

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.

**Relationships Between Poverty and Psychopathology: A Natural Experiment**

*Costello EJ, Compton SN, Keeler G, et al.*

**Background:** Social selection (downward mobility from familial liability to mental illness) versus social causation (adversity and stress) are 2 competing theories regarding the origins of mental illness. Using a natural experiment, this study tested the role of social selection versus social causation of childhood psychopathology. **Method:** In this quasi-experimental, longitudinal study, annual psychiatric assessments were given to a representative sample of 1420 rural children aged 9 to 13 years (at intake) for 8 years (1993–2000). One quarter of the sample were American Indian, and the remaining children were predominantly white. A casino opened on the Indian reservation halfway through the study, providing every American Indian an income supplement that increased annually. This supplement moved 14% of families out of poverty; 53% remained poor and 32% were never poor. Non-Indian family incomes were not affected. DSM-IV psychiatric symptoms in never-poor, persistently poor, and ex-poor children were compared for the 4 years before and after the casino opened. **Results:** The persistently poor and ex-poor children had more psychiatric symptoms (4.38 and 4.28, respectively) before the casino opened than the never-poor children (2.75). But levels among the ex-poor fell to those of the never-poor children after the opening, while levels among those who were persistently poor remained high (odds ratio, 1.50; 95% confidence interval, 1.08 to 2.09; and odds ratio, 0.91; 95% confidence interval, 0.77 to 1.07, respectively). The effect was specific to symptoms of conduct and oppositional defiant disorders; depression and anxiety symptoms were unaffected. Similar results were found in non-Indian children whose families moved out of poverty during the same period. **Conclusions:** Results support a social causation explanation for conduct and oppositional disorder, but not for depression or anxiety. An income intervention that moved families out of poverty for reasons that cannot be ascribed to family characteristics had a major effect on some types of children's psychiatric disorders, but not on others.

*(JAMA 2003;290:2023–2029)*

**Economic Consequences of Not Recognizing Bipolar Disorder Patients: A Cross-Sectional Descriptive Analysis**

*Birnbaum HG, Shi L, Dial E, et al.*

**Background:** This retrospective study compared treatment patterns and costs for patients with recognized and unrecognized bipolar disorder with those of depressed patients without a bipolar disorder claim. **Method:** Claims data for 7 large national employers covering 585,584 persons aged less than 65 years were used to identify patients diagnosed with depression and initially treated with antidepressants. Data on employees, as well as spouses and dependents, for the period 1998 to mid-2001 were used. Patients were identified as bipolar based on the criteria of a bipolar diagnosis claim (ICD-9 codes: 296.0, 296.1, 296.4–296.8) and/or a mood stabilizer prescription claim. Of the patients identified as bipolar, unrecognized bipolar disorder (unrecognized-BP) patients met the criteria after antidepressant initiation, while recognized bipolar disorder (recognized-BP) patients met the criteria at or before initiation. The remaining patients in the sample were non-bipolar depressed (non-BP) patients. Outcome measures included treatment patterns and monthly medical costs in the 12 months subsequent to initiation of antidepressant treatment. **Results:** Of the 9009 patients treated for depression with antidepressants, there were 8383 non-BP patients (93.1%), 293 recognized-BP patients (3.3%), and 333 unrecognized-BP patients (3.7%). Use of combination therapies varied among the non-BP (11%), unrecognized-BP (32%), and recognized-BP patients (44%) (all pairwise  $p < .01$ ). Use of mood stabilizers was less frequent among unrecognized-BP patients (14%) than recognized-BP patients (34%) ( $p < .0001$ ). Unrecognized-BP patients incurred significantly greater ( $p < .05$ ) mean monthly medical costs (\$1179) in the 12 months following initiation of antidepressant treatment compared with recognized-BP patients (\$801) and non-BP patients (\$585). Monthly indirect costs were significantly greater ( $p < .05$ ) for unrecognized-BP (\$570)

and recognized-BP (\$514) employees compared with non-BP employees (\$335) in the 12 months following antidepressant initiation. **Conclusions:** Patterns of medication treatment for bipolar disorder were suboptimal. Accurate and timely recognition of bipolar disease was associated with lower medical costs and lower indirect costs due to work loss.

(*J Clin Psychiatry* 2003;64:1201–1209)

### Pharmacologic Treatment of Alzheimer's Disease: An Update

Delagarza VW

Alzheimer's disease is characterized by the development of senile plaques and neurofibrillary tangles, which are associated with neuronal degeneration, especially in cholinergic neurons. The mainstays of therapy are drugs that inhibit the degradation of acetylcholine within synapses. Galantamine, donepezil, and rivastigmine are safe but have cholinergic side effects that are potentially troublesome such as weight loss, diarrhea, nausea, vomiting, and anorexia. These adverse reactions can be minimized by slow drug titration and are often self-limited. Although the magnitude of benefit may be greater in clinical trials than in practice, acetylcholinesterase inhibitors appear to be effective. Evidence is less robust for benefits in delaying nursing home placement and improving functional ability and behaviors, but the drugs clearly improve cognition. While supporting evidence is not strong, benefit for selegiline or vitamin E has been suggested. Guidelines for monitoring drug therapy in patients with Alzheimer's disease generally recommend periodic measurements of functional ability and cognition but advise against continuing therapy with acetylcholinesterase inhibitors when dementia becomes severe.

