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Research report

Clinical effectiveness: The importance of psychosocial functioning outcomes

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ABSTRACT

Background: Major depressive disorder (MDD) is associated with significant impairment in quality of life and psychosocial functioning, including social and occupational/role functioning. Evaluation of clinical effectiveness of treatments for depression must include improvement in these important functional outcomes. However, clinical trials for depression have primarily focused on reduction in symptoms, as measured by symptom severity scales such as the HDRS and MADRS or by standard definitions of response and remission.
Method: The rationale and necessity for accessing both symptom and functional outcomes in clinical trials for MDD are reviewed, and examples of validated scales for measuring QoL and social and occupational functioning are provided.
Results: Emerging data suggest that treatment effects assessed with functioning scales may differ from those captured by symptoms scales. Many validated scales are available to measure global and specific aspects of functional outcomes, including QoL, psychosocial functioning and occupational functioning. Nevertheless, systematic reviews have shown that functional outcome scales are used in fewer than 5% of trials.
Conclusions: Given the importance of psychosocial functioning for the individual with MDD as well as for society, greater attention must be focused on the assessment of functional outcomes in clinical trials for MDD, as well as in the clinical management of people with depression.

1. Introduction

Depression is now widely recognized as one of the greatest contributors to health burden to society. Major depressive disorder (MDD) is currently the fourth leading medical condition contributing to global burden of disease, and is estimated to rise to second by the year 2030 (Mathers and Loncar, 2006). For example, the overall costs of depression have been estimated at over C$6 billion in Canada (Stephens and Joubert, 2001), US$83 billion in the United States (Greenberg et al., 2003), and €118 billion in Europe (Sobocki et al., 2006). Much of this burden relates to the economic losses suffered (both personal and to society) when people are depressed, and by impairment in their quality of life and relationships.

The physical, cognitive and emotional symptoms of MDD lead to considerable impairment in psychosocial functioning. The DSM-IV recognizes the importance of functioning by coding functional impairment on Axis V in its multiaxial diagnostic system. In addition, the criteria for diagnoses include the stipulation that symptoms must "represent a change from previous functioning" and that they cause "clinically significant distress or impairment in social, occupational, or other important areas of functioning".

Given the intimate association of depressive symptoms and functioning in MDD, treatments for MDD must not only target symptoms but also the significant impairment in psychosocial functioning experienced by people with depression. Indeed, patients with MDD rate treatment outcomes such as well-being, quality of life, and functioning as more important than symptom relief (Zimmerman et al., 2006). Any measure of clinical effectiveness of treatment for MDD, then, should encompass improvement in psychosocial functioning. In fact, most clinical practice guidelines state that a

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primary goal of depression treatment is restoration of functioning (e.g., Lam et al., 2009a).

If functional impairment is such an integral consequence of depression and restoration of functioning is a treatment goal, it stands to reason that depression treatment studies should be evaluating improvement in psychosocial functioning. Surprisingly, this is not the case. Systematic reviews of over 90 meta-analyses have shown that less than 5% of clinical trials in depression report functional outcomes. The main focus of treatment studies is in symptom improvement using symptom rating scales such as the clinician-rated Hamilton Depression Rating Scale (HDRS, Hamilton, 1960) or Montgomery Åsberg Depression Rating Scale (MADRS, Montgomery and Åsberg, 1979). Even "clinically relevant" outcomes, such as clinical response and remission, are based primarily on symptom scale scores. These clinical outcomes are important because they provide detail of specific patient outcomes that are more informative than average HDRS or MADRS scores. However, these scales do not fully assess functioning. For example, in the HDRS, there is only one item that assesses work/activities, but this item has response descriptors that include symptoms (interest, fatigue, and weakness) as well as functioning (decrease of time spent in activities and stopped working).

DSM-IV operationalizes functional impairment with the Global Assessment of Functioning (GAF) scale (Endicott et al., 1976). However, the GAF obscures a true assessment of functioning because the anchor point descriptions for ratings on the GAF also include severity of symptoms. To remedy this problem, the Social and Occupational Functioning Assessment Scale (SOFAS) was developed, which is identical to the GAF except that the anchor points only include the functional impairment descriptions (Hilsenroth et al., 2000).

