

EDITOR'S NOTE

This column reflects our commitment to provide you, the primary care physician, with information that will prove helpful in making informed decisions about the care of your patients who suffer from psychiatric disorders. We will highlight abstracts of high interest to you from our sister publication, *The Journal of Clinical Psychiatry*, and summarize pertinent articles from the general scientific literature. We hope that this section is clinically relevant to your practice and that it will encourage you to expand your horizons.

Effectiveness of a Quality Improvement Intervention for Adolescent Depression in Primary Care Clinics: A Randomized Controlled Trial

Asarnow JR, Jaycox LH, Duan N, et al.
JAMA 2005;293:311-319

Background: Depression is a common condition that is associated with significant morbidity in adolescents. In primary care settings, few depressed adolescents receive effective treatment for depression.

Objective: To evaluate the effectiveness of a quality improvement intervention targeted at increasing access to evidence-based treatments for depression (particularly cognitive-behavior therapy and antidepressant medication), relative to usual care, among adolescents in primary care practices.

Design, Setting, and Participants: Randomized controlled trial conducted between 1999 and 2003 enrolling 418 primary care patients with current depressive symptoms, aged 13 through 21 years, from 5 health care organizations purposively selected to include managed care, public sector, and academic medical center clinics in the United States.

Intervention: Usual care (N = 207) or 6-month quality improvement intervention (N = 211) including expert leader teams at each site, care managers who supported primary care clinicians in evaluating and managing patients' depression, training for care managers in manualized cognitive-behavior therapy for depression, and patient and clinician choice regarding treatment modality. In addition, participating clinicians received education regarding depression evaluation, management, and pharmacologic and psychosocial treatment.

Main Outcome Measures: Depressive symptoms assessed by Center for Epidemiological Studies-Depression Scale (CES-D) score. Secondary outcomes were mental health-related quality of life assessed by Mental Health Summary Score (MCS-12) and satisfaction with mental health care assessed using a 5-point scale.

Results: Six months after baseline assessments, intervention patients, compared with usual care patients, reported significantly fewer depressive symptoms (mean [SD] CES-D scores = 19.0 [11.9] vs. 21.4 [13.1]; $p = .02$), higher mental health-related quality of life (mean [SD] MCS-12 scores = 44.6 [11.3] vs. 42.8 [12.9]; $p = .03$), and greater satisfaction with mental health care (mean [SD] scores = 3.8 [0.9] vs. 3.5 [1.0]; $p = .004$). Intervention patients also reported significantly higher rates of mental health care (32.1% vs. 17.2%, $p < .001$) and psychotherapy or counseling (32.0% vs. 21.2%, $p = .007$).

Conclusions: A 6-month quality improvement intervention targeted at improving access to evidence-based depression treatments through primary care was significantly more effective than usual care for depressed adolescents from diverse primary care practices. The greater uptake of counseling versus medication under the intervention reinforces the importance of practice interventions that include resources to enable evidence-based psychotherapy for depressed adolescents.

Cerebrovascular Disease and Late-Life Depression

Kales HC, Maixner DF, Mellow AM
Am J Geriatr Psychiatry 2005;13:88-98

Background: Depression may be a result of vascular disease in a significant subpopulation of elderly persons. The high rate of depression in patients with vascular disease, the frequency of "silent stroke" and white-matter hyperintensities in late-life depression, and the lower frequency of positive family histories of depression in such patients provide indirect support for vascular disease as an underlying etiology of late-life depression.

Objective and Data Sources: The associations of late-life depression with cerebrovascular disease were evaluated by reviewing the existing pathophysiologic, prognosis, and treatment-outcomes studies. The current literature was systematically searched in electronic databases.

Data Synthesis: A high frequency of depression in older patients with cardiovascular and cerebrovascular diseases and the possibility of a bidirectional relationship between depression and vascular disease were indicated by the findings of this review. Studies have found different symptom profiles, greater disability,

and higher risk for poorer outcomes in patients with vascular depression than in those with nonvascular depression. Since the vascular depression hypothesis was proposed as a conceptual framework, accumulating evidence indicates that patients with vascular depression may have poorer outcomes related in part to executive dysfunction and consequent disability. The association of vascular risk factors with geriatric depression has been inconsistent in studies to date.

