Collaborative care for depression in primary care. Making sense of a complex intervention: systematic review and meta-regression

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CRD summary
Meta-regression was used to identify the 'active ingredients' in primary care collaborative models for depression management. Key predictors of depressive symptom outcomes included systematic patient identification, professional staff background and specialist supervision. No significant predictors emerged for antidepressant use. The analysis was exploratory and the results were not definitive. Meta-regression may be useful for identifying key elements of complex interventions.

Authors' objectives
The authors aimed to identify the 'active ingredients' in collaborative care models for the management of depression in primary care, by means of meta-regression.

Searching
MEDLINE, EMBASE, CINAHL and the Cochrane Library were searched from inception to November 2005. The search terms were not reported but are available from the authors on request.

Study selection
Study designs of evaluations included in the review
No inclusion criteria were specified with regard to the study design. Only randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Collaborative care interventions for patients with depression in primary care were eligible for inclusion. These were defined as multifaceted organisational interventions such as the introduction of case managers, mechanisms to improve liaison between primary care clinicians and mental health specialists, and systems to manage information on the progress of individual patients. The authors excluded educational and training initiatives and the provision of brief psychological therapy where these were the sole intervention.

The specific interventions in the individual studies were not described, but a table reported intervention content variables of interest for the eight variables included in analysis. Of the 34 studies, primary care physicians received training in 15, case managers had a mental health background in 17, the number of case management sessions was five or more in 21, and case managers had regular or planned supervision in 24. The case management content included medication management in all studies but also included psychological therapy in 13 of the 34 studies. Other variables of interest concerned the study setting and methodology. Most of the studies (27 out of 34) were set in the USA.

Participants included in the review
Participants eligible for inclusion were patients with depressive symptoms, or with a diagnosis of depression, in a primary care setting.

Where the information was reported, the participants in the included studies were adults (26 studies) or elderly people (6 studies) in primary care. A single study was restricted to adult women. The participants had either depressive symptoms (5 studies) or a formal diagnosis of depression (27 studies). In almost half of the studies the participants were starting treatment, generally with a new antidepressant, or were changing treatment (16 studies). In several studies the patients had co-morbidities such as dysthymia (10 studies), diabetes, substance abuse or minor depression (1 study each), or were at high risk of relapse or recurrence (3 studies).

Outcomes assessed in the review
Outcomes eligible for inclusion were changes in measures of antidepressant use and a reduction in depressive symptoms. Where alternative measures of depressive outcomes were reported, priority was given to the primary study outcome and then to observer-rated scales over self-report measures. All studies reported one or both of the outcomes of interest. The analysis was restricted to short-term outcomes (at approximately 6 months follow-up) in order to maximise the data available.

How were decisions on the relevance of primary studies made?
The authors did not state how the studies were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Two members of the research team working independently extracted data on allocation concealment in the included studies, with any disagreements resolved by discussion. Allocation concealment was the only methodological quality variable to be included in the regression model.

Data extraction
Data extraction methods were developed and piloted a priori. Two members of the research team working independently extracted the data. Any disagreements were resolved by discussion.

Measures of antidepressant use were extracted as dichotomous outcomes and analysed using odds ratios (ORs). Continuous measures of depressive symptoms were translated into standardised effect sizes by dividing the difference between the group means by the pooled standard deviation. Dichotomous measures of depressive symptoms were also translated into standardised effect sizes, using the logit transformation. In 5 (8%) of 62 comparisons, missing data were imputed from other relevant studies. Studies using cluster randomisation were checked for unit of analysis errors and, where necessary, their precision was adjusted in the meta-analysis. The effects of adjustment were examined in a sensitivity analysis.

Data were also extracted on the content of the interventions in the included studies, using a coding frame with codes to represent potential elements of a prototypical collaborative care model. This included variables related to professional training, case management, liaison mechanisms and information systems. Additional codes related to study characteristics.

