2016 in Review

The Editors are pleased to offer personal selections of some of the articles they found particularly interesting and important in this year's *Journal*.

The Colliding Crises of Greece and Syria

Robert Freedman, M.D.

One-fourth of the articles published in the *American Journal of Psychiatry* this year were written by authors outside the United States. Most of these articles are from countries across the globe with well-established clinical and research institutions. Nonetheless, some of them come from countries where neither clinical nor research efforts are well-supported, either because they have never developed or because they have been destroyed by armed conflicts or by fiscal crises. We wanted to give these colleagues a voice in the *Journal*. They bring perspective for our readers on what is happening to them in their part of the world that cannot be obtained through network newscasts or newspapers. The "Perspectives in Global Mental Health" section of the *Journal* is a recent feature for our fellow psychiatrists and other mental health professionals in these countries. The article in this series by Anagnostopoulos et al. (1), "A Compounding Mental Health Crisis: Reflections From the Greek Experience With Syrian Refugees," describes two crises that have intersected. The financial crisis in Greece has the consequence of high unemployment, as well as loss of support for mental health services. Yet Greece is also one of the closest Western countries to Syria, and it has been inundated with refugees arriving nearly daily in open boats despite the high risk of such voyages. The authors describe a 14-year-old Syrian boy who came to Greece with his father, after his mother and sister were killed in the streets of Syria. He is ridiculed by his classmates for his poor academic development, and his father, stressed by unemployment, is unable to help him manage his anger and dissociation. The boy was assessed by our colleagues, and fortunately they found a place for him at a day center established by a nongovernmental organization. The determination of these psychiatrists to continue providing the best clinical care possible and to write about the experience, regardless of difficult conditions, earns my respect and admiration.

Mortality in Women With Psychiatric Diagnoses

David A. Lewis, M.D.

The increased risk of depression and suicide in mothers during the postpartum period has been well-known for years but remains a substantial clinical problem. The study by Johannsen and colleagues (2) provides additional perspective on the scope of the problem by examining mortality from all causes in women with an onset of psychiatric illness during the 3 months following childbirth (postpartum-onset mothers). Using records available from four Danish population registries, the authors found that postpartum-onset mothers had a mortality rate ratio 3.75 times higher than mothers with no psychiatric history. However, this rate was also elevated in mothers with onset of psychiatric disorders outside of the postpartum period (2.73) and even higher still in childless women with psychiatric diagnoses (6.15). The authors offer reasonable interpretations for these differences, but given the epidemiological nature of the study, these explanations remain speculative. However, the findings of this study clearly demonstrate the increased risk of premature death from multiple causes in women diagnosed with psychiatric disorders, especially when comorbid with a substance use disorder. This study also provides another reminder of the clinical importance of maintaining alertness to the potential emergence of mood, anxiety, and/or psychotic symptoms in the postpartum period. Current initiatives to integrate clinicians with mental health expertise into obstetrical-gynecological practices will hopefully both increase awareness and improve detection of psychiatric symptoms in the postpartum period and improve access to mental health services focused on preemption and treatment. The integration of mental health services into women's health programs more broadly may also serve to reduce the elevated rates of premature death in all women with a psychiatric illness.

The Value of Long-Term Follow-Up

Robert Michels, M.D.

There are several images of what a "typical" mental disorder is, in the minds of both the public and the profession. For many years, this term implied a lifelong deficit; this was certainly the dominant notion of the 19th century and early 20th century. Related to this, a major theme of research was tracing the life course of patients and their disorders. Emil Kraepelin's name is often associated with this approach.

In the last few decades, particularly in the United States, an alternate model has become popular. A primary example is Adolf Meyer's concept of "reaction" and the notion of an individual's being exposed to a "precipitant" that leads to a reaction, which is a mental disorder that begins, and then ends, with a course that may be influenced by an intervention along the way. This was a much more optimistic picture, and it fit the culture well. The research models associated with this view consisted of cross-sectional studies of groups of subjects, along with studies of the impact of interventions, perhaps biologic or psychosocial, and most often involving follow-up for a period of weeks or months. Lengths of hospitalization and treatments became briefer, and today it is not uncommon for a psychiatry resident to complete training having followed few or even no patients for more than a few months.

Yet we know that many, and probably most, of our patients have life courses that are influenced by their disorders, with episodes of remission and exacerbation, and symptoms that wax and wane.

