

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.

Screening for Bipolar Disorder in a Primary Care Practice

Das AK, Olfson M, Geleroff MJ, et al.

JAMA 2005;293:956-963

Context: Bipolar disorder is characterized by episodes of mania and depression. Screening for depression in primary care patients without assessing for a history of manic symptoms can lead to incorrect diagnosis and treatment of bipolar disorder.

Objectives: To screen for and examine the clinical presentation and effect on functioning of bipolar disorder in adults in a primary care setting.

Design, Setting, and Participants: 1157 patients aged between 18 and 70 years seeking care at an urban general medicine clinic serving a low-income population. The study was conducted between December 2001 and January 2003.

Main Outcome Measures: Prevalence and treatment of bipolar disorder and patient functioning. The Mood Disorder Questionnaire, the Primary Care Evaluation of Mental Disorders (PRIME-MD) Patient Health Questionnaire, the Medical Outcomes Study 12-Item Short Form health survey, and the Sheehan Disability Scale were the measures used. Also included were data on past mental health treatments and a review of medical records and ICD-9 codes for each visit beginning from 6 months prior to the screening day.

Results: The prevalence of a positive screen for lifetime bipolar disorder was 9.8% (N = 112; 95% CI = 8.0% to 11.5%) and did not differ significantly by age, sex, or race/ethnicity. 81 patients (72.3%) who screened positive for bipolar disorder sought professional help for their symptoms, but only 9 (8.4%) reported being diagnosed with bipolar disorder. Current major depressive episode or an anxiety or substance use disorder was found in 75 patients (68.2%) who screened positive for bipolar disorder. Only 7 (6.5%) of 112 patients reported taking a mood-stabilizer in the past month. Evidence of current depression was recorded by primary care physicians in 47 patients (49.0%) who screened positive for bipolar disorder, but a diagnosis of bipolar disorder was not recorded either in administrative billing or the medical record of any of these patients. Worse health-related quality of life and increased social and family life impairment was reported in patients who screened positive for bipolar disorder compared with those who screened negative.

Conclusions: A positive screen for bipolar disorder appears to be common, clinically significant, and underrecognized in an urban general medicine clinic. Risks associated with treating bipolar disorder with antidepressant monotherapy necessitate education about screening, management, and pharmacotherapy of bipolar disorders for primary care physicians.

Long-Term, Open-Label Study of the Safety and Efficacy of Atomoxetine in Adults With Attention-Deficit/Hyperactivity Disorder: An Interim Analysis

Adler LA, Spencer TJ, Milton DR, et al.

J Clin Psychiatry 2005;66:294-299

Background: Attention-deficit/hyperactivity disorder (ADHD) is an early-onset neuropsychiatric disorder that affects 3% to 7% of school-age children and 4% of adults. Its pathophysiology is thought to involve the dopaminergic and noradrenergic pathways associated with attention control and impulsivity. These symptoms have largely been defined in the childhood population, but the course of the condition and expression in the adult population are not as well characterized.

Method: This is an ongoing, 3-year, open-label study consisting of adults with DSM-IV ADHD who were previously enrolled in 1 of 2 double-blind, acute-treatment studies of atomoxetine. The results of the interim analysis reported here were derived from 384 patients at 31 sites who had been studied for a period of up to 97 weeks. The primary efficacy measure was the Conners' Adult ADHD Rating Scale-Investigator Rated: Screening Version (CAARS-Inv:SV) total ADHD symptom score. In addition, safety, adverse events, and vital sign measurements were assessed.

Results: Significant improvement was noted with atomoxetine therapy, with mean CAARS-Inv:SV total ADHD symptom scores decreasing 33.2% from

29.2 (baseline of open-label therapy) to 19.5 (endpoint of open-label therapy) ($p < .001$). Similar and significant decreases were noted for the secondary efficacy measures. Adverse events consisted primarily of pharmacologically (noradrenergic) expected effects, such as increases in heart rate and blood pressure and a slight decrease in weight.

Conclusion: The results of this interim analysis of an ongoing, open-label study of adults with ADHD support the long-term efficacy, safety, and tolerability of atomoxetine for the treatment of adult ADHD.

Efficacy and Tolerability of Citalopram in the Treatment of Late-Life Anxiety Disorders: Results From an 8-Week Randomized, Placebo-Controlled Trial

Lenze EJ, Mulsant BH, Shear MK, et al.
Am J Psychiatry 2005;162:146–150

Background: Although anxiety disorders are commonly seen in the elderly population, there is a paucity of data concerning the treatment of these disorders in this population. The efficacy of the selective serotonin reuptake inhibitor (SSRI) medication citalopram in the treatment of late-life anxiety disorders was evaluated.

