

treatment is considered prohibitively expensive. Not only do they point out costs because of the length of phase-oriented treatment² and its unpredictable non-linear course, they also highlight the costs involved in the training of staff because DID treatment requires specialised skills currently not developed during psychiatrists' training. They conclude that the evidence for DID should be followed by clinicians and that appropriate treatment will cost less overall than leaving disorders involving pathological dissociation untreated.

An important avenue that might reduce treatment length, and therefore treatment costs, is pharmacological intervention. Corrigan & Hull state that medication is of limited value, but to date no double-blind placebo-controlled studies have been performed with the aim to develop evidence-based pharmacotherapy to alleviate pathological dissociative symptoms in DID. However, it has been proposed that kappa-opioid receptor antagonists may be of interest for the selective pharmacological targeting of debilitating dissociative symptoms in post-traumatic stress disorder and trans-diagnostically.³ Abnormal serotonin neurotransmission in frontal and temporal regions has been found in relation to dissociative amnesia in a positron emission tomography receptor binding study³ and therefore serotonergic medication might also be of interest to treat pathological dissociative symptoms. In addition, the authors would like to offer the consideration of a glutamate hypothesis for dissociation on the basis of scientific evidence that (a) the glutamatergic agent ketamine induces dissociative symptoms in humans⁴ and in animal models,⁵ (b) the psychotropic drug lamotrigine can reduce dissociative symptoms induced by ketamine in healthy individuals,⁶ (c) glutamatergic hyperactivity could be relevant in the neurobiology of depersonalisation and (d) lamotrigine can be an augmenting treatment to reduce dissociative symptoms in depersonalisation disorder,⁶ and (e) anterior cingulate glutamate concentration correlates positively with dissociative symptoms in individuals with borderline personality.³ Glutamate concentrations in the brain of individuals with pathological dissociation can relatively easily be measured using magnetic resonance spectroscopy, which may provide information on whether glutamate is a neurochemical biomarker of dissociation.

Although more has become known about what happens in the dissociated brain and functional neurocorrelates of pathological dissociation^{1,3} are being unravelled, it remains largely unknown how dissociative symptoms are mediated in the brain at a neurotransmitter level. Neurobiological research into the neurochemical biomarkers of pathological dissociation could possibly lead to the development of pharmacological agents that facilitate more rapid symptom alleviation. Although the development of such pharmacological interventions offers a challenge for the scientific community, they are expected to reduce the treatment costs of individuals with DID.

Declaration of interest

None.

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Letter to the editor about 'Context and outcome of first-episode psychosis in India and Canada'

The study by Malla et al¹ explored the differences in the 2-year outcome of first-episode psychosis at two sites, one in Montreal, Canada, and the other in Chennai, India. The study concluded a better outcome for negative symptoms in low- and middle-income contexts compared with a high-income context, concurring somewhat with the long-held notion of a better outcome in psychosis, particularly schizophrenia.² More family support partly explained this outcome. Evidence against this axiom has also been published³ in light of methodological limitations of studies supporting this hypothesis, human rights abuses in people with mental illness prevalent in low- and middle-income contexts, and socio-cultural transformations occurring in this part of the world. Notwithstanding these debates, we wish to point out a few issues with the present study.¹

Primarily the way family support was evaluated and used as a statistical metric. The two items (support and family relationship) from the Wisconsin Quality of Life Index – Provider Version were scored on a Likert-type scale; support on a scale of 1–3, and family relationship on a scale of 0–5. For a single-weighted score of family support, both the scores were multiplied, thus ending up with zero total scores occasionally if the latter was scored zero despite a variable score on the former item. Its significance is related to the variation in environmental support and family relationship in the two sites.

Another essential variable of interest missing from the study is the aspect of income (or family income adjusted to the gross domestic product per capita) and controlling for it for site difference other than family support at month 3.

For the examination of predictors of negative symptoms, remission and remission status at month 24, the adherence to medication variable was dropped. We do not find any reason for doing so.

The high-income context site had one-third of participants with affective psychosis versus 10% in the low- and middle-income context site. Patients with affective psychosis are more prone to extrapyramidal symptoms from antipsychotics than those with non-affective psychosis.⁴ The higher chances of categorising depressive and extrapyramidal symptoms as negative symptoms without an evaluation of side-effects results in the possibility of inflating the findings.

Finally, concerning individuals who were non-completers of the study, first, mortality in four participants (three because of suicide) in the India site, to us, needs greater emphasis (and may be interpreted as a unique aspect in outcomes research for psychiatric disorders). Second, the disproportionately small number of participants lost to follow-up in the India site is not well explained. The latter could probably be as a result of a combination of family

support, aspect of the patient–provider relationship and the value of free medications (provided at Schizophrenia Research Foundation (SCARF), India) in improving treatment adherence in this context.

Declaration of interest

None

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Author's response

We thank Kumar & Das for raising some important issues about our published article.¹ We hope that our findings do not suggest or support the better outcome in low-middle-income countries as an axiom. Our findings are, in fact, limited to the two specific contexts in which the study was carried out. Here we attempt to address each of the issues raised by them.

First, family support. We acknowledge that the measure of family support used in this study has its limitations, especially in terms of not being able to explore greater detail. The authors of the letter are correct in their interpretation of the scoring of this measure that, theoretically, a participant could end up with a score of zero, if one of the two questions had a score of zero. We had verified this as part of our analysis and none of the patients had a score of zero on either of the two questions. Therefore, the variance in the scoring of the measure was retained.

Second, family income. The authors raise an important point regarding family income adjusted to gross domestic product. Although we attempted to collect these data, unfortunately they were available infrequently and not always reliably. For some patients this meant individual income (Montréal) whereas others interpreted it as family collective income (Chennai). As a result of the unreliability of the comparative nature of the data across the two sites, we did not use it as part of our analysis. However, future studies should make an effort to do so.

Third, extrapyramidal symptoms (EPS). Given that almost invariably second-generation antipsychotic medications were used at both sites, the frequency of EPS was expectedly low. We used the prescription of anticholinergic medication as a proxy for EPS because it was collected consistently. The rate of such use was similar for patients with affective and non-affective psychotic disorders (mean rate over 24 months 9.0% and 7.5%, respectively for schizophrenia spectrum and affective psychoses, in Montréal). Only 1/15 patients with affective psychosis in Chennai received anticholinergic medication.

Fourth, patient mortality. We agree that this issue needs 'greater emphasis'. Greater details were provided in the original submission but could not be accommodated in the final version in response to one of reviewer's comments as this was not the focus of the study. Briefly, all deaths occurred in the first 3 months of treatment and all had a diagnosis within the schizophrenia spectrum disorders.

Fifth, differences in attrition rates. The highly significant difference in attrition from treatment and the study across the two sites are presented and discussed in detail in a separate publication.²

Sixth, medication and adherence. Medications were available to all patients free of cost if they could not afford them (Chennai) and/or through a mandatory state-funded system if they did not have private insurance (Montréal). Rates of adherence to medication were similar in Montréal and Chennai (modal adherence rate 80% and 82% in Montréal and Chennai, respectively). Hence this variable was not entered into the regression analysis.

We hope that we have addressed the important questions raised by Kumar & Das.

Declaration of interest

None.

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