



## **FUNCTIONAL OUTCOMES IN MAJOR DEPRESSIVE DISORDER**

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### DISCUSSANT

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### **ABSTRACT**

When treating chronic diseases, physicians have long recognized the importance of focusing on the restoration of functioning, in conjunction with alleviating the overt signs and symptoms of such disorders. Until recently, practitioners who treat patients with major depressive disorder (MDD) have typically not prioritized the measurement of functional outcomes, despite the wealth of empirical data quantifying the workplace and interpersonal disability that is associated with MDD. Emerging evidence suggests that the emotional and physical symptoms of MDD as well as the cognitive deficits associated with the disorder are major contributing factors to the psychosocial dysfunction and workforce maladjustment seen in affected patients. Validated measurement devices that assess disability and monitor improvement across the spectrum of functional domains related to MDD may help improve outcomes in patients with the disorder. The use of a scale that measures work, social, and familial disability, such as the Sheehan Disability Scale, in conjunction with a symptom measurement scale, is recommended to quantify the level of impairment and to measure treatment effects in patients with MDD.

The following question-and-answer session was prepared from a discussion with Roger S. McIntyre, MD, FRCPC, moderated by Diane M. Sloan, PharmD, of Advogent.

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## Q&A Session

### FUNCTIONAL OUTCOMES IN MAJOR DEPRESSIVE DISORDER

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#### What level of disability has been shown to be associated with major depressive disorder (MDD)?

Several community-based epidemiological studies have documented that the majority of patients who screen positive for MDD experience significant disability in workforce and overall psychosocial functioning.<sup>1-5</sup> According to the National Comorbidity Survey-Replication, patients with MDD experienced ~30 days/year when they were unable to perform their expected work and/or social roles.<sup>6</sup>

Several international studies have also reported on the extent of disability in the workforce and the direct and indirect costs associated with MDD.<sup>7,8</sup> When functional outcomes include measures of disability beyond work—such as being able to participate meaningfully in life, days spent with family, or, conversely, days spent in bed—MDD is as impairing if not more impairing than other chronic medical disorders, such as hypertension,<sup>9</sup> diabetes,<sup>9,10</sup> and cardiovascular disease.<sup>9</sup>

#### Should physicians be cognizant of any particular symptoms of MDD that are associated with functional impairment?

During the last decade, the field has learned from several population-based and clinical studies that there is an inverse and parallel relationship between the severity of MDD symptoms and the level of functioning among patients with MDD (Figure). As the severity of MDD symptoms increases, the less likely it is that the patient will be functioning optimally.<sup>6</sup> Attempts to elucidate specific symptoms that are associated with impaired functioning have underscored the persistent neurocognitive impairment associated with MDD. Commonly encountered neurocognitive deficits are disturbances in attention, memory, concentration, executive function, and information processing speed.<sup>11-13</sup> Although the effect size of the neurocognitive deficits in patients with schizophrenia and bipolar disorder are greater than MDD, symptomatic (and asymptomatic) patients with MDD frequently exhibit clinically meaningful deficits in neurocognitive func-

tioning. It is hypothesized that the deficits that are encountered in patients with MDD relate to the neurodegenerative changes associated with MDD.<sup>14</sup> Moreover, neurocognitive function may be secondarily affected by classic symptoms of MDD, such as loss of energy, motivation, interest, and vitality.

