Achieving Effective Antidepressant Pharmacotherapy in Primary Care: The Role of Depression Care Management in Treating Late-Life Depression

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OBJECTIVES: To estimate the effect of an evidence-based depression care management (DCM) intervention on the initiation and appropriate use of antidepressant in primary care patients with late-life depression.

DESIGN: Secondary analysis of data from a randomized trial.

SETTING: Community, primary care.

PARTICIPANTS: Randomly selected individuals aged 60 and older with routine appointments at 20 primary care clinics randomized to provide a systematic DCM intervention or care as usual.

METHODS: Rates of antidepressant use and dose adequacy of patients in the two study arms were compared at each patient assessment (baseline, 4, 8, and 12 months). For patients without any antidepressant treatment at baseline, a longitudinal analysis was conducted using multilevel logistic models to compare the rate of antidepressant treatment initiation, dose adequacy when initiation was first recorded, and continued therapy for at least 4 months after initiation between study arms. All analyses were conducted for the entire sample and then repeated for the subsample with major or clinically significant minor depression at baseline.

RESULTS: Rates of antidepressant use and dose adequacy increased over the first year in patients assigned to the DCM intervention, whereas the same rates held constant in usual care patients. In longitudinal analyses, the DCM intervention had a significant effect on initiation of antidepressant treatment (adjusted odds ratio (OR) = 5.63, $P < .001$) and continuation of antidepressant medication for at least 4 months (OR = 6.57, $P = .04$) for patients who were depressed at baseline.

CONCLUSIONS: Evidence-based DCM models are highly effective at improving antidepressant treatment in older primary care patients. **J Am Geriatr Soc 57:895–900, 2009.**

Key words: depression care management; collaborative care models; antidepressant treatment; process outcomes

Depression in older adults is a common and debilitating disease. It is estimated to affect approximately 3% of community-dwelling older people and as many as 10% of older primary care patients.[1–3] It is associated with significant emotional morbidity, serious functional decline,[4,5] and risk of death from suicide and other medical illnesses.[6] Despite the existence of effective treatment for depression, late-life depression remains seriously underdetected and under- or mistreated in primary care.[7–9]

Antidepressant medications are the most commonly used treatments for depression in primary care. The keys to effective antidepressant therapy, once initiated, are close follow-up and regimen adjustment based on side effects, drug interactions, and treatment response during the initial 8 to 10 weeks of treatment[10] and longer-term continuation after remission to prevent recurrence of depression.[11,12] In reality, suboptimal dosages and failure to complete an adequate course of therapy often characterize antidepressant treatment.[13,14] In older patients with depression, declining physical health and cognitive abilities make effective antidepressant treatment an even more daunting task.

The Prevention of Suicide in Primary Care Elderly: Collaborative Trial (PROSPECT) developed a systematic depression care management (DCM) program targeting late-life depression in primary care.[15] The program featured practice-based depression care managers (e.g., nurses or social workers) who collaborated with physicians by help-

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ing them recognize depression (and therefore initiate treatment) in older adults, offered guideline-based recommendations, closely monitored patient status, and provided follow-up care. This intervention proved highly effective, compared with care as usual, in reducing suicidal ideation[15] and mortality[16] in older patients with depression, as well as in reducing depressive symptoms in older patients with major depression.

This study assessed the effect of the PROSPECT DCM program on effective antidepressant treatment in older patients with depression, a major intended process outcome of the intervention, to help elucidate how the intervention achieved better depression outcomes. Longitudinal data from four patient assessments conducted in the first year of the PROSPECT study were analyzed to estimate the effect of DCM on the initiation and appropriate use of antidepressants in primary care patients with late-life depression. Because pharmacotherapy is the predominant modality of treatment for depression in primary care settings[17] and because psychotherapy use in the PROSPECT data was not clinically well defined, given that data available for all patients were based on patient self-report, it was decided to focus on engagement in antidepressant treatment as the primary outcome of interest in this study.

METHODS

Design of the PROSPECT Study

The PROSPECT study recruited 20 primary care practices located in greater New York City, Philadelphia, and Pittsburgh and randomized them to intervention or to care as usual. The intervention had two major components: physician education regarding treating geriatric depression and treatment management operationalized by a care manager. The clinical algorithms of the intervention recommended a selective serotonin reuptake inhibitor (SSRI) as first-line depression treatment, but physicians could refer patients for interpersonal psychotherapy provided by the care manager if patients refused or failed to respond to antidepressants. The intervention protocol was designed to target the acute, continuation, and maintenance phases of treatment. Previous publications[15,18] have described PROSPECT study design, recruitment, and intervention procedures in detail.

