



Department of Psychiatry
RESEARCH WATCH



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Research Watch is an initiative by the residents of University Hospitals/ Case Western Reserve University; it aims to inform psychiatry residents and faculty of notable articles published in prominent research journals.

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

- FDA's reduction of citalopram's max dose to 40 mg/day appears to have been associated with increase in rates of hospitalization for patients previously treated with a higher dose. (AJP)
- Continued treatment with escitalopram for body dysmorphic disorder for 6 months beyond acute treatment delays time to relapse. (AJP)
- Adjunctive antidepressant use in schizophrenia appears to have small but beneficial effect on depressive and negative symptoms. (AJP)
- Danish population study reports association between hospitalization with infection and the risk of death by suicide. (JAMA-P)
- RCT shows adjunctive raloxifene reduces illness severity and increases the probability of a clinical response in women with refractory schizophrenia. (JAMA-P)
- A large cohort study shows no increased risk of congenital malformations with first-trimester antipsychotic exposure, with a possible exception of risperidone. (JAMA-P)
- In a 15-year observational study from Germany open psychiatric wards did not have increased rates of suicide, suicide attempts and absconding compared to locked wards. (LP)
- Mexican field study suggests that distress and dysfunction associated with transgender identity may be related to experiences of social rejection and violence rather than being inherent features of transgender identity. (LP)
- A large epidemiological study reveals that while PTSD psychotherapy trials have good generalizability to community population, majority of PTSD patients in routine clinical practice would be excluded in a typical PTSD pharmacological trial. (JCP)
- Study suggests that residual subsyndromal depressive symptoms are a continuation of major depressive episode, and should not be considered equivalent to asymptomatic recovery. (JCP)
- Prenatal maternal smoking was associated with increased risk of development of Tourette's & chronic tic disorder in a large Danish cohort. (JAACAP)

The American Journal of Psychiatry

Volume 173, Issue 9

Efficacy and Safety of Antidepressants Added to Antipsychotics for Schizophrenia: A Systematic Review and Meta-analysis

Helfer, et al.

This review and meta-analysis included 82 randomized controlled trials of any adjunct antidepressant treatment compared to placebo or no-treatment in patients with schizophrenia. Results showed adjunct antidepressants were more efficacious than controls for depressive symptoms and negative symptoms, as well as overall symptoms, positive symptoms and overall quality of life, with generally small effect sizes. Additionally, no differences were found between the two groups for exacerbation of psychosis, premature discontinuation, or adverse events.

Pharmacotherapy Relapse Prevention in Body Dysmorphic Disorder: A Double-Blind Placebo-Controlled Trial

Phillips, et al.

The authors present findings from the first prospective relapse study in body dysmorphic disorder. In the first phase of this trial, 100 patients were treated with open-label escitalopram for 14 weeks with 81.1% response. In phase 2, 58 responders were randomized to either double-blind continuation therapy with escitalopram or switch to placebo. Treatment with escitalopram significantly increased time to relapse versus placebo and decreased symptom severity during the six-month continuation phase. No significant differences were shown between groups in body dysmorphic disorder severity or insight, depressive symptoms, psychosocial function or quality of life.

Outcomes of Citalopram Dosage Risk Mitigation in a Veteran Population

Rector, et al.

This retrospective study evaluated an at-risk cohort of 35,848 veterans who had citalopram prescriptions for 64mg/day on average. Six months after the FDA issued guidance discouraging citalopram dosages of more than 40mg/day due to risk for dosage-dependent QT interval prolongation, 60% of the cohort filled prescriptions for ≤ 40 mg/day. All-cause hospitalizations or deaths were found to significantly increase after dosage reductions, as well as hospitalizations due to depression. However, mortality and hospitalizations due to arrhythmias did not decline.

Effect of Marriage on Risk for Onset of Alcohol Use Disorder: A Longitudinal and Co-Relative Analysis in a Swedish National Sample

Kendler, et al.

The association between marital status and risk for alcohol use disorder was assessed in a population-based cohort using longitudinal time-dependent survival and co-relative designs. The study showed that a first marriage was associated with a substantial decline in risk for onset of alcohol use disorder in men and women. The association was slightly stronger if a spouse did not have a lifetime alcohol use disorder, and risk was increased if a spouse did have an alcohol use disorder. In both sexes, the protective effect was stronger in individuals with than without a family history of alcohol use disorder.

