Department of Psychiatry
RESEARCH WATCH

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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)

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Highlights

- A systematic review and meta-analysis showed greater patient insight was associated with better psychotherapy outcomes across disorders and psychotherapy types. (AJP)
- A new model utilizing electronic medical record data effectively predicts suicide attempts and suicide deaths in the 90 days following a mental health diagnosis. (AJP)
- A total population cohort study shows decreased rates of suicidal behavior, unintentional substance overdose, and criminal activity with use of methadone, naltrexone, and buprenorphine, respectively. (AJP)
- An RCT suggests that peer comparison letters sent to prescribers substantially reduced quetiapine prescribing, with no evidence of negative effects on patients. (JAMA-P)
- A meta-analysis demonstrates that antenatal anxiety is associated with multiple adverse perinatal outcomes. (JCP)
- A retrospective comparative effectiveness study shows equivalence among evidence-based medications for treatment of PTSD but significant benefit to concurrent evidence-based psychotherapy. (JCP)
- Results of a three-phase switching study suggest benefit to early use of clozapine after non-response to a single antipsychotic trial in first-episode schizophrenia. (LP)
- A cross-sectional multimodal imaging study shows an inverse relationship between striatal dopamine synthesis capacity and psychosis. (LP)
- A retrospective-prospective cohort study of first suicide attempts in youth, showed that three-fourths of completed youth suicides occurring on index attempts with 85% of these involving a firearm. (JAACAP)

Association Between Insight and Outcome of Psychotherapy: Systematic Review and Meta-Analysis

Jennissen, et al.

This systematic review and meta-analysis examined the association between patient insight and psychotherapy outcome across a range of treatment modalities. Insight was defined as patients' understanding of associations between past and present experiences, typical relationship patterns, and the relation between interpersonal challenges, emotional experience, and psychological symptoms. From 13, 849 initially identified abstracts, authors assessed 261 full manuscripts and extracted 23 independent effect sizes. Random-effects meta-analysis assessed the magnitude of the insight-outcome relationship. Among the 22 final studies, twelve employed psychodynamic treatments and 11 were other treatments, such as cognitive-behavioral, emotion-focused, client-centered, and interpersonal psychotherapy. The studies used 27 different outcome measures and 18 different insight measures with a majority of measures being clinician-rated. Overall, there existed a significant, moderate correlation (r=0.31) between insight and treatment outcome.

Predicting Suicide Attempts and Suicide Deaths Following Outpatient Visits Using Electronic Health Records

Simon, et al.

Authors developed and validated a model utilizing electronic health data to predict suicide attempts and deaths following an outpatient visit. More than 2.9 million patients made 10,275,853 specialty mental health visits and 9,685,206 primary care visits with mental health diagnoses between Jan. 1, 2009, and June 30, 2015. Health system records and death certificate data identified suicide attempts (N=24,133) and deaths (N=1,240) over 90 days following each visit. Authors identified 313 demographic and clinical characteristics as potential predictors. Logistic regression models predicting suicide attempt and death were developed in a random sample of 65% of the visits and validated the remaining 35%. Mental health specialty visits with risk scores in the top 5% accounted for 43% of subsequent suicide attempts and 48% of deaths. Primary care visits with scores in the top 5% accounted for 48% of subsequent suicide attempts and 43% of deaths. The top 1% of individuals identified as "high risk" by the model were nearly 20 times more likely to have a suicide attempt or death than average. This group constituted between 10% and 15% of all eventual suicide deaths or attempts.

Medications for Alcohol and Opioid Use Disorders and Risk of Suicidal Behavior, Accidental Overdoses, and Crime

Molero, et al.

Using data from Swedish population-based registries between 2005 and 2013, authors conducted a total population cohort study in which they examined individuals who were treated with either acamprosate

or oral naltrexone for alcohol use disorder or with buprenorphine or methadone for opioid use disorder (N=21,281). Rates of suicidal behavior, unintentional substance overdose, and criminal activity during periods of medication adherence were compared with periods in which medications were not prescribed or taken. No significant associations with any of the primary outcomes were found for acamprosate. For naltrexone, there was a reduction in the hazard ratio for accidental overdoses during periods of treatment relative to periods of non-treatment (HR=0.82, 95% CI=0.70, 0.96). Buprenorphine was associated with reduced arrest rates for all crime categories (i.e., violent, nonviolent, and substance-related), as well as reduction in accidental overdoses (HR=0.75, 95% CI=0.60, 0.93). For methadone, there were significant reductions in the rate of suicidal behaviors (HR=0.60, 95% CI=0.40–0.88) and reductions in all crime. There was an increased risk for accidental overdoses among individuals taking methadone (HR=1.25, 95% CI=1.13, 1.38). Patients who took naltrexone or acamprosate, as well as a benzodiazepine had increased suicidal behavior.