The article by Mary Zanarini and her associates (3) describes a large cohort of patients with borderline personality disorder followed for 16 years with individual assessments every 2 years. The work involved is prodigious: 231 patients and 58 comparison subjects were interviewed at each of eight follow-up waves over a period of 16 years—a total of 4,624 individual clinical assessments! No single clinician, and very few groups, could accumulate that much experience, and each assessment was standardized and involved instruments of known reliability. What emerges is a finely textured clinical picture of an important disorder (one whose very existence was long questioned and that only recently has been demonstrated to have acceptable diagnostic reliability).

Zanarini and colleagues have previously demonstrated that the disorder is far from hopeless; 80% of patients had a remission lasting 8 years, with only 10% having a subsequent recurrence. Here they extend their study to patterns of remission and recurrence of individual symptoms. They identified two clusters: chronic "temperamental" symptoms that remit only briefly and then recur, such as chronic depression, hopelessness, anxiety, anger, and loneliness; and "acute" symptoms that have higher rates of remission and lower rates of recurrence. These symptoms include affective instability, stormy relationships, and self-mutilation. The picture that emerges is of a complex disorder with some stable traits of less diagnostic specificity and of other less stable and often more dramatic symptoms that are more likely to remit. A picture of the natural course of the disorder, such as this one, is essential as a basis for planning, conducting, or evaluating a treatment.

Finding a Favorite in Treatment

Daniel S. Pine, M.D.

Articles on treatment hold a special place in the *Journal*, as they communicate new findings that might immediately impact the care of patients. My favorite article in this year's *Journal* reports data from a randomized controlled trial for treatment-resistant depression, a condition where novel therapeutics are needed desperately. In this article, Singh and colleagues (4) compare the efficacy of intravenous ketamine and placebo in patients receiving multiple infusions for as long as 4 weeks.

Two features excite me about this report. First, research on ketamine deeply melds basic and clinical approaches because ideas about its therapeutic potential initially emerged from a clinical observation, and this observation then later spawned basic science, which continues to grow rapidly. Second, while many studies report acute effects of ketamine on depression, Singh and colleagues report one of the first attempts to use ketamine for more extended periods, by comparing regimens involving repeated dosing. This research seeks procedures for safely extending the acute mood-elevating effects of ketamine in a way that might have the maximal beneficial effect on patients.

Family History: A GPS for Early Screening and Intervention for Mood and Anxiety Disorders

A. John Rush, M.D.

The report by Weissman and colleagues (5), "Offspring of Depressed Parents: 30 Years Later," presents the longest follow-up of children and adolescents from families with at least one parent who received treatment for major depressive disorder and a comparable control group of children and adolescents without parental history of major depressive disorder. These results are clinically actionable as they have implications for adult psychiatric and pediatric practice, systems of care delivery, and research funders.

What did Weissman and colleagues find? The high-risk offspring had thrice the risk for major depressive disorder as controls, the majority of whom had their first episode before age 21. Prepubertal onset, while uncommon, was 10-fold greater in the high-risk offspring. These offspring also had more general medical burden in earlier adult years, more mental health inpatient and outpatient treatment, and greater mortality from unnatural causes (5.5% compared with 2.5%).

Clinicians who treat adults with major depression—especially if there are other affected family members or if the course is recurrent—could be of great service by offering a screening visit from time to time, or pediatricians could include a depression screen in the "annual checkup" visit. The early and frequent onset of anxiety disorders, which also occurred in these high-risk offspring, offers another opportunity for early detection in pediatric or psychiatric practices by simple screening methods. A web site offering free screening tests may be a more attractive alternative to some adolescents.

For care systems, early free screening could reduce the long-term costs of undetected but expensive mental and general medical conditions.

For research funders, the value of longer-term studies like this one is obvious, but long-term clinically oriented research funding is virtually unheard of. We need to put patients back into the funding prioritization.

The long delay between symptomatic expression and proper diagnosis with treatment can be life-destroying, especially for

adolescents. We can now focus our efforts at least in part based on family history. Had we a patient with a history of parental death from a myocardial infarction at age 36 or breast cancer at age 34, or familial melanoma, would we not screen these offspring earlier and more often? A change in psychiatric, pediatric, and school health practices is overdue.

Thoughtful Strategies Needed for Behavioral Symptoms in Dementia

Susan K. Schultz, M.D.