Conclusion: Although an association between a subset of late-life depression and vascular disease is clear, there remain significant gaps in our understanding.

The Effect of Clozapine on Factors Controlling Glucose Homeostasis

Howes OD, Gaughran FP, Amiel SA, et al.
J Clin Psychiatry 2004;65:1352–1355

Background: This prospective study examines the effect of clozapine on factors determining glucose homeostasis.

Method: The sample consisted of all patients meeting DSM-IV criteria for schizophrenia who commenced clozapine treatment within the South London and Maudsley hospitals during 1 year (2000–2001). Growth hormone (GH), insulin-like growth factor-1 (IGF-1), and IGF binding protein-1 (IGFBP-1) were measured in 19 patients (10 female; mean age = 31.1 years [SD = 5.8]; 9 black British/African, 10 white British) before and after a mean of 2.5 (SD = 0.9) months of clozapine treatment.

Results: Baseline IGFBP-1 was low. IGFBP-1, GH, and IGF-1 were not significantly changed by clozapine treatment.

Conclusions: Clozapine does not alter GH, IGF-1, or IGFBP-1 within 3 months of commencing treatment, indicating that alteration in glucose tolerance associated with clozapine treatment involves other mechanisms yet to be elucidated. Baseline abnormalities in IGFBP-1 indicate a preexisting susceptibility to glucoregulatory dysfunction.

Beliefs and Attitudes Associated With the Intention to Not Accept the Diagnosis of Depression Among Young Adults

Van Voorhees BW, Fogel J, Houston TK, et al.
Ann Fam Med 2005;3:38–46

Purpose: Many young adults may be prevented from accepting a diagnosis and treatment for depression by negative attitudes and beliefs about depression treatment. The purpose of this study was to determine the association of depressive symptom severity, beliefs about and attitudes toward treatment, subjective social norms, and past behavior with intent to not accept a physician's diagnosis of depression.

Method: A cross-sectional study was conducted of 10,962 persons aged 16 to 29 years who participated in an Internet-based public health depression screening program and had positive screening results on the Center for Epidemiologic Studies Depression Scale (CES-D). Participants reported whether they would accept their physician's diagnosis of depression. Based on the theory of reasoned action, a multivariate model of the factors that predict intent to not accept a diagnosis of depression was developed.

Results: Twenty-six percent of the participants stated their intent to not accept their physician's diagnosis of depression. The following factors were associated with the intent not to accept a diagnosis of depression: (1) disagreeing that medications

are effective in treating depression (strongly disagree, OR = 6.5, 95% CI = 4.6 to 9.3), (2) disagreeing that there is a biological cause for depression (strongly disagree, OR = 1.9, 95% CI = 1.3 to 2.7), and (3) agreeing that it would be embarrassing if friends knew about the depression (strongly agree, OR = 2.3, 95% CI = 1.8 to 2.9). Beliefs and attitudes, subjective social norms, and past behavior explained most of the variance in this model (84%).

Conclusions: Negative beliefs and attitudes, subjective social norms, and lack of past helpful treatment experiences are associated with the intent to not accept the diagnosis of depression and may contribute to low rates of treatment among young adults.

Effects of Long-Term Administration of Nicotine and Fluoxetine on Sleep in Depressed Patients

Haro R, Drucker-Colin R
Arch Med Res 2004;35:499–506

Background: This study investigated the long-term effects of transdermal nicotine and fluoxetine on sleep and major depression.

Method: Subjects included 2 independent groups of 12 non-smoking patients with major depression (Hamilton Rating Scale for Depression [HAM-D] score \geq 18). One group received transdermal nicotine (17.5 mg) and another group received an oral dose of fluoxetine (20 mg/day), 5 days a week for 6 months, 3 days a week at month 7, and 1 day per week at month 8. From the 9th to the 14th month, a patch without nicotine and an oral placebo substituted nicotine and fluoxetine once per week. Polysomnographic recordings were conducted; depressive symptoms were evaluated at baseline and on a monthly basis during medication and during withdrawal.