(*Am Fam Physician* 2003;68:1365–1372)

### Suicide Risk in Bipolar Disorder During Treatment With Lithium and Divalproex

Goodwin FK, Fireman B, Simon GE, et al.

**Background:** Lithium treatment has been suggested to reduce risk of suicide in bipolar disorder in several studies. Although divalproex is the most commonly prescribed mood-stabilizing drug in the United States, no research has examined suicide risk during treatment. This study was designed to compare risk of suicide attempt and suicide death during divalproex treatment with that during lithium treatment. **Design and Setting:** Retrospective cohort study in California and Washington conducted at 2 large integrated health plans with a population-based sample of 20,638 health plan members aged 14 years or older. All participants had at least 1 outpatient diagnosis of bipolar disorder and at least 1 filled prescription between January 1, 1994, and December 31, 2001, for carbamazepine, lithium, or divalproex. Follow-up for each patient began with first qualifying prescription and ended with disenrollment from the study plan, death, or end of study period. The main outcome measures were suicide attempt, recorded as a hospital discharge diagnosis or an emergency department diagnosis and suicide death, recorded on death certificate. **Results:** In both health plans, unadjusted rates were greater during treatment with divalproex than during treatment with lithium for emergency department suicide attempt (31.3 vs. 10.8 per 1000 person-years;  $p < .001$ ), suicide attempt resulting in hospitalization (10.5 vs. 4.2 per 1000 per-

son-years;  $p < .001$ ), and suicide death (1.7 vs. 0.7 per 1000 person-years;  $p = .04$ ). Risk of suicide death was 2.7 times higher (95% confidence interval [CI] = 1.1 to 6.3;  $p = .03$ ) during treatment with divalproex than during treatment with lithium, after adjustment for sex, age, health plan, year of diagnosis, comorbid psychiatric and medical conditions, and concomitant use of other psychotropic drugs. Corresponding hazard ratios for nonfatal attempts were 1.7 (95% CI = 1.2 to 2.3;  $p = .002$ ) for attempts resulting in hospitalization and 1.8 (95% CI = 1.4 to 2.2;  $p < .001$ ) for attempts diagnosed in the emergency department. **Conclusion:** Risk of suicide attempt and suicide death is lower during treatment with lithium than during treatment with divalproex among patients treated for bipolar disorder.

(*JAMA* 2003;290:1467–1473)

### Occult Mood Disorders in 104 Consecutively Presenting Children Referred for the Treatment of Attention-Deficit/Hyperactivity Disorder in a Community Mental Health Clinic

Dilsaver SC, Henderson-Fuller S, Akiskal HS

**Objective:** To ascertain the prevalence of mood disorders among consecutively evaluated prepubertal children presenting for the treatment of attention-deficit/hyperactivity disorder (ADHD) in a community mental health clinic. **Method:** 104 children received systematic assessments designed to identify individuals meeting the DSM-IV criteria for major depressive disorder (MDD), mania, and ADHD. "Standard" and "modified" criteria for mania were employed. Modified criteria, in an effort to minimize false-positive diagnoses of mania, required the presence of euphoria and/or flight of ideas. A child meeting the criteria for MDD or either set of criteria for mania was categorized as having a mood disorder. Mood disorders in first-degree relatives were assessed using a systematic interview. Data were gathered from 2000 to 2002. **Results:** Sixty-two children (59.6%) had a mood disorder. Compared with those who did not have a mood disorder, they were 3.3 times more likely (54.8% vs. 16.7%) to have a family history of any affective disorder ( $p < .0001$ ) and 18.3 times more likely (43.5% vs. 2.4%) to have a family history of bipolar disorder ( $p < .0001$ ). Twenty (32.3%) of the children with and none without a mood disorder had psychotic features ( $p < .0001$ ). Compared with those meeting only the standard criteria for mania, those meeting the modified criteria were 9.1 times more likely (69.8% vs. 7.7%) to have a family history of an affective disorder ( $p < .0001$ ) and 7.3 times more likely (55.8% vs. 7.7%) to have a family history of bipolar disorder ( $p = .002$ ). **Conclusion:** Children who presumably have ADHD often have unrecognized affective illness. Our findings support the view that children meeting the modified criteria for mania have veritable bipolar disorder. These findings, which were derived in the course of delivering routine clinical services in a community mental health clinic, are consistent with those obtained in research settings suggesting that children presenting with ADHD often have occult mood disorders, especially unrecognized bipolarity. We suggest that clinicians encountering children with prominent features of ADHD inquire about the presence of euphoria and flight of ideas. We submit that the presence of these "classic" manifestations of mania strongly suggests the presence of occult bipolarity, even if course of illness otherwise markedly deviates from "classic" descriptions.

