See article by van der Voort et al

Major Depressive Disorder: Treat the Disability, Not the Diagnosis

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The article by van der Voort and colleagues in the present issue of the *Journal*[1] is a timely reminder that major depressive disorder (MDD) is not just a diagnosis. It creates disability. Data from a naturalistic cohort with a representative range of care settings in the Netherlands give a renewed understanding of the impact of illness severity on outcomes. The primary measure of function covered impairment in 6 domains: cognition (understanding and communicating), mobility (moving and getting around), self-care (hygiene, dressing, eating, and staying alone), getting along (interacting with other people), life activities (domestic responsibilities, leisure, work, and school; in fact, this item was dropped from the analysis because of missing values), and participation (joining in community activities). The findings resonate for a number or reasons.

First, they underline that major depressive episodes entail functional impairment, not just symptoms. Indeed, it is impairments of function that make major depression a disorder rather than a collection of emotional biases. The impairments may take a long time to resolve, usually much longer than the relatively short periods of time for patients to show a treatment response in clinical trials. Finally, there are important differences in the times individuals take to respond. Patients with a single episode were much more likely to be in stable remission after 1 year and had probably responded more quickly and completely. The recurrent and bipolar subgroups described here were more likely to be in partial remission. Patients with repeated episodes or a bipolar diagnosis also tended to be more impaired in the early stages of remission.

Second, the importance of actually measuring depression severity remains unrecognized in ordinary practice. This study used the 30-item Inventory of Depressive Symptomatology (IDS),[2] which is well characterized and can be employed in a shortened ("Quick") form (QIDS) as a clinician- or patient- (ie, self-)rated scale. It has a factor structure characterized by a general factor, an anxiety factor, and an atypical symptom feature factor. The items contributing to the general factor are loss of interest or pleasure, sad mood, dissatisfaction and negative views of the self, lack of energy (including psychomotor retardation and inability to work), inability to make decisions or concentrate, reactive mood, irritability, and future pessimism. The subfactors within the scale essentially map onto *DSM* criteria, but of course they are scored for severity. Whereas diagnosis sets a minimum hurdle, the IDS score offers an estimate of how high the depressive episode is over the bar. It can be used reliably to identify a depressive episode as mild, moderate, or severe. It also appears to be a proxy measure of impairment from the present study. A much more careful use of severity criteria in ordinary practice would drive more rational prescribing of appropriate treatments.

The severity issue is important because of the criticisms that have been made of "antidepressant" prescribing on the back of findings that use has increased at a population level in the last decade. This increase has been assumed to result from lowered thresholds for treating depression, and it plays to the particular preoccupation of some critics that psychiatrists are bent on pathologizing normal experience.[3] The interpretation of these findings is both confused and confusing. First, there is clear evidence, in the United Kingdom anyway, that increased numbers of prescriptions for depression are actually a result of longer-term treatment, not increased rates of diagnosis.[4,5] The present study teaches us that longer-term treatment may be highly appropriate for the most impaired patients with slow treatment response profiles and recurrent episodes. Second, the clear danger of the irresponsible polemics around this issue is that rates of diagnosis and treatment of more severe depression will fall. Third, to define a drug by its indication as an "antidepressant" leads to a tautology: increased use must mean more prescriptions for depression. In fact, serotonergic drugs are often highly effective for anxiety disorders and pain states, which are very common indeed and often untreated. Increased prescribing may in part represent appropriate treatment for disorders other than depression.

Whatever the source of the overtreatment fallacy, it could only be helped by improved methods for recording symptom severity in patients. Advances in digital technology mean that patient self-rating should be an increasing part of patient care and clearly recommended in guidelines.

Beyond their clear correlation, the relationship between depressive symptoms and functional impairment remains uncertain. Two potential mediators are of interest: anhedonia and impairment of cognition per se. Anhedonia, or emotional blunting, is a relatively unexplored correlate of poor functional outcomes. Arguably, normal behavior and experience must require adequate motivation and reward. While these are dimensions that are clearly impaired in depression, they are assessed in the mix with negative emotion. The return of positive emotion per se may be

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underestimated as a predictor and requirement for good outcomes. Moreover, serotonergic drugs may act to reduce both negative and positive emotional processing and so contribute to incomplete recovery in a subgroup of patients.[6]

Cognitive impairment means poor concentration and difficulty making decisions, items already included in the IDS metric. Hence, there is little scope for teasing out its specific contribution to poor outcome. Directly measured cognitive impairment is an obvious candidate for further exploration. Indeed, enhanced remediation of cognitive performance may be an appropriate treatment target for patients with incomplete functional recovery. This is the current focus for proof-of-concept studies with drugs and psychological interventions. It represents an area in which real innovation and treatment enhancement may be possible. The present data show how much they are still needed.

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