Methods of synthesis
How were the studies combined?
In a preliminary analysis, the studies were combined using a random-effects model to provide an overall pooled measure of the effect of collaborative care on antidepressant use and depressive symptoms. The main analysis used random-effects meta-regression to provide estimates of the relationship between eight intervention content variables and the two outcomes. A second meta-regression assessed the relationship between these outcomes.

How were differences between studies investigated?
Heterogeneity between the studies was the main focus of the analysis. Different combinations of variables were examined by meta-regression to determine which model provided the biggest reduction in heterogeneity. Heterogeneity was quantified using the I-squared statistic, which estimates the percentage of variation that can be attributed to differences between the studies rather than chance.

Results of the review
Thirty-four RCTs with a total of 12,294 participants were included.

There were problems of inconsistent reporting in the included studies and many data were missing. Allocation concealment was not clearly described in most studies, and comprehensive data could be extracted on only eight of the 27 intervention content variables of interest.

The meta-analysis showed a statistically significant beneficial effect for collaborative care on antidepressant use (OR
1.92, 95% confidence interval, CI: 1.54, 2.39) and on depressive outcomes (standardised mean difference 0.24, 95% CI: 0.17, 0.32). These estimates were associated with high and moderate heterogeneity (I-squared estimates 80% and 54%), respectively.

The meta-regression found none of the intervention content variables to be significantly associated with antidepressant use, and so no multivariate model was estimated for this outcome. Three variables predicted improvement in depression symptoms: recruitment of patients by systematic identification (as opposed to referral by clinicians) (p=0.061), case managers having a specific mental health background (p=0.004), and the provision of regular supervision for case managers (p=0.033). The most robust multivariate model for improvement in depression symptoms incorporated the above three variables plus the variable for a non-US setting; the combination of these four variables reduced overall heterogeneity (I-squared) to 36% (low to moderate).

The additional meta-regression found a positive association between antidepressant use and depressive symptoms (p=0.028), suggesting that the effect of collaborative care on depressive symptoms may be mediated through antidepressant use.

Sensitivity analyses on the effect of cluster randomisation did not materially affect these results.

**Authors’ conclusions**

Meta-regression techniques indicated that key predictors of the effect of collaborative care on depressive symptoms in primary care were systematic identification of the patients, professional background of the staff and specialist supervision. No significant predictor of the effect of collaborative care on antidepressant use was identified. Meta-regression is a feasible way of examining the active constituents in complex health interventions, but it has its limitations.

**CRD commentary**

The review question was clear, the literature search was satisfactory and the data synthesis was clearly described. The analytical methods used in the review were clearly reported and referenced, and appeared appropriate. The inclusion criteria were of necessity quite loose, because the study focused on the degree to which variability in collaborative care models influences the outcomes. The authors acknowledged that study choice might have important implications, but unfortunately did not report the number of reviewers involved in selecting the studies, whether their assessment was independent, or how any disagreements were resolved. Moreover, there was minimal information about the quality of the included studies: allocation concealment was the only aspect of methodological quality assessed. It is possible that other differences in quality, which were not assessed, may be significant predictors of outcome.

As the authors pointed out, there were several reasons why their findings should be considered exploratory rather than definitive: the validity of their coding scheme has not been confirmed, a large number of data were missing, it was possible that significant variables were not included in the analysis, and the meta-regression was unable to detect ‘active ingredients’ that did not vary between interventions. Much of the data related to the USA and the findings might not be generalisable to other countries, as setting was a significant predictor of outcomes. In addition, the results might have been influenced by the study selection process.

**Implications of the review for practice and research**

Practice: The authors stated that key predictors of the effect of collaborative care on depressive symptoms were systematic identification of the patients, professional background of the staff and specialist supervision. They further suggested that the effects of collaborative care on depression symptoms may be mediated through changes in antidepressant use.

Research: The authors stated that meta-regression may be useful in identifying the active constituents of complex interventions in mental health. Such research would be facilitated by a more standardised approach to the reporting of complex interventions. In addition, analytical techniques such as path analysis may help elucidate the causal pathways between variables and outcomes. Qualitative research may also be useful to explore the effect mechanisms of variables identified as significant.
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