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Predictors of Poor Response to Depression Treatment in Primary Care

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Objective: Depression is pervasive and costly, and the majority of depression is treated in primary care. The objective of this study was to identify patient characteristics predictive of poor depression outcomes in primary care clinics.

Methods: This observational study followed 792 patients receiving usual care for depression in 83 clinics across Minnesota for at least six months between 2008 and 2010. The primary outcome was an ordinal outcome of remission or response without remission ("response") six months after the start of treatment. The outcome was assessed via telephone administration of the Patient Health Questionnaire-9. Associations of patient characteristics with the primary outcome were assessed by using ordinal logistic regression.

Results: The majority of patients were female, Caucasian, and employed, and most had some college education and good,

very good, or excellent self-rated health. At baseline, 32% had mild depression, 40% moderate depression, 20% moderately severe depression, and 8% severe depression. One-third of patients had psychotherapy or psychiatric care in addition to antidepressant medications. At six months, only 47% of patients obtained depression remission or response. Patients were significantly less likely to experience remission or response if they rated their health as poor or fair or if they were unemployed and were more likely to achieve remission or response if they were younger or had mild depression.

Conclusions: Patients with poor or fair health or who were unemployed were less likely to respond to usual depression care and may be good candidates for limited, but potentially more effective, intensive treatment resources for depression.

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Depression is the second most common chronic condition treated by primary care providers, with an estimated 12% of primary care patients experiencing major depression (1,2). Despite the prevalence of depression and the availability of effective evidence-based treatments, most depressed patients do not have adequate treatment outcomes. In primary care, the most common treatment for depression is antidepressant medications (3), with second-generation antidepressants accounting for over 90% of prescriptions for depression among primary care patients (4). However, in a study by Solberg and colleagues (5), only 50% of primary care patients who received antidepressants as their main treatment demonstrated improvement after three months, and 15% experienced increased depression severity. Another study, by Vuorilehto and colleagues (6), found that only 25% of primary care patients with major depression achieved and maintained remission at 18 months. Clearly there is room for improvement in primary depression care.

Developing a clearer idea of which patients are least likely to respond to usual care may help providers to focus more intensive interventions, including stepped care or collaborative care, on these patients to improve their chances of recovering from depression. Prior research has shown that comorbid

psychiatric (7-9) and general medical conditions (10,11), chronic pain (7), early age of depression onset (7,9), recurrent depressive episodes (9), severity of depression (7,9), and lower socioeconomic status (12,13) are predictors of poor depression remission or response. However, much of these data were collected as part of clinical trials with select patient populations or in psychiatric care settings rather than in primary care settings. The few studies of depression in primary care have been limited by selection bias, small sample sizes, and short follow-up times (14). As part of evaluating a statewide effort to improve primary care of depression through a collaborative care initiative, we had the opportunity to evaluate a large group of primary care patients receiving usual care for depression prior to implementation of the new depression care model. This study determined which patient characteristics best predicted poor depression outcomes in primary care.

METHODS

Setting

Patients were enrolled in 83 urban and rural primary care clinics representing 23 medical groups across Minnesota prior

to the clinics' participation in a statewide collaborative care initiative (15). This study examined baseline and six-month data that were collected between March 2008 and November 2010, prior to the implementation of collaborative care in these primary care clinics. This study was reviewed, approved, and monitored by the HealthPartners Institutional Review Board.

Participants

Inclusion and exclusion criteria were designed to include only adult patients receiving treatment for a new episode of depression in primary care. Of the 11,889 patients identified via antidepressant pharmacy claims, patients were excluded because of inability to be contacted because of incorrect information (N=2,684), inability to be reached within 21 days (N=2,451), refusal of screening (N=1,986), having a Patient Health Questionnaire-9 (PHQ-9) (16) score less than 7 (N=1,723), filling a prescription for an antidepressant for an indication other than depression (N=1,481), not being treated in a participating clinic (N=247), not filling an antidepressant prescription (N=110), or inability to complete the screen because of language or cognitive barriers or time constraints (N=420). A total of 1,168 patients completed a baseline survey, and 793 patients completed a six-month follow-up survey. One patient did not complete a PHQ-9 at six months, leaving 792 patients in the final sample.

Usual Care for Depression

Patients received usual care for depression in their primary care clinics. Few if any clinics systematically performed depression screening for patients; diagnosis occurred primarily during the routine course of clinic visits. All patients in this sample received antidepressants for depression. Co-management of depression by psychotherapists or psychiatrists was permitted.

Measures

Patient self-report questionnaires were completed via phone interviews and provided information on patient demographic characteristics, health status, depression severity, functional impairment, and past and current depression episodes and treatment. Health status was assessed via a single item from the Short Form 36 (SF-36) asking patients to rate their overall health, commonly referred to as the SF-1 (17). Functional impairment was assessed by using an item from the Work Productivity and Activity Impairment Questionnaire (18), which asks what percentage of a patient's life is impaired by the patient's health.