Study Sample

The PROSPECT study enrolled randomly selected individuals aged 60 and older with routine primary care appointments at the study sites. Of the 1,226 patients who completed the baseline interview, 599 were identified as having major depression or clinically significant minor depression based on the Structured Clinical Interview for Axis I *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (SCID),[19] with criteria for minor depression modified by requiring four depressive symptoms of at least 4 weeks and a Hamilton Depression Rating Scale (HDRS) score of 10 or higher. Several previous reports evaluated outcomes for this subsample of patients,[15,16,20] because these were the patients clinically eligible for the intervention at baseline. Although the remaining 627 patients did not have a clinical diagnosis based on the SCID, 72 had an HDRS score of 10 or higher at baseline (indicating transient depressive symptoms). Analyses of the entire cohort ($N = 1,226$) were conducted, as well as of the subsample of patients with depression at baseline ($n = 599$).

Measures

Antidepressant Medication

The Composite Antidepressant (CAD) Score[21] was used to construct several measures of antidepressant use. Patients were asked to bring all medications that they were currently taking to in-person interviews at baseline and 12 months. At the 4- and 8-month telephone interviews, they were asked to bring medications to the phone. The interviewers recorded the name, dosage, and prescribed frequency of administration for each medication. Based on information provided on antidepressants, a CAD score was constructed to reflect the presence and dose adequacy of antidepressant therapy for each patient at each assessment time point. The CAD score took integer values and ranged from 0 to 4, with 0 indicating no antidepressant, 1 to 2 indicating antidepressant treatment with an inadequate dose, and 3 to 4 indicating antidepressant treatment with an adequate dose.

For cross-sectional analyses using data from each of the 4-month interviews, dichotomous measures of any antidepressant use (CAD score >0 vs 0) and antidepressant treatment with adequate dosage (CAD score ≥ 3 vs <3) were constructed.

For longitudinal analyses, patients who were not taking an antidepressant at baseline were focused on, and new initiation of antidepressant within 4 or 8 months after baseline, adequate dosage at the time new initiation was recorded (at the 4- or 8-month assessment), and continued treatment for at least 4 months after initiation were measured. New initiation was determined if the patient subsequently had some antidepressant use at 4 months (CAD score >0), regardless of their treatment status at 8 or 12 months, or if they had no antidepressant use at 4 months but had use at 8 months, regardless of their treatment status at 12 months. Adequacy of dosage was defined as a CAD score of 3 or greater at 4 months if newly initiated in the interim before the 4-month interview or at 8 months if newly initiated in the interim between the 4- and 8-month interviews. Continued treatment was identified by determining whether the patient, once initiated on an antidepressant, was still taking an antidepressant at the next interview (8 or 12 months). Because these measures were based on information collected at discrete assessment points (rather than continuously over time), they did not capture dose changes or interruptions in pharmacotherapy in the intervening time between assessments.

Baseline Depression Severity and Comorbidities

Depression severity at baseline was assessed using the 24-item HDRS,[22] which ranges from 0 to 40, with higher scores indicating greater severity.

A Charlson Comorbidity Index[23] was constructed based on patient self-reports at baseline about major health events and chronic conditions.

Analysis

Two sets of analyses were performed: descriptive analyses of each cross-sectional and longitudinal outcome measure

Table 1. Baseline Patient Characteristics of Study Samples According to Intervention Status

Characteristic	All Patients			Patients with Clinical Depression*		
	Intervention (n = 609)	Usual Care (n = 617)	*P*-Value	Intervention (n = 320)	Usual Care (n = 279)	*P*-Value
Demographic, %						
Female	68.1	71.6	.29	69.1	74.6	.20
Aged ≥75	35.1	34.8	.95	31.9	29.7	.63
Racial or ethnic minority	28.7	36.8	.62	29.1	36.8	.63
Married	39.5	37.7	.82	36.4	37.7	.89
Living with someone else	56.3	56.1	.96	43.5	43.7	.97
Clinical						
Diagnosis of depression, %*	52.5	45.2	.16	100.0	100.0	—
Mean HDRS score	12.0	10.8	.25	18.4	17.4	.16
Mean Center for Epidemiologic Studies Depression Scale score	21.0	20.4	.62	27.2	27.2	.99
Charlson Comorbidity Index	2.7	2.6	.64	3.1	2.9	.53