Antipsychotic medications for dementia-related symptoms such as aggression have been the focus of safety concerns for some time. As a result, a number of initiatives have sought to reduce prescribing to elderly patients, particularly in the nursing home setting. This scenario has occurred against the backdrop of dramatic increases in the burden of care with a growing dementia population. Consequently, there is an urgent need for new strategies to improve quality of life for patients suffering from Alzheimer's disease, vascular dementia, traumatic brain injury, and other neurodegenerative conditions. Clive Ballard and colleagues (6) provide new insight into this difficult problem through an innovative study that addresses the role of concurrent intervention strategies. Ballard et al. examined the effects of antipsychotic medication review and reduction among persons with dementia living in nursing facilities. Specifically, they measured whether the medication reduction occurred in the presence or absence of concurrent nonpharmacologic interventions, such as a social interaction and an exercise treatment plan. The study showed that in the absence of a concurrent nonpharmacologic intervention, antipsychotic reduction was more often associated with a deleterious outcome on ratings of neuropsychiatric symptoms compared with the presence of a concurrent social intervention. The beauty of this study is its relevance to real-world care delivery in dementia. It compels us to shift away from studies that ask "which treatment is better"—rather, it compels us to consider how to manage the interdependence of multiple safety interventions in the nursing home setting. Our care systems may find themselves in a place where responding to a policy directive regarding medication reduction results in poor patient outcomes if the setting is not able to manage in a compensatory way with social interventions. This leaves us with a challenging question: If nonpharmacologic interventions must be provided simultaneously with antipsychotic reductions to permit a positive outcome, how can resources be mobilized, created, or implemented to ensure a successful result for the patient?

Predicting Psychosis Onset in Individual Patients

Carol A. Tamminga, M.D.

Identification of risk features for the development of a psychotic illness, designed to be effective on an individual level, has reached a new milestone with the publication of the Cannon et al. article (7) by the North American Prodrome Longitudinal Study (NAPLS-2) investigators. The risk group was composed of individuals meeting criteria for clinical high risk for psychosis; even at this threshold, there is a conversion rate to psychosis of only 16% (in this study) or slightly higher (in other studies) over 2 years. These investigators used the large number of individuals who were thoroughly evaluated over time in the NAPLS-2 study to develop a "risk calculator" where unusual thoughts, poor verbal memory, slow processing speed, young age, and reduced social functioning were discovered to generate, together, a predictive factor score to indicate conversion to clinical psychosis. Given the importance of this tool, the risk calculator was replicated in an independent sample (8) (by Carrión et al., in collaboration with the Early Detection, Intervention, and Prevention of Psychosis Program) of young people at clinical high risk for psychosis and published alongside the Cannon article. Both studies show a high predictive ability for psychosis: .71 for Cannon et al. and .79 for Carrión et al. This level of predictive ability is not only medically important but will allow for the selection of individuals at highest risk for the study of psychosis biology and for the use of stronger treatment interventions in prepsychosis individuals.

From the *Residents' Journal*: Exploring Psychopathology in LGBT Refugees

Katherine Pier, M.D.

"Mental Health in LGBT Refugee Populations," published in July 2016 by Mark Messih (9), a resident at Drexel University, is emblematic of the bold voice of psychiatry trainees that the *American Journal of Psychiatry Residents' Journal* hopes to capture. The article emphasizes how safety, community, and access to mental health care are elusive for many individuals seeking asylum in the United States. During our recent humanitarian crisis, 3.8%−10% of individuals fleeing their countries identify as lesbian, gay, bisexual, or transgender (LGBT) upon resettling in the United States (9). Dr. Messih explores the ways that identity confusion, persecution, and trauma accumulate in LGBT refugees, increasing their vulnerability to mental illness over time. He describes "pre-flight" stressors prior to exile, with corrective rape and other forms of torture remaining pervasive in many of the countries from which LGBTs originate. Years of oppression, discrimination, and violence erode human attachment styles, which Messih identifies as "especially troubling given that patients who access community resources and group activity have better outcomes than patients in isolation" (9). Dr. Messih reminds providers treating this population to look for complex trauma symptoms, including somatization, identity disturbance, and disorganized attachment styles. He lends a nuanced perspective on the reasons our field might reconsider the diagnosis of disorders of extreme stress or complex posttraumatic stress disorder to classify the psychopathology that results from protracted physical, sexual, and emotional abuse. Until

psychiatrists can effectively detect and treat presentations of trauma in LGBT refugees, basic human rights, such as the freedom to express one's gender and sexual orientation, will remain out of reach. If the United States aspires to become home for these patients, we should not only prevent further detriment but also provide an environment that allows refugees to heal.

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