Individual Treatment of Posttraumatic Stress Disorder Using Mantram Repetition: A Randomized Clinical Trial
Bormann, et al.

This randomized controlled study of 173 veterans with military-related PTSD compared present-centered therapy and individually delivered "mantram" (sacred word) repetition therapy – both non-trauma-focused interventions. Authors report that mantram repetition therapy is associated with greater improvement in symptoms on the Clinician-Administered PTSD Scale (CAPS) and the insomnia severity index at posttreatment and 2-month follow-up assessments as compared with present-centered therapy (effect sizes [Cohen's d], 0.49 at posttreatment assessment and 0.46 at 2-month follow-up). Approximately 75% of participants in the mantram group had greater than a 10-point decrease on the CAPS; at the posttreatment assessment, 48% no longer met criteria for PTSD. At 2-month follow-up, 59% no longer met criteria (p<0.04).

JAMA Psychiatry
Volume 75, Issue 10

Functional Connectivities in the Brain That Mediate the Association Between Depressive Problems and Sleep Quality
Cheng, et al.

This study of 1,017 participants from the Human Connectome Project, from the general population of the United States aged 22-35 years, sought to identify the brain areas that mediate the association of depressive symptoms with poor sleep quality. Using the Achenbach Adult Self-Report for Ages 18-59, a survey of self-reported sleep quality and functional magnetic resonance imaging (fMRI), this study determined that the Depressive Problems score was positively correlated with poor sleep quality. Of the 166 functional connectivity links associated with sleep, 39 were also associated with the Depressive Problems score including the lateral orbitofrontal cortex, dorsolateral prefrontal cortex, anterior and

posterior cingulate cortices, insula, parahippocampal gyrus, hippocampus, amygdala, temporal cortex, and precuneus. These finding imply that increase functional connectivity between these regions may be the neural basis for the association between depression and poor sleep quality.

Effect of Peer Comparison Letters for High-Volume Primary Care Prescribers of Quetiapine in Older and Disabled Adults: A Randomized Clinical Trial
Sacarny, et al.

This randomized clinical trial targeted the 5,055 highest-volume primary care prescribers of quetiapine for the Medicare population in 2013 and 2014 and randomized them to either receive a placebo letter or three peer-comparison letters that stated their quetiapine prescribing was high relative to their peers and was under review by Medicare. Over nine months, the treatment arm supplied 11.1% fewer quetiapine days per prescriber than the control arm (P<0.001) which persisted through two years. At the patient level, individuals in the treatment arm received fewer days of quetiapine, with a larger decreased among patients with low-value indications without evidence of substitution to other antipsychotics, indicating that peer comparison letters caused substantial and durable reductions in quetiapine prescribing with no evidence of negative effects on patients.

Risk Factors Associated With Attempted Suicide Among US Army Soldiers Without a History of Mental Health Diagnosis
Ursano, et al.

In this retrospective longitudinal cohort study using administrative date from the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS), person-month records were identified for all active-duty Regular Army enlisted soldiers with a medically-documented suicide attempt between 2004 and 2009, and compared this with a sample of control person-months. Of the enlisted soldiers with a documented suicide attempt, 36.3% did not have a previous mental health diagnosis. Among that 36.3%, female sex, less than high school education, first year of service, previously deployed, promotion delayed 2 months or less, past-year demotion, 8 or more outpatient physical health care visits within the prior 2 months, past-month injury-related outpatient and inpatient health care visits, prior combat injury, victimization by minor violent crime, perpetration of major violent crime, and family violence were all associated with suicide attempts. These factors were also associated with suicide attempts in those soldiers with a prior mental health diagnosis, although the strengths of associations varied. Based on this study, administrative records may assist in identifying soldiers at risk.

Evaluation of the Concurrent Trajectories of Cardiometabolic Risk Factors in the 14 Years Before Dementia
Wagner, et al.

This case-control study of a French population-based cohort of persons 65 years of age and older included 6 home visits with neuropsychological testing between 1999 and 2014. Dementia cases were matched by sex, age, and educational level with controls. The dementia cases presented a faster decline in body mass

index (BMI), slower increase of systolic blood pressure, and constantly lower diastolic blood pressure. Mean fasting glucose values, however, were higher among those cases with dementia. There were no significant case-control differences in blood lipid levels. Thus, this study indicates that decline of BMI may reflect early preclinical changes associated with dementia while higher blood glucose levels may constitute a risk factor for dementia in this population.

The Journal of Clinical Psychiatry
Volume 79, Issue 5

Maternal Anxiety During Pregnancy and the Association With Adverse Perinatal Outcomes: Systematic Review and Meta-Analysis
Grigoriadis, et al.