Method: 34 subjects aged ≥ 60 years with a DSM-IV anxiety disorder and a Hamilton Rating Scale for Anxiety (HAM-A) score of 17 or higher were randomly assigned to double-blind treatment with citalopram ($N = 17$) or placebo ($N = 17$). Measures of response were a score of 1 or 2 (very much or much improved) on the Clinical Global Impressions-Improvement scale or a 50% reduction in HAM-A score. Comparisons of response and side effects between the 2 treatment conditions were made using χ^2 tests and linear modeling.

Results: 65% of the citalopram patients showed a response at 8 weeks versus 24% of the placebo patients. Sedation was the most common side effect for the citalopram group.

Conclusion: This study supports the use of citalopram as an effective and safe treatment for late-life anxiety disorders.

The Safety of Newer Antidepressants in Pregnancy and Breastfeeding

Gentile S
Drug Saf 2005;28:137–152

Background: Particularly for women with preexisting psychiatric illnesses, pregnancy and postpartum are considered relatively high risk periods for depressive episodes. Beginning or continuing pharmacologic treatment of depression during these periods may therefore be necessary.

Study Selection: This article reviews data on the effects of exposure to various antidepressant medications on the fetus and infant through the placenta and maternal milk. Articles reviewed included data on the antidepressants fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, escitalopram, mirtazapine, venlafaxine, reboxetine, and bupropion.

Data Synthesis: Teratogenic risks, perinatal toxicity, and effects on newborn neurobehavioral development associated with exposure to these medications through the placenta or maternal milk should be carefully assessed before starting psychopharmacologic treatment in pregnant or lactating women. Despite limitations of some studies reviewed, older selective serotonin

reuptake inhibitors (SSRIs) and venlafaxine seem to be devoid of teratogenic risks (awaiting further data on escitalopram). Data concerning possible effects on neonatal adaptation and long-term infant neurocognitive development from exposure to SSRIs via the placenta and breast milk are still controversial. Reports have shown, however, that there may exist an association between placental exposure to SSRIs and adverse but self-limiting effects on neonatal adaptation. Information on both teratogenic and functional teratogenic risks associated with exposure to bupropion, mirtazapine, and reboxetine is incomplete or absent. Therefore, at present, these compounds should not be used as first-line treatments for depression during pregnancy and breastfeeding.

Conclusions: Untreated maternal depression carries its own risks including negative impact on the emotional development of children and attempted suicide and infanticide. Consequently, the role of the clinician must be to help mothers weigh the risks of prenatal exposure of the fetus to drugs against the potential risks of untreated depression or abrupt discontinuation of pharmacologic treatment. Since degree of severity appears to be the most relevant parameter to guide the use of psychopharmacologic treatments in pregnant or breastfeeding women with depression, careful evaluation of psychopathologic condition must precede this decision.

A Retrospective Study of SSRI Treatment in Adolescent Anorexia Nervosa: Insufficient Evidence for Efficacy

Holtkamp K, Konrad K, Kaiser N, et al.
J Psychiatr Res 2005 May;39:303–310

Background: Limited efficacy has been shown with selective serotonin reuptake inhibitors (SSRIs) in the treatment of eating disorder psychopathology and comorbid symptoms of malnourished patients with anorexia nervosa. Recent data suggest that SSRIs may prevent relapse among weight-restored patients. Although some previous studies included patients in late adolescence, most subjects have been adults. This study sought to determine the effects of SSRI treatment in partially weight-restored children and adolescents with anorexia nervosa.

Method: This retrospective study included 32 females with anorexia nervosa (mean age = 14.5 ± 1.4 years). BMI, eating disorder psychopathology, depressive symptoms, and obsessive-compulsive symptoms were evaluated during inpatient treatment and at 3- and 6-month follow-up. At the 6-month follow-up, medication history during inpatient and outpatient treatment was reconstructed. 19 patients were treated with SSRIs; 13 subjects were unmedicated.

Results: While patients in the SSRI group had BMI and obsessive-compulsive symptoms similar to those in the non-SSRI group, their levels of core eating disorder psychopathology and depressive symptoms were higher at the start of medication. Readmission rates were 36% in the SSRI group and 31% in the non-SSRI group ($p = .72$). Repeated measures analysis of variance revealed no significant group with time interactions for BMI ($p = .84$), core eating disorder symptoms ($p = .79$), depressive symptoms ($p = .75$), and obsessive-compulsive symptoms ($p = .40$), indicating minimal or no effects of SSRIs on their course.

