This issue starts with a special article by Paul Bebbington\[1\] and two commentaries on the article, one by Jim van Os\[2\] and one by Xin Yu.\[3\] Bebbington’s article discusses how research over the last 20 years in psychosocial epidemiology and cognitive behaviour therapy has led to new thinking about the etiology and development of psychoses. Despite the frequently reported centrality of heritable genetic factors, social environment and the occurrence of so-called non-psychotic symptoms such as disturbances in affect and sleep play key roles in the onset and persistence of psychotic disorders. These findings have important implications for our understanding of the multiple pathways that lead to psychotic symptoms and, more importantly, for the development of interventions that can prevent or ameliorate these symptoms. Van Os highlights the diagnostic implications of this revised understanding of psychosis. If psychosis is a ‘transdiagnostic dimension’, that is, a category of symptoms that reflect severity in a variety of diagnostic categories, then the rigid psychotic versus non-psychotic dichotomy that has dominated diagnostic considerations for decades needs to be re-considered. This dimensional approach was considered in the preliminary discussions of DSM-5 but was eventually dropped because of the complexity of integrating dichotomous diagnoses and dimensional scores; van Os believes that integrating both approaches is necessary to improving our understanding of how symptoms interact with each other and respond to environmental influences.\[4,5\] Yu Xin considers the multi-dimensional approach to diagnoses proposed by Bebbington a substantial improvement on the traditional dichotomous classification system, but remains concerned about the lack of methodological rigor of assessment methods of concurrent psychotic and non-psychotic symptoms. He is also skeptical about the use of the presence of concurrent non-psychotic symptoms or responsiveness to cognitive behavioral therapy as parameters for subclassifying psychotic disorders.

The review article by Freedman and Ross\[6\] raises the enticing possibility that prenatal dietary supplementation with phosphatidyl-choline could prevent the subsequent development of schizophrenia, similar to prenatal folate supplementation to prevent cleft palate and spina bifida.\[7,8\] The authors integrate a small but growing literature with findings from their own studies to suggest that cholinergic neurotransmission at nicotinic receptors is essential to normal brain circuit development and, more importantly, that choline supplementation in the second and third trimesters is associated with improved inhibitory neuronal functions—functions that are associated with schizophrenia and attention deficit disorder. Given the long time-lag between the intervention and the target outcome (schizophrenia), providing convincing proof of the benefit of prenatal choline supplementation will be difficult. But the huge potential public health benefits of this simple, safe, inexpensive, and short-term intervention may be sufficient to justify promoting choline supplementation before definitive proof of its efficacy is available.

The first original research article in this issue by Xie and colleagues\[9\] is a randomized controlled trial involving the administration of ‘shuganjieyu’, the first Chinese traditional medicine approved for use in the treatment of depression by the Chinese drug regulatory authorities. The efficacy and safety of shuganjieyu, which is composed of St. John’s wort and extracts of Siberian ginseng, has been reported in previous studies.\[10,11\] The current study assesses the relative efficacy of shuganjieyu with or without adjunctive repetitive transcranial magnetic stimulation (rTMS) in the treatment of 65 elderly inpatients with depression. All participants received daily shuganjieyu and were randomly assigned to active or sham rTMS treatment (5 days a week for 4 weeks). The trial continued for 6 weeks but only 1 patient dropped out of the experimental group and 2 patients from the control group. None of the participants had serious adverse effects. Blinded assessment of outcome using the Hamilton Rating Scale for Depression (HAMD-17) found that both groups improved significantly after the first 2 weeks of treatment, but after 6 weeks of treatment only one-fifth of participants had a greater than 50% drop in the severity of depression from baseline. There were no significant differences between groups, so there appears to be no benefit of combined treatment with shuganjieyu and rTMS. The relatively low 20% rate of substantial improvement after 6 weeks of treatment suggests that further placebo-controlled trials with shuganjieyu are needed.

The second original research article by Zuo and colleagues\[12\] is a secondary data analysis that uses both gene-based and pathway-based methods to analyze data from several large genome-wide-association-studies (GWAS) of alcohol dependence. Though more complicated, gene-based and pathway-based methods have several advantages over the more traditional single nucleotide polymorphism (SNP) method; it is, for example, easier to associate biological functions with specific genes and pathways than with specific SNPs. The combined dataset used in the analysis included 1409 European-American and 681 African-American alcohol dependent individuals and 1518 European-American and 508 African-American healthy controls. After applying statistical adjustments, the ‘cell-extracellular matrix interactions’ pathway and the PXN gene (which encodes paxillin) within this pathway were the most promising risk factors for alcohol dependence. This new analytic approach identified several genes and signalling pathways of potential importance to the onset and development of alcohol dependence that are not evident when limiting the analysis to SNPs.

The forum addresses an issue of increasing importance in China and other rapidly aging middle-income countries: the diagnosis of Alzheimer’s disease.

A full-text Chinese translation of this article will be available at http://dx.doi.org/10.11919/j.issn.1002-0829.215047 on June 6, 2015.
(AD). Yang and Xiao\(^{[13]}\) discuss how substantial advances over the last 2 decades in the understanding of the etiology and progressive deterioration characteristic of AD have led to refinements in the diagnostic criteria for AD. However, these criteria now require highly trained clinicians to make fine clinical distinctions and, often, advanced equipment to assess the presence of an increasing number of potential biomarkers. The criteria are, therefore, of little use in locations where high-level clinicians and advanced equipment are not available. Chen\(^{[14]}\) concurs that the new criteria are of little practical use in routine care and highlights the ethical problems of making early diagnoses for a condition for which there is, as yet, not effective treatment. However, he believes that biomarkers are essential in clinical and pharmacological research about AD because their use allows for a more precise identification of the condition, earlier institution of treatment, and more accurate assessment of the effectiveness of proposed treatments.

The case report from India by Sachdeva and colleagues\(^{[15]}\) described a 36-year-old patient with an 8-year history of moderately severe social phobia and agoraphobia with panic attacks who had experienced concurrent visual and auditory hallucinations that occurred multiple times a day over the 2 months prior to admission. Treatment of the anxiety disorder with sertraline over 4 weeks significantly improved the anxiety symptoms; the hallucinations also resolved completely over this 4-week period—without resorting to the use of antipsychotic medication. This case provides support for the approach to psychosis promoted by Bebbington in this issue’s special article\(^{[11]}\) and by van Os in the commentary;\(^{[16]}\) they consider psychosis a transdiagnostic dimensional group of symptoms that are often markers of the severity of underlying disorders.

The biostatistics in psychiatry piece by Song and Lu\(^{[17]}\) introduces the decision tree method that is particularly useful for identifying homogenous subgroups of subjects in large complex data sets and for developing prediction algorithms for outcomes of interest. This non-parametric analytic method has fewer underlying assumptions than other methods so it is better able to deal with data sets that have missing values and to rank the relative importance of different potential predictor variables. The article provides a general description of the method and of the available algorithms and software packages for building decision tree models.

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