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### Journals covered in the issue:

- \* American Journal of Psychiatry (AJP)
- \* JAMA Psychiatry (JAMA-P)
- \* The Journal of Clinical Psychiatry (JCP)
- \* Lancet Psychiatry (LP)
- \* Journal of the American Academy of Child & Adolescent Psychiatry (JAACAP)
- \* British Journal of Psychiatry (BJP)
- \* Acta Psychiatrica Scandinavica (APS)

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### Highlights

- Hormonal contraceptive use in females was tied to a 2-3 times greater risk for suicide attempt and completed suicide in a Danish nationwide cohort study. (AJP)
- Adjunctive ketamine demonstrated a greater reduction in clinically significant suicidal ideation in depressed inpatients within 24 hours compared to midazolam in an RCT. (AJP)
- US epidemiological survey reveals anxious distress and mixed-features specifiers for major depression are associated with early onset, poor course, and suicidality. (JAMA-P)
- In a Finnish nationwide study of bipolar disorder, long-acting injectable antipsychotics were associated with 30% lower risk of rehospitalization compared with their equivalent oral counterparts. (JAMA-P)
- Swedish cohort study reveals associations of childhood infections with lower IQ and risk of adult non-affective psychosis. (JAMA-P)
- Rate of hippocampal atrophy progression in first-episode psychosis correlates with the duration of untreated psychosis. (JAMA-P)
- Meta-analysis shows that antidepressant response can be experienced up to 12 weeks of treatment, but in the majority of responders, response is achieved by 8 weeks. (JCP)
- Danish cohort study shows ECT is not associated with increased risk of incidental dementia in patients with affective disorders. (LP)
- SSRIs show superiority over SNRIs for the treatment of pediatric anxiety disorders in a meta-analysis of RCTs. (JAACAP)
- ADHD was a risk factor for suicide attempt and a predictor of repeated suicide attempts in a longitudinal cohort study from Taiwan. (BJP)
- In a Swedish cohort study, first suicide attempt is associated with a dramatic reduction in subsequent life expectancy. (APS)
- French study of new anxiolytic benzodiazepine users aged 50 and older shows four trajectories: occasional use (60%), early increasing use (10%), late increasing use (17%) and increasing/decreasing use (13%). (APS)

## **The American Journal of Psychiatry**

### **Volume 175, Issue 4**

#### **Association of Hormonal Contraception With Suicide Attempts and Suicides**

Skovlund, et al.

This prospective nationwide cohort study examined associations between hormonal contraceptive use and subsequent suicide attempt and suicide. Women from Denmark with no previous psychiatric diagnoses, antidepressant use, or suicide attempts who turned 15 during the study period (from 1996 to 2013) were followed. The study population (n= 475,802) had a mean age of 21 (SD 4), a mean follow-up period of 8.3 years, and 54% were current or recent hormonal contraceptive users. Overall, 6,999 first suicide attempts and 71 suicides were detected. Relative risk among current or recent hormonal contraceptive users compared to never users was 1.97 (95% CI= 1.85-2.10) for suicide attempt and 3.08 (95% CI=1.34-7.08) for suicide. Suicide attempt risks estimates were 1.91 (95% CI=1.79-2.03) for oral combined pills, 2.29 (95% CI=1.77-2.95) for oral progestin only pills, 2.58 (95% CI= 2.06-3.22) for vaginal ring, and 3.28 (95% CI=2.08-5.16) for the patch. Relative risk for suicide attempt increased rapidly, peaking after two months of contraceptive initiation.

#### **Ketamine for Rapid Reduction of Suicidal Thoughts in Major Depression: A Midazolam-Controlled Randomized Clinical Trial**

Grunebaum, et al.

