

## Highlights of this issue

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I write my last Highlights column with a sense of loss but also one of fulfilment. I have stood on the shoulders of giants and seen our specialty continue to occupy a privileged position in medicine – one that combines research and practice to advance our understanding of mental disorders. It is a very special place to be.

As a profession, psychiatry remains forward-thinking in its understanding of diagnosis and treatment. Tyrer's editorial on Galenic syndromes (pp. 309–310) reinforces this vision. The author immerses us in a different mindset around personality and how it is inextricably bound with depressive and anxiety-related disorders, substance use disorders and autism spectrum disorder. In a similar vein, Woo (pp. 311–313) hones in on the true meaning of harm reduction in cannabinoid use. A mechanical approach to assessment that simply stops at quantity, frequency and duration – while having some intrinsic value in gauging risk – is incomplete without wider psychoeducation around risk and benefit in a way that does not judge or shame.

### Powers of prediction

Younger people living with severe mental illness are known to show persistent deficits in functional outcomes. For this group, prediction of social and role functioning is central to the prevention of disability. In a study of 102 participants with psychosis and 114 with depression as part of the Personalised Prognostic Tools for Early Psychosis Management (PRONIA) study, Rosen et al (pp. 318–321) used machine learning models to predict social and role functioning using clinical phenotyping with a combination of rating scales. Compared with relying on neuro-imaging to guide prognosis, such phenotyping holds promise for earlier targeted intervention in clinical settings. While we are on the theme of prediction, the study by Xi et al (pp. 339–346), adds yet another layer of knowledge. Their study from China used magnetic resonance imaging to gauge predicted brain age in participants aged between 18 and 44 years with a diagnosis of schizophrenia through measures of white matter disorganisation. A unique finding was that early treatment with antipsychotic drugs reduced predicted brain age by 2.7 years after an average of 4 months of drug treatment. These findings hold promise for targeted treatments in earlier brain ageing and the benefits of antipsychotic drugs in the reversal of structural brain damage.

### Clozapine: beyond the granulocyte

Clozapine remains widely used in treatment-resistant schizophrenia and psychosis in Parkinson's disease. It is also used off-licence to treat a range of other mental disorders and has stood the test of time with respect to treatment adherence. A study by Brodeur et al (pp. 347–354) involving 3228 participants in Canada found

that prior poor adherence to antipsychotics was associated with poor adherence after clozapine initiation. However, the absolute risk of poor adherence to treatment was low, with more than 68% of patients adhering to their treatment after initiating clozapine. The authors conclude that clozapine should still be used where indicated in everyday clinical practice. That said, the need for pharmacovigilance cannot be understated. And that means looking beyond blood dyscrasias. Constipation is a manifestation of clozapine-induced gastrointestinal hypomotility (CIGH) and is three times more prevalent with clozapine than with other antipsychotics. This means that early detection of potentially harmful CIGH – predominantly abdominal pain and abdominal distension – is central in the prevention of adverse outcomes. A study by Handley et al (pp. 355–363) of spontaneous UK pharmacovigilance reports that were recorded as clozapine-related gastrointestinal adverse drug reactions over a 25 year time frame found 527 such reports, of which 33% involved patient death. Surgical intervention occurred in 26% of those with non-fatal CIGH. There is clearly a need to monitor bowel function actively and to have a low threshold for prescribing and continuing laxatives for the duration of clozapine treatment. The authors also consider it good practice to record clozapine prescription on the patient's electronic prescribing record, so that it appears in the patient's summary care records if they are admitted to hospital.

### A wave of optimism

To conclude, we visit the arena of delirium research – an area not readily frequented by research in our pages, that is, outside the realms of phenomenology and assessment. Delirium is present in up to 50% of patients admitted to general medical wards, up to 53% undergoing post-operative recovery and up to 87% on intensive care units (ICUs). It is a strong predictor of mortality, length of hospital stay and the likelihood of long-term care placement. Standardised questionnaires to detect delirium lack sensitivity, with fewer than 50% of patients correctly identified in busy clinical settings such as ICUs. There is clearly a need for better detection. The presence of low-frequency brain signals is characteristic of delirium, but the value of the electroencephalogram (EEG) has hitherto been squandered owing to the need for skilled interpretation by suitable trained professionals. In this regard, the study by Yamanashi et al (pp. 322–329) breaks new ground. Through the development of a novel bispectral EEG (BSEEG) – one that uses only two EEG channels – patterns of electrical activity can be interpreted and acted on by non-experts. The study enrolled 279 participants with an average age of 71 and clinical evidence of delirium, with BSEEG used to predict outcomes. The authors found BSEEG scores to be higher in the group scoring positive for delirium on the Confusion Assessment Method for the ICU (CAM-ICU) than in the CAM-ICU-negative group. Death rate and length of stay in the BSEEG positive group were significantly higher than those in the BSEEG negative group. This heralds a new dawn for the use of EEG in everyday care of patients with delirium.

This where I leave you. I wish my successor the best of luck in continuing to bring you a Highlights section that will be as stimulating and informative as it always has been.