Article

Depression remission after six months of collaborative care management: role of initial severity of depression in outcome

Kurt B Angstman MS MD
Department of Family Medicine, Mayo Clinic, Rochester, Minnesota, USA

Pamela Pietruszewski MA
Program Lead, Institute for Clinical Systems Improvement, Bloomington, Minnesota, USA

Norman H Rasmussen EdD
Departments of Family Medicine and Psychiatry and Psychology

John M Wilkinson MD
Department of Family Medicine

David J Katzelnick MD
Department of Psychiatry

Mayo Clinic, Rochester, Minnesota, USA

ABSTRACT

Aim The impact of initial severity of depression on the rate of remission has not been well studied. The hypothesis for this study was that increased depression severity would have an inverse relationship on clinical remission at six months while in collaborative care management.

Participants The study cohort was 1128 primary care patients from a south-eastern Minnesota practice and was a longitudinal retrospective chart review analysis.

Results Clinical remission at six months was less likely in the severe depression group at 29.6% compared with 36.9% in the moderately severe group and 45.6% in the moderate depression group \((P<0.001)\). Multivariate analysis of a subgroup demonstrated that increased initial anxiety symptoms (odds ratio [OR] 0.9645, 95% confidence interval [CI] 0.9345–0.9954, \(P = 0.0248\)) and an abnormal screening for bipolar disorder (OR 0.4856, 95% CI 0.2659–0.8868, \(P = 0.0187\)) predicted not achieving remission at six months. A patient with severe depression was significantly less likely to achieve remission at six months (OR 0.6040, 95% CI 0.3803–0.9592, \(P = 0.0327\)) compared with moderate depression, but not moderately severe depression \((P = 0.2324)\). There was no statistical difference in the adjusted means of the PHQ-9 score for those patients who were in remission at six months. However, in the unremitted patients, the six-month PHQ-9 score was significantly increased by initial depression severity when controlling for all other variables.

Conclusion Multivariate analysis in our study demonstrated that patients with severe depression have a decreased OR for remission at six months compared with moderate depression. Also, there was a significant increase in the six-month PHQ-9 score for those unremitted patients in the severe vs. moderate depression groups.

Keywords: collaborative care management, depression, primary care
Introduction

Unrecognised depression carries as much disability as chronic medical conditions such as low back pain and heart disease. Disability cost-estimates related to depression were as high as $83 billion dollars in the USA alone in 2000. Up to 25% of women and 12% of men will experience depression and once diagnosed the likelihood of recurrence increases even when remission is initially achieved. Although there is a likelihood of recurrence of depressive symptoms in any patient who has been diagnosed with depression, it is particularly high in depressed patients who do not achieve at least an initial remission of their symptoms. Therefore, complete remission, rather than simply an improvement, is the ultimate goal of treatment. Collaborative care management (CCM) for depression, based on the IMPACT study and others, has demonstrated consistent improvement in outcomes for depression care, compared with usual care.

STAR*D showed a cumulative 67% remission rate after four treatment steps, with the majority of those occurring in the first two steps. It was found that keeping patients engaged and providing early aggressive treatment provided ongoing strategies for improved depression treatment. Other studies have also demonstrated that early treatment response predicted response and remission for major depressive disorder.

In 2005, the Institute for Clinical Systems Improvement (ICSI) convened a group of stakeholders including health plans, medical clinics, patients and employer groups to redesign care and payment for depression in adults in the primary care setting. 'Depression Improvement Across Minnesota – Offering a New Direction' (DIAMOND) was first implemented in March 2008 starting with 5 of the 74 clinics currently certified to offer the programme. DIAMOND is based upon the collaborative care model and incorporates principles developed for the IMPACT study. The model includes six care components:

- the use of the PHQ-9 for assessment and ongoing management
- a registry for systematic tracking and follow-up
- the use of evidence-based guidelines for stepped care treatment modification/intensification
- relapse prevention planning
- a case manager located in the primary care clinic to provide ongoing support, education and coordination
- a consulting psychiatrist to meet onsite weekly with the care manager for case review and treatment recommendations.

Payment redesign was established to allow for a monthly fee paid to DIAMOND-certified sites for the bundle of services provided in the care model.