Authors conducted this RCT to examine the effects of adjunctive ketamine versus midazolam infusion on clinically significant suicidal ideation in adult patients with major depressive disorder. Patients (n=80) who were voluntarily admitted to an inpatient psychiatric unit were randomly assigned to receive adjunctive IV racemic ketamine hydrochloride 0.5 mg/kg or midazolam 0.02 mg/kg in 100 mL NS over 40 minutes. Primary outcome measure was the score on the Scale for Suicidal Ideation (SSI) 24 hours post infusion. Adverse effects were monitored using the Systematic Assessment for Treatment Emergent Events-General Inquiry, Clinician-Administered Dissociative States Scale (CADSS), and the positive symptom subscale of the Brief Psychiatric Rating Scale (BPRS). SSI score after 1 day was 4.96 points lower for the ketamine group versus midazolam group (95% CI=2.33,7.59; Cohen's d=0.75). Overall, 55% of the ketamine group were responders (at least 50% reduction in SSI score) vs. 30% of those who received midazolam (OR=2.85, 95% CI=1.14, 7.15; NNT=4).

#### **Rates and Predictors of Conversion to Schizophrenia or Bipolar Disorder Following Substance-Induced Psychosis**

Starzer, et al.

This study aimed to identify the rate of patients diagnosed with substance induced psychosis who later develop schizophrenia and bipolar disorder and to identify risk factors associated with conversion. Patient information was extracted from the Danish Civil Registration System and included all persons

diagnosed with substance induced psychosis and matched comparison subjects from 1994 to 2014. Data from the Psychiatric Central Research Register and the National Patient Register were used to assess predictors of conversion and subjects were followed until first diagnosis with schizophrenia or bipolar disorder, death, emigration, or study end point. The resulting study population included 6,788 patients with an incident diagnosis of substance induced psychosis and 67,227 matched comparisons. At end point, 32.2% (95% CI=29.7-34.9) of patients with substance induced psychosis developed schizophrenia or bipolar disorder within 20 years. The highest conversion rate, 47.4% (95% CI= 42.7-52.3) was for cannabis-induced psychosis converting to schizophrenia or bipolar. Higher risk for conversion to schizophrenia was associated with younger age. Self-harm following substance induced psychosis was associated with a higher risk of conversion to either schizophrenia or bipolar disorder. Conversion for half of the cases to schizophrenia occurred so within 3.1 years versus bipolar disorder which half did so in 4.4 years.

## **JAMA Psychiatry**

### **Volume 75, Issue 4**

#### **Association of Hippocampal Atrophy With Duration of Untreated Psychosis and Molecular Biomarkers During Initial Antipsychotic Treatment of First-Episode Psychosis**

Goff, et al.

This longitudinal case-control study of 71 individuals with non-affective first-episode psychosis (FEP) before-and-after initiation of antipsychotic medications sought to better understand the relationship between hippocampal volume and duration of untreated psychosis. Hippocampus volume integrity was measured at study baseline. Compared with 73 age and sex-matched healthy controls, FEP group demonstrated greater hippocampal atrophy (lower median left hippocampus volume integrity). Furthermore, during roughly 8 weeks of antipsychotic treatment, left hippocampus volume integrity decreased in an annualized change of -4.1% in the FEP group. In comparison, the controls showed an increase of 0.13%. The rate of progression of left hippocampal atrophy was significantly correlated with the duration of untreated psychosis ( $r = -0.61$ ;  $P = .002$ ). Similar results were found for the right hippocampus volume integrity, which did not achieve statistical significance. Exploratory analyses revealed an association between left hippocampus volume integrity and markers of inflammation, oxidative stress, brain-derived neurotrophic factor, glial injury, and markers reflecting dopaminergic and glutamatergic transmission.

#### **Epidemiology of Adult DSM-5 Major Depressive Disorder and Its Specifiers in the United States**

Hasin D, et al.

Data analysis of the 2012-2013 National Epidemiologic Survey on Alcohol and Related Conditions III (NESARC-III), which consisted of in-person interviews with a representative sample of US noninstitutionalized civilian adults ( $\geq 18$  years) ( $n = 36,309$ ). The 12-month prevalence of MDD was 10.4% and the lifetime prevalence was 20.6%. Most lifetime MDD cases were moderate (39.7%) or severe

(49.5%). Odds of 12-month MDD was significantly lower in men, higher in younger adults and in those with low incomes. There were significant associations with other psychiatric disorders, such as anxiety disorders and substance use disorders. Functioning among those with severe MDD was approximately 1 SD below the national mean. Among 12.9% of those with lifetime MDD, all episodes occurred just after the death of someone close and lasted less than 2 months. The anxious/distressed specifier characterized 74.6% of MDD cases, and the mixed-features specifier characterized 15.5%. Controlling for severity, both specifiers were associated with early onset, poor course and functioning, and suicidality.