Another important factor that may mediate the psychosocial, physical, and neurocognitive dysfunction in patients with MDD is the presence of medical comorbidities. Patients with MDD are differentially affected by several “stress-sensitive” medical disorders, such as cardiovascular disease,<sup>15</sup> arthritis,<sup>16</sup> obesity,<sup>17</sup> diabetes,<sup>9</sup> multiple sclerosis,<sup>18</sup> and metabolic bone disease.<sup>19</sup> Increasingly, MDD is conceptualized as an independent risk factor for incident medical illness, which suggests a neurobiological overlap between MDD and some commonly occurring somatic comorbidities.<sup>20,21</sup> Medical comorbidities in MDD are associated with increased medical service utilization and overall health care cost.<sup>9,22-24</sup> The presence of comorbid general medical disorders in patients with MDD may also exert an additive effect on overall functional decline and a deteriorating effect on quality of life.<sup>25</sup> Taken together, the hazard posed by ubiquitous medical comorbidities in patients with MDD supports the recommendations for systematic screening, prevention, detection, and management of comorbid somatic health issues in patients with MDD.

### Are data available that examine the ways in which impairment is seen across the different domains of functioning?

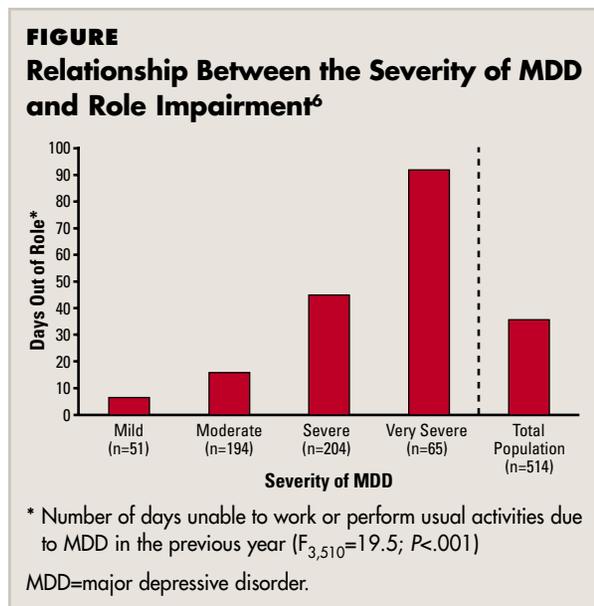
MDD is an “equal opportunity disabler” and as such it is rare to encounter abject impairment in one area and meaningful functionality in other areas. Nevertheless, anecdotally physicians do encounter some situations in which a person is certainly more impaired in one area than another. For example, someone who has a cognitively demanding job such as a banker, an accountant, or a school teacher, may be more likely to be affected by MDD in the workforce.

In my experience, the effect of MDD on a patient’s functioning is heterogeneous. Nevertheless, many patients who are suffering from MDD are severely impaired in the workforce because clinicians are increasingly finding patients with cognitively demanding jobs being referred for assessment and treatment. Although they are experiencing difficulties from an interpersonal perspective, the impairment may not be as severe as in the workplace. Speculatively, this may be due in part to the protective and supportive mechanisms that are provided by the patient’s interpersonal relationships.

As a clinician, I have frequently encountered the bidirectional relationship between MDD and psychosocial functioning. For example, although it seems axiomatic that MDD adversely affects functional outcomes, suboptimal functioning can also portend non-recovery in MDD.<sup>26,27</sup> In everyday clinical practice, mental health professionals occasionally encounter clinical scenarios where a patient has achieved symptomatic remission, but continues to be highly distressed by the fact that they have been unable to recover functionally.

### How does the psychosocial disability associated with MDD manifest in a patient’s life?

The psychosocial dysfunction observed in patients with MDD is often apparent in their interpersonal lives and is typically expressed as an increasing distance and disengagement in interpersonal, social, and familial activity. However, it is not uncommon for deficits in



psychosocial functioning to impair workforce performance as well.

