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Brief report

Persistence in the long term of the effects of a collaborative care programme for depression in primary care

Enric Aragonès *, Antonia Caballero, Josep-Lluís Piñol, Germán López-Cortacans

Tarragona-Reus Primary Care Area, Catalan Health Institute, IDIAP (Primary Care Research Institute) Jordi Gol, Barcelona, Spain

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ABSTRACT

Background: A collaborative care programme for depression in primary care has proven clinical effectiveness over a 12-months period. Because depression tends to relapse and to chronic course, our aim was to determine whether the effectiveness observed in the first year persists during 3 years of monitoring.
Methods: Randomised controlled trial with twenty primary care centres were allocated to intervention group or usual care group. The intervention consisted of a collaborative care programme with clinical, educational and organisational procedures. Outcomes were monitored by a blinded interviewer at baseline, 12 and 36 months. Clinical outcomes were response to treatment and remission rates, depression severity and health-related quality of life. Trial registration: ISRCTN16384353.
Results: A total of 338 adult patients with major depression (DSM-IV) were assessed at baseline. At 36 months, 137 patients in the intervention group and 97 in the control group were assessed (attrition 31%). The severity of depression (mean Patient Health Questionnaire-9 score) was 0.95 points lower in the intervention group [6.31 versus 7.25; $p=0.324$]. The treatment response rate was 5.6% higher in the intervention group than in the control group [66.4% versus 60.8%; $p=0.379$] and the remission rate was 9.2% higher [57.7% versus 48.5%; $p=0.164$]. No difference reached statistical significance.
Limitations: The number of patients lost (31%) before follow-up may have introduced a bias.
Conclusions: Clinical benefits shown in the first year were not maintained beyond: at 36 months the differences between the control group and the intervention group reduced in all the analysed variables.

1. Introduction

Deficiencies have been described in the clinical management of depressed patients that affect negatively the clinical results, particularly in primary care (Wittchen et al., 2001). It is difficult to properly identify and diagnose patients with depression, and among patients under antidepressant treatment, there is no planned clinical monitoring and contacts after the start of the treatment are scarce and irregular. In this situation, you lose the opportunity to adjust the treatment to the patient's clinical status and to improve adherence to treatment (Pinto-Meza et al., 2008; Fernández et al., 2010).

The clinical effectiveness and usefulness of disease management models for depression that involve changes in the various components of the care process (Thota et al., 2012) have been proved. INDI (INterventions for Depression Improvement) is a collaborative care programme designed to optimise patient care and clinical outcomes of depression in primary care. The assessment of its effectiveness in the first year has been published in 2012 (Aragonès et al., 2012). In patients treated with this programme, compared to those treated according to usual criteria, the severity of depressive symptoms and quality of life evolved more positively and response to the treatment and remission rates were significantly higher. Due to the chronic nature of depression, often with incomplete recovery, residual symptoms, frequent relapses and recurrences, it is important to assess the long-term effects of this intervention. The aim of this paper is therefore to determine whether the effectiveness shown in the first year of the programme persists during 3 years of monitoring.

2. Methods

This is a randomised controlled trial with primary care centres participating in the intervention group – where a programme to improve the clinical management of depression is applied, or

* correspondence to: Centre d'Atenció Primària de Constantí, Carrer dels Horts, 6 43120, Constantí (Tarragona), Spain Tel.: +34 977524109, +34 680 766 92.
E-mail address: earagones.tarte.ics@gencat.cat (E. Aragonès).

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to the control group – where depression is treated according to the usual standards.

The Research Ethics Committee of the Jordi Gol Primary Care Research Institute (IDIAP) approved the study protocol in Barcelona, on 29 March 2006 (Ref. P06/16). All the participants provided written informed consent. This study is registered as ISRCTN16384353 and a detailed description of its design has been published previously (Aragonès et al., 2012, 2007).

2.1. Location and patients

The study was carried out in 20 primary care centres in Catalonia, Spain. Inclusion criteria for patients: age ≥ 18 years, suffering from a moderate or severe major depressive episode (score >14 according to the Patient Health Questionnaire, PHQ-9) or a mild depression (PHQ-9 score of 10–14) that persists for over a month, and no antidepressant medication during the past three months. Patients with psychotic or bipolar disorders, alcohol or drug dependency, physical, mental or language limitations or concurrent illness that would prevent them from participating in the evaluation study, and pregnant or lactating women were excluded.