Performance of DSM-5 Persistent Complex Bereavement Disorder Criteria in a Community Sample of Bereaved Military Family Members

Cozza, et al.

This study examined the accuracy of DSM-5 proposed criteria for persistent complex bereavement disorder as well as prolonged grief disorder and complicated grief. Criteria sets varied in their ability to identify clinical cases. The DSM-5 persistent complex bereavement disorder criteria accurately exclude nonclinical, normative grief, but also exclude nearly half of clinical cases. Complicated grief criteria in comparison exclude nonclinical cases while identifying more than 90% of clinical cases, suggesting it is more accurate than the current DSM-5 diagnostic criteria for persistent complex bereavement disorder.

JAMA Psychiatry

Volume 73, Issue 9

Effect of Adjunctive Raloxifene Therapy on Severity of Refractory Schizophrenia in Women: A Randomized Clinical Trial

Kulkarni, et al.

This 12-week, double-blind, placebo-controlled, randomized clinical trial sought to determine whether adjunctive use of the selective estrogen receptor modulator, raloxifene hydrochloride, could reduce illness severity in women with refractory schizophrenia. At doses of 120mg/d, raloxifene produced a greater reduction in the PANSS total score relative to placebo and an increased probability of a clinical response in women with refractory schizophrenia. No statistically significant treatment effect on PANSS positive symptoms scores was seen in patients who completed the full 12-week trial. Change in mood, cognition, and reproductive hormone levels and the rate of adverse events did not differ between groups.

Age-Dependent Effects of Methylphenidate on the Human Dopaminergic System in Young vs Adult Patients With Attention-Deficit/Hyperactivity Disorder - A Randomized Clinical Trial

Schranter, et al.

In this randomized, double-blind, placebo-controlled trial of 99 male patients with attention-deficit/hyperactivity disorder, sixteen weeks of methylphenidate treatment increased the cerebral blood flow response to methylphenidate within the thalamus of children aged 10 to 12 but not in older children

or adults or in the placebo group. In the striatum, the methylphenidate condition differed significantly from placebo in children but not in adults.

Analysis of Intellectual Disability Copy Number Variants for Association With Schizophrenia

Rees, et al.

Single-nucleotide polymorphism array data on 20,403 individuals with schizophrenia and 26,628 controls were used to evaluate 51 copy number variants (CNVs) implicated in intellectual disability.

Intellectual disability loci were significantly enriched in patients with schizophrenia compared with controls. One novel deletion at 16p12.1 was significantly associated with schizophrenia after correcting for multiple testing, and 2 additional loci reached nominal levels of significance. This analysis indicated that intellectual disability CNVs are likely to represent novel schizophrenia risk loci, but larger samples are required for their identification.

A 30-Year Study of 3 Generations at High Risk and Low Risk for Depression

Weissman, et al.

This longitudinal retrospective cohort family study looked to examine the familial aggregation of psychiatric disorders and functioning in grandchildren by their biological parents' and grandparents' depression status. It showed that the biological offspring with 2 previous generations affected with major depressive disorder (MDD) were the highest-risk group, with more than a 3-fold increased risk of MDD; grandchildren with both a depressed parent and grandparent were at highest risk for MDD.

Comparative Effectiveness of Cognitive Therapy and Dynamic Psychotherapy for Major Depressive Disorder in a Community Mental Health Setting

Connolly-Gibbons, et al.

A randomized clinical non-inferiority trial of directly compared cognitive therapy (CT) with short-term dynamic psychotherapy (DT) in the treatment of 237 adults with major depressive disorder in a single community mental health center. Study participants underwent 16 sessions of either DT or CT completed over five months. Expert blind evaluators completed a final assessment using the 17-item Hamilton Rating Scale to evaluate. Change in depressive symptoms for the DT group was statistically not inferior to that observed in the CT condition.

A Nationwide Cohort Study of the Association Between Hospitalization with Infection and Risk of Death by Suicide

Lund-Sorensen, et al.