Results: Nicotine diminished wakefulness and stage 1 and increased REM sleep latency and slow wave sleep throughout the study. Upon nicotine withdrawal, a small decrease of REM sleep duration was observed. Fluoxetine decreased the sleep efficiency index and increased wakefulness, stage 1 duration, and REM latency. According to HAM-D scores, both nicotine and fluoxetine improved mood.

Conclusions: Nicotine and fluoxetine showed equivalent antidepressant efficacy. Important differences in sleep parameters were observed between nicotine and fluoxetine, however, both during their administration and following withdrawal.

Follow-Up Care of Children Identified With ADHD by Primary Care Clinicians: A Prospective Cohort Study

Gardner W, Kelleher KJ, Pajer K, et al.
J Pediatr 2004;145:767–771

Background: The authors' objective was to document the follow-up care received by children identified with attention-deficit/hyperactivity disorder (ADHD) by primary care clinicians (PCCs).

Study Design: Families of children 4 to 15 years of age who had been diagnosed with ADHD were surveyed. At an index office visit, parents and clinicians completed questionnaires; 6 months later, parents completed a questionnaire (N = 659 returned surveys, 68% return rate). The number of visits with PCCs or mental health specialists during the 6 months after the index visit was the main outcome measure.

Results: Children had a median of 1 PCC visit over a 6-month period. Children who had prescriptions for psychotropic medi-

cations (78%) did not differ from others in the number of visits. Follow-up visits with the child's own doctor were more common when the PCC had completed mental health training. Only 26% of patients saw a mental health specialist. Children who were black, were on Medicaid, or had higher levels of internalizing symptoms were more likely to see a mental health specialist. **Conclusions:** Children treated for ADHD need more follow-up visits to permit adjustment of medication and support continuation in treatment. The authors state that systematic quality improvement efforts are warranted.

Risk Factors for Geriatric Depression: The Importance of Executive Functioning Within the Vascular Depression Hypothesis

*Mast BT, Yochim B, Macneill SE, et al.
J Gerontol A Biol Sci Med Sci 2004;59:1290-1294*

Background: In recent studies addressing the vascular depression hypothesis, results have been mixed, with cerebrovascular risk factors (CVRFs) predicting depression in some geriatric patients but not in others. The researchers examined executive dysfunction as a potential moderator of the relationship between CVRFs and depressive symptoms.

Method: Data on CVRFs, executive functioning, and depressive symptoms from 77 geriatric rehabilitation patients were used to test the hypothesis that patients with executive dysfunction and greater CVRFs would show the highest levels of depression over time. CVRFs (diabetes, hypertension, atrial fibrillation) were measured via diagnosis by treating physician. Depression was assessed with the 15-item Geriatric Depression Scale (GDS) at baseline and at 6-month and 18-month follow-ups. Executive functioning was measured at baseline using the initiation/perseveration (IP) subtest of the Mattis Dementia Rating Scale.

Results: A significant statistical interaction between the number of CVRFs and scores on the IP subtest on depressive symptoms was shown by multivariate analysis of variance. Patients with 2 or more CVRFs and lower IP scores had significantly greater depressive symptoms at baseline and at 18-month follow-up than patients with fewer CVRFs and higher IP scores. The univariate effect at 6 months was not significant.

Conclusion: Scores on an index of executive functioning may moderate the relationship between CVRFs and depressive symptoms. The authors interpret these findings in the context of the vascular depression hypothesis and related frontostriatal dysfunction. Patients with greater burden of CVRF and poor executive functioning may be at particularly high risk for depression.

Fluoxetine Treatment for Prevention of Relapse of Depression in Children and Adolescents: A Double-Blind, Placebo-Controlled Study

*Emslie GJ, Heiligenstein JH, Hoog SL, et al.
J Am Acad Child Adolesc Psychiatry 2004;43:1397-1405*

Background: Fluoxetine 20 to 60 mg/day was compared with placebo for prevention of relapse of major depressive disorder in children and adolescents who had achieved scores of ≤ 28 on the Children's Depression Rating Scale, Revised during treatment with fluoxetine 20 to 60 mg.