2.2. Randomisation

Participating centres agreed to take part in the study before their assignment to the intervention group or to the control group. Centres were matched according to similar characteristics and for each pair, centres were assigned to each study group following a random procedure.

3. Intervention

This is a programme of collaborative care to improve the management of depression. It is based on the chronic care model (Bodenheimer et al., 2002) adapted to primary care in the Spanish public health system. It is a multi-component programme with elements of improvement in the organisation of depression care within the primary care team (case management, professional roles, care circuits) and the primary care–psychiatry interface, training of professionals, elements to help decision-making and clinical management of depression (clinical guidelines, algorithms, registration systems, etc.) and a psychoeducational programme for patients and their families.

The interventions included in the programme are well established and highly structured for the acute and continuation phase of treatment (usually over the first year). Also, long-term monitoring of patients is recommended to support treatment compliance (in those patients in whom a maintenance treatment is established) and to detect a possible symptomatic worsening and/or recurrence. The details of this programme can be found in previous articles (Aragonès et al., 2007, 2008).

3.1. Usual care

Patients with depression in centres of the control group were treated according to standard criteria using all available resources that the doctor considers appropriate.

3.2. Measurements and masking

The outcomes were monitored using standard questionnaires applied through telephone interviews by an interviewer 'blinded' to the patients' study group. In this article we consider assessments at baseline, 12 and 36 months. The main outcome variables are the treatment response and remission rates, and severity of depressive symptoms. The severity of depression was assessed using PHQ-9. A PHQ-9 score <5 indicates clinical remission. The response is defined as a 50% reduction in the severity of symptoms (measured with the PHQ-9) compared to baseline. Quality of life related to health was measured with the SF-12 health questionnaire that provides the physical component score (PCS) and mental component score (MCS). The following variables related to the process of care were also measured: persistence of the antidepressant treatment, and number and type of primary care visits and psychiatry visits caused by the depression.

3.3. Statistical methods

The unit of analysis was the patient. The analysis was performed allowing for the clinical and process outcomes in each group on the basis of the initial assignment to the study groups, regardless of the adherence to programme guidelines of the patient, health professionals or health centre. We used data from those patients who remained in the study sample at each cut-point, and missing values were not imputed. In continuous variables, we calculated averages, standard deviations and differences between the two groups (with a confidence interval at 95%; CI 95%). For categorical variables, we calculated the percentages in each group and differences between groups (CI 95%).

4. Results

At the beginning of the study, 338 patients were evaluated. At 12 months, the figure was 302 patients (11% loss) and at 36 months, 234 patients were participating (31% loss). At 12 months 19 patients were no longer in the control group, and 17 were no longer in the intervention group, primarily because it was impossible to contact them. However, three patients in the control group revoked their consent and two patients in the intervention group were excluded because of illnesses which impeded their participation. At 36 months, the patients lost (53 in control group and 52 in intervention group) were largely unreachable, except the patients withdrawn at 12 months due to illness and non-consent, and one patient in the intervention group who had died. At baseline, patients in both study groups were comparable in their sociodemographic and clinical characteristics. The patients were aged around 47 years on average and eight out of ten were women. The baseline severity of depression was in the range of moderate depression (about 18 points on the PHQ-9) and for half of these patients, it was a recurrent episode. A table with the basal characteristics of the patients can be found in the on-line appendix. Regarding the individuals who remained in the study, the lost patients were most frequently men (29.8% versus 16.7%; $p=0.006$), were younger (43.5 years versus 49.5 years; $p=0.001$) and there were no significant differences in the severity of depression or the measurement of quality of life.

4.1. Outcomes

Although at 12 months, the proportions of response and remission were significantly higher in the intervention group (difference of 15.4% and 13.4%, respectively), there were less differences at 36 months (5.6% and 9.2%, respectively) and these did not reach statistical significance. In the first 12 months, the severity of depressive symptoms decreased in both groups, but the clinical status was significantly better in the intervention group. At 36 months, the difference between the groups is not statistically significant (Table 1).

