña D, Mendive J, Aranda-Regules JM, Rodriguez-Morejón A, Salvador-Carulla L, de Dios Luna J. Preventing the onset of major depression based on the level and profile of risk of primary care attendees: protocol of a cluster randomised trial (the predictD-CCRT study). BMC Psychiatry. 2013 Jun 19;13:171.

### **Background:**

The 'predictD algorithm' provides an estimate of the level and profile of risk of the onset of major depression in primary care attendees. This gives us the opportunity to develop interventions to prevent depression in a personalized way. We aim to evaluate the effectiveness, cost-effectiveness and cost-utility of a new intervention, personalized and implemented by family physicians (FPs), to prevent the onset of episodes of major depression.

### **Methods/design:**

This is a multicenter randomized controlled trial (RCT), with cluster assignment by health center and two parallel arms. Two interventions will be applied by FPs, usual care versus the new intervention predictD-CCRT. The latter has four components: a training workshop for FPs; communicating the level and profile of risk of depression; building up a tailored bio-psycho-family-social intervention by FPs to prevent depression; offering a booklet to prevent depression; and activating and empowering patients. We will recruit a systematic random sample of 3286 non-depressed adult patients (1643 in each trial arm), nested in 140 FPs and 70 health centers from 7 Spanish cities. All patients will be evaluated at baseline, 6, 12 and 18 months. The level and profile of risk of depression will be communicated to patients by the FPs in the intervention practices at baseline, 6 and 12 months. Our primary outcome will be the cumulative incidence of major depression (measured by CIDI each 6 months) over

18 months of follow-up. Secondary outcomes will be health-related quality of life (SF-12 and EuroQol), and measurements of cost-effectiveness and cost-utility. The inferences will be made at patient level. We shall undertake an intention-to-treat effectiveness analysis and will handle missing data using multiple imputations. We will perform multi-level logistic regressions and will adjust for the probability of the onset of major depression at 12 months measured at baseline as well as for unbalanced variables if appropriate. The economic evaluation will be approached from two perspectives, societal and health system.

**Discussion:**

To our knowledge, this will be the first RCT of universal primary prevention for depression in adults and the first to test a personalized intervention implemented by FPs. We discuss possible biases as well as other limitations.

**Trial registration:**

ClinicalTrials.gov identifier: NCT01151982.

**DOI:** 10.1186/1471-244X-13-171

**Publicación 3ª**

Bellón JÁ, Conejo-Cerón S, Moreno-Peral P, King M, Nazareth I, Martín-Pérez C, Fernández-Alonso C, Rodríguez-Bayón A, Fernández A, Aiarzaguena JM, Montón-Franco C, Ibanez-Casas I, Rodríguez-Sánchez E, Ballesta-Rodríguez MI, Serrano-Blanco A, Gómez MC, LaFuente P, Muñoz-García Mdel M, Mínguez-Gonzalo P, Araujo L, Palao D, Bully P, Zubiaga F, Navas-Campaña D, Mendive J, Aranda-Regules JM, Rodriguez-Morejón A, Salvador-Carulla L, de Dios Luna J. Intervention to prevent major depression in primary care: a cluster randomized trial. *Ann Intern Med.* 2016 May 17;164(10):656-65.

**Background:**

Not enough is known about universal prevention of depression in adults.

**Objective:**

To evaluate the effectiveness of an intervention to prevent major depression.

**Design:**

Multicenter, cluster randomized trial with sites randomly assigned to usual care or an intervention. (ClinicalTrials.gov: NCT01151982).

**Setting:**

10 primary care centers in each of 7 cities in Spain.

**Participants:**

Two primary care physicians (PCPs) and 5236 nondepressed adult patients were randomly sampled from each center; 3326 patients consented and were eligible to participate.

**Intervention:**

For each patient, PCPs communicated individual risk for depression and personal predictors of risk and developed a psychosocial program tailored to prevent depression.

**Measurements:**

New cases of major depression, assessed every 6 months for 18 months.

**Results:**

At 18 months, 7.39% of patients in the intervention group (95% CI, 5.85% to 8.95%) developed major depression compared with 9.40% in the control (usual care) group (CI, 7.89% to 10.92%) (absolute difference, -2.01 percentage points [CI, -4.18 to 0.16 percentage points];  $P = 0.070$ ). Depression incidence was lower in the intervention centers in 5 cities and similar between intervention and control centers in 2 cities.

**Limitation:**

Potential self-selection bias due to nonconsenting patients.

**Conclusion:**

Compared with usual care, an intervention based on personal predictors of risk for depression implemented by PCPs provided a modest but nonsignificant reduction in the incidence of major depression. Additional study of this approach may be warranted.

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