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RESEARCH ARTICLE

The effect of remission status on work functioning in employed patients treated for major depressive disorder

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BACKGROUND: The ability to function at work is impaired in patients with major depressive disorder (MDD) but few clinical trials include occupational outcome assessments. This study examined whether symptom remission following treatment for MDD is associated with work functioning improvement.

METHODS: We conducted a secondary analysis of a 12-week randomized clinical trial comparing escitalopram with or without telephone-administered cognitive therapy in employed patients with MDD (N = 86). Outcomes included the Montgomery-Åsberg Depression Rating Scale (MADRS) and validated, self-rated work functioning scales including the Lam Employment Absence and Productivity Scale (LEAPS), Work Performance Questionnaire (HPQ), and Sheehan Disability Scale (SDS). Remission was defined as MADRS score ≤10 at 12 weeks. Data were evaluated using analysis of covariance with baseline score as covariates.

RESULTS: Remission status was associated with significant improvement in work performance as assessed by the LEAPS productivity subscale, HPQ overall performance, and the SDS work/school item; a trend ($P = .08$) was observed with the HPQ productivity subscale. The effect sizes ($d = 0.23$, 0.51, 0.36, and 0.43, respectively) indicate small to medium effects that are likely clinically significant.

CONCLUSIONS: The results of our study confirm that symptom remission following treatment is associated significantly with improvement in work performance and productivity, as measured by validated work functioning scales. Measurement-based care for MDD should include both symptom and functional outcome assessments.

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INTRODUCTION

The prevalence of major depressive disorder (MDD) is highest among individuals of typical working age (15 to 64).[1] Given the physical and cognitive symptoms associated with MDD, it is not surprising that occupational functioning is affected severely by the disorder. MDD is now one of the leading causes of work-related disability and lost work productivity.[2,3] The costs of depression-related absenteeism (time off work) are high, but because community prevalence studies have shown that 7 out of 10 people with MDD still are working while depressed,[4] the impact of "presenteeism," ie, lost productivity while still at work, is much more significant. For example, the average productivity loss due to depression-related presenteeism is estimated at 15.3%, compared with 10.7% due to absenteeism.[5] MDD thus has a significant negative impact on workers, employers, and the economy as a whole.

Despite the importance of occupational outcomes in MDD, few clinical studies have examined work functioning or productivity changes in employed patients with MDD. A Cochrane systematic review[6] found only 23 studies looking at sickness absence as an outcome in MDD; only 8 studies used work functioning scales as an outcome measure, and only 2 recruited patients in the workplace. The review found moderate quality evidence that adding a work-directed intervention to clinical treatment diminished the number of days on sick leave compared with clinical treatment alone,[6] and recommended that clinical intervention studies should include work outcomes to increase our knowledge of occupational outcomes in depression. Further, a recent systematic review and meta-analysis examined the effects of newer antidepressants on occupational impairment in MDD and found only 28 randomized controlled trials (RCTs) that included data on occupational outcomes; only 1 trial targeted an employed population.[7]

The necessity for including work functioning measures in treatment trials is underscored by systematic reviews showing that symptom outcomes often are not correlated with functional outcomes.[8] In a 12-week RCT of employed patients with MDD, we compared the combination of escitalopram and telephone-administered cognitive-behavioral therapy (CBT) with escitalopram alone.[9] We found that combined treatment produced superior improvement in work functioning measures, but no difference in symptom outcomes, including response and remission, compared with escitalopram monotherapy.[9] Results such as these highlight the importance of examining both functional and symptom outcomes in treatment trials for MDD.

Remission of symptoms is an important clinical outcome and a target for acute treatment of MDD in most clinical guidelines.[10-12] Patients who do not achieve symptom remission have poor outcomes, including higher relapse rates and poorer functional outcomes,[13] including occupational outcomes. For example, patients with MDD in remission were less likely to be on sick leave and had fewer absent work days in the past 3 months, compared with patients in partial remission.[14] However, there are few studies specifically examining work functioning and productivity outcomes in remitted patients following treatment for MDD. Hence, we conducted a secondary analysis of our previous trial to investigate the relationship between remission and work functioning outcomes. We hypothesized that symptom remission following treatment would be a predictor of improved work functioning and productivity in employed patients with MDD, irrespective of treatment condition.

METHODS

This *post hoc* analysis was based on data from a previous study, with details of the study design and methods previously reported.[9] Briefly, inclusion criteria for participants included age 19 to 65; a diagnosis of MDD by DSM-IV criteria; a score of at least 19 on the Montgomery-Åsberg Depression Rating Scale (MADRS, indicating at least moderate severity)[15]; and employed at least 15 hours per week. The main exclusion criteria included being on short or long-term disability; having an organic mental disorder, a psychotic disorder, another primary psychiatric diagnosis, or substance misuse in the past year; treatment resistance in the current depressive episode; or prior use of CBT or escitalopram for depression. Eligible participants received open-label treatment with escitalopram, 10 to 20 mg/d, for the 12-week study period, and were randomized at baseline to receive either telephone-administered CBT or telephone adherence-reminder calls (control condition) for 8 weekly sessions. Participants who completed the 12-week study were included in this analysis.