The GAF and SOFAS can be considered global clinical scales, since they comprised only a single item rated by the clinician. They are comparable to the Clinical Global Impression scale, and thus are useful to provide an overall rating of functioning. However, we know from principles of measurement-based clinical care that global ratings alone are not sufficient to track outcomes, so more specific and comprehensive scales are required to provide additional information on symptoms and functioning (Patten et al., 2009; Greer et al., 2010). In addition, constructs such as quality of life are best assessed using self-rated scales. In this paper, we briefly review the issues in measurement of psychosocial functioning, and describe some selected validated tools.

2. What are functional outcomes?

The term "functional outcome" can encompass many different concepts and domains, including quality of life (QoL) and psychosocial functioning. Although QoL and functioning are often used interchangeably or subsumed together, they are separate but complementary constructs. QoL is also variably defined, but the World Health Organization definition includes "*an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns*" (The WHOQOL Group, 1995). In medicine, we usually refer more specifically to Health Related Quality of Life (HRQoL), a multidimensional evaluation of health (both physical and mental) and its treatment on a person's daily life and well-being. However, given the importance of physical and mental processes in a person's life, there seems to be great overlap between QoL and HRQoL, so we will use QoL for both constructs.

In contrast to QoL, psychosocial functioning usually refers to the person's ability to perform daily tasks and to interact with others and with society in a mutually satisfying manner. Functioning can therefore be narrowly defined by specific domain (e.g., marital functioning; social functioning; occupational, school and role functioning; and physical functioning) whereas QoL, by definition, includes multiple domains. Unlike QoL, which remains primarily a subjective evaluation, psychosocial functioning can sometimes be assessed objectively.

Despite these various definitions and the complexity of concepts, functional outcomes can be reliably assessed using clinician- and patient-rated instruments. There are many validated scales available that measure global and specific aspects of functional outcomes, including QoL and psychosocial functioning. Some scales have data on population norms so that functioning in patients with MDD can be compared to general populations. Other scales of psychosocial functioning are sensitive to change, making them useful as outcome measures for clinical trials.

3. How do functional outcomes differ from symptom outcomes?

Although functioning is such an important aspect of depression, especially for the patient, it may be surprising to learn that there is inadequate attention to measurement of functional outcomes in clinical trials of MDD. For example, a systematic review of 203 depression trials (77% medication and 23% psychotherapy studies) found that, of the most frequently used health status scales, all of the top 10 scales were symptom scales and only 3 of the top 20 were functional outcome scales (Brockow et al., 2004). In fact, functional outcome scales were used in less than 5% of trials. This finding was replicated in another systematic review that also found less than 5% of clinical trials in depression study meta-analyses reported outcomes using a QoL or functioning scale (McKnight and Kashdan, 2009).

Given that impairment in functioning results from depressive symptoms, does measuring functioning provide additional information to measuring symptoms? A systematic review of treatment studies in MDD found only a "tenuous relationship" between scores on symptom and functioning scales (McKnight and Kashdan, 2009). For example, the mean correlation between scores on the GAF and a depression symptom scale in 10 studies (total $n = 2733$ patients) was about -0.65 (representing less than 45% of the variance), with a 95% confidence interval ranging from -0.25 to -0.75. Similar findings were reported for other QoL, social and occupational functioning scales.

Emerging data also suggest that treatment effects assessed with functioning scales may differ from those captured by symptom scales. For example, a 24-week study comparing escitalopram with duloxetine in patients with MDD found that remission rates as defined by MADRS scores were not significantly different (73% versus 70%, respectively) between medications, but escitalopram-treated patients had greater improvement in the Sheehan Disability Scale (SDS, Leon et al., 1997), in both SDS total scores and the SDS work subscale scores (Wade et al., 2007). This suggests that there is no complete correspondence between symptom remission and functioning.

Similarly, in a pooled analysis of two aripiprazole augmentation studies for antidepressant non-responders, Trivedi et al. (2009) found that improvement on the SDS was greater in patients who were in remission on the MADRS compared to those who had a response but were not in remission; in turn, responders had greater improvement on the SDS than non-responders. However, in an analysis using structural equation modeling, they were able to show that the degree of change in SDS scores was not related to change in depression score or in side effect scores (Trivedi et al., 2009). These results indicate that other factors beyond symptoms and side effects are also important in determining improvement in functioning, and that symptom scales and functioning scales may provide different and complementary information for clinical trials.