* Major or clinically significant minor depressive disorder based on the Structured Clinical Interview for Axis I *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, with criteria for minor depression modified by requiring four depressive symptoms of at least 4 weeks and a Hamilton Depression Rating Scale (HDRS) score of 10 or higher.

and a model-based analysis of longitudinal outcomes. In the descriptive analyses, means of each outcome were calculated, and differences were tested for across the two study arms. Statistical inferences were based on a Pearson chi-square test of independence with a correction of degrees of freedom to account for the design effect as a result of patients being clustered within primary care practices.[24,25] For each longitudinal outcome in patients not taking antidepressants at baseline (i.e., initiation of antidepressant by 4 or 8 months, adequate dosage at the time initiation was first recorded, and continued treatment for at least 4 months), a multilevel logistic model was estimated with a practice-level random effect to account for correlated outcomes of patients within the same practice. Patient sex, baseline age, marital status, living status (with someone vs alone), baseline HDRS score, and Charlson Comorbidity Index were controlled for. Adjusted odds ratios (ORs) associated with the intervention status (vs usual care) are reported for each outcome.

Additional analyses were conducted to assess the extent to which the effect of the DCM intervention on depression outcomes operated through better pharmacotherapy, psychotherapy, or both. Three outcomes were considered: response to treatment indicated by a 50% reduction in the HDRS score from baseline, remission defined as having a HDRS score less than 7, and remission defined as having a HDRS score less than 10.[15] Focusing on patients with major or clinically significant minor depression but no antidepressant at baseline, a model of each of the depression outcomes at each assessment (4, 8, and 12 months) was first estimated as a function of the DCM intervention, controlling for baseline HDRS, suicidal ideation, and major versus minor depression to assess the intention-to-treat intervention effect. Dichotomous indicators of any antidepressant use and dose adequacy at the time of the assessment and any psychotherapy use during the 4 months before the assessment were then added to examine the mediating effects of depression treatment.

RESULTS

Patient baseline demographic and depression-related clinical characteristics are summarized in Table 1 for all patients and for the subsample with major or clinically significant minor depression at baseline. A majority of study patients were female, and more than one-third were aged 75 and older. Although patients in the intervention arm were less likely to be racial or ethnic minorities, more likely to have a clinical depressive diagnosis at baseline, and had higher HDRS and CES-D scores, none of these differences was statistically significant. Other than having greater severity and more symptoms of depression, patients with a diagnosis of depression at baseline were younger and less likely to be living with someone else than the entire sample. The two study arms were balanced in terms of patient characteristics in the subsample with depression.

Table 2 presents cross-sectional measures of antidepressant use. Of the entire sample, 31% of the intervention patients were taking an antidepressant at baseline, compared with 29% of the usual care patients. Although the treatment rate in usual care patients remained relatively constant during the next 12 months, the rate in the intervention patients continued to rise; by the end of the first year, 46% were taking antidepressant medication ($P < .05$ for comparisons at 8 and 12 months). A similar pattern held for adequacy of antidepressant dosage; the proportion of patients who received antidepressant treatment with adequate dosage increased from 23% at baseline to 36% at 12 months in intervention patients, whereas the same measure stayed almost constant in the usual care patients throughout the first year. Again, differences according to intervention status achieved statistical significance with $P < .05$ starting from 8 months. Antidepressant use in patients with

Table 2. Antidepressant Use According to Intervention Status: Cross-Sectional Analysis