A nationwide, population-based, prospective cohort study investigated the association between risk of death by suicide and hospitalization with infection. Data were drawn from Danish longitudinal registers with 7.22 million individuals observed during a 32-year follow-up period. Among 32,683 suicides observed, 24% of individuals had previously been diagnosed as having an infection during a

hospitalization. Hospitalization with infection was linked to an elevated suicide risk compared with those without prior infection. Dose-response relationships were observed with respect to number of hospitalizations with different infections. There is no known causation based on this corollary data, but the authors hypothesized that infections may have a role in the pathophysiological mechanisms of suicidal behaviors.

Association of Reports of Childhood Abuse and All-Cause Mortality Rates in Women

Chen, et al.

A national sample of adults were surveyed to collect baseline psychosocial data, including self-reported childhood emotional abuse, moderate physical abuse, and severe physical abuse. Follow-up mortality data was tracked over the next 20 years. Women who reported childhood emotional abuse, moderate physical abuse, and severe physical abuse were at an increased risk for all-cause mortality. Reports of more types of abuse were also associated with an increased risk; no associations were observed in men. There was no mention of childhood sexual abuse in this study or exact age at time of reported abuse.

Metformin for Treatment of Overweight Induced by Atypical Antipsychotic Medication in Young People With Autism Spectrum Disorder: A Randomized Clinical Trial

Anagnostou, et al.

A 16 week, double-blind, placebo-controlled RTC was conducted at 4 North American centers to evaluate the efficacy of metformin for weight gain associated with atypical antipsychotics in children with ASD. Metformin was titrated to 500mg twice daily for children aged 6 to 9 years or 850mg twice daily for those 10 to 17 years. Metformin reduced BMI z scores from baseline to week 16 significantly more than placebo. There were also statistically significant improvements in secondary body composition measures and raw weight but not metabolic variables. Only 5 of 60 participants discontinued treatment due to adverse of events (agitation or sedation).

Antipsychotic Use in Pregnancy and the Risk for Congenital Malformations

Huybrechts, et al.

A cohort study of 1.3 million pregnant women sought to examine the risk for congenital malformations overall and cardiac malformations associated with first-trimester exposure to antipsychotics. Data from a nationwide sample of pregnant women enrolled in Medicaid were analyzed from three months prior to pregnancy through at least 1 month after delivery. Major congenital malformations, including specific cardiac malformations, were identified during the first 90 days after delivery. After accounting for psychiatric conditions and other potential confounding variables, no increased risk for congenital malformations was found for typical or atypical antipsychotics. A possible exception was noted with a small increased risk in all malformations and cardiac malformations with risperidone, indicating need for further investigation in this regard.

The Journal of Clinical Psychiatry

Volume 3, Issue 8

Generalizability of Pharmacologic and Psychotherapy Clinical Trial Results for Posttraumatic Stress Disorder to Community Samples

Franco, et al.

Data derived from the 2004–2005 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a large nationally representative sample of the adult US population indicated that more than 6 of 10 respondents from the overall PTSD sample and more than 7 of 10 respondents seeking treatment for PTSD would have been excluded by 1 exclusion criterion or more in a typical pharmacologic trial. In contrast, about 2 of 10 participants in the full sample and about 3 of 10 participants seeking treatment for PTSD would have been excluded in a typical psychotherapy efficacy trial, indicating that while psychotherapy trial results may be applied to most patients with PTSD in routine clinical practice, results of pharmacological trials are not generalizable.

A New Empirical Definition of Major Depressive Episode Recovery and Its Positive Impact on Future Course of Illness

Judd, et al.

Aim of the study was two-fold: 1) to provide the first head-to-head test of the predictive validity of 2 resolution levels of major depressive episode (MDE) recovery, and 2) provide a definition of the end of an MDE. Subject population consisted of 322 participants entering the NIMH Collaborative Depression Study with MDE in 1978–1981, and followed thereafter for up to 31 years. They were divided into those with 8 consecutive weeks of asymptomatic MDE recovery or residual subsyndromal depressive symptom (SSD) resolution of their index MDE. Compared to asymptomatic recovery, SSD resolution was associated with significantly longer and more severe index MDEs, with more miscellaneous psychopathology as well as increased long-term psychosocial dysfunction and a greater depressive illness burden during the ensuing 10 or 20 years. Eight consecutive weeks of asymptomatic recovery had 93% overlap with a 4-week definition and conferred little benefit over 4 weeks. Four consecutive weeks of asymptomatic recovery appears to define the end of an MDE; residual symptom resolution appears to be a continuation of an active state of MDE.