(*J Clin Psychiatry* 2003;64:1170–1176)

### Increased Medical Costs of a Population-Based Sample of Depressed Elderly Patients

Katon WJ, Lin E, Russo J, et al.

**Background:** This study compared older adults with depressive symptoms below the diagnostic threshold and those with DSM-IV major depression and/or dysthymia with older adults without depression to determine which group has higher medical costs. **Methods:** Patients of 2 large primary care clinics of a staff-model health maintenance organization in Seattle, Wash., were mailed the 2-item PRIME-MD depression screen. All patients 60 years and older (N = 11,679) with primary care providers at the participating clinics were included; 8894 (76.2%) were enrolled. An additional 107 patients were referred to the study by their primary care physician. Nonrespondents had higher inpatient medical costs in the previous 6 months and were slightly younger. Patients referred by their primary care physicians or with positive findings on at least 1 item were offered an interview with the Structured Clinical Interview for DSM-IV. The total cost of medical services for the 6 months before the study was obtained from the health maintenance organization's cost accounting system. **Results:** After adjustment for chronic medical illness, total ambulatory costs were 43% to 52% higher and total ambulatory and inpatient costs were 47% to 51% higher in depressed compared with nondepressed elderly patients. Cost increase was evident in all health care components, with only a small percentage due to mental health treatment. Depressed elderly patients averaged an increase of \$763 to \$979 in ambulatory costs and \$1045 to \$1700 in ambulatory and inpatient costs. No cost differences were noted between patients with DSM-IV depressive disorders and those with subthreshold depressive syndromes. **Conclusions:** Even after adjustment for chronic medical illness, depressive symptoms and DSM-IV depressive disorders in elderly patients are associated with significantly higher health care costs.

(*Arch Gen Psychiatry* 2003;60:897-903)

### Citalopram in the Treatment of Binge-Eating Disorder: A Placebo-Controlled Trial

McElroy SL, Hudson JI, Malhotra S, et al.

**Background:** Binge-eating disorder is a newly recognized eating disorder characterized by recurrent episodes of binge eating without compensatory weight loss behaviors. It commonly co-occurs with depressive disorders and obesity. Citalopram is a highly selective serotonin reuptake inhibitor antidepressant. The purpose of this study was to assess the efficacy and safety of citalopram in the treatment of binge-eating disorder. **Method:** Thirty-eight outpatients with a DSM-IV diagnosis of binge-eating disorder were enrolled in the study between August 2000 and July 2001 and were randomly assigned to receive either citalopram (N = 19) or placebo (N = 19) in a 6-week, double-blind, flexible-dose (20-60 mg/day) study. The primary measure of efficacy was frequency of binge-eating episodes. Secondary measures included frequency of binge days, body mass index (BMI), weight, Clinical Global Impressions-Severity of Illness scale scores, Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating (YBOCS-BE) scores, Hamilton Rating Scale for Depression (HAM-D) scores, and response categories. The outcome measures were analyzed using 2 random regression methods, with a time trend analysis (primary analysis) and an endpoint analysis. In addition, response categories were analyzed using an exact trend test. **Results:** Compared with

placebo-treated subjects, subjects receiving citalopram (mean dose of 57.9 mg/day) had a significantly greater rate of reduction in frequency of binge eating (p = .003), frequency of binge days (p < .001), BMI (p < .001), weight (p < .001), severity of illness (p = .028), and YBOCS-BE score (p = .007) and a marginally significant rate of reduction in HAM-D score (p = .053). Differences between groups in response categories were marginally significant (p = .068 for intent-to-treat analysis). **Conclusion:** In a 6-week, placebo-controlled, flexible-dose trial, citalopram was efficacious in reducing binge-eating frequency, weight, and severity of illness and was generally well tolerated in subjects with binge-eating disorder.