The physical component of the SF-12 was stable in both groups during follow-up. The mental health component progressed more

Table 1
Depression outcomes by study group at baseline, 12 months, and 36 months.

Clinical outcomes	Intervention group ($N=189$)[a] % (n/N)	Usual care group ($N=149$)[a] % (n/N)	Difference between groups (95% CI)	p-Value
Response[b]				
12 months	66.9% (115/172)	51.5% (67/130)	15.4% (4.3% to 26.5%)	0.007
36 months	66.4% (91/137)	60.8% (59/97)	5.6% (−6.9% to 18.1%)	0.379
Remission[c]				
12 months	48.8% (84/172)	35.4% (46/130)	13.4% (2.3% to 24.5%)	0.020
36 months	57.7% (79/137)	48.5% (47/97)	9.2% (−3.7% to 22.1%)	0.164
PHQ-9 score[d]	**Mean (SD)**	**Mean (SD)**		
Baseline	18.10 (5.20)	17.66 (4.79)	−0.44 (−1.52 to 0.65)	0.429
12 months	7.15 (7.11)	8.78 (6.99)	1.63 (0.02 to 3.25)	0.048
36 months	6.31 (7.11)	7.25 (7.26)	0.95 (−0.94 to 2.82)	0.324
SF12 mental health[e]				
Baseline	22.26 (9.05)	22.73 (10.44)	0.47 (−1.62 to 2.55)	0.661
12 months	43.39 (14.12)	38.49 (15.32)	−4.90 (−8.28 to −1.52)	0.005
36 months	47.98 (14.10)	46.17 (14.26)	−1.81 (−5.52 to 1.90)	0.338
SF12 physical health[e]				
Baseline	47.47 (10.98)	48.23 (11.23)	0.76 (−1.63 to 3.15)	0.533
12 months	47.06 (10.19)	46.99 (10.30)	−0.07 (−2.44 to 2.29)	0.951
36 months	46.15 (9.51)	45.60 (9.22)	−0.56 (−3.02 to 1.91)	0.657

[a] Total number of patients randomized to each group at enrolment.
[b] Response: decrease $\geq 50\%$ in PHQ-9 score from baseline.
[c] Remission: PHQ-9 depression score < 5.
[d] Range: 0–27.
[e] Range: 0–100.

Table 2
Process of care variables in depressed patients being managed with the depression management model versus usual care.

Process of care variables	Intervention group ($N=189$)[a] Mean (SD)	Usual care group ($N=149$)[a] Mean (SD)	Difference between groups (95% CI)	p-Value
Visits for depression to the primary care physician in the past year				
At 12 months	8.2 (7.1)	8.2 (7.8)	0.0 (−1.7 to 1.7)	0.999
At 36 months	1.1 (2.1)	1.1 (2.5)	0.2 (−0.6 to 0.6)	0.948
Visits for depression to the primary care nurse in the past year				
At 12 months	5.0 (4.9)	1.9 (3.7)	−3.1 (−4.1 to −2.1)	0.000
At 36 months	0.9 (4.6)	0.3 (1,4)	−0.6 (−1.4 to 0.3)	0.198
Visits to the psychiatrist in the past year				
At 12 months	1.1 (4.1)	0.6 (1.4)	−0.5 (−1.2 to 0.2)	0.150
At 36 months	0.2 (0.9)	0.1 (0.6)	−0.0 (−0.2 to 0.2)	0.684
Visits to the psychologist in the past year				
At 12 months	2.3 (5.7)	1.7 (3.9)	−0.6 (−1.8 to 0.6)	0.311
At 36 months	0.7 (4.4)	0.3 (1.0)	−0.3 (−1.2 to 0.6)	0.463
Persistence of antidepressant treatment	**% (n/N)**	**% (n/N)**		
At 12 months	62.2% (107/172)	56.2% (73/130)	6.0% (−5.1% to 17.2%)	0.293
At 36 months	37.2% (51/137)	32.3% (31/96)	4.9% (−7.4% to 17.3%)	0.441

[a]Total number of patients randomized to each group at enrolment.

satisfactorily in the intervention group during the first year, but the differences disappeared at 36 months (Table 1).