TABLE 1
Baseline clinical and demographic information for remitters and non-remitters (N = 86)

	Remitters (MADRS ≤10) n = 41	Non-remitters (MADRS ≥11) n = 45
Age, mean years (SD)	41.7 (11.6)	44.8 (9.3)
Marital status, n (%)		
Married, cohabiting	15 (36.5%)	18 (40%)
Separated, divorced, widowed	11 (27%)	17 (38%)
Never married	15 (36.5%)	10 (22%)
Sex, n (%)		
Male	18 (44%)	19 (42%)
Female	23 (56%)	26 (58%)
Single vs recurrent episodes, n (%)		
Single episode	18 (44%)	13 (29%)
Recurrent	23 (56%)	32 (71%)
Number of episodes, mean (SD)	3.5 (8.3)	3.6 (4.9)
Baseline scores, mean (SD)		
MADRS	26.2 (5.5)	28.5 (4.6)
CGI severity	4.2 (0.62)	4.2 (0.61)
LEAPS Productivity Subscale	5.4 (2.6)	6.2 (2.1)
HPQ Performance Item	5.5 (1.8)	5.4 (1.7)
HPQ Productivity Subscale	12.1 (2.8)	11.7 (2.1)
SDS Work/School Item	5.4 (2.1)	6.5 (2.2)

CGI: Clinical Global Impression; HPQ: Health and Work Performance Questionnaire; LEAPS: Lam Employment Absence and Productivity Scale; MADRS: Montgomery-Åsberg Depression Rating Scale; SD: standard deviation; SDS: Sheehan Disability Scale.

Symptom and work functioning outcomes were assessed at baseline and end-point. Outcome measures included the MADRS, the Lam Employment Absence and Productivity Scale (LEAPS),[16] the Health and Work Performance Questionnaire (HPQ),[17] and the Sheehan Disability Scale (SDS).[18] Symptom remission was defined as MADRS score ≤10 at 12 weeks. The LEAPS is a self-report 7-item measure that includes a 3-item productivity subscale with items including doing less work, doing poorer quality work, and making mistakes (score range 0 to 12, higher scores indicate worse productivity). The HPQ is a comprehensive self-report questionnaire that includes an item for overall performance (score range 0 to 10, higher scores indicate better work performance) and a calculated productivity subscale (score range 0 to 37, higher scores indicating better productivity). The SDS is a self-report 3-item scale that includes 1 item assessing impairment at work or school (score range 0 to 10, higher scores indicate greater impairment in work/school functioning).

A series of analyses of covariance (ANCOVA) were conducted to determine predictors of change from baseline to endpoint on each of the LEAPS productivity subscale, HPQ productivity subscale, HPQ performance item, and SDS work/school item. The MADRS remission status and baseline scores on the relevant subscale were used as covariates in each model. For example, when analyzing the change on the LEAPS productivity subscale scores, the baseline score on the LEAPS productivity subscale was used as the covariate. The data are presented as means (standard deviations, SD). All the ANCOVA models met Levene's Test of Equality of Error Variances. Effect sizes were calculated using Cohen's *d*.[19]

RESULTS

Ninety nine patients were randomized to treatment and 86 completed the 12-week protocol and were available for analysis. Demographics and baseline symptom and work functioning scores were not significantly different between MADRS remitters (n = 41) and non-remitters (n = 45) (**TABLE 1**). The mean ages for both groups were,

respectively, 41.7 and 44.8 years. Sex distribution was similar (56% and 58% female, respectively) and proportion of patients who were married was similar across both groups (36.5% and 40%, respectively). The mean baseline scores on the MADRS and Clinical Global Impression–Severity scale reflected a moderately depressed patient population, with no significant differences based on remission status. Baseline scores in the work functioning scales were also similar for the HPQ performance item, HPQ productivity subscale, SDS work/school item, and LEAPS productivity subscale (**TABLE 1**).

The overall results of the ANCOVA models are shown in **TABLE 2**. For the LEAPS productivity subscale, MADRS remission status had significant main effect (F = 11.49, P = .001, partial η^2 = 0.12), with the mean change significantly higher in remitters (3.5, SD 2.4) than non-remitters (2.9, SD 2.8). The effect size was d = 0.23. Similarly, for the SDS work/school item, MADRS remission status (F = 14.05, P < .001, partial η^2 = 0.15) had a significant main effect. The mean change in score for remitters and non-remitters was 3.5 (2.8) compared with 2.5 (2.8), with an effect size of d = 0.36.

For the HPQ overall performance item, MADRS remission status (F = 6.674, P = .01, partial η^2 = 0.08) had a significant main effect. The mean change in performance for remitters was 1.3 (1.7), compared with 0.48 (1.5) for non-remitters, for an effect size of d = 0.51. However, for the HPQ productivity subscale, MADRS remission status did not have a significant main effect (F = 3.188, P = .08, partial η^2 = 0.04). Remitters had a mean change of 3.6 (2.9), and non-remitters 2.4 (2.7), for an effect size of d = 0.43.

