Reviewer's report

Title: Major Depressive Disorder as a Nonlinear Dynamic System: Bimodality in the Frequency Distribution of Depressive Symptoms over Time

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Reviewer: Sean Lynch

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I thought overall that this was a stimulating and well-written paper. It is certainly innovative in approach and could be useful in leading to greater understanding of recovery trajectory and normal time course of depressive episodes.

The strengths are that the cohort studied is selected from primary care as far as I can understand and is a reasonable size for an initial “proof-of-concept” study. The sample is thus less likely to be treatment resistant or have complex comorbidity. Data has been collected on mood shifts over a two year period for a reasonable proportion of the sample, sufficient to begin exploratory mathematical modelling. However, data loss is substantial and needs far fuller discussion. However, the authors should be commended on obtaining the amount of individual data on mood changes in this group. The interventions that have been used in the patients are also referenced e.g. psycho-education, CBT, antidepressant therapy, psychiatric treatment.

There are a few issues I have in terms of methodology and other possible limitations of the study. The degree (severity) of depression and number of previous episodes are not defined. Particularly whether this has resulted in self harm, contact with secondary mental health care services or hospitalisation. It is not clear whether patients had completed a treatment protocol / programme during entry to the study or whether this study was designed to be more naturalistic. This leads on to questions as to whether patients continued to have treatment and their degree of response, conventional categorical methods could be used e.g. 50% reduction in initial score (response), 25-50% reduction in initial score (non-response), full remission and response (do not meet diagnostic criteria and low score), which I am sure could be considered by the authors. Other data which I think should be briefly mentioned are any psychiatric co-morbidity (even if not meeting exclusion criteria) or physical co-morbidity, alcohol, smoking and substance use and basic economic and socio-demographic data.

As the authors stated, a major methodological weakness is in recall bias due to retrospective recollection of mood score. If this was the most feasible method, possibly a small subgroup could be studied to compare both prospective and retrospective methods of collecting this data? Other options are to look at modern technologies to instantly upload mood scores. Little data is given on any changes in external life events or stressors or in treatment plan.
The statistics are described in detail, but threats to their interpretation e.g. modest numbers and repeated (possibly related) measures need fuller discussion. I think that for all the above reasons if the authors were to state that this is a preliminary or “proof-of-concept” study, this might be much clearer for the readers of the journal.

Although the authors are enthusiastic about the possible bimodality or multi-modality constructs for depression, how can they be certain that these are distinct states i.e. “depressive” and “non-depressive”? Also, it is important to consider typology of depressive disorder i.e. interpretation of data could also depend on whether severe and moderate severity forms of depression are seen as within the same spectrum of disorders or as being different disorders, as is the view of some researchers. It is possible that there may be several states e.g. full episode, partial remission, subsyndromal (but not in normal range) and normal mood reactivity states? I would like to see the authors engage in much more detailed discussion of these issues.

The authors should finally discuss how they would like to see research develop e.g. if larger and multi-centre prospective studies.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.