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Toward Personalized Treatment in Psychiatry

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In recent years, there has been, inspired by developments in other areas of medicine like oncology, an increasing interest in the potential possibilities of personalized medicine in psychiatry. One of the motivating factors behind this interest in the field of mood disorders is the growing awareness among clinicians and researchers that the "one size fits all" approach to the treatment of major depression is not fruitful. An increasing number of reviews and meta-analyses have shown that many acute-phase treatments show comparable efficacy in the treatment of major depression.[1] This finding, originally in the field of psychotherapy research, has become known as the Dodo-bird verdict.[2] The Dodo-bird verdict was interpreted as evidence that all treatments are equivalent because they share common factors.[3] This has led to a lively debate in the literature, with opponents arguing that there is ample evidence for clinically meaningful differences in effect sizes between treatments, indicating that therapy-specific factors, and not common factors, are indeed responsible for these differences.[4]

However, a totally different point of view has entered the debate. It has been convincingly argued that clinically meaningful differences between treatments are obscured by the large amount of symptomatic and etiologic heterogeneity within the current *DSM*-based, categorical, single-entity concept of major depression.[5,6] By ignoring this heterogeneity and holding on to the "one size fits all" approach, the field will not succeed in increasing the effectiveness of evidence-based treatments for depression. Many have expressed their confidence that results from new fundamental research into etiology, phenomenology, and endophenotypes will yield a more basic understanding of the heterogeneity of depression. A recent example is the National Institute of Mental Health–initiated Research Domain Criteria project.[7]

As early as 1993, Fava and Kellner[8] suggested a somewhat related but more clinically orientated approach. They introduced a staging approach to mental disorders that could operate as a model for treatment planning. They argued that, within this framework, subjects at high risk for the development of an episode of major depression qualify for different interventions than individuals with a far more advanced stage, eg, multiple episodes with residual symptoms, of the disorder. In recent years, McGorry and colleagues have drawn much attention to the use of clinical staging models in the development and course of psychopathology,[9] which are now available for many psychiatric disorders.[10] In addition to staging, the profiling of patients may be very helpful in deciding which treatment is most indicated for each patient. Profiling refers to characteristics that may further help in choosing a personalized, evidence-based treatment for each individual patient. A clear example would be a patient suffering from psychotic depression with a prior history of 3 episodes in 10 years. In terms of *staging*, the prior history would indicate advanced illness severity warranting prophylactic treatment after recovery. Additionally, the psychotic features as a *profiling* characteristic would qualify for combined treatment with an antidepressant and an antipsychotic.

Optimism has been expressed that, based on the staging and profiling models, more knowledge will accumulate that will help clinicians decide which patient will profit most from which treatment during which stage of the disorder. To be useful in daily clinical practice, the variables of interest need to be easy to administer. Although results from brain-imaging procedures may be highly informative in indicating that a given patient will profit more from pharmacotherapy than from short-term psychotherapy, implementation of this knowledge is hardly feasible; most clinical facilities will not be able to use the results from such studies in routine practice. To date, most of this type of research has been devoted to the planning of acute-phase treatment. A beautiful example of profiling in the acute phase is a recent study in a large sample that reported superior treatment outcome of combined pharmacotherapy and psychotherapy for only those patients with severe depression. Monotherapy with cognitive behavioral therapy was equally efficacious as combined therapy in patients with mild to moderate severity.[11] Depression severity serves here as a profiling element.

There is growing awareness of the recurrent nature of depression, especially in patients presenting in specialized treatment care. One of the key questions is which interventions are indicated in patients that are at risk for recurrence after recovery of their index episode. An example of such approach is the finding that mindfulness-based cognitive therapy is probably effective only in patients with 3 or more depressive episodes and not effective for those with fewer episodes.[12] Thus, prior history is a *staging* element that can help clinicians and patients to decide if mindfulness-based cognitive therapy will have value in a treatment strategy aimed at reducing the risk of recurrence.

A good example of the use of *staging* and *profiling* characteristics can be found in this issue of the *Journal*.

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J Clin Psychiatry 2015;76(10):e1313–e1314
dx.doi.org/10.4088/JCP.14com09737

Figueroa and colleagues[13] conducted a very interesting study in which they found that cognitive reactivity in euthymic patients, assessed with a relatively simple instrument, predicted relapse over a 3.5-year follow-up period. Moreover, by combining the number of previous episodes and the magnitude of cognitive reactivity with the use of a mild mood induction, the authors present an elegant table displaying the risk of relapse in a given patient. As they outline in their article, much research has been carried out into the persistence of dysfunctional cognitions in depressed patients after their recovery. The majority of these studies report that dysfunctional cognitions are present during an episode of major depression but are not found after recovery, indicative of a state, and not a trait, characteristic. Accordingly, assessing dysfunctional cognitions after successful treatment is not helpful in the prediction of the risk for future recurrence of depression. Figueroa and colleagues[13] introduce a rather novel instrument, the Leiden Index of Depression Sensitivity (LEIDS), which measures cognitive reactivity without complex mood induction procedures.

This study[13] may be one that adds to our knowledge about which of our patients are at the highest risk for developing a new depressive episode in the near future. The LEIDS is easily implemented in daily practice, and assessing cognitive reactivity in a given patient may help to decide if ongoing treatment is advisable in the face of risk for recurrence. Some limitations hamper current implementation in clinical care. As the authors themselves indicate, the sample size is somewhat modest, and their results may apply only to their sample.[13] Replication, preferably in larger samples, is therefore required. Research, like this article by Figueroa and colleagues, directed at assessing staging and profiling characteristics with the aim of informing clinicians and patients as to which intervention is most likely to be successful, will increase the effectiveness of our treatments significantly.

Submitted: December 15, 2014; accepted December 23, 2014.
Potential conflicts of interest: None reported.
Funding/support: None reported.

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