### **What impact does MDD have on a patient's psychosocial functioning at work?**

The mechanisms wherein MDD affects the ability to work relates to patient factors as well as interpersonal factors arising from the individual's social/occupational network. Clinicians know that MDD diminishes functioning, job performance, and the ability to perform commensurate with their aptitude, which may affect the opportunity for job advancement and security. In the workforce, presenteeism is more often a consequence of MDD than is absenteeism.<sup>28</sup>

MDD also has a virulent effect on the social network within the workforce. Most individuals with MDD work in an environment that includes other coworkers who together create a complicated group dynamic. For example, if an individual is suffering from MDD in an office setting, it often implies that issues of stigma and alienation are introduced. The reactions of other group members toward a patient with MDD may be negative and unsupportive. For example, coworkers may have concerns about work-sharing when a coworker with MDD is unable to fulfill his or her responsibilities. This makes it very difficult for patients in the workplace who have MDD to manage both the burden of their own illness and also reactions from their coworkers, supervisors, direct reports, etc. Available evidence indicates that the probability of returning to the workforce and assuming the previously held, premorbid position diminishes significantly, especially if they are unable to return to work for protracted periods of time (ie,  $\geq 6$  months).<sup>29-31</sup>

Fortunately, many companies have become aware that mood disorders (and psychiatric disorders more broadly) are a significant burden on their employees and overall company performance. As a result, there has been interest by many companies in designing and executing a variety of education-based programs that generally focus on risk factor detection, primary prevention screening, and evidence-based interventions.

### **How does MDD specifically impact a patient's personal life?**

There has been a tacit assumption in psychiatry that the absence of psychopathology (ie, remission of MDD symptoms) equates to the existence of health. Unfortunately, many patients with MDD, despite the objective verification of MDD symptom abatement, are left with persistent deficits in functioning and detriments in quality of life.

Recently, several objective scales have been developed in an attempt to objectively measure the "happiness" that is often eroded, if not fully abrogated, by MDD. This domain is a relatively new construct dealing with self-regard, self-esteem, and quality of life.

### **When patients seek treatment or enter the physician's office presenting with MDD symptoms, do they generally volunteer information regarding disability?**

Although I have observed that patients spontaneously mention psychosocial and work-related dysfunction, it still requires careful probing to explore the quality and the quantity of the impairment on the part of the clinician. For example, patients with MDD are not frequently asked "What is your job? Describe the expectations that your employer has for you. What deliverables are expected from you, and how has your performance aligned with these expectations?" The relative lack of attention to workforce aspects of patients' lives is in part related to medical education and curricula that does not focus on this aspect of assessing and managing MDD.

Until recently, the effect of MDD on the workforce has been underemphasized by patients, families, and practitioners. More recently, however, mental health care providers are beginning to collaborate with various private sector professionals, such as vocational rehabilitation counselors, as part of a chronic disease management approach to treating MDD. The intensified interest in the effect of MDD on the workforce is in part due to destigmatization campaigns, greater public awareness, and the acceptance of the impact that MDD has on employees.

### **Do clinicians routinely inquire about the disability associated with MDD at the time of diagnosis?**

My impression is that clinicians do routinely inquire about disability, but what is missing is a sharpening of focus. In other words, there should be a much more measurement-based approach to quantifying patient functioning. Assessing functional outcomes enables practitioners and patients to more precisely estimate the severity of their functional difficulties. It also refines the measuring of subdomains of functioning (eg, workforce) that require greater attention, providing a more careful evaluation of treatment effectiveness. Moreover, measurement-based care provides a language for communicating with patients, families, employers, and other key stakeholders.

### **How can clinicians monitor functional impairment across its various domains over the course of treatment?**

It is extremely important when clinicians diagnose MDD that they incorporate an evidence-based, algorithmic sequence of pharmacotherapy and psychosocial treatment, but they should also evaluate and measure outcomes with appropriate metrics that have been validated to assess the severity of MDD and the degree of functional impairment. At the Mood Disorder Psychopharmacology Unit at the University Health Network in Toronto, patients with MDD are routinely evaluated with a symptom measurement tool. The tools include the 9-item Patient Health Questionnaire (PHQ-9),<sup>32</sup> which is easy to use and serves not only as a symptom measurement device that can establish and compare the efficacy of antidepressant interventions, but also as an MDD screening tool. Other scales include the shortened, 7-item version of the 17-item Hamilton Rating Scale for Depression (HAM-D<sub>7</sub>)<sup>33</sup> and the Inventory for Depressive Symptoms or the Quick Inventory for Depressive Symptoms (QIDS).<sup>34,35</sup> The patient's functional performance was also measured using the Sheehan Disability Scale (SDS).<sup>36</sup> The SDS is also easy to use and evaluates patients on three areas of functioning: work, social, and family. These three domains give a clear picture of how the patient is per-