This systematic review and meta-analysis examined the association between maternal antenatal anxiety (AA) and a range of perinatal outcomes. Six databases were searched through May 31, 2016 using controlled vocabulary and key-words. Of 1,458 abstracts reviewed, 306 articles were retrieved, and 29 articles were included. Random-effects models were utilized for outcomes (≥3 studies). Subanalyses examined potential effect moderators including study quality and diagnostic versus self-reported anxiety among others. Antenatal anxiety was associated with increased odds for preterm birth (pooled odds ratio [OR]=1.54; 95% CI, 1.39 to 1.70, 16 studies) and spontaneous preterm birth (OR=1.41; 95% CI, 1.13 to 1.75), lower mean birth weight, increased odds for low birth weight, earlier gestational age (mean difference = −0.13 wk; 95% CI, −0.22 to −0.04 wk), increased odds for being small for gestational age (OR=1.48; 95% CI, 1.26 to 1.74), and smaller head circumference (mean difference = −0.25 cm; 95% CI, −0.45 to −0.06 cm). Heterogeneity between studies was not significant for most outcomes. Subanalyses for birth weight found women with diagnosed anxiety had infants with significantly lower birth weight (P<.03) compared to those identified with rating scales (although both subanalyses were significant [P<.01]). Associations between anxiety and preeclampsia, cesarean delivery, and Apgar scores were nonsignificant.

A Retrospective Comparative Effectiveness Study of Medications for Posttraumatic Stress Disorder in Routine Practice
Shiner, et al.

Authors conducted a retrospective comparison effectiveness study of fluoxetine, paroxetine, sertraline, topiramate, and venlafaxine for treatment of posttraumatic stress disorder (PTSD). Utilizing electronic medical record, data, 2,931 Department of Veterans Affairs outpatients were identified as initiating treatment for PTSD between 2004 and 2013. Included patients received with one of the five target medications at adequate dose and duration, combined with baseline and endpoint PTSD Checklist (PCL) measurements. Comparisons were made between continuous changes on total PCL score, symptom cluster scores, and sleep items, as well as categorial changes including reliable improvement and loss of PTSD diagnosis, using weighted regression analysis. Patients improved by a mean of 5-6 points on the PCL

over approximately 6 months of treatment. While half of patients had a reliable improvement of 5 points or more on the PCL, less than a fifth achieved loss of diagnosis. There were no differences between medications. The only significant predictor (P<0.001) of loss of PTSD diagnosis was concurrent treatment with evidence-based pharmacotherapy.

The Lancet Psychiatry
Volume 5, Issue 10

Amisulpride and olanzapine followed by open-label treatment with clozapine in first-episode schizophrenia and schizophreniform disorder (OPTiMiSE): a three-phase switching study
Kahn, et al.

A three-phase study performed in 27 medical centers sought to evaluate the benefit of switching antipsychotics versus early use of clozapine in first-episode schizophrenia. Patients who met DSM-IV criteria for schizophrenia, schizophreniform disorder, or schizoaffective disorder were treated for 4 weeks with up to 800 mg/day amisulpride orally in an open-label design. Patients who did not meet symptomatic remission criteria at 4 weeks were assigned randomly to continue amisulpride or switch to olanzapine (≤20 mg/day) during a 6-week double-blind phase (phase 2). Patients who were not in remission at 10 weeks were given clozapine (≤900 mg/day) for an additional 12 weeks in an open-label design (phase 3). The primary outcome was the number of patients who achieved symptomatic remission at the final visits of phases 1, 2, and 3, measured by intention-to-treat analysis. Among 446 patients, 371 completed amisulpride treatment with 250 (56%) achieving remission after phase 1. Patients not in remission (N=93) continued to the 6-week double-blind switching trial, with 72 (72%) completing the trial (39 on olanzapine, 33 on amisulpride); 15 (45%) on amisulpride versus 17 (44%) on olanzapine achieved remission (p=0.87). Of 40 patients not in remission after 10 weeks of treatment, 28 (70%) started on clozapine; 18 (64%) patients completed the 12-week treatment, and five (28%) achieved remission. Authors suggest that the current guideline that clozapine should only be used after patients fail treatment with two different antipsychotics should be reexamined.

The relationship between cortical glutamate and striatal dopamine in first-episode psychosis: a cross-sectional multimodal PET and magnetic resonance spectroscopy imaging study
Jauhar, et al.