At 12 months, significant differences were only observable in the number of visits made by patients of depression to the primary care nurse; but not to other involved health professionals. Despite the fact that at 36 months a tendency to attend more to the nurse in the intervention group patients remains, the difference is not significant (Table 2).

5. Discussion

In this study on the long-term effects of a collaborative care programme for the management of depression in primary care, we have found that the clinical benefits that were demonstrated in the first year of implementation do not persist with the same magnitude in the long term: at 36 months, despite more favourable clinical results observed in the intervention group, the

differences had greatly reduced in all analysed variables and are no longer statistically significant.

In a previous article on the effect of the programme during the first 12 months of follow-up, we had already reported that the effects were more important at 3 and 6 months and observed a relative reduction of differences between groups in the evaluation at 12 months (Aragonès et al., 2012). This trend continues and grows at 36 months.

A limitation of this study is that a significant proportion of patients assessed at baseline – 31% – could not be contacted at 36 months. We did not observe differences between patients who remained in the study regarding severity of the depression but can not rule out that this loss of information caused a bias in the results. In any case, the smaller number of individuals in the sample represents a loss of statistical power.

In a metanalysis, Gilbody et al. (2006) reported eleven studies that provided better long-term outcomes of up to 5 years with collaborative care compared with standard care. However, the pooled effects were of small magnitude (effect size from 0.31 at 1 year to 0.15 at 2 and 5 years) and there was substantial heterogeneity between the studies. Therefore, there was some uncertainty regarding these long-term outcomes.

Rost et al. (2002) reported that an enhanced care programme with an initial intervention (up to six months) followed by a structured continuing intervention (7–24 months) leads to persistent better clinical outcomes and concluded that improving primary care depression management on an ongoing basis should be needed to achieve and sustain significant improvements in the health of the depressed patients.

Several reasons may account for the dilution of the effects of the INDI programme in the long term. The programme's design focused on practicality with 'low intensity' interventions, to ease implementation. Moreover, although the programme includes recommendations on the management of patients in the continuation and maintenance phases of treatment, measures of clinical support and psychoeducation of patients are more concentrated and intense in the acute phase of treatment (during the first months). Also the professional training activities were concentrated in the first year of programme implementation. The implementation of programme included organisational changes – both within in the primary care team as in the relation between primary care and psychiatry – but these changes lacked support and continued feedback and did not persist over time. The reduction of the effects of the INDI programme in clinical practice over time is reflected in the sharp drop observed in contacts with various medical devices because of depression in the third year of follow-up compared to the figures of the first year. This leads to a similar intensity in the use of health resources and in the reduction of the differences initially observed between groups.

It should be noted that at 36 months, although the average severity of depression is below the standard diagnosis threshold (PHQ-9 <10 points), in a third of patients, there was not a minimally satisfactory clinical response regarding their baseline state and approximately half of the patients have not achieved clinical remission (that is the target for the treatment of depression).

The results suggest the need to improve the intervention with measures to extend the beneficial effects shown in the short and medium term to the long term and achieve higher effectiveness rates. Benchmarking with other interventions that have proven effective in the long term (Rost et al., 2002; Katon et al., 2002; Hunkeler et al., 2006; Sherbourne et al., 2001), we concluded that the programme must be redesigned to be performed on an ongoing basis. Miller et al. (2013) indicate that the implementation and maintenance of care models require support from the healthcare organisation and implementation strategies to back the adoption and sustainability of the model in a clinical environment. Therefore, we should focus on the inclusion of support mechanisms and on the continuous improvement of organisational changes (e.g., by including the implementation of the programme in contracts and management agreements of healthcare centres and professionals), and also on the continuous training of professionals. Systems to aid clinical decision making (e.g., clinical guidelines, algorithms or schedules of recommended visits) contained in the programme must include explicit guidance on the clinical management of situations with incomplete resolution and chronification of depression, and psychoeducative interventions should provide reinforcement interventions and periodic updates, particularly for those patients with incomplete resolution or following antidepressant treatment.

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Conflict of interest

E Aragonès has received honoraria for educational activities, from Esteve and Lilly, and as research advisor, and meeting expenses, from Lilly. All authors declare no other relationships, interests or activities that could appear to have influenced the submitted work.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jad.2014.05.003.

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