DISCUSSION

The results of our secondary analysis show that symptom remission, as measured by the MADRS, is associated significantly with improvement in work performance and productivity, as assessed by several self-report work functioning scales, irrespective of the type of treatment. This was most apparent with the HPQ overall performance item, SDS work/school item, and LEAPS productivity subscale. Only the HPQ productivity subscale was not significantly different between remitters and non-remitters. However, given the trend P (.08) and effect size of d = 0.43, which is similar to the effect sizes of the other work functioning measures that did show significance, this may be a Type II error. A larger sample size with sufficient power may be required to demonstrate significant differences with the HPQ productivity subscale.

There is no consensus on what are clinically meaningful changes on functional outcome measures like the LEAPS, HPQ, or SDS yet. The effect sizes ranged from 0.23 for the LEAPS productivity subscale to 0.51 for the HPQ overall performance, representing small to moderate magnitudes of effect that generally would be considered clinically relevant. For the HPQ overall performance item, patients in symptom remission showed a mean change in score of 1.3, an almost 3-fold mean improvement relative to non-remitters. A previous RCT looking at the impact of telephone screening, outreach, and care management for depressed workers found improvement in the HPQ performance item of 0.8 (intervention group) and 0.7 (usual care group), at 6 months after randomization.[20] Similarly, the significant difference on the SDS work/school item (3.5 vs 2.5 for remitters vs non-remitters) is consistent with prior studies. In a placebo-controlled RCT to assess the efficacy of desvenlafaxine in employed patients with MDD,[21] the SDS Work/School item was improved significantly in the desvenlafaxine-treated group vs the placebo group, with differences of 3.0 and 2.5, respectively, after 12 weeks.

In addition, the mean percent (%) improvement in scores after treatment showed important changes. For the LEAPS productivity subscale and SDS work/school item, remitters improved by 69% and 66%, respectively. By contrast, non-remitters showed improvements of 46% and 38% on the same scales. Considering that clinical response often is defined as a reduction of at least 50% on a given symptom scale, these results suggest that remission status predicts clinically important improvements in work functioning and productivity. For the HPQ productivity item, remitters improved by 23% compared with 9% for non-remitters, an almost 3-fold difference.

Our results are also consistent with other studies examining remission status and functional outcomes. In the large STAR*D effectiveness study, symptom remission after 12 weeks of citalopram was associated with significant improvement in the Work and Social Adjustment Scale, a measure of functioning at work, social relationships, and home tasks, compared with both patients with partial response and those with no response.[22]

These findings have important implications for clinicians managing patients with MDD. First, our results confirm the importance of symptom remis-

TABLE 2
MADRS remission status and change scores between baseline and week 12 for each work functioning scale

		Remitters (MADRS ≤10)	Non-remitters (MADRS ≥11)	*P*[a]
LEAPS Productivity subscale	n	41	45	
	Mean change (SD)	3.5 (2.4)	2.9 (2.8)	.001[a]
	% improvement	69%	46%	
HPQ Performance item	n	39	42	
	Mean change (SD)	1.3 (1.7)	0.48 (1.5)	.01[a]
	% improvement	23%	9%	
HPQ Productivity subscale	n	39	42	
	Mean change (SD)	3.6 (2.9)	2.4 (2.7)	.08[a]
	% improvement	31%	21%	
SDS Work/School	n	41	43	
	Mean change (SD)	3.5 (2.8)	2.5 (2.8)	<.001[a]
	% improvement	66%	38%	

[a]Analyses of covariance (ANCOVA) with baseline scores on the relevant subscale as a covariate.

HPQ: Health and Work Performance Questionnaire; LEAPS: Lam Employment Absence and Productivity Scale; MADRS: Montgomery-Åsberg Depression Rating Scale; SD: standard deviation; SDS: Sheehan Disability Scale.

sion for optimizing functioning, including work functioning. Second, measurement-based care, in which outcome assessment using validated symptom scales is used to guide clinical decisions, has been shown in RCTs to improve clinical outcomes.[23,24] Given the importance of both symptom and functional outcomes,[25] it is also important to include assessments of work functioning within the clinical evaluation and management of working patients with depression.[26] In this context, the HPQ is a comprehensive questionnaire but, at 45 items, is too long and complex for busy clinical settings. However, both the LEAPS and SDS, which can be completed and scored in less than 3 minutes, can be incorporated readily into routine measurement-based care.

Limitations of this study include the *post hoc* analysis, so the results will have to be confirmed with prospective studies. We used self-report work functioning measures that potentially may be biased by negative depressive cognitions. However, the HPQ has been validated in depressed patients against objective measures of productivity.[16] Further research will be required to determine the clinical significance of changes in self-report functional outcome scales and to assess objective measures of work performance. ■

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