

psychiatry, namely whether we need models for different disorders if their trajectories (especially early on) overlap in so many ways (e.g., genetics, neuropsychological profile, oxidative stress, sleep-wake cycle).¹⁵ Pluripotential outcomes, transdiagnostic risk factors that could explain mental and physical comorbidities, age at peak onset and transitions of subthreshold syndromes often defy classification under current schema, but are likely to be a key part of the new psychiatry.¹⁶ If we decide to adopt clinical staging models, whichever version we choose will challenge us all, as it is not just a case of putting old wine into new bottles (or young wine into old ones!).

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Author response

We are thankful to Drs. Shah and Scott for their comments on our editorial. Their letter gives us an opportunity to expand on and clarify the most relevant points. Our main argument has been that the staging model may not be as fully developed as to be ready for clinical application, but it has had healthy stimulating effect on our field, and we see the letter by Shah and Scott as a testimony to that.

It was not our intention to focus just on stages in fully manifest illness. The importance of recognizing clinical heterogeneity of bipolar disorder is supported by studies of prodromal stages as well. We have been involved in some of the longitudinal high-risk studies of young people at risk for bipolar disorder.¹⁻³ These studies, among others, described early stages of the illness and their comorbidities⁴ as well as neuropsychological functioning⁵ and structural brain findings.⁶ Based on these studies as well as on

observations of other authors, we believe that the point of heterogeneity of bipolar disorder and the need to separate it from the concept of uniformly progressing illness are equally applicable in the early stages as in the latter ones. The prodromes may appear non-specific and uninformative with respect to future illness trajectories when viewed through the prism of current diagnostic classification. But an alternate phenotypic characterization may identify well circumscribed and more homogeneous subgroups of illness that are continuous with the later stages. This is exemplified by the studies of children of lithium-responsive and nonresponsive parents, showing concordance of the patterns of clinical course (as well as treatment response) between generations.^{4,7}

Another point raised by Shah and Scott pertains to the risk:benefit ratio of treatments in different stages, considered more favourable early on. We agree that this is a reasonable assumption, but it remains to be tested, and such testing may not be easy to carry out. A recent review lists a handful of studies, some showing short-term relief of clinical symptoms in young people (frequently treated with medication).⁸ However, the lower risk:benefit ratio of these mostly psychosocial treatments is implicitly assumed rather than derived from appropriate comparisons.

We agree with Drs. Shah and Scott that more attention needs to be paid to the early stages of major psychiatric disorders. We also believe that the staging concept is important for psychiatry heuristically as it challenges some of the basic concepts of bipolar disorder. However, before it can be applied clinically, the staging model deserves deeper scrutiny and more support from longitudinal studies.

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