### **Real-world Effectiveness of Pharmacologic Treatments for the Prevention of Rehospitalization in a Finnish Nationwide Cohort of Patients With Bipolar Disorder**

Lähteenvuo M, et al

Finnish nationwide databases were used to conduct a population-based cohort study of patients hospitalized for bipolar disorder between 1987 and 2012 (N = 18,018; mean follow-up time, 7.2 years) to examine the risk of psychiatric and all-cause hospitalization. The primary analysis was within-individual analysis, in which each individual was used as his or her own control. A total of 9,721 patients (54.0%) had at least 1 psychiatric rehospitalization. The medications associated with the lowest risk of psychiatric rehospitalization were lithium carbonate (HR 0.67), gabapentin (HR 0.58), and perphenazine long-acting injection (HR 0.60). Regarding all-cause hospitalization, lithium (HR 0.71) was associated with the lowest risk. Quetiapine showed very modest, if any, effectiveness in reducing risk of psychiatric rehospitalization (HR 0.92 [95% CI, 0.85-0.98]) and risk of all-cause hospitalization (HR 0.93 [95% CI, 0.88-0.98]). Long-acting injection antipsychotics were associated with 30% lower risk of rehospitalization compared with their equivalent oral counterparts (risk of psychiatric rehospitalization: HR 0.70; risk of all-cause hospitalization: HR 0.70).

### **Association of Childhood Infection With IQ and Adult Nonaffective Psychosis in Swedish Men**

Khandaker G, et al.

Authors analyzed data from a population-based longitudinal cohort study which included all Swedish men – born between 1973 and 1992, followed until the end of 2010 – who had been hospitalized with infection and nonaffective psychosis (n = 647,515 participants analyzed). Infections at birth to age 4 years, but not 5 to 13 years, were associated with a modest increased risk of nonaffective psychosis. Infections at birth to age 1 to 9 years, but not 10 to 13 years, were associated with lower IQ. There was a linear association between lower premorbid IQ and adult nonaffective psychosis, which persisted after excluding prodromal cases (adjusted hazard ratio per 1-point increase in IQ: 0.976). The infection-psychosis and IQ-psychosis associations were similar in the general population and in full-sibling pairs discordant for exposure. Childhood infection had a greater association with nonaffective psychosis risk in the lower IQ range.

## **The Journal of Clinical Psychiatry**

### **Volume 79, Issue 3**

#### **Executive Function Predicts Antidepressant Treatment Noncompletion in Late-Life Depression**

Cristancho, et al.

This prospective study sought to evaluate the association of executive function (EF) and nonremission and noncompletion of antidepressant pharmacotherapy among older adults (n=468) with major depressive episodes (DSM-IV). Participants received 12 weeks of venlafaxine extended release with the goal of remission. Baseline EF and other cognitive variables were assessed via Delis-Kaplan Executive Function System subtests and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Among those evaluated, 96 (21%) failed to complete the treatment trial, 191 (41%) completed and remitted, and 181 (39%) completed and did not remit. Some EFs (set-shifting and semantic fluency) and cognitive variables including attention, immediate memory, visuospatial ability and global cognition predicted treatment noncompletion. No cognitive variables predicted nonremission. Semantic fluency (P=0.003), comorbid medical burden (P < .001), and early nonadherence (P<.001) were significant predictors of treatment noncompletion.

#### **Effects of Antipsychotics on Secular Mortality Trends in Patients With Alzheimer's Disease**

Nielsen, et al.

A 12-year nationwide, retrospective cohort study investigated changes in mortality rates between patients with Alzheimer's disease (AD) and the general population, as well as changes in antipsychotic drug treatment and the association between treatment and mortality. Among 32,001 Danish patients, antipsychotic dosages from dementia diagnosis until end of study were calculated and categorized according to WHO Defined Daily Doses (DDD). During the study period, an increasing trend was found in median survival time without decline in standardized mortality ratios. A decline was noted in proportion of patients with incident AD exposed to antipsychotic drugs, as well as in mean annual cumulative DDDs. Current exposure to antipsychotic drugs was associated with increased mortality. However, hazard ratios declined during the study period from 2.24 (95% CI, 2.07-2.43) in 2000-2002 to 1.24 (95% CI, 1.09-1.41) in 2009-2011, with p values <0.001.