The impact of the initial severity of depression on the rate of remission, and the likelihood of relapse, has not been well studied or quantified. In 1998, in a cohort follow-up study of 251 primary care patients, Lin et al found that depression severity at baseline was not predictive of relapse at 7 months. In contrast, time to relapse and recurrence were robustly predicted by depression severity in a cohort of primary care patients in Finland. A recent study by Beck et al demonstrated that the severity of depression at the time of diagnosis had a significant impact on productivity loss (absenteeism and presenteeism). Our literature search identified no studies looking directly at the impact of the severity of the depression by the initial PHQ-9 score on the outcomes of depression treatment while the patient is enrolled in CCM. A recent study of 12- and 24-week remission rates for psychiatry (not primary care) patients, with a multivariate analysis, demonstrated that a higher PHQ-9 score at the time of initial diagnosis was inversely related to the odds of remission. Our group has evaluated pilot studies on the effectiveness of the initial implementation of CCM for depression in a primary care practice, as well as the mental health comorbid risk factors for not clinically responding after six months of therapy.

If the primary care provider is able to assess the odds of improvement based on depression severity at the time of diagnosis and communicate this to the patient, this may improve the provider/patient interaction and help the patient understand potential future changes in therapy if treatment targets are not met. The hypothesis for this study was that increased depression severity (classified as moderate, moderately severe or severe) as noted on the initial evaluation would have an inverse relationship with clinical remission at six months.

Methods

The collaborative care model utilised for this study has been described previously. Briefly, any adult (age 18 years and older) patient with a diagnosis by their primary care provider of major depression or dysthymia and a score of 10 or greater on the Patient Health Questionnaire 9-item screen (PHQ-9) qualified for admission into CCM. Intake assessment also included screening tools for anxiety (Generalized Anxiety Disorder questionnaire, GAD-7) and bipolar depression (Mood Disorder Questionnaire, MDQ)
and alcoholism (Alcohol Use Disorders Identification Test, AUDIT)\(^2\).

The CCM programme for depression has been used in primary care practices in Rochester, Minnesota since 1 March 2008. The Mayo Clinic participated in the development of the programme via representation on the DIAMOND Steering Committee, development subgroups and the ICSI Depression Guideline work group. Five Mayo Clinic sites completed certification training to offer the programme.

There were 1143 patients who met the criteria and were admitted to the CCM programme to 30 June 2010, allowing for six months of follow-up analysis. Fifteen patients moved out of our service area and were removed from the study. The study cohort was 1128 primary care patients from a south-eastern Minnesota primary care practice. This study was a longitudinal retrospective chart review analysis.

The primary dependent variables in this study were if the patient had clinical remission of depression at six months (defined as a PHQ-9 score of < 5) and clinical response at six months (defined as a six-month PHQ-9 score ≤ 50% of baseline). The independent variables were age, gender, marital status (married or not), race (white or non-white), initial PHQ-9 score, AUDIT score, GAD-7 score and MDQ score. The PHQ-9 score was categorised further as moderate depression (10–14); moderately severe depression (15–19) or severe depression (≥ 20). The MDQ was considered negative if the patient had a score of < 7 and a negative response on questions 2 and 3; otherwise the MDQ was noted as abnormal.

Categorical variables were tested using chi-square analysis. Means across multiple groups were tested with one-way analysis of covariance (ANCOVA). In a subset of the patients who had complete data sets, a multiple logistic regression model was developed to identify independent predictors of clinical response and remission utilising all independent variables (age, gender, marital status, race, initial PHQ-9 category, AUDIT score, GAD-7 score and MDQ result). Comparison of the adjusted means of the six-month PHQ-9 score for those remitted and unremitting patients was controlled for the independent variables with ANCOVA. Statistical analysis was carried out using MedCalc software (v. 11.6.1, www.medcalc.org). The study was approved by the institutional review board of the Mayo Clinic, Rochester, USA.