(*J Clin Psychiatry* 2003;64:807-813)

### Managing Multiple Morbidity in Mid-Life: A Qualitative Study of Attitudes to Drug Use

Townsend A, Hunt K, Wyke S

**Background:** This qualitative study used detailed interviews to examine attitudes regarding drug use among middle-aged respondents with high levels of chronic morbidity. All participants had 4 or more chronic illnesses. The primary outcome measure was participants' feelings about long-term use of drugs to manage chronic multiple morbidity. **Method:** Study participants included 23 men and women from west of Scotland with a mean age of 50 years. Interviews (each lasting about an hour) were conducted between Oct. 2001 and July 2002. **Results:** Drugs occupied a central place in the respondents' lives, aiding in the management of multiple chronic conditions. Participants expressed an aversion to taking drugs, but acknowledged that they depended on the drugs to lead normal lives. Ambivalence toward drug use was expressed in various ways. Respondents adopted regular and flexible regimens, adhering to a regular regimen to treat 1 condition (e.g., hypertension) while adopting a flexible regimen that accommodated changing circumstances. Respondents also expressed a dislike of drugs but an inability to be free of the medications. Also, drugs both facilitated performance of social roles and served as evidence of an inability to perform such roles. **Conclusions:** Insight into the tension experienced by people managing multiple chronic illness with complex drug regimens may help health care professionals to support self-care practices among patients and to optimize concordance in their use of prescribed drugs.

(*BMJ* 2003;327:837-840)

### Exercise Plus Behavioral Management in Patients With Alzheimer Disease: A Randomized Controlled Trial

Teri L, Gibbons LE, McCurry SM, et al.

**Background:** The purpose of this study was to determine whether a home-based exercise program for Alzheimer patients in conjunction with caregiver training in behavior management would reduce functional dependence and delay institutionalization among patients with Alzheimer disease. **Method:** This randomized controlled trial was conducted between June 1994 and April 1999. Study participants included 153 community-dwelling patients meeting National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer Disease and Related Disorders Association criteria for Alzheimer disease. Patient-caregiver dyads were randomly assigned to either

routine medical care (RMC) or the combined exercise and caregiver training program, Reducing Disability in Alzheimer Disease (RDAD), conducted in the patients' homes for 3 months. Outcome measures included physical health and function (36-item Short-Form Health Survey's physical functioning and physical role functioning subscales and Sickness Impact Profile's Mobility subscale) and affective status (Hamilton Depression Rating Scale and Cornell Depression Scale for Depression in Dementia). **Results:** In comparison with the RMC group, more patients in the RDAD group exercised at least 60 min/wk (odds ratio [OR], 2.82; 95% confidence interval [CI] = 1.25 to 6.39;  $p = .01$ ) and had fewer days of restricted activity (OR, 3.10; 95% CI = 1.08 to 8.95;  $p < .001$ ) at 3 months. The RDAD group had improved scores for physical role functioning compared with worse scores for RMC patients (mean difference, 19.29; 95% CI = 8.75 to 29.83;  $p < .001$ ). The RDAD group had improved Cornell Depression Scale for Depression in Dementia scores while the RMC patients had worse scores (mean difference, -1.03; 95% CI = -0.17 to -1.91;  $p = .02$ ). At 2 years, the RDAD patients showed a trend (19% vs. 50%) for less institutionalization due to behavioral disturbance and continued to have better physical role functioning scores than the RMC patients (mean difference, 10.89; 95% CI = 3.62 to 18.16;  $p = .003$ ). For patients with higher depression scores at baseline, those in the RDAD group improved significantly more at 3 months on the Hamilton Depression Rating Scale (mean difference, 2.21; 95% CI = 0.22 to 4.20;  $p = .04$ ) and maintained that improvement at 24 months (mean difference, 2.14; 95% CI = 0.14 to 4.17;  $p = .04$ ). **Conclusion:** Exercise and caregiver training in behavioral management techniques improved physical health and depression in patients with Alzheimer disease.

(*JAMA* 2003;290:2015-2022)

### Mental Disorder and Serious Violence: The Victims

Johnston I, Taylor PJ

**Background:** Media representation of violence by people with mental disorder tends toward images of random, serious violence to strangers. Studies of general psychiatric patients do not support this representation, but include few cases of serious or homicidal violence. This study describes the relationship of mentally disordered offenders to victims of an attack that was serious enough to result in the offender's detention in a high-security hospital. Hypotheses tested were that perpetrators of stranger violence would be more likely than those targeting people they know to be male, nonwhite, and younger and have a violence history and less likely to have psychotic features. **Method:** A clinical register and record study of all patients with an index offense of interpersonal violence who were resident in English high-security hospitals Jan. 1, 1993, to June 30, 1993, was conducted. **Results:** Among 887 men and 88 women, 33% had attacked strangers. After adjustment for the high proportion of men in this male-dominated population, men were still more likely than women to have attacked strangers. There was no independent association between stranger victimization and perpetrator's age, ethnic group, or violence history. Stranger victimization was, however, more likely to have been committed by those with personality disorder than those with psychosis. The most serious violence and homicide were more likely to be against intimates than strangers. **Conclusion:** Among patients selected for high risk to the public, high rates of stranger victimization would be expected. The rates appeared, however, only slightly higher than in other reported patient samples and lower than in an untreated sample. The safety of people close to such patients urgently needs improvement.

(*J Clin Psychiatry* 2003;64:819-824)