#### **Trajectories of Acute Antidepressant Efficacy: How Long to Wait for Response? A Systematic Review and Meta-Analysis of Long-Term, Placebo-Controlled Acute Treatment Trials**

Henssler, et al.

The extant literature was reviewed to evaluate response to antidepressant pharmacotherapy. MEDLINE, Embase, PsycINFO, and CENTRAL databases were searched using terms for depressive or affective disorders, individual drug names, and placebo to identify double-blind, randomized studies with continuous outcome reporting from 4 weeks to 12 weeks, comparing antidepressant monotherapy to placebo in adult patients suffering from acute depressive disorder. Authors screened 6,043 articles and

selected 9 studies including 3,466 patients. Altogether 21.6% of previously nonresponsive patients achieved response with ongoing antidepressant treatment between weeks 5 and 8, and 9.9% (7.5%, 12.7%), between weeks 9 and 12. Probability of response while taking placebo was 13.0% between weeks 5 and 8 and 2.4% between weeks 9 and 12. Difference in the probability of response between antidepressant and placebo translated into a number needed to treat of 11 after 4 weeks and 17 after 8 weeks.

## **The Lancet Psychiatry**

### **Volume 5, Issue 4**

#### **Five novel loci associated with antipsychotic treatment response in patients with schizophrenia: a genome-wide association study**

Hao Yu Et al.

This genome-wide association study was carried out to gain a superior understanding of genetic factors associated with antipsychotic treatment response. In the combined sample of the discovery and validation cohorts, researchers identified five novel loci showing genome-wide significant associations with general antipsychotic treatment response (rs72790443, rs1471786, rs9291547, rs12711680, and rs6444970). In antipsychotic-specific groups, after the combination of results from both samples, the rs2239063 SNP was associated with treatment response to olanzapine ( $p=1.10 \times 10^{-8}$ ), rs16921385 in SLC1A1 was associated with treatment response to risperidone ( $p=4.40 \times 10^{-8}$ ), and rs17022006 in CNTN4 was associated with treatment response to aripiprazole ( $p=2.58 \times 10^{-8}$ ).

#### **Does depression treatment improve the survival of depressed patients with cancer? A long-term follow-up of participants in the SMaRT Oncology-2 and 3 trials**

Mulick Et al.

In the SMaRT Oncology-2 (good prognosis cancers) and SMaRT Oncology-3 (lung cancer, a poor prognosis cancer) trials, the researchers had found that a depression treatment programme, Depression Care for People with Cancer (DCPC), was effective in reducing comorbid major depression. In this analytical study, the researchers aimed to identify if depression care also had effect on survival. The researchers followed up SMaRT Oncology-2 (N=500) and SMaRT Oncology-3 (N=142) participants for a median of 5 years and 1 year, respectively. 27% of 500 SMaRT Oncology-2 participants and 80% of 142 SMaRT Oncology-3 participants died within this period. No significant effect was found of DCPC on survival in the total follow-up period for either SMaRT Oncology 2 or SMaRT Oncology-3.

#### **Electroconvulsive therapy and risk of dementia in patients with affective disorders: a cohort study**

Osler Et al

This cohort study from Denmark aimed to examine the association between ECT and risk of subsequent dementia in patients with first-time hospital diagnosis of affective disorder. During the median follow-up

of 4.9 years and 872,874 person-years, 3.6% of the patients treated with ECT developed dementia, whereas of patients not treated with ECT 3.1% developed dementia. In patients younger than 70 years, ECT was not associated with a risk of dementia compared with age-matched controls. In patients aged 70 years and older, ECT was associated with a decreased rate of dementia (0.68,  $p < 0.0001$ ), however, after correcting for the potential effect of patient selection or competing mortality, ECT was not associated with risk of incidental dementia in patients with affective disorders. The findings from this study support the continued use of ECT in patients with severe episodes of mood disorders, including geriatric subjects.

## **Journal of the American Academy of Child and Adolescent Psychiatry**

### **Volume 57, Issue 4**

#### **The Impact of Antidepressant Dose and Class on Treatment Response in Pediatric Anxiety Disorders: A Meta-Analysis**

Strawn, et al.