Conclusion: These results challenge the efficacy of SSRI medication for eating disorder psychopathology as well as comorbid depressive and obsessive-compulsive symptoms in adolescent anorexia nervosa. Clinicians should be cautious in treating adolescent anorexia nervosa with SSRIs.

Pregnancy Outcome of Women Exposed to Bupropion During Pregnancy: A Prospective Comparative Study

Chun-Fai-Chan B, Koren G, Fayez I, et al.

Am J Obstet Gynecol 2005;192:932-936

Objective: Bupropion, originally developed to treat depression, was later found to be effective for smoking cessation. No prospective comparative studies exist to date examining its safety in pregnancy. This study sought primarily to determine whether bupropion increases the risks for major malformations above baseline. Authors also recorded the rates of live births, stillbirths, and spontaneous and therapeutic abortions; mean birth weight; and gestational age at birth.

Study design: Subjects were women taking bupropion who were pregnant or planning to become pregnant. Pregnancy outcome follow-up was performed between 4 months and 1 year postpartum. The 3 comparison groups were (1) women taking bupropion versus those taking a nonteratogen, (2) women taking bupropion for depression versus those taking other antidepressants, versus those taking a nonteratogen, (3) spontaneous abortions occurring in women taking bupropion for depression, versus those taking another antidepressant versus those taking a nonteratogen.

Results: Follow-up was completed for 136 women taking bupropion during the first trimester of pregnancy. There were 105 live births and no major malformations. Mean birth weight was 3450 g, and mean gestational age at delivery was 40 weeks. There were 20 spontaneous abortions, 10 therapeutic abortions, 1 stillbirth, and 1 neonatal death. No statistically significant differences were found for any endpoint examined between the exposed and comparison groups, except that there were significantly more spontaneous abortions in the bupropion group ($p = .009$).

Conclusion: The results suggest that bupropion does not increase rates of major fetal malformations above baseline. Other studies examining the safety of antidepressants during pregnancy have found similarly high rates of spontaneous abortions.

Effect of Gender on Suicide Attempters Versus Nonattempters in an Adolescent Inpatient Unit

Fennig S, Geva K, Zalzman G, et al.

Compr Psychiatry 2005;46:90-97

Background: Gender differences have been noted in risk factors for suicide and attempted suicide. Comparative studies to date have used only 2 groups and a limited number of measures. This cross-sectional study compared the effect of gender on suicide in 4 groups of adolescent psychiatric inpatients.

Method: 404 patients, aged between 12 and 21 years, were divided into groups of male suicide attempters ($N = 76$), male nonattempters ($N = 103$), female suicide attempters ($N = 143$), and female nonattempters ($N = 82$). The Child Suicide Potential Scale, Beck Depression Inventory, State-Trait Anxiety Inventory, Overt Aggression Scale, Multidimensional Anger Inventory, Impulsivity Control Scale, and Life Style Index were used to evaluate patients for life events, affective disorders, aggression, impulsivity, ego defense mechanisms, and death perception. Multivariate regression with stepwise logistic models was used for analyses.

Results: The prevalence of depression and anxiety was higher in female nonattempters than male nonattempters, but no such gender differences existed among the attempters. Prevalence of antisocial behavior was higher in male attempters

than female attempters, but no such gender differences existed among the nonattempters. Gender differences were found for defense mechanisms in the attempters. Separate logistic regression models for male and female patients revealed that antisocial behavior and anxiety were common predictors of suicide attempt, destructiveness was a predictor in female patients only, and depression was associated with suicide attempt in male patients only.

Conclusions: Distinct differences are seen in psychopathology, ego defense mechanisms, and life events in suicide-prone male and female adolescent inpatients compared to adolescent inpatients without a history of suicide attempt. Deviation from gender-specific behaviors must raise suspicion of a risk of attempted suicide.

A Population-Based Study of Anxiety as a Precursor for Depression in Childhood and Adolescence

Rice F, van den Bree MB, Thapar A

BMC Psychiatry 2004;4:43

Background: Anxiety and depression co-occur in children and adolescents; anxiety commonly precedes depression. Although some evidence suggests that the association between early anxiety and later depression is explained by a shared genetic etiology, the contribution of environmental factors is less well examined, and whether anxiety itself is a phenotypic risk factor for later depression is unknown.