4. What are differences between functional outcome scales?

Generally, there are a number of factors that can differentiate individual scales. For example, scales can be clinician-rated or patient-rated. Clinician-rated scales can have an advantage in that clinical expertise may help clarify patient responses to ensure that they are valid and reliable. However, they also usually require special training to administer and take time to conduct, which makes them less useful for large-sample studies or busy clinical settings. Patient self-rated scales are simple and easy to use, and self-monitoring by patients may improve adherence to treatment. However, patient-rated scales can also be limited by response bias (e.g., over-reporting or under-reporting), which is especially important for health conditions like depression where negative cognitive distortions may be present.

Global scales composed of one or two items can provide a brief assessment of overall rating, but specific scales can provide greater and richer detail about specific domains of functioning. However, comprehensive scales have greater respondent burden and are less useful in clinical practice. Generic scales, designed to be used in a wide variety of health conditions, are especially useful to compare functioning between disease conditions and often have normative data from general population samples. However, disease-specific scales may offer more important clinical information about specific impairments experienced by patients with a certain health condition.

The selection of a particular scale is dependent upon the population, setting and purpose for the scale. Studies examining etiological and contributing factors in depression require comprehensive scales measuring specific theoretical constructs of psychosocial functioning. Studies comparing functional impairment across different disease conditions require scales that reflect general or non-specific pathology. Clinical trials usually require functional outcome scales that assess specific aspects of functioning and that are sensitive to change. Finally, scales for clinical settings must be brief and simple to use and interpret. In the following sections, we provide some examples of functional outcome scales that can be used in these different situations.

5. Quality of life and social functioning scales

There is a rich literature on social functioning assessment in depression, so it is not surprising that there are many QoL and social functioning assessments available (Coons et al., 2000; Bech, 2005). Table 1 lists some commonly used QoL and social functioning scales. The Medical Outcomes Study SF-36 (Ware and Sherbourne, 1992) is a generic QoL scale with 41 items that assess symptoms, physical health, work and family satisfaction, and disability. The SF-36 has been used in more than a thousand depression studies (McKnight and Kashdan, 2009).

In contrast to the generic SF-36, a QoL scale that is more specific to psychiatric conditions is the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q, Endicott et al., 1993). The original version of the Q-LES-Q had 93 items that assessed degree of enjoyment or satisfaction in a variety of domains, including work, home or school activities. A shorter 16-item version is also available. The Q-LES-Q has been used in many clinical trials and has been shown to be sensitive to treatment effects, even in short term acute phase treatment trials of depression and anxiety (e.g., Michalak et al., 2007).

An example of a depression-specific QoL scale is the Quality of Life in Depression Scale (QLDS, Hunt and McKenna, 1992). This 34-item, self-rated scale is based on the premise that QoL is dependent on the ability of a person to satisfy her/his needs. The QLDS has been validated in several different languages, shows good sensitivity to depression severity, and has been used in clinical trials of antidepressants (Tuynman-Qua et al., 1997). For example, an 8-week clinical trial involving 511 patients with MDD found that agomelatine was superior to placebo in improving QLDS total and subscale scores (Zajecka et al., 2010).

Social functioning is often assessed as a separate domain within many QoL scales, especially those that are more comprehensive in scope. In contrast, an example of a specific social functioning scale is the widely used Social Adjustment Scale, available as a self-rated version (SAS-SR, Weissman et al., 1978). The SAS-SR has 54 items that assess performance in several areas of functioning, including work (within and outside the home), social and leisure activities, family relationships, and roles within marriage and family.

While there are many studies of social functioning in depression, there are fewer clinical trials that have incorporated QoL and social functioning assessment (Weissman, 2000). Reviews of these studies show an overlap in treatment effectiveness as compared to symptom scales, but functional assessments provided important additional information about residual symptoms and differential responses to medications (Kennedy et al., 2001; Greer et al., 2010). It is important to note that the trajectory for response in functional outcomes may not parallel that for symptom response. Although improvement in psychosocial functioning can be demonstrated in short term depression treatment studies of 8 weeks or less, it may take longer (12 weeks or more) for functioning to improve to general population norms (Bech, 2005).

