This issue starts with a meta-analysis by Liu and colleagues1 about the effectiveness of adjunctive treatment with metformin to reduce the weight gain associated with clozapine use in patients with schizophrenia. The relatively common occurrence of the metabolic syndrome among individuals taking clozapine2 is a major problem for the minority of difficult-to-treat patients for whom clozapine is the only effective agent for treating their psychosis. One option is to concurrently treat these patients with clozapine and another agent that reduces the risk of the negative effects of clozapine. Metformin has previously been shown to reduce the weight gain associated with the use of other antipsychotic medications, but there is, to date, no meta-analysis specifically focused on its utility when used as an adjunctive treatment for clozapine. This study identified 6 randomized controlled studies on this issue—three of which were only published in the Chinese literature—with a pooled sample of 414 subjects. The meta-analysis found that metformin did, indeed, both reduce the weight gain and decrease the increase of body mass index (BMI) typically associated with clozapine use in patients with schizophrenia. The quality of the evidence for these conclusions was rated as ‘moderate’ and ‘high,’ respectively, but the follow-up time in the studies was only 6 to 24 weeks, so the long-term effectiveness of this adjunctive treatment remains unknown.

The first original research article by Yang and colleagues3 is a case control study that compares the density of GABA (gamma-aminobutyric acid) in the ventromedial prefrontal cortex (vmPFC) of 22 individuals with first-onset psychosis (10 with schizophrenia and 12 with schizophreniform disorder) to that in the vmPFC of 23 healthy controls. Previous studies have reported higher levels of GABA in the vmPFC and suggest that the density of GABA may be related to the severity of the psychotic symptoms,4 but the results may have been confounded by the prior use of antipsychotic medication, so this study enrolled drug-naive individuals with first-onset psychosis. The authors used single-voxel 1H-MRS (magnetic resonance spectroscopy) to assess the concentration of GABA and the Positive and Negative Syndrome Scale (PANS) to evaluate the severity of psychotic symptoms in the patient group. They found that the concentration of GABA in the vmPFC was significantly greater in the patient group than in the control group, confirming that this abnormality is independent of medication use. However, they did not confirm the previously reported association between the density of GABA and the severity of psychotic symptoms.

The second original research article by Hu and colleagues5 follows up on previous studies about the relationship of specific single nucleotide polymorphisms (SNPs) of the Disrupted-in-Schizophrenia 1 (DISC1) gene to the onset of schizophrenia. The weight of previous research indicates that the rs821633(C) allele is more prevalent in schizophrenia than in healthy controls,7 but no previous study has assessed whether this association is stronger in (presumably) more genetically heterogeneous early-onset patients than in less genetically heterogeneous late-onset patients. The authors used TaqMan genotyping technology to assess the rs821633 SNP in 315 early-onset patients with schizophrenia (i.e., onset of hallucinations or delusions before age of 19), 407 late-onset patients (i.e., onset after age of 19), and 482 healthy controls. They found that compared to healthy controls, the prevalence of the C/C genotype of rs821633 and of the rs821633(C) risk allele were significantly higher in both the early-onset and late-onset patient groups. However, there was no significant difference in prevalence of the C/C genotype or the rs821633(C) risk allele between early-onset and late-onset patients. Moreover, based on Kaplan-Meier survival analysis, there was no association between the presence of the rs821633(C) risk allele and the age of onset.

The third original research article by Xia and colleagues8 considers the prevalence of comorbid anxiety and depressive symptoms in children with attention deficit hyperactivity disorder (ADHD), and the relationship of self-reported symptoms of ADHD, anxiety, and depression between children with ADHD and their parents. A two-stage diagnostic assessment using the Schedule for Affective Disorder and Schizophrenia for School-Aged Children (K-SADS-PL) identified 135 children 7–10 years of age who met diagnostic criteria of ADHD and 65 control children without ADHD. The high prevalence of comorbid anxiety disorders (42%) and comorbid depressive disorders (33%) found in the children with ADHD confirmed results from previous studies.9 Self-reported ADHD symptoms were significantly higher in parents of children with ADHD than in parents of children without ADHD, particularly the mothers. This result both highlights the heritability of the disorder and the presence of ADHD symptoms—primarily inattention symptoms—in adults. However, in the patient group, there was no significant relationship between the severity of parents’ self-reported ADHD symptoms and the severity of their child’s ADHD symptoms (r=0.35, p=0.342). But the severity of parents’ self-reported anxious and depressive symptoms were significantly correlated with the severity of self-reported anxious symptoms (r=0.58, p<0.001) and depressive symptoms (r=0.59, p=0.030) in their children.