Antidepressant Use	Intervention	Usual Care	*P*-Value
	%		
All patients			
Any antidepressant use			
Baseline	31.1	28.6	.57
4 months	38.5	27.8	.09
8 months	43.7	27.5	.02
12 months	45.6	29.6	.03
Antidepressant treatment with adequate dose			
Baseline	23.1	18.8	.35
4 months	30.3	19.4	.09
8 months	34.1	20.5	.03
12 months	35.7	20.1	.03
Patients with clinical depression			
Any antidepressant use			
Baseline	41.7	40.2	.81
4 months	56.5	38.9	.02
8 months	64.5	42.6	.006
12 months	69.1	44.0	.007
Antidepressant treatment with adequate dose			
Baseline	33.2	27.5	.39
4 months	46.9	28.1	.04
8 months	53.2	34.2	.02
12 months	55.0	33.3	.03

clinical depression, for whom antidepressant treatment is most clearly indicated, presented a similar, if not stronger, pattern; the rate of treatment with adequate dose increased more than 1.6 times in intervention patients, from 33.2% at baseline to 55.0% at 12 months, whereas the rate of treatment increased slightly in the usual care arm. The inter-arm differences achieved statistical significance ($P < .05$) starting with the 4-month interview.

Results of descriptive and model-based analyses of longitudinal outcomes for the group with no antidepressant treatment at baseline are reported in Table 3. In the descriptive analysis, intervention patients were more than twice as likely to have initiated antidepressant by 8 months as usual care patients ($P = .003$ for all patients; $P = .001$ for patients with depressive diagnosis). Of those with newly initiated antidepressant use, the rate of adequate dosage when antidepressant pharmacotherapy was subsequently first recorded did not differ significantly between the two study arms, although a substantially higher proportion of intervention than usual care patients continued the medication for at least 4 months once initiated ($P < .05$ in both analysis samples).

Based on results of the covariate-adjusted analysis, the DCM intervention was associated with ORs of 2.77 in the entire sample and 5.63 in the sample with clinical depression for initiation of antidepressant treatment ($P < .001$ in both cases). For adequate dosage at the time initiation was recorded, the adjusted analysis yielded ORs of 3.11 for the entire sample and 0.90 for the subsample with depression, neither of which was statistically significant. For the outcome of continued antidepressant use for at least 4 months after initiation, the adjusted analysis yielded ORs of 10.46 ($P = .009$) for the entire sample and 6.57 ($P = .04$) for the subsample with depression.

Patient characteristics controlled for in the adjusted analysis did not predict medication outcomes, except that patients with depression aged 75 and older were much more likely than those aged 60 to 74 to have initiated antidepressant treatment by 8 months (OR = 2.37, $P = .03$).

In the mediating analysis, the intention-to-treat effect of the intervention was found to be close to statistical significance only at 4 months. In these models, ORs associated with the DCM intervention were 1.88 ($P = .06$) for treatment response, 1.67 ($P = .09$) for remission with a HDRS score less than 7, and 1.93 ($P = .06$) for remission with a HDRS score less than 10. When treatment indicators for antidepressant initiation and dose adequacy recorded at 4 months and any psychotherapy use in the first 4 months

Table 3. Antidepressant Initiation, Dose Adequacy, and Continuation in Patients Not Taking an Antidepressant at Baseline

	Unadjusted			Adjusted*	
Antidepressant Use	Intervention	Usual Care	*P*-Value	Odds Ratio	*P*-Value
	%				
All patients					
Initiated antidepressant by 4 or 8 months	26.4	12.4	.003	2.77	.00
Adequate dosage when initiation was recorded	69.2	51.5	.17	3.11	.15
Continued antidepressant for at least 4 months	81.8	39.1	.01	10.46	.009
Patients with clinical depression at baseline					
Initiated antidepressant by 4 or 8 months	51.9	19.4	.001	5.63	.00
Adequate dosage when initiation was recorded	66.7	68.4	.89	0.90	.76
Continued antidepressant for at least 4 months	83.0	50.0	.04	6.57	.04

* Adjusted for patient sex, baseline age, marital status, living status (with someone vs alone), baseline Hamilton Depression Rating Scale score and Charlson Comorbidity Index.

were added, the ORs were invariably reduced in magnitude and lost statistical significance (1.06, $P = .90$; 1.36, $P = .49$; and 1.50, $P = .37$, respectively), suggesting that at least part of the intervention effect was mediated through treatment, but it was not possible to statistically determine which dimension of pharmacotherapy (initiation vs dose adequacy) had a stronger effect, because confidence intervals of the two largely overlapped.