6. Occupational functioning scales

Occupational functioning is a particularly important aspect of functioning for individuals and for society at large. The constellation of core symptoms of depression includes both physical (decreased energy and sleep disturbance) and

Table 1
Examples of quality of life and social functioning scales.

General scales	Psychopathology non-specific scales	Depression-specific scales
• Medical Outcomes Study Short Form (SF-36)	• General Health Questionnaire (GHQ)	• Quality of Life in Depression Scale (QLDS)
• Social Adjustment Scale (SAS-SR)	• Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q)	• Sertraline Quality of Life Battery (SQOLB)
• EuroQoL 5 Dimension (EQ-5D)	• Sheehan Disability Scale (SDS)	• Social Adaptation and Self-evaluation Scale (SASS)
• Satisfaction with Life Scale (SWLS)	• Sickness Impact Profile (SIP)	

cognitive (reduced interest and motivation, difficulty with concentration and attention) symptoms that would be expected to impair functioning in all types of work, so it is not surprising that 79% of people experiencing MDD in the previous year reported some interference with their work functioning (Gilmour and Patten, 2007). Although the cost of absenteeism (time off work) is high in MDD, even greater cost is attributed to "presenteeism", or reduced productivity while still attending work. One report estimated the average productivity loss due to depression-related presenteeism as 15.3%, compared to 10.7% loss due to absenteeism (Goetzel et al., 2004).

A number of scales are available to measure work functioning and productivity (Table 2). The SDS is an example of a global scale that has a single item assessing work or role functioning, and many QoL scales also include at least 1 item in the work domain. Specific work productivity scales provide greater detail in describing specific productivity problems that can be impaired by health concerns. Most are generic scales that can be used in a number of health conditions, such as the Work Limitations Questionnaire (WLQ, Lerner et al., 2001) and the Stanford Presenteeism Scale (SPS, Koopman et al., 2002). It should be noted that very few productivity scales have been used or validated in clinical trials, and that some may be more sensitive to change than others (Sanderson et al., 2007).

In addition, few work functioning scales have been developed specifically for depression. The "gold standard" is currently the Health and Work Performance Questionnaire (HPQ), developed for the World Health Organization (Kessler et al., 2003). The HPQ has been used in randomized treatment studies, e.g., finding that telephone care management for employees with depression offers cost savings for businesses (Wang et al., 2007). However, the HPQ is too long to be useful in clinical practice. A recently validated brief productivity scale, the Lam Employment Absence and Productivity Scale (LEAPS), was developed specifically for clinical use in patients with depression (Lam et al., 2009b). It consists of 7 items, takes 3–5 min to complete, and can be used to monitor clinical treatment.

Table 2
Examples of occupational functioning scales.

Global scales	Specific scales
• Global Assessment of Functioning (GAF)	• Endicott Work Productivity Scale (EWPS)
• Medical Outcomes Study Short Form (SF-36)	• Lam Employment Absence and Productivity Scale (LEAPS)
• Sheehan Disability Scale (SDS)	• Stanford Presenteeism Scale (SPS)
• Social Adjustment Scale (SAS-SR)	• Work Limitations Questionnaire (WLQ)
• Social and Occupational Functioning Assessment Scale (SOFAS)	• Work Productivity and Activity Impairment Questionnaire (WPAI)
• WHO Psychiatric Disability Assessment Schedule (DAS)	• Work and Social Adjustment Scale (WSAS)

7. Conclusions

Psychosocial functioning, which includes QoL and social and occupational functioning, is arguably the most important concern for patients with MDD, hence any evaluation of clinical effectiveness of treatments should encompass these functional outcomes. While there is overlap in treatment effects on symptoms and on psychosocial functioning, assessment of the latter provides information that is different from, and complementary to, the former. A number of validated instruments are available that assess both general and specific aspects of psychosocial functioning, and that are sensitive to change. The selection of any particular functional outcome scale depends upon the specific purpose for which they are used. However, despite the importance of functional outcomes and the availability of tools that measure them, they are still underutilized in treatment studies of MDD. It is no longer adequate for depression treatment studies to simply focus on a proxy measure of improvement such as symptom change. Given their importance to patients and to society, functional outcomes should become the primary endpoints for clinical trials for MDD, especially in the assessment of clinical effectiveness for new and novel treatments for depression.

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