Depression severity was assessed by using the PHQ-9 (16), with scores of 7–9 indicating mild depression; 10–14, moderate depression; 15–19, moderately severe depression; and ≥ 20 , severe depression. The primary outcome was an ordinal outcome of remission or response without remission. Remission was defined as achieving a follow-up PHQ-9 score of ≤ 5 ; if patients met criteria for remission, they were not eligible to meet criteria for response (16). Response was defined as a follow-up PHQ-9 score that was at least 50% lower than the patient's baseline score (16).

Data Analysis

Descriptive statistics were used to characterize the study sample. First, the associations between the ordinal outcome for remission or response without remission and each patient characteristic were assessed with ordinal logistic regression analysis adjusted for baseline PHQ-9. The underlying assumption of this model is that the odds between patient characteristics and the ordered categories (remission versus response without remission [hereafter referred to "response"] versus neither) are proportional. Next, a fully adjusted analysis was conducted by using an ordinal logistic regression model that included all factors from each individual model that were statistically associated ($p < .2$) with remission or response to evaluate the independent effect of each patient characteristic on the outcome variable. Consistency between the results of the two models indicated that other variables included in the first model (adjusted only for PHQ-9) did not affect the association between a particular variable and the outcome, whereas differences between the results of the two models indicated that other factors were associated with both the factor of interest and the outcome. A p value cutpoint of .2 was chosen to retain possible contributors to nonresponse in the model while excluding those that were clearly not associated. A p value of $< .2$ was able to detect an absolute difference of 10% between patients who achieved remission or response and those who did not. Associations are presented as odds ratios (ORs) and 95% confidence intervals. All analysis was done in SAS/STAT software, version 9.3.

RESULTS

A total of 792 primary care patients received usual care for depression (Table 1). Patient ages ranged from 18 to 88, with a mean \pm SD age of 46 ± 14 years. Women comprised 75% of patients, and most patients were white and had at least some college education. Over half of patients were in relationships, and two-thirds were employed. A majority reported a household income equal to at least twice the federal poverty level, and most reported good, very good, or excellent health.

At baseline, 255 (32%) patients had mild depression, 315 (40%) moderate depression, 161 (20%) moderately severe depression, and 61 (8%) severe depression, as measured by the PHQ-9. In addition to receiving primary care treatment of depression, 43 (5%) received treatment from a psychiatrist, 201 (25%) participated in individual psychotherapy, and 26 (3%) participated in group therapy; in all, 230 (29%) patients received some psychiatric or psychological treatment. This was the first episode of depression treatment for 307 (39%) patients, whereas 185 (23%) had been treated for one prior episode, and 300 (38%) had at least two prior episodes of depression. Over half of patients (N=445) felt that their functioning was impaired by at least 50% because of their health.

At six months, 47% of patients achieved a combined ordinal outcome of remission (N=292) or response (N=83).

TABLE 1. Baseline characteristics of 792 patients who were treated for depression in primary care, by treatment outcome at six months^a

Characteristic	N	%	Outcome					
			Remission		Response		Neither	
			N	Row %	N	Row %	N	Row %
Total	792	100	292	37	83	10	417	53
Age								
<35	196	25	86	44	15	8	95	49
35–49	273	35	93	34	25	9	155	57
50–64	251	32	86	34	32	13	133	53
≥65	72	9	27	38	11	15	34	47
Gender								
Female	591	75	218	37	59	10	314	53
Male	201	25	74	37	24	12	103	51
Race-ethnicity								
White	711	90	265	37	76	11	370	52
Hispanic	19	2	8	42	3	16	8	42
Other	62	8	19	31	4	6	39	63
Relationship status								
Partnered	486	61	185	38	53	11	248	51
Single	306	39	107	35	30	10	169	55
Location of clinic								
Urban	493	62	184	37	50	10	259	53
Rural	299	38	108	36	33	11	158	53
Employed								
Yes	532	67	212	40	57	10	263	49
No	260	33	80	31	26	10	154	59
Education								
High school or less	208	26	72	35	20	10	116	56
Some college or technical school	313	40	110	35	37	12	166	53
College graduate	271	34	110	41	26	10	135	50
Income								
>2 × FPL ^b	544	69	214	40	59	11	271	50
≤2 × FPL ^b	248	31	78	32	24	10	146	59
Health status								
Excellent, very good, or good	573	72	237	41	56	10	280	49
Fair or poor	219	28	55	25	27	12	137	63
PHQ-9 score								
7–9	255	32	126	49		0	129	51
10–14	315	40	118	38	35	11	162	51
15–19	161	20	40	25	30	19	91	57
≥20	61	8	8	13	18	30	35	57
Percentage of life impaired due to health								
<50	337	43	143	42	29	9	165	49
≥50	455	57	149	33	54	12	252	55
Treatment by a psychiatrist								
Yes	43	5	72	31	28	12	130	57
No	749	95	220	39	55	10	287	51
Treatment by a psychotherapist								
Yes	201	25	62	31	23	11	116	58
No	591	75	230	39	60	10	301	51
Group therapy								
Yes	26	3	9	35		0	17	65
No	766	97	283	37	83	11	400	52
Times treated for depression in past								
0	307	39	116	38	27	9	164	53
1	185	23	74	40	25	14	86	47
≥2	300	38	102	34	31	10	167	56