DISCUSSION

Collaborative depression care models developed in the past decade have proven highly effective in improving depression treatment outcomes for older patients in primary care. This study used data from the PROSPECT study to perform an in-depth examination of one intended process outcome of the intervention: use of antidepressant medication in accordance with clinical guidelines.[26,27] It found that receiving the DCM intervention was associated with a substantially greater likelihood of receiving antidepressant medication and with adequate medication dose at 8 and 12 months into the intervention. It also found that the intervention had a statistically and clinically significant effect on whether older patients who were not receiving antidepressant pharmacotherapy subsequently initiated antidepressant treatment within 8 months. Furthermore, in those who newly initiated medication, the DCM intervention was associated with an OR of at least 6 for continued medication for at least 4 months.

A statistically significant association was not found between DCM and dose adequacy when newly initiated antidepressant was first recorded. The intervention may not have had an effect on adequate dosage at treatment initiation, because up-titration in the early stage of pharmacotherapy is an essential element of effective antidepressant treatment. Hence, dose adequacy shortly after a patient newly initiates pharmacotherapy may be an overly stringent benchmark for interventions that nonetheless effectively engage patients in evidence-based depression treatment.

Antidepressant treatment, the outcome of interest in the study, was not the primary outcome of the PROSPECT study. Because the measures in the current study were based on data collected at discrete assessment points, the outcome of receiving antidepressant therapy at least 4 months after treatment initiation may not accurately represent continuous antidepressant treatment during that time period, but the randomized design of the PROSPECT study makes it likely that any systematic bias in the measure would be balanced across the two arms. The PROSPECT study did not collect data on medication side effects or drug interactions. It was therefore not possible to examine the reasons underlying antidepressant use with inadequate dose or premature discontinuation.

Although it was explicitly decided to focus on antidepressant medication as a process outcome, psychotherapy remains an alternative or complementary treatment with known efficacy. Of patients with depression who were not treated with antidepressants at baseline, 50% reported some kind of psychotherapy at the 4- or 8-month assessment. By offering free interpersonal psychotherapy conducted by the care managers, the PROSPECT intervention greatly facilitated access to psychotherapy.[15] By 8 months, in patients with depression with no antidepressants at baseline, 86% of patients in the intervention arm reported some kind of psychotherapy, compared with 11% of those in the usual care arm. The mediating analysis, which controlled for psychotherapy use in addition to medication, provided evidence that psychotherapy accounted for some of the intervention effect at 4 months, although ORs between the psychotherapy indicator and the outcomes did not achieve statistical significance. By not considering use of psychotherapy in the analysis, it is likely that findings reflect more-conservative estimates of the intervention effect on antidepressant treatment engagement and adequacy than if the intervention had not also lowered the cost and improved the accessibility of psychotherapy.

In summary, one of the mechanisms by which DCM is intended to achieve improved depression treatment for older primary care patients was investigated: by achieving guideline-concordant, effective antidepressant treatment. Given that antidepressant medication is first-line treatment for depression in primary care settings, it is likely that DCM models that help achieve effective pharmacotherapy will provide the greatest benefit. This is especially true for older primary care patients, for whom underdetection and undertreatment of depression poses a greater challenge, because depression may be more seriously stigmatized,[28] considered a normal part of aging,[29] or considered to be an incidental epiphenomenon of other chronic conditions rather than a serious condition in need of treatment.

The findings of the current study provide evidence that implementing collaborative depression care management models will help primary care practices meet nationally recognized "best practice" guidelines for antidepressant management such as those in the Healthcare Effectiveness Data and Information Set[30] and, in turn, improve outcomes for their older patients with depression, although implementing evidence-based DCM in real-world settings requires overcoming a wide array of barriers.[31,32] The most pressing issues are the need to reorient and restructure primary care practices from a focus on acute care to chronic condition management and aligning payment and financing systems toward providing sufficient incentives for the delivery of evidence-based depression care. Efforts to reform the delivery and payment systems for primary care in general include initiatives surrounding the "Medical Home" concept.[33,34] In the arena of DCM, one ongoing initiative is Depression Improvement Across Minnesota, Offering a New Direction, which offers a bundled payment negotiated between health plans and medical groups that covers key components of DCM activities.[35] Finally, the Veterans Health Administration is making major financial and systems changes to integrate DCM and collocated collaborative mental health professionals into primary care clinics.[36] Lessons learned from these and other implementation efforts around the country will facilitate translation of evidence-based DCM into primary care practice.

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