The Lancet Psychiatry

Volume 3, Issue 9

Suicide risk and absconding in psychiatric hospitals with and without open door policies: a 15 year, observational study.

Huber, et al.

A 15 year, naturalistic observational study compared hospitals with and without locked wards to evaluate the effect of hospital type on inpatient suicide and secondary outcomes of suicide attempts and absconding with and without return in patients at risk of self-endangering behavior. Propensity score matching analysis of almost 350,000 admissions to 21 German psychiatric hospitals suggested that suicide, suicide attempts, and absconding with return and without return were not increased in hospitals with an open door policy. Compared with treatment in locked wards, treatment on open wards was associated with a decreased probability of suicide attempts, absconding with return, and absconding without returns, but not completed suicide.

Removing transgender identity from the classification of mental disorders: A Mexican field study for ICD-11

Robles, et al.

A field study utilizing a retrospective interview design sought to address the WHO proposal to remove categories related to gender identity from the ICD-11 Mental and Behavioral Disorders chapter by examining whether distress and impairment, considered essential characteristics of mental disorders, could be explained by experiences of social rejection and violence rather than being inherent features of transgender identity. Multivariate logistic regression models of data collected from 250 transgender adults receiving general health care services indicated that distress and all types of dysfunction were strongly predicted by experiences of social rejection and violence. A current male gender identity also predicted distress. Among indicators of gender incongruence, only request for treatment as a different gender was a significant predictor, and only of work or scholastic dysfunction.

Journal of the American Academy of Child and Adolescent Psychiatry **Volume 55, Issue 9**

Prenatal Maternal Smoking and Increased Risk for Tourette Syndrome and Chronic Tic Disorders

Browne, et al.

Using the Danish National Birth Cohort, this study assessed the role of prenatal maternal smoking in risk for Tourette syndrome and chronic tic disorder in 73, 073 single pregnancies. Heavy smoking was associated with a 66% increased risk for chronic tic disorder and Tourette's syndrome. It was also associated with a 2-fold increased risk for comorbid ADHD, and both light and heavy smoking were associated with a more than 2-fold increased risk for Tourette's syndrome and chronic tic disorder with any non-ADHD psychiatric comorbidity even when adjusting for maternal psychiatric history, socioeconomic status, and partner smoking.

Lack of Gender-Related Differences in Childhood-Onset Schizophrenia

Ordonez, et al.

This aim of this study was to evaluate gender differences in childhood-onset schizophrenia. The study population consisted of 133 patients with childhood onset schizophrenia. Males with childhood onset schizophrenia had a small but significant younger age of onset than females with childhood onset schizophrenia, higher verbal IQ scores and higher rate of comorbid pervasive developmental disorder and ADHD. However, this gender ratio is similar to what is seen in the general population and was not thought to be specific to childhood onset schizophrenia-related gender differences. Overall, few gender differences were noted in childhood onset schizophrenia.

A Randomized Controlled Trial of a School-Implemented School-Home Intervention for Attention Deficit/Hyperactivity Disorder Symptoms and Impairment

Pfiffner, et al.

This study evaluated the efficacy of Collaborative Life Skills (CLS), a new psychosocial intervention for primary-school students with ADHD symptoms. The intervention is a 12-week program consisting of integrated school, parent, and student treatments delivered by school-based mental health providers. Schools in a large urban public school district were randomly assigned to CLS versus usual services. Students from schools assigned to CLS compared with those assigned to usual services had significantly greater improvement on parent and teacher ratings of ADHD symptom severity and organizational functioning, teacher-rated academic performance, and parent ratings of oppositional defiant disorder symptoms as well as social/interpersonal skills. Findings support the modification of existing school-based mental health resources to assist with treatment of inattentive and disruptive behavior in school.