**Results**

For the 1143 patients admitted to CCM, when evaluated by the clinical outcomes on an intention to treat method (if follow-up was not obtained, it was assumed that the patient did not improve), the clinical response was 52.3%. The response ranged from 48.4% to 53.3% across the groups of depression severity and was not statistically different after six months of therapy. Clinical remission at six months was 39.6% for the entire cohort and was less likely in the severe depression group at 29.6%, compared with 36.9% in the moderately severe group and 45.6% in the moderate depression group (\(P < 0.001\)) (Figure 1). An intention to treat method assumes a ‘real-world’ result, while outcomes for those patients who are re-measured at six months may give an indication of the potential benefit from the treatment if all patients were able to receive treatment. Figure 2 shows that clinical response is again not statistically significant for the re-measured patients at six months (68.4% vs. 73.2% vs. 70.1%, \(P = 0.387\), based on their initial depression severity, but clinical remission was observed significantly less often in the moderately severe (50.7%) and severe (42.9%) depression groups when compared with those with moderate depression (59.1%, \(P = 0.002\)). Using re-measured data, overall the cohort had a six-month follow-up response rate of 70.3% and a remission rate of 53.5%.

In a subgroup of 698 patients who had complete data sets, univariate analysis demonstrated no difference in the depression severity groups in terms of age, race, percent married or diagnosis. The percentage of women in each group declined as the severity of depression increased (78.4% vs. 69.9% vs. 66.4%, \(P = 0.011\)). There was a statistically significant increase in all intake comorbid mental health screening tests as depression severity increased. The AUDIT score increased from 2.4 in the moderate group to 3.4 in the severe depression group (\(P = 0.01\)). The GAD-7 score varied from 9.3 in the moderate group to 11.9 in the moderately severe and 14.2 in the severely depressed group (\(P < 0.001\)). The percentage of abnormal MDQ scores increased from 5.1% to 8.4% to 16.0% (\(P < 0.001\)). Clinical response was not different between the groups (\(P = 0.913\)), but clinical remission at six months was improved in the moderate depression group (64.0%) vs. the moderately severe group at 55.3% and the severe depression group (45.3%, \(P = 0.001\)) (Table 1).

Multivariate analysis of the independent variables for those patients who achieved clinical remission is shown in Table 2. An increased initial GAD-7 score (odds ratio [OR] 0.9645, 95% confidence interval [CI] 0.9345–0.9954, \(P = 0.0248\)) and an abnormal MDQ score (OR 0.4856, 95% CI 0.2659–0.8868, \(P = 0.0187\)) remained as independent predictors of not achieving remission at six months. In comparison with those patients with moderate depression, a patient with severe depression was significantly less likely to achieve remission at six months (OR
Figure 1 Clinical response and remission after 6 months of treatment for depression in CCM of depression (intention to treat method).

Figure 2 Clinical response and remission after 6 months of treatment for depression in CCM of depression in re-measured patients.
### Table 1  Demographic and clinical factors for patients enrolled in CCM for the treatment of depression, by initial depression severity

<table>
<thead>
<tr>
<th></th>
<th>Moderate depression</th>
<th>Moderately severe depression</th>
<th>Severe depression</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PHQ-9 score 10–14</td>
<td>PHQ-9 score 15–19</td>
<td>PHQ-9 score ≥ 20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N= 353</td>
<td>N= 226</td>
<td>N= 213</td>
<td></td>
</tr>
<tr>
<td>Age, years (range)</td>
<td>41.6 (18–87)</td>
<td>40.0 (18–88)</td>
<td>42.7 (18–79)</td>
<td>0.236</td>
</tr>
<tr>
<td>Gender (percent female)</td>
<td>78.4</td>
<td>69.9</td>
<td>66.4</td>
<td>0.011</td>
</tr>
<tr>
<td>Race (percent Caucasian)</td>
<td>91.8</td>
<td>92.0</td>
<td>92.4</td>
<td>0.974</td>
</tr>
<tr>
<td>Marital status (percent married)</td>
<td>60.3</td>
<td>60.6</td>
<td>49.6</td>
<td>0.090</td>
</tr>
<tr>
<td>AUDIT score (range)</td>
<td>2.4 (0–23)</td>
<td>3.3 (0–29)</td>
<td>3.4 (0–30)</td>
<td>0.010</td>
</tr>
<tr>
<td>GAD-7 score (range)</td>
<td>9.3 (0–21)</td>
<td>11.9 (0–21)</td>
<td>14.2 (2–21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Percent MDQ abnormal</td>
<td>5.1</td>
<td>8.4</td>
<td>16.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
<td>0.213</td>
</tr>
<tr>
<td>Percent dysthymia</td>
<td>4.8</td>
<td>3.1</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>Percent first episode</td>
<td>59.5</td>
<td>55.3</td>
<td>51.3</td>
<td></td>
</tr>
<tr>
<td>Percent recurrent</td>
<td>35.7</td>
<td>41.6</td>
<td>46.2</td>
<td></td>
</tr>
<tr>
<td>Percent clinical response at 6 months</td>
<td>72.8</td>
<td>73.5</td>
<td>74.8</td>
<td>0.913</td>
</tr>
<tr>
<td>Clinical remission at six months</td>
<td>64.0%</td>
<td>55.3%</td>
<td>45.3%</td>
<td>0.001</td>
</tr>
</tbody>
</table>