^a Remission was defined as achieving a follow-up Patient Health Questionnaire–9 (PHQ-9) score of ≤5. Response was defined as a follow-up PHQ-9 score that was at least 50% lower than the patient's baseline score. Patients who met criteria for remission were not eligible to meet criteria for response. PHQ-9 scores of 7–9 indicate mild depression; 10–14, moderate depression; 15–19, moderately severe depression; and ≥20, severe depression.

^b Federal poverty level

Health status was the most strongly associated with depression remission or response: patients who reported fair or poor health were significantly less likely to experience depression remission or response compared with patients with good, very good, or excellent health (OR=.58, model 1 [adjusted for baseline PHQ-9 score]; adjusted OR [AOR]=.63, model 2 [adjusted for all other variables in the model]) (Table 2). Patients who were unemployed were also less likely to achieve remission or response (OR=.70), although this association was no longer significant in the fully adjusted model. Patients who had lower incomes or who were treated by a psychiatrist or psychotherapist tended to have lower rates of remission or response, but these associations did not achieve statistical significance. In contrast, although there was not a monotonic association between age and remission or response, we found that patients under age 35 were more likely to achieve remission or response compared with patients ages 35 to 49 (OR=1.46; AOR=1.49). Similarly, patients with mild depression were more likely to achieve depression remission or response compared with patients with severe depression (OR=2.16), but this association was no longer significant in the fully adjusted model.

DISCUSSION

Our results from this large sample of primary care patients indicate that patients were significantly less likely to achieve depression remission or response at six months if their self-rated health status was poor or

TABLE 2. Odds of achieving remission or response at six months among 792 patients who were treated for depression in primary care, by patient characteristic at baseline^a

Characteristic	Model 1 ^b			Model 2 ^c		
	OR	95% CI	p ^d	OR	95% CI	p ^d
Age (reference: 35–49)			.18			.12
<35	1.46	1.02–2.09		1.49	1.03–2.15	
50–64	1.10	.78–1.53		1.07	.76–1.51	
≥65	1.33	.80–2.20		1.48	.86–2.56	
Female (reference: male)	.95	.70–1.30	.75			
Race-ethnicity (reference: white)			.36			
Hispanic	1.41	.59–3.41				
Other	.73	.43–1.24				
Single (reference: partnered)	.90	.68–1.20	.48			
Urban clinic location (reference: rural)	1.01	.76–1.33	.96			
Not employed (reference: yes)	.70	.52–.93	.02	.76	.54–1.07	.12
Education (reference: some college or technical school)			.61			
High school or less	.93	.66–1.32				
College graduate	1.11	.81–1.53				
Income ≤2 × FPL (reference: >2 × FPL) ^e	.74	.55–1.01	.052	.80	.58–1.11	.17
Fair or poor health (reference: excellent, very good, or good)	.58	.42–.80	<.001	.63	.46–.88	.01
PHQ-9 score (reference: ≥20) ^f			.005			.12
7–9	2.16	1.23–3.79		1.60	.88–2.89	
10–14	1.67	.96–2.90		1.40	.79–2.48	
15–19	1.20	.66–2.18		1.03	.56–1.91	
≥50% of life impaired due to health (reference: <50%)	.80	.61–1.06	.12	.88	.66–1.17	.38
Treatment by a psychiatrist (reference: no)	.57	.30–1.09	.09	.61	.32–1.19	.15
Treatment by a psychotherapist (reference: no)	.74	.54–1.02	.07	.73	.52–1.01	.06
Group therapy (reference: no)	.66	.30–1.45	.30			
Times treated for depression in past (reference: 0)			.31			
1	1.18	.84–1.69				
≥2	.90	.66–1.23				

^a Outcome variables were coded as follows: 1, remission; 2, response without remission; and 3, none. Remission was defined as achieving a follow-up Patient Health Questionnaire–9 (PHQ-9) score of ≤5. Response was defined as a follow-up PHQ-9 score that was at least 50% lower than the patient’s baseline score. Patients who met criteria for remission were not eligible to meet criteria for response. PHQ-9 scores of 7–9 indicate mild depression; 10–14, moderate depression; 15–19, moderately severe depression; and ≥20, severe depression.