The Forum includes two contributions about the issue of antipsychotic polypharmacy.10,11 Use of relatively high doses of antipsychotic medication and the concurrent use of multiple antipsychotic medications in the treatment of patients with schizophrenia are common problems in China and

A full-text Chinese translation of this article will be available at http://dx.doi.org/10.11919/j.issn.1002-0829.216028 on April 25, 2016.
other Asian countries. Professor Chuanyue Wang\textsuperscript{[11]} discusses the failure of such approaches to achieve the intended improved clinical outcomes and the increased risks of serious adverse events of high-dose treatment and antipsychotic polypharmacy, including the recently acknowledged exacerbation of the cognitive impairment that occurs in schizophrenia due to medication-induced reduction in synaptic plasticity. Professor Yifeng Xu\textsuperscript{[12]} discusses the factors that have promoted these clinically unsound practices in China and elsewhere, including the role of training, pharmaceutical marketing, Traditional Chinese Medicine (TCM) prescribing practices (which encourage polypharmacy), financial incentives, and the limited research about antipsychotic polypharmacy. The treatment of psychotic disorders is the core function of most psychiatrists in China and in many other low- and middle-income countries, so changing attitudes and practices about high-dose treatments and about antipsychotic polypharmacy should become a high-priority activity for national and regional professional associations.

The first case report by Chen and colleagues\textsuperscript{[13]} discusses a case of quetiapine-induced eosinophilia. Eosinophilia is a rare allergic response to antipsychotic medications that can lead to myocardial damage and even death if it goes undetected. The case report describes a man with alcohol-induced psychotic disorder who developed dramatic eosinophilia (7.63 \times 10^9/L; normal range, <0.5 \times 10^9/L) four weeks after starting a standard dose of quetiapine. The patient had no symptoms of the eosinophilia and complained of no adverse reactions to the quetiapine. It was only recognized as part of a routine blood count test conducted during the treatment. After stopping the medication his eosinophil count returned to normal over a 4-week period and there was no myocardial damage. The case highlights the importance of routine blood tests, particularly during the early phases of treatment with antipsychotic medication, and the need for clinicians who use antipsychotic medications to be ever-vigilant about the possibility of rare but clinically important adverse events.

The case report by Ye and colleagues\textsuperscript{[14]} discusses the treatment of panic attacks with low-dose citalopram in a 22-year-old woman who developed serious panic attacks (that were probably induced by a psychological stressor) ten years following cardiac transplantation. Despite the seriousness of her attacks, which resulted in twice-weekly emergency room visits for several weeks, she adamantly refused any type of psychotherapeutic help. However, with the strong encouragement of the clinicians who had regularly followed her heart condition, it was possible to start her on citalopram 10 mg/d. Her symptoms significantly improved within 2 weeks and completely resolved after 8 weeks of treatment. There are no clinical guidelines for the treatment of psychiatric conditions in patients who are taking anti-rejection drugs and other medications following organ transplantation. As is the case for all patients with serious medical conditions who develop psychiatric disorders, the possibility of serious drug interactions understandably makes clinicians very conservative in their pharmacological treatment of such patients. If feasible, the first line of treatment with such patients should be psychotherapy, but carefully monitored administration of psychiatric medications in collaboration with the treating clinicians should definitely be considered if psychotherapy is not feasible or ineffective.

The Biostatistics in Psychiatry article by Lu and Belitskaya-Levy\textsuperscript{[15]} discusses recent debates about problems in the use of the p-value – the most widely employed statistic in biomedical (and most other scientific) research. Some authors\textsuperscript{[16]} have suggested that misuse of the p-value is the root cause for the lack of repeatability of research findings, a serious problem that limits the conversion of clinical research findings into clinical practice. Based on this, some journals have taken the extreme step of banning p-values completely from their pages.\textsuperscript{[17]} The authors provide a layman’s introduction to the p-value and suggest that despite some real limitations, there is no better alternative than the p-value method for testing the hypotheses that are central to all research efforts. They also suggest that the poor design and implementation of research studies and the frequent use of sub-optimal sample sizes in studies are much more likely causes of the poor repeatability of research findings than the misuse of p-values in the analysis of research results.

The letter by Tonna and colleagues\textsuperscript{[18]} provides additional information related to their Forum\textsuperscript{[19]} in the previous issue that discussed comorbid obsessive compulsive disorder and bipolar disorder (BD-OCD). In support of their hypothesis that this condition is a subtype of bipolar disorder rather than the co-occurrence of two separate disorders, they discuss the limited data available about BD-OCD in pediatric patients. In most such patients, OCD symptoms initially coexist with BD symptoms (and may even cycle with mood symptoms), but they gradually decrease with increasing age and the BD symptoms become more prominent. This supports the contention that in these cases the OCD symptoms are part of the developmental trajectory of BD, not a separate disorder.

\textsuperscript{[Shanghai Arch Psychiatry. 2015; 27(6):328-330. doi: http://dx.doi.org/10.11919/j.issn.1002-0829.216028]}
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