Authors conducted a meta-analysis to determine the trajectory and magnitude of SSRI/SNRI response in pediatric anxiety disorders. Data were extracted from randomized, parallel group, placebo-controlled trials of SSRIs and SNRIs in pediatric anxiety disorders (generalized, separation, and/or social anxiety disorders). Change in symptom severity was evaluated as a function of time, class and, for SSRIs, standardized dose. Data from 9 trials (SSRIs:  $n = 5$ ; SNRIs,  $n = 4$ ) evaluating 7 medications in 1,673 youth was included. Significant treatment effects emerged within 2 weeks of beginning treatment and by week 6, clinically significant differences emerged ( $p = .001$ , approximate Cohen's  $d = 0.44$ ). Compared to SNRIs, SSRIs resulted in significantly greater improvement, and this advantage remained statistically significant through week 2 to 12. Improvement occurred earlier with high-dose SSRI treatment (week 2) compared to low-dose treatment (week 10), but SSRI dose did not have an impact on overall response trajectory.

## **The British Journal of Psychiatry**

### **Volume 212, Issues 4**

#### **Risk of suicide attempts in adolescents and young adults with attention-deficit hyperactivity disorder: a nationwide longitudinal study**

Huang, et al.

Authors sought to evaluate the risk of suicide attempt in adolescents and young adults with ADHD using a nationwide, population-based insurance claims database in Taiwan. The longitudinal cohort study enrolled 20,574 adolescents and young adults with ADHD and 61,722 age- and gender-matched controls between 2001 and 2009. Any suicide attempt was identified from enrolment to 31 December 2011. The association between ADHD medications and the likelihood of suicide attempt was assessed. ADHD was an independent risk factor for any suicide attempt (hazard ratio = 3.84) and repeated suicide attempts

(hazard ratio = 6.52). Long-term methylphenidate treatment was associated with a significantly decreased risk of repeated suicide attempts in men (hazard ratio = 0.46).

### **Adolescent cannabis use, baseline prodromal symptoms and the risk of psychosis**

Mustonen, et al.

Aim of this study was to examine the association between cannabis use in adolescence and the risk of psychosis after adjustment for prodromal symptoms and other potential confounders. The sample (n = 6534) was composed of the prospective general population-based Northern Finland Birth Cohort of 1986. Information on prodromal symptoms of psychosis and cannabis use was collected using questionnaires at age 15–16 years. Participants were followed up for ICD-10 psychotic disorders until age 30 years using nationwide registers. The risk of psychosis was elevated in individuals who had tried cannabis 5 times or more (hazard ratio = 6.5). The association remained statistically significant even when adjusted for prodromal symptoms, other substance use and parental psychosis (HR= 3.0).

## **Acta Psychiatrica Scandinavica**

### **Volume 137, Issue 4**

#### **Trajectory analysis of anxiolytic dispensing over 10 years among new users aged 50 and older**

Verger, et al.

Using French national health records from 2006 through 2015, treatment patterns among new anxiolytic benzodiazepine users aged 50 and older demonstrated four trajectories: occasional use (60% of users), early increasing use (10% users), late increasing use (17% users) and increasing/decreasing use (13% users). In women, prevalence of occasional use decreased with age, but this was not observed in men. Duration of treatment episodes and doses differed between trajectories. These trajectories indicated that each trajectory may face different difficulties in quitting or reducing consumption, requiring customized approaches.

#### **Life expectancy after the first suicide attempt**

Jokinen, et al.

Using the nationwide cohort of 187,894 Swedish persons 18 years of age or older who were hospitalized for a first suicide attempt between 1971 and 2019, this study attempted to assess excess mortality as compared to the general population. Analysis of these records shows that men with a first suicide attempt at age 20 experienced a reduction in life span of 18 years, while the reduction for men with a first suicide attempt at age 50 was 10 years. For women, the life expectancy was shortened for those with first suicide attempt at age 20 by 11 years and for those with first suicide attempt at age 50 by 8 years. The gender difference in shortened life expectancy resolved by age 70. Suicide deaths explained approximately 20% of total mortality within the first 10 years of the attempt and 5% within the first 40 years of the attempt.