forming prior to treatment, and the scores can be combined to provide an overall level of global functioning. At each visit, clinicians evaluate a patient's symptoms with a brief MDD rating scale and contemporaneously assess their functioning with the SDS.

Historically, physicians and other health care providers who treat patients with MDD have utilized the Global Assessment of Functioning (GAF), which is a continuous scale that comprises Axis 5 in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*.<sup>37</sup> The GAF provides a global estimate of general functioning. However, for a more refined evaluation particularly across the multiple spheres of functioning, a measurement-based device, such as the SDS, offers an opportunity for more specific evaluation.

### **What additional tools may be useful to assist with measuring or tracking disability in clinical practice?**

There are several other tools that have been used in clinical practice for evaluating disability in patients with MDD. Examples include, but are not limited to, the GAF and the 5-item World Health Organization Well-Being Index.<sup>38</sup> In addition, there are several work performance tools that have been employed primarily in research settings as well as other scales that are an admixture of functional outcome and quality-of-life measures. The 36-item Short-Form Health Survey<sup>39</sup> and the Quality of Life Enjoyment and Satisfaction Questionnaire<sup>40</sup> are examples of such tools. Many quality-of-life scales are broad-based and are not specific to psychiatry.

In routine clinical practice, it is preferred to use one of the MDD metrics mentioned previously, such as the PHQ-9, HAM-D<sub>7</sub>, or the QIDS in conjunction with the SDS. Results from the Sequenced Treatment Alternatives to Relieve Depression study<sup>41</sup> and other empirical studies,<sup>42</sup> have documented that measurement-based care improves symptomatic and functional outcomes in patients with MDD. Notwithstanding the availability of multiple scales, each with their own merits and limitations, the guiding principle should be the use of a measurement-based approach to treating the symptoms and functional impairment associated with MDD.

## What should the goal of treatment be with regard to the restoration of functioning or reduction of functional impairment associated with MDD?

During the past decade, the therapeutic objectives of managing patients with MDD have been refined. The overarching aim in managing a patient with MDD should be a restoration of functioning. Toward that aim, a full and sustained symptomatic remission will increase the probability that a restoration of premorbid functioning will occur.

There are clinical scenarios (eg, chronicity or a recalcitrance of MDD symptoms) where an affected patient has received multiple antidepressants and adequate psychosocial or novel interventions yet remains symptomatic. The goals of treatment for such patients may have to shift toward improving quality of life and living with a chronic illness. Fortunately, most patients with MDD can expect some degree of responsivity to disparate treatment modalities.

Notwithstanding the availability of many United States Food and Drug Administration-approved conventional antidepressants, efficacious manual-based psychotherapies as well as novel neuromodulatory approaches, most patients with MDD in primary care continue to receive guideline-discordant care. Several lines of evidence indicate that the use of decision support (eg, MDD treatment guidelines) as part of a multidimensional chronic disease management model can significantly improve outcomes in patients with MDD.<sup>41,42</sup>

