

## Depressions black and blue: changing the *Zeitgeist*

*A new model of depression with meaningful subtypes will avoid simplistic treatments*

WHEN YOU HEAR the term “major depression”, you imagine a clinically meaningful entity. Think “pseudoentity”, know “paradigm failure”.<sup>1</sup> If I took my tegument for dermatological inspection, a diagnosis of “major” or “minor” blotches would be uninformative. I would need more categorical information (eg, freckle, melanoma) to make rational treatment choices. However, non-specificity now rules in depression modelling and treatment.

“Depression” is currently viewed as a single disorder, varying dimensionally. The World Health Organization’s international classification of diseases, 10th revision (ICD-10), specifies “mild”, “moderate” and “severe” episodes.<sup>2</sup> The US *Diagnostic and statistical manual of mental disorders*, 4th edition (DSM-IV)<sup>3</sup> categorises depression as “major depression” (episodes requiring at least five symptoms present for two weeks) and other (including “minor”) disorders. The Plimsoll line for “caseness” (ie, for diagnosis of a depressive disorder) has been further lowered, with two or more depressive symptoms held to define “new” (“sub-syndromal” or “subclinical”) mood disorders.<sup>4</sup> If the criteria for caseness are progressively loosened so as to capture most of the “blue” population, isn’t the meaning of a “depressive disorder” lost? The logical inconsistency of positing a “subclinical” disorder as a clinical disorder has not, however, discouraged efforts to prove high prevalence, functional impairment and need for treatment.

The dominant *Zeitgeist* views depression as an “it”, a disease having nothing to do with the individual’s personality, and, because “it” is caused by chemical brain changes, requiring an antidepressant drug. However, for those with an antipathy to antidepressants, there are equally effective psychotherapies. Thus, all roads lead to Rome. Such “homogenising” has resulted in efficacy studies (the largest database in psychiatry) producing quite meaningless results.<sup>5</sup> “Evidence-based psychiatry” is at risk of becoming an oxymoron.

Mere polemic? Let’s consider some data. For “major depression”, efficacy studies quantify all antidepressants (old and new classes compared between and within classes) as equally efficacious,<sup>6</sup> and the overall antidepressant drug response as comparable to that for St John’s wort, cognitive behaviour therapy (CBT), other psychotherapies and counselling.<sup>5</sup> Why?

Data from efficacy studies submitted by pharmaceutical companies for product licensing are problematic. One analysis of data for antidepressants submitted to the US Food and Drug Administration (FDA) showed that, of 47 trials for major depression, there was no drug effect in nine, and a drug–placebo difference of questionable significance for the remainder.<sup>7</sup> In another analysis of 52 pivotal placebo-controlled FDA-submitted studies,<sup>8</sup> half showed no advantage to the antidepressant drug. “Homogenising” depression and implying “universal” application for treatments

leads to the inability to distinguish between differing effects according to differing depressive subtypes. Furthermore, trial selection of pristine subjects (eg, those without comorbidity, in whom melancholic depression is rare) ensures a high response rate in trials (to both active treatment and placebo) and thus their minimal separation. Yet these are the data on which current practice and treatment guidelines are based.<sup>9</sup>

So, everyone’s a winner — and a loser. Winners? All therapies can claim efficacy. Treatment then risks being determined more by the therapist’s discipline or interest — a Procrustean approach that fits the patient to the therapist’s preferred treatment. Losers? The pharmaceutical companies are challenged for “overselling” the properties of antidepressant drugs, patients feel demeaned in reading that antidepressant drugs are akin to placebos, and practitioner credibility is challenged.

Moving along the “overselling” dimension, we are informed that the benefits of CBT have been scientifically proven and that it is the benchmark non-drug therapy. While CBT has credibility, a recent review<sup>10</sup> of its efficacy returned the Scottish verdict of “not proven”, in that it lacked any superiority over other psychotherapies or “clinical management”. Despite CBT being held to be useful for multiple psychosocial problems, a recent Cochrane review<sup>11</sup> of psychosocial interventions delivered in general practice found “good evidence that problem-solving treatment by general practitioners is effective for major depression”, but limited or conflicting evidence for CBT. As for antidepressant drugs, a potentially useful treatment may “fail” or appear weak if it is not tested on people with subtypes of depression who are likely to benefit.

Let’s broaden the argument. Would we be sanguine about grouping all breast lumps (ranging from benign cysts to malignant cancers), testing myriad treatments as universal ones, interpreting the “homogenised” group data as indicative of comparable efficacy, and having an individual’s treatment determined largely by the treating practitioner’s discipline or enthusiasm? We would surely expect that a subtyping diagnosis would be made and that any treatment would be empirically based. Such a standard should also be demanded for diagnosing and managing the depressive disorders.

While it is important that the mood disorders be destigmatised and that people be encouraged to seek assessment, it is equally important that they then receive appropriate diagnosis and treatment. Unpublished data from our clinics suggest that bipolar disorder is often missed or misdiagnosed, that the more biological (“black”) depressive disorders are undertreated, and that there is too much reliance on pharmacological treatments for managing non-melancholic disorders.

### Recommendations

- Treatment guidelines for managing the depressive disorders that rely on efficacy data should be regarded as providing tentative information at best.
- There is no “universal treatment” for depression. As it encompasses mood disturbances, syndromes, disorders and diseases, clinicians should expect heterogeneity, resist simplification, and reject the plausibility of any “universal treatment” model.
- Clinicians should seek to identify and address the causes of an individual’s disorder, allowing that causes may be biological, psychological and/or social.
- Assessing disorder “pattern” and aetiology (as against depression severity) allows clarification of the differential impact of various treatments on different disorder “types”.
- Clinical effectiveness data (assessing the full range of mood disorders and associated comorbidity in “real-world” conditions) should be given more airtime in developing a disorder–treatment matrix.

We favour a model for identifying meaningful depressive subtypes that incorporates aetiology, development of a matrix linking subtypes to specific (and non-specific) treatments, testing the model’s utility in “real-world” clinical studies, and promoting broader education of professionals. The model is not intrinsically complex. The complexity lies in recognising and changing the *Zeitgeist* (see Box). While there is an argument for destigmatising depression with a

simple message, there is no argument for doctors continuing to buy simplistic “one-size-fits-all” management recommendations for patients who present for assessment.

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