A cross-sectional multimodal imaging study evaluated the relationship between cortical glutamate concentrations and striatal dopamine synthesis capacity, and psychotic symptoms. A total of 28 individuals with first-episode psychosis and 20 healthy controls underwent ^{18}F-DOPA PET (measuring striatal dopamine synthesis capacity), and proton magnetic resonance spectroscopy (measuring anterior cingulate cortex glutamate concentrations). Symptoms were measured using the Positive and Negative Syndrome Scale (PANSS). The primary endpoint was the relationship between anterior cingulate cortex glutamate concentrations and striatal dopamine synthesis capacity in individuals with their first episode of psychosis as shown by imaging, examined by linear regression. Glutamate concentrations showed a

significant inverse relationship with striatal dopamine synthesis capacity in patients with psychosis. This relationship remained significant after the addition of age, gender, ethnicity, and medication status to the model (p=0.015). In healthy controls, there was no significant relationship between dopamine and glutamate measures. PANSS positive psychotic symptoms were positively associated with striatal dopamine synthesis capacity and showed an inverse relationship with anterior cingulate glutamate concentrations. No relationships were seen with negative symptoms (positive symptoms, mean [SD] −18.4 (6.6) negative symptoms, mean [SD] −15.4 [6.1]).

Trends in attention-deficit hyperactivity disorder medication use: a retrospective observational study using population-based databases
Raman, et al.

Authors conducted a retrospective, observational study using population-based databases from 13 countries and one Special Administrative Region (SAR) to determine regional and national prevalences of ADHD medication use in children and adults, with a specific focus on time trends in ADHD medication prevalence. Study populations consisted of 154.5 million individuals aged 3 years or older between Jan 1, 2001, and Dec 31, 2015. ADHD medication use prevalence in 2010 (in children aged 3–18 years) varied between 0.27% and 6.69% in the countries and SAR assessed (0.95% in Asia and Australia, 4.48% in North America, 1.95% in northern Europe, and 0.70% in western Europe). The prevalence of ADHD medication use among children increased over time in all countries and regions, and the absolute increase per year ranged from 0.02% to 0.26%. Among adults aged 19 years or older, the prevalence of any ADHD medication use in 2010 varied between 0.003% and 1.48% (0.05% in Asia and Australia, 1.42% in North America, 0.47% in northern Europe, and 0.03% in western Europe). The absolute increase in ADHD medication use prevalence per year ranged from 0.0006% to 0.12%. Methylphenidate was the most commonly used ADHD medication in most countries.

Journal of the American Academy of Child and Adolescent Psychiatry
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Prevalence and Characteristics of Self-Harm in Adolescents: Meta-Analysis of Community-Based Studies 1990-2015
Gillies, et al.

This meta-analysis sought to estimate the prevalence and characteristics of all self-harm (SH) in adolescents (ages 12-18). International cohort and cross-sectional studies that examined deliberate self-harm (DSH) and nonsuicidal self-injury (NSSI) between 1990-2015 were included in the analysis. Of >597,548 participants, 51.09% were female, with a mean age of 15.41 years. Lifetime prevalence of SH was 16.9% with RR for female vs. male of 1.72. Subset analysis yielded DSH rates of 11.4% and NSSI rates of 22.9% at a mean start age of 12.81 years. The most common form of and reason for SH was cutting and "to obtain relief from feelings or thoughts," respectively. The RR of SI in adolescents who engaged in SH

vs. those who did not was 4.97; RR of reported suicide attempts was 9.14 and not significantly different between DSH vs. NSSI. More frequent SH was correlated with increased RR of suicide attempt.

Rethinking Lethality in Youth Suicide Attempts: First Suicide Attempt Outcomes in Youth Ages 10 to 24
McKean, et al.

The authors of this retrospective-prospective cohort study assessed lethality and methodology of suicide attempt in youth ages 10-24 beginning at the time of their first medically recorded suicide attempt (index attempt [IA]). Of 813 youth identified (males, N=258, females N=555), 29 died from suicide, with 71.4% of completed suicides occurring at the IA at a mean age of 19.3 years (SD 2.9). The most youth IAs (53.1%) occurred between ages 15-19, however the 20-24-year-old group completed suicide at the highest rate. Male youth disproportionately contributed to IA deaths (n = 23/29; OR 6.6, 95% CI 1.394-34.716, p=.018). Eighty-five percent of all IA deaths involved firearms. Hospitalizations after IA did not achieve statistical significance for decreasing risk of subsequent death by suicide.

A Risk Calculator to Predict the Individual Risk of Conversion From Subthreshold Bipolar Symptoms to Bipolar Disorder I or II in Youth
Birmaher, et al.

This prospective cohort study utilized data from the longitudinal Course and Outcome of Bipolar Youth (COBY) study to develop a 5-year individual risk calculator of conversion from BP-NOS to BP-I/II. A total of 140 youths with BP-NOS were evaluated at a median of every 7 months over 11.5 years. Seventy-five (53.6%) converted to BP-I (N=27) or BP-II (N=48). Risk of conversion increased with age but was decreased in boys and African American patients. The statistically significant risk factors identified in the calculator were early onset of BP-NOS, family history of mania, and mood lability. The risk calculator showed excellent consistency, good discrimination (area under the curve 0.71, CI 0.67-0.74), and 75% externally validity in an independent sample. Unlike other studies, SES, comorbid disorders, family history of unipolar depression, and exposure to negative events did not influence risk.