Method: The authors report on the 32-week relapse-prevention phase of a 51-week, double-blind, multicenter, placebo-

controlled study. Twenty patients continued to receive their fixed dose of fluoxetine, while 20 similar patients were switched to placebo. The definition of relapse for the primary analysis was a score of > 40 on the Children's Depression Rating Scale, Revised with a 2-week history of clinical deterioration or relapse in the opinion of the physician. Discontinuation-emergent adverse events were assessed by comparison of adverse events between groups.

Results: Mean time to relapse was longer in the fluoxetine recipients than in the placebo recipients ($p = .046$). The fluoxetine cohort had a relapse rate of approximately 34% compared with 60% in the placebo group. Both groups were similar in the incidence of adverse events and tolerability, suggesting that fluoxetine is not associated with significant discontinuation events.

Conclusion: Fluoxetine 20 to 60 mg/day was well tolerated and can significantly delay relapse of symptoms of major depressive disorder in children and adolescents.

Assessing Demoralization and Depression in the Setting of Medical Disease

*Mangelli L, Fava GA, Grandi S, et al.
J Clin Psychiatry 2005;66:391-394*

Objective: The aim of this study was to assess the presence of demoralization and major depression in the setting of medical disease.

Method: 807 consecutive outpatients recruited from different medical settings (gastroenterology, cardiology, endocrinology, and oncology) were assessed according to DSM-IV criteria and Diagnostic Criteria for Psychosomatic Research, using semi-structured research interviews.

Results: Demoralization was identified in 245 patients (30.4%), while major depression was present in 135 patients (16.7%). Even though there was a considerable overlap between the 2 diagnoses, 59 patients (43.7%) with major depression were not classified as demoralized, and 169 patients (69.0%) with demoralization did not satisfy the criteria for major depression.

Conclusions: The findings suggest a high prevalence of demoralization in the medically ill and the feasibility of a differentiation between demoralization and depression. Further research may determine whether demoralization, alone or in association with major depression, entails prognostic and clinical implications.

Overweight Status and Depressive Symptoms During Adolescence

*Needham BL, Crosnoe R
J Adolesc Health 2005;36:48-55*

Objectives: The authors cited 3 objectives: to extend previous research on the association between overweight status and depressive symptoms among adults to adolescents, to explore whether this association varies across social structural contexts and school context, and to investigate additional mechanisms that link overweight status to depressive symptoms.

Method: Survey regression procedures were used to analyze data from the first wave of the National Longitudinal Study of Adolescent Health. Degree of overweight was indicated by body mass index, which was calculated using self-reported height and weight information, whereas depressive symptoms were assessed with the Center for Epidemiologic Studies Depression Scale. Data were analyzed to determine (1) the social groups in

which being overweight was least common, (2) the association between overweight status and depressive symptoms, and (3) potential mediators of the association between relative weight and symptoms of depression, including dieting and self-rated health.

Subjects: The analytic sample contained 18,924 adolescents aged 11 to 21 years (mean age = 915.68) of whom approximately half were female (N = 9634).

Results: Relative weight was found to be associated with depressive symptoms for girls but not boys after adjusting for exercise and sociodemographic characteristics. For both, the association between overweight status and symptoms of depression was stronger among adolescents in lower grades. Dieting explained the positive association between relative weight and depressive symptoms for girls, whereas self-rated health mediated the association between relative weight and symptoms of depression for adolescents in lower grades.

Conclusion: The social dimension of weight must be examined to fully understand both the physical and mental health consequences of adolescent obesity.

The Use of Paroxetine and Cognitive-Behavioral Therapy in Postpartum Depression and Anxiety: A Randomized Controlled Trial

Misri S, Reebye P, Corral M, et al.
J Clin Psychiatry 2004;65:1236–1241

Background: Approximately 10% to 16% of women experience a major depressive episode after childbirth. A significant proportion of these women also suffer from comorbid anxiety disorders. The purpose of this study was to evaluate whether the addition of cognitive-behavioral therapy (CBT) to standard antidepressant therapy offers additional benefits in the treatment of postpartum depression with comorbid anxiety disorders.