### Table 2  Multiple regression analysis for clinical remission at 6 months of independent variables for patients in CCM for depression

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>95 % CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.0114</td>
<td>0.9999–1.0230</td>
<td>0.0519</td>
</tr>
<tr>
<td>Gender (female vs. male)</td>
<td>1.0436</td>
<td>0.7220–1.5086</td>
<td>0.8203</td>
</tr>
<tr>
<td>Race (white vs. non-white)</td>
<td>1.1578</td>
<td>0.6567–2.0412</td>
<td>0.6125</td>
</tr>
<tr>
<td>Marital status (married)</td>
<td>1.0921</td>
<td>0.7863–1.5167</td>
<td>0.5992</td>
</tr>
<tr>
<td>AUDIT score</td>
<td>1.0007</td>
<td>0.9630–1.0399</td>
<td>0.9724</td>
</tr>
<tr>
<td>GAD-7 score</td>
<td>0.9645</td>
<td>0.9345–0.9954</td>
<td>0.0248</td>
</tr>
<tr>
<td>MDQ (abnormal vs. negative)</td>
<td>0.4856</td>
<td>0.2659–0.8868</td>
<td>0.0187</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First episode</td>
<td>Referent</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>Recurrent depression</td>
<td>0.7509</td>
<td>0.5430–1.0384</td>
<td>0.0832</td>
</tr>
<tr>
<td>Dysthymia</td>
<td>1.0341</td>
<td>0.4539–2.3561</td>
<td>0.9364</td>
</tr>
<tr>
<td>PHQ-9 score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate (10–14)</td>
<td>Referent</td>
<td>Referent</td>
<td>Referent</td>
</tr>
<tr>
<td>Moderately severe (15–19)</td>
<td>0.8043</td>
<td>0.5626–1.1499</td>
<td>0.2324</td>
</tr>
<tr>
<td>Severe (≥ 20)</td>
<td>0.6040</td>
<td>0.3803–0.9592</td>
<td>0.0327</td>
</tr>
</tbody>
</table>
Adjusted means of the six-month PHQ-9 scores were evaluated by initial depression severity for those patients who achieved remission (PHQ-9 score < 5) and those who did not. This will allow determination of the impact that the other clinical and demographic characteristics have on the six-month PHQ-9 in these two groups of patients. When controlling for all independent variables, there was no statistical difference in the adjusted means of the PHQ-9 score (1.8 vs. 1.9 vs. 1.7, \(P = 1.0\)) for those patients who were in remission at six months (Figure 3). However, in the patients who were not in remission, the six-month PHQ-9 score was significantly increased by initial depression severity when controlling for all other variables. Those diagnosed with moderate depression and not in remission at six months had an adjusted mean for the PHQ-9 at repeat testing of 9.0. This was significantly smaller than the unremitted group of initial moderately severe depressed patients (10.6, \(P = 0.0212\)) and severely depressed patients (11.1, \(P = 0.0092\)). There was no statistically significant difference in the adjusted means of the six-month PHQ-9 score between the moderately severe and severely depressed groups (Figure 3).