## REFERENCES

- Berndt ER, Finkelstein SN, Greenberg PE, et al. Workplace performance effects from chronic depression and its treatment. *J Health Econ.* 1998;17(5):511-535.
- Judd LL, Akiskal HS, Zeller PJ, et al. Psychosocial disability during the long-term course of unipolar major depressive disorder. *Arch Gen Psychiatry.* 2000;57(4):375-380.
- Kessler RC, Akiskal HS, Ames M, et al. Prevalence and effects of mood disorders on work performance in a nationally representative sample of U.S. workers. *Am J Psychiatry.* 2006;163(9):1561-1568.
- Spitzer RL, Kroenke K, Linzer M, et al. Health-related quality of life in primary care patients with mental disorders. Results from the PRIME-MD 1000 Study. *JAMA.* 1995;274(19):1511-1517.
- Wells KB, Stewart A, Hays RD, et al. The functioning and well-being of depressed patients. Results from the Medical Outcomes Study. *JAMA.* 1989;262(7):914-919.
- Kessler RC, Berglund P, Demler O, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA.* 2003;289(23):3095-3105.
- Saarijärvi S, Salminen JK, Toikka T, Raitasalo R. Health-related quality of life among patients with major depression. *Nord J Psychiatry.* 2002;56(4):261-264.
- Sobocki P, Jönsson B, Angst J, Rehnberg C. Cost of depression in Europe. *J Ment Health Policy Econ.* 2006;9(2):87-98.
- Druss BG, Rosenheck RA, Sledge WH. Health and disability costs of depressive illness in a major U.S. corporation. *Am J Psychiatry.* 2000;157(8):1274-1278.
- Egede LE. Diabetes, major depression, and functional disability among U.S. adults. *Diabetes Care.* 2004;27(2):421-428.
- Holmes AJ, Pizzagalli DA. Spatiotemporal dynamics of error processing dysfunctions in major depressive disorder. *Arch Gen Psychiatry.* 2008;65(2):179-188.
- Mondal S, Sharma VK, Das S, Goswami U, Gandhi A. Neuro-cognitive functions in patients of major depression. *Indian J Physiol Pharmacol.* 2007;51(1):69-75.
- Wang PS, Beck AL, Berglund P, et al. Effects of major depression on moment-in-time work performance. *Am J Psychiatry.* 2004;161(10):1885-1891.
- Smith DJ, Muir WJ, Blackwood DH. Neurocognitive impairment in euthymic young adults with bipolar spectrum disorder and recurrent major depressive disorder. *Bipolar Disord.* 2006;8(1):40-46.
- Penninx BW, Beekman AT, Honig A, et al. Depression and cardiac mortality: results from a community-based longitudinal study. *Arch Gen Psychiatry.* 2001;58(3):221-227.
- Kessler RC, Ormel J, Demler O, Stang PE. Comorbid mental disorders account for the role impairment of commonly occurring chronic physical disorders: results from the National Comorbidity Survey. *J Occup Environ Med.* 2003;45(12):1257-1266.
- de Wit LM, van Straten A, van Herten M, Penninx BW, Cuijpers P. Depression and body mass index, a u-shaped association. *BMC Public Health.* 2009;9:14.
- Janssens AC, van Doorn PA, de Boer JB, et al. Anxiety and depression influence the relation between disability status and quality of life in multiple sclerosis. *Mult Scler.* 2003;9(4):397-403.
- Williams LJ, Pasco JA, Jacka FN, Henry MJ, Dodd S, Berk M. Depression and bone metabolism. A review. *Psychother Psychosom.* 2009;78(1):16-25.
- Barefoot JC, Helms MJ, Mark DB, et al. Depression and long-term mortality risk in patients with coronary artery disease. *Am J Cardiol.* 1996;78(6):613-617.
- Kaufmann MW, Fitzgibbons JP, Sussman EJ, et al. Relation between myocardial infarction, depression, hostility, and death. *Am Heart J.* 1999;138(3 pt. 1):549-554.
- Beekman AT, Penninx BW, Deeg DJ, de Beurs E, Geerling SW, van Tilburg W. The impact of depression on the well-being, disability and use of services in older adults: a longitudinal perspective. *Acta Psychiatr Scand.* 2002;105(1):20-27.
- Carta MG, Hardoy MC, Kovess V, Dell'Osso L, Carpiniello B. Could health care costs for depression be decreased if the disorder were correctly diagnosed and treated? *Soc Psychiatry Psychiatr Epidemiol.* 2003;38(9):490-492.
- McIntyre RS, Konarski JZ, Soczynska JK, et al. Medical comorbidity in bipolar disorder: implications for functional outcomes and health service utilization. *Psychiatr Serv.* 2006;57(8):1140-1144.
- Baune BT, Adrian I, Jacobi F. Medical disorders affect health outcome and general functioning depending on comorbid major depression in the general population. *J Psychosom Res.* 2007;62(2):109-118.
- Solomon DA, Leon AC, Coryell W, et al. Predicting recovery from episodes of major depression. *J Affect Disord.* 2008;107(1-3):285-291.