Objective: To evaluate these explanations of the association between early anxiety and later depression.

Method: Anxiety and depressive symptoms were assessed longitudinally in a U.K. population-based sample of 676 twins aged 5 to 17 years at baseline by parental questionnaire. Depression was assessed 3 years later by parental and adolescent questionnaire.

Results: The authors found shared genetic effects between early anxiety and later depression. A model of a phenotypic risk effect from early anxiety on later depression provided a poor fit to the data. However, significant genetic effects were specific to later depression, showing that early anxiety and later depression do not index entirely the same genetic risk.

Conclusion: Anxiety and depression are associated over time because they share a partly common genetic etiology, not because the anxiety phenotype leads to later depression.

Treatment of Depression Improves Physical Functioning in Older Adults

Callahan CM, Kroenke K, Counsell SR, et al, for the IMPACT Investigators

J Am Geriatr Soc 2005;53:367-373

Objective: To determine the effect of collaborative care management for depression on physical functioning in older adults.

Design: Multisite randomized clinical trial.

Setting: 18 primary care clinics from 8 health care organizations.

Participants: Patients aged ≥ 60 years with major depressive disorder ($N = 1801$).

Intervention: Patients were randomly assigned to the Improving Mood: Promoting Access to Collaborative Treatment (IMPACT) intervention ($N = 906$) or to a control group ($N = 895$). Patients in the control group had access to all health ser-

vices available as part of usual care; those in the intervention group had access to a depression clinical specialist who coordinated depression care with their primary care physician for 12 months.

Measurements: The 12-item short form Physical Component Summary (PCS) score (range: 0–100) and instrumental activities of daily living (IADLs) (range: 0–7).

Results: Mean age of subjects was 71.2 years, 65% were women, and 77% were white. At baseline, the mean PCS score was 40.2 and the mean number of IADL dependencies was 0.7; 45% of participants rated their health as fair or poor. Intervention patients, compared with usual-care patients, had significantly better physical functioning at 1 year according to a between-group difference in PCS scores of 1.71 (95% CI = 0.96 to 2.46) and in IADLs of -0.15 (95% CI = -0.29 to -0.01). Intervention patients were also less likely than usual-care patients to rate their health as fair or poor (37.3% vs. 52.4%, $p < .001$). All patients with improved depression were more likely to experience improved physical functioning.

Conclusion: The authors concluded that the IMPACT collaborative care model for late-life depression improves physical function more than usual care.

Pain Reactivity in 2-Month-Old Infants After Prenatal and Postnatal Serotonin Reuptake Inhibitor Medication Exposure

Oberlander TF, Grunau RE, Fitzgerald C, et al.
Pediatrics 2005;115:411–425

Objective: This prospective study evaluated biobehavioral responses to acute procedural pain in infants aged 2 months with prenatal and postnatal selective serotonin reuptake inhibitor (SSRI) medication exposure. Previous findings have shown reduced pain responses in newborns after prenatal exposure; therefore, altered pain reactivity may also be expected at 2 months of age.

Method: 11 infants with prenatal only SSRI exposure (fluoxetine, $N = 2$; paroxetine, $N = 9$); 30 infants with prenatal and postnatal (via breast milk) SSRI exposure (fluoxetine, $N = 6$; paroxetine, $N = 20$; sertraline, $N = 4$); and 22 unexposed control infants were compared in terms of facial action (Neonatal Facial Coding System) and cardiac autonomic reactivity derived from the respiratory activity and heart rate variability (HRV) responses to a painful event (heel lance) at baseline, during the painful event, and during the recovery periods. Bayley Scales of Infant Development-II were administered at ages 2 and 8 months, and measures of maternal mood and drug levels were also obtained.

Results: Facial action increased in all groups immediately after the lance but was significantly lower during the painful event in the group of infants exposed during the prenatal period only. Heart rate was significantly lower during recovery among infants in the prenatal exposure group and the prenatal and postnatal exposure group. Exposed infants had a greater return of parasympathetic cardiac modulation in the recovery period using measures of HRV and the transfer relationship between heart rate and respiration, whereas a sustained sympathetic response continued in control infants. Although postnatal exposure via breast milk was extremely low when infant drug levels could be detected in the prenatal and postnatal exposure group, changes in heart rate and HRV from painful event to recovery were greater among those infants with drug levels too low to be quantified. Neither maternal mood nor the presence of clonazepam influenced pain responses.