**Discussion**

Prior studies have shown differences in mental health comorbidity on the outcome of remission for depression treatment in CCM\(^4\) and the overall effectiveness of this type of treatment.\(^4\) For patients diagnosed with depression and enrolled in CCM, our initial hypothesis was partially correct, in that severe depression at the time of diagnosis was associated with a decreased likelihood of remission at six months in both a univariate and multivariate analysis. However, patients with moderately severe depression, when controlling for all other variables, did not have a statistically significant difference in the odds of remission at six months compared with those patients with moderate depression.

In patients with severe depression, this study demonstrated a six-month remission rate of 29.6–42.9\% (intention to treat model vs. re-measured patients) while in CCM. With multivariate analysis, there appeared to be 60\% odds of achieving remission at six months compared with those patients with a diagnosis of moderate depression. Patients with an initial higher baseline PHQ-9 need to have a greater absolute change in PHQ-9 score to reach remission. Of the adjusted six-month PHQ-9 scores in remitted patients, depression severity was not a factor. However, the difference in those patients not in remission by initial depression severity, suggested that the remission rate variations noted were from this group. Lower remission rates at six months were
associated with higher adjusted follow-up PHQ-9 scores. Future prospective evaluations of the factors influencing non-remission would be helpful.

Although, remission is the goal, the data were encouraging when evaluating CCM treatment by clinical response. This study would suggest that for primary care clinics utilising CCM there appeared to be no significant difference in clinical response rates over a period of six months from enrolment based on initial depression severity. This would give hope to the providers and patients that even though the depression may be categorised as severe, while in CCM, the patient should generally expect improvement over a six-month time frame. It is possible that the time to achieve the goal of remission may be longer than six months as is methodologically employed in this study and thus longer follow-up is needed. Determining the average time of a patient in CCM to remission based on depression severity would also help answer this point for the clinician and the patient.

This study only compared those patients in CCM and there was no ‘usual care’ group to serve as a comparison or reference group. The patients were from a large primary care community-based practice and may not be comparable with other primary or specialty care practices. Because there was minimal variation in several demographic variables such as insurance coverage or ethnicity, the lack of diversity may further hamper comparisons with other sites. No determination of the types of therapies or medications utilised was carried out in this study. There was significant attrition because this was a retrospective analysis of a clinical, not a research, population. Also, the patients were ‘real world’ and had other psychiatric and mental health comorbidities that might have impacted the outcomes. Future studies examining the impact of different modalities within CCM and the impact on remission rates are needed. Based on the data from this study, a prospective evaluation of treatments for those patients who were severely depressed at the initial diagnosis and at higher risk for not remitting (e.g. an elevated GAD-7 score or abnormal MDQ score) could be undertaken.

**Conclusions**

Although patients with depression and treated with CCM can achieve remission by six months of therapy with any initial severity of depression, multivariate analysis in our study population demonstrated that patients with severe depression have an OR for remission at six months of 60% compared with moderate depression, when controlling for all other variables. Also, there was a significant increase in the six-month PHQ-9 score for those patients who did not achieve remission at six months in the severe vs. moderate depression groups. Because remitted patients had no difference in the six-month PHQ-9 score based on initial depression severity, it was postulated that the variations seen in clinical remission were based on the increased severity of those patients who had not achieved remission by six months.

**ETHICAL APPROVAL**

This study was reviewed and approved by Mayo Clinic Institutional Review Board.

**FUNDING**

Departmental source.

**CONFLICTS OF INTEREST**

The authors have no conflict of interest to report.

**ACKNOWLEDGEMENTS**

Isaac Johnson assisted with abstraction and collection of the data.

**REFERENCES**

7 Szegedi A, Jansen WT, van Willigenburg AP, van der Meulen E, Stassen HH, Thase ME (2009) Early
improvement in the first 2 weeks as a predictor of treatment outcome in patients with major depressive disorder: a meta-analysis including 6562 patients. *Journal of Clinical Psychiatry* 70: 344–53.


**ADDRESS FOR CORRESPONDENCE**
Kurt B Angstman, Department of Family Medicine, Mayo Clinic, 200 First St. SW, Rochester, MN 55905, USA; Tel: +1 507 284 2511; fax: +1 507 538 8543; email: angstman.kurt@mayo.edu

Accepted April 2012