^b Odds ratios were estimated by using an ordinal logistic regression and were adjusted for baseline PHQ-9 score.

^c Odds ratios were estimated by using an ordinal logistic regression and were adjusted for all other variables in the model. Model 2 included only variables with a significance level of p<.2 in model 1.

^d Values correspond to type 3 Wald chi-square analyses testing the variable as a whole.

^e Federal poverty level

^f In model 1, the ORs for PHQ-9 score are unadjusted estimates.

fair or if they were unemployed and were more likely to achieve remission or response if they were younger or had mild depression. Patients with lower incomes and those who received specialty mental health care tended to have lower rates of remission or response that did not reach statistical significance.

Poorer self-rated health was by far the strongest predictor of depression remission or response in our population and the only significant predictor in the fully adjusted model. Several studies have shown that adults with depression function poorly and that their level of functioning is on par with persons with chronic medical conditions such as cardiopulmonary disease, arthritis, hypertension, and diabetes (19–21). Studies also show that depression can prolong the recovery from certain medical illnesses and increase the risk of mortality (22,23). Further, depression can decrease energy

and motivation and lead to poorer self-care behaviors (24). Ultimately, patients with poorer health are more likely to develop depression (25), and our study shows that these patients were also less likely to achieve depression remission or response as a result of usual care. Most primary care providers have easy access to patients’ problem lists or past medical histories, which, as surrogates for health status, have been found in other studies to be associated with poor depression outcomes (26). In this manner, providers could identify patients who are less likely to respond to usual depression care. Even easier, perhaps, would be to ask patients to rate their own health, given that self-rated health was a robust predictor of depression remission or response in our sample.

Other predictors of poorer depression outcomes in our study included unemployment and lower income. A systematic review of observational studies in primary care similarly found lower education and unemployment to be significant risk factors for persistent depression (14). Other studies have shown a

correlation between unemployment, lower income, and the prevalence of depression (27–30). The relationship between depression and employment and income is thought to be bidirectional, with depression impairing one’s ability to obtain and maintain employment and income level, and unemployment and poverty increasing one’s risk of depression. In other research, poverty has been one of the most consistent predictors of depression (31), and common correlates of low income (including a disadvantaged neighborhood, less access to educational and employment opportunities, and concerns about safety and resources) have significant detrimental effects on mental health beyond the direct effects of poverty itself (32), particularly for women (33,34). We should note that in our sample, the association between employment and depression outcomes was no longer significant in the fully adjusted model, likely because this

association was confounded with health status. Regardless, our results show that when disadvantaged people develop depression, their depression, unfortunately, is less likely to respond to usual care.

Overall, 53% of patients in our sample had persistent depression without remission or response at six months. This rate of nonresponse is consistent with the few other studies of usual care of depression in primary care, which have found nonresponse rates ranging from 24% to 81% at six to 12 months (35–40). This rate of continued depression is troublesome, particularly given the significant morbidity and mortality that accompany depression (41,42). It may be that providing more intense depression treatment for patients at higher risk of nonresponse—those with poor health, more severe depression, or unemployment or lower income—could improve these relatively dismal rates of improvement, and this is an area for future study.

Our study had several potential limitations. Although we interviewed patients within 21 days of their index prescription for depression, some may have responded to depression treatment by the time of the interview. This may have resulted in patients having lower PHQ-9 scores at baseline than they might have had at the time of treatment initiation, possibly excluding some otherwise eligible patients from our sample. We studied patients receiving usual care in their primary care clinics and thus could not control factors that we might have been able to control in a randomized controlled trial, such as additional treatment by mental health providers. Our sample included only patients who started antidepressant medications, and results cannot be generalized to other groups, such as patients receiving only psychotherapy or those who opted for no treatment. In addition, the generalizability of our data is limited by the fact that only 792 patients out of a potential sample of 11,889 patients completed our baseline and six-month surveys. Some of these patients were excluded because they did not have depression or could not complete the measures, but others were excluded because we were unable to reach them or they refused screening, and thus potential selection bias may have influenced our results. Further, it is likely that patients who were willing to participate in our surveys may have been less severely depressed and perhaps had better health status than patients who declined. Generalizability was also limited because our sample was predominantly white and of relatively high socioeconomic status.

CONCLUSIONS

Poor or fair health, unemployment, and more severe depression were significantly associated with lower rates of depression remission or response. Ideally, being better able to identify such predictors of poor depression outcomes may help clinics and care systems determine where limited but potentially effective intensive and evidence-based treatment resources for depression may be most helpful.

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