27. Sotsky SM, Glass DR, Shea MT, et al. Patient predictors of response to psychotherapy and pharmacotherapy: findings in the NIMH Treatment of Depression Collaborative Research Program. *Am J Psychiatry*. 1991;148(8):997-1008.
28. Stewart WF, Ricci JA, Chee E, Hahn SR, Morganstein D. Cost of lost productive work time among US workers with depression. *JAMA*. 2003;289(23):3135-3144.
29. Kessler RC, Barber C, Birnbaum HG, et al. Depression in the workplace: effects on short-term disability. *Health Aff (Millwood)*. 1999;18(5):163-71.
30. Lerner D, Adler DA, Chang H, et al. The clinical and occupational correlates of work productivity loss among employed patients with depression. *J Occup Environ Med*. 2004;46(6 suppl):S46-S55.
31. McIntyre RS, Wilkins K, Gilmour H, et al. The effect of bipolar I disorder and major depressive disorder on work-force function. *Chronic Dis Can*. 2008;28(3):84-91.
32. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. *JAMA*. 1999;282(18):1737-1744.
33. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23:56-62.
34. Rush AJ, Trivedi MH, Ibrahim HM, et al. The 16-Item Quick Inventory of Depressive Symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. *Biol Psychiatry*. 2003;54(5):573-583.
35. Trivedi MH, Rush AJ, Ibrahim HM, et al. The Inventory of Depressive Symptomatology, Clinician Rating (IDS-C) and Self-Report (IDS-SR), and the Quick Inventory of Depressive Symptomatology, Clinician Rating (QIDS-C) and Self-Report (QIDS-SR) in public sector patients with mood disorders: a psychometric evaluation. *Psychol Med*. 2004;34(1):73-82.
36. Sheehan DV. Sheehan Disability Scale. In: Rush AJ, Pincus HA, First MB, et al, eds. *Handbook of Psychiatric Measures*. 1st ed. Washington, DC: American Psychiatric Association; 2000:113-115.
37. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed, text rev. Washington, DC: American Psychiatric Association; 2000.
38. World Health Organization. Wellbeing measures in primary health care/the deprecare project. Copenhagen, Denmark: WHO Regional Office for Europe; 1998.
39. van der Heijden PG, van Buuren S, Fekkes M, Radder J, Verrips E. Unidimensionality and reliability under Mokken scaling of the Dutch language version of the SF-36. *Qual Life Res*. 2003;12(2):189-198.
40. Endicott J, Nee J, Harrison W, Blumenthal R. Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. *Psychopharmacol Bull*. 1993;29(2):321-326.
41. Trivedi MH, Rush AJ, Wisniewski SR, et al, and the STAR\*D Study Team. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR\*D: implications for clinical practice. *Am J Psychiatry*. 2006;163(1):28-40.
42. Trivedi MH, Rush AJ, Crismon ML, et al. Clinical results for patients with major depressive disorder in the Texas Medication Algorithm Project. *Arch Gen Psychiatry*. 2004;61(7):669-680.