Method: Thirty-five women referred to a tertiary care hospital outpatient program with a DSM-IV diagnosis of postpartum depression with comorbid anxiety disorder were randomly assigned to 1 of 2 treatment groups—paroxetine-only monotherapy group (N = 16) or paroxetine plus 12 sessions of CBT combination therapy group (N = 19)—for a 12-week trial. Progress was monitored by a psychiatrist blinded to treatment group, using the Hamilton Rating Scale for Depression, Hamilton Rating Scale for Anxiety, Yale-Brown Obsessive Compulsive Scale, Clinical Global Impressions scale, and Edinburgh Postnatal Depression Scale. Data were analyzed using 2-tailed statistical tests at an alpha level of .05. The study was conducted from April 1, 2002, to June 30, 2003.

Results: Both treatment groups showed a highly significant improvement ($p < .01$) in mood and anxiety symptoms. Groups did not differ significantly in week of recovery, dose of paroxetine at remission, or measures of depression, anxiety, and obsessive-compulsive symptoms at outcome.

Conclusion: Antidepressant monotherapy and combination therapy with antidepressants and CBT were both efficacious in reducing depression and anxiety symptoms. However, in this sample of acutely depressed/anxious postpartum women, there were no additional benefits from combining the 2 treatment modalities. Further research into the efficacy of combination therapy in the treatment of moderate-to-severe depression with comorbid disorders in postpartum women is recommended.

Antidepressant Pharmacotherapy in the Treatment of Depression in the Very Old: A Randomized, Placebo-Controlled Trial

Roose SP, Sackeim HA, Krishnan KR, et al.
Am J Psychiatry 2004;161:2050–2059

Background: This study determined the efficacy of antidepressant medication for the treatment of depression in the “old-old.”

Method: In this 8-week randomized medication trial, citalopram (10–40 mg/day) was compared with placebo in the treatment of patients with unipolar depression aged 75 years and older.

Results: A total of 174 patients (58% women) with a mean age of 79.6 years (SD = 4.4) and a mean baseline Hamilton Rating Scale for Depression (HAM-D) score of 24.3 (SD = 4.1) were randomly assigned to treatment at 15 sites. There was a main effect for site but not for treatment condition. The remission rate, defined as a final HAM-D score < 10 , was 35% for the citalopram group and 33% for the placebo group. Patients with severe depression (baseline HAM-D score > 24), however, tended to have a higher remission rate with medication than with placebo (35% versus 19%).

Conclusions: Medication was not more effective than placebo for the treatment of depression in this oldest group of community-dwelling patients to be studied to date. The considerable psychosocial support given to all patients, however, represents more than the ingestion of an inactive pill for the placebo condition. There was considerable range in response to medication across sites, 18% to 82%, and to placebo, 16% to 80%.

Iron Deficiency in Children With Attention-Deficit/Hyperactivity Disorder

Konofal E, Lecendreux M, Arnulf I, et al.
Arch Pediatr Adolesc Med 2004;158:1113–1115

Background: Iron deficiency, which causes abnormal dopaminergic neurotransmission, may contribute to the pathophysiology of attention-deficit/hyperactivity disorder (ADHD).

Objective: To evaluate iron deficiency in children with ADHD compared with iron deficiency in an age- and sex-matched control group.

Design: Controlled group comparison study.

Setting: Child and Adolescent Psychopathology Department in European Pediatric Hospital, Paris, France.

Patients: Fifty-three children with ADHD aged 4 to 14 years (mean \pm SD = 9.2 \pm 2.2 years) and 27 controls (mean \pm SD = 9.5 \pm 2.8 years).

Main Outcome Measures: Serum ferritin levels evaluating iron stores and Conners' Parent Rating Scale scores measuring severity of ADHD symptoms.

Results: Mean serum ferritin levels were lower in the children with ADHD (mean \pm SD = 23 \pm 13 ng/mL) than in the controls (mean \pm SD = 44 \pm 22 ng/mL; $p < .001$). Serum ferritin levels were abnormal (< 30 ng/mL) in 84% of children with ADHD and 18% of controls ($p < .001$). Low serum ferritin levels were also correlated with more severe general ADHD symptoms measured with Conners' Parent Rating Scale (Pearson correlation coefficient, $r = -0.34$; $p < .02$) and greater cognitive deficits ($r = -0.38$; $p < .01$).

Conclusions: Low iron stores may contribute to ADHD and ADHD children may benefit from iron supplementation.