Conclusions: Infants with prenatal SSRI exposure alone exhibited blunted facial-action responses, and reduced parasympathetic withdrawal and increased parasympathetic cardiac modulation were observed in infants with both prenatal and postnatal exposure during recovery from a painful event. Data are consistent with patterns of pain reactivity observed in the same cohort during the newborn period. Postnatal exposure via breast milk was extremely low, and altered biobehavioral pain reactivity was not associated with levels of maternal reports of depression; therefore, these data suggest possible sustained neurobehavioral outcomes beyond the newborn period. As the first study of pain reactivity in infants with prenatal and postnatal SSRI exposure, findings were limited by the lack of an unmedicated depressed control group, small sample size, and understanding of infant behaviors associated with pain reactivity that could have also been influenced by prenatal SSRI exposure. Developmental and clinical implications remain unclear, as do mechanisms that may have altered serotonin-mediated pain modulation in infants after SSRI exposure. The treatment of maternal depression with antidepressants both during and after pregnancy and the promotion of breastfeeding remains a key goal for all clinicians. Additional study is needed on the long-term effects of prenatal and early postnatal SSRI exposure.

Relation of the Tocopherol Forms to Incident Alzheimer Disease and to Cognitive Change

Morris MC, Evans DA, Tangney CC, et al.
Am J Clin Nutr 2005;81:508–514

Background: High intake of vitamin E from food (tocopherol) is inversely associated with Alzheimer's disease, while high intake of vitamin E from supplements, which usually contain alpha-tocopherol, is not.

Objective: To determine whether food intakes of vitamin E, alpha-tocopherol equivalents (a measure of the relative biologic activity of tocopherols and tocotrienols), or individual tocopherols would protect against incident Alzheimer's disease and cognitive decline over a 6-year period in Chicago Health and Aging Project participants.

Design: Four cognitive tests and clinical evaluations for Alzheimer's disease were administered to community residents aged ≥ 65 years, and a food-frequency questionnaire was used for dietary assessment. The study was conducted from 1993 to 2002.

Results: In 1041 participants who were clinically evaluated ($N = 162$ incident cases), tocopherol intake from food was related to 4-year incidence of Alzheimer's disease, determined by logistic regression, and, in 3718 participants, to change in global cognitive score, determined by mixed models. Separate multiple-adjusted models that included intakes of saturated and trans fats and docosahexaenoic acid revealed an association between higher intakes of vitamin E (relative risk = 0.74 per 5-mg/day increase; 95% CI = 0.62 to 0.88) and alpha-tocopherol equivalents (relative risk = 0.56 per 5-mg/day increase; 95% CI = 0.32 to 0.98) and reduced incidence of Alzheimer's disease. Independent associations were found for alpha- and gamma-tocopherol. A slower rate of cognitive decline was associated with intake of vitamin E, alpha-tocopherol equivalents, and alpha- and gamma-tocopherols in separate mixed models.

Conclusion: Tocopherol forms other than alpha-tocopherol alone may be important in the protective association of vitamin E with Alzheimer's disease.

Maternal Depressive Symptoms and Children's Receipt of Health Care in the First 3 Years of Life

Minkovitz CS, Strobino D, Scharfstein D, et al.

Pediatrics 2005;115:306–314

Background: Maternal depression has a detrimental effect on mother-child interactions and child behavior and development. Little is known, however, about the association between maternal depression and children's receipt of health care.

Objective: To determine if maternal depressive symptoms are associated with children's receipt of acute and preventive health care services in the first 30 months postpartum.

Design: Data collected prospectively as part of the National Evaluation of Healthy Steps for Young Children (HS) were examined, and sources included medical records abstracted for the first 32 months, enrollment questionnaires, and parent interviews at 2 to 4 and 30 to 33 months postpartum. Acute care was defined as hospitalizations and emergency department visits, and preventive care was defined as well-child visits and vaccinations. The Center for Epidemiologic Studies-Depression Scale was used to evaluate maternal depressive symptoms. Logistic regression for dichotomous outcomes and Poisson regression for count outcomes were used to estimate the effect of maternal depressive symptoms on children's receipt of health care. Models were adjusted for baseline demographic characteristics, child health status, participation in HS, and site of enrollment.

Results: Of the 5565 families enrolled in HS, 88% completed the parent interviews at 2 to 4 months, 67% completed the parent interviews at 30 to 33 months, and 96% had medical records abstracted. 17.8% of mothers reported depressive symptoms at 2 to 4 months, 15.5% at 30 to 33 months, and 6.4% at both. Increased use of acute care, including emergency department visits in the past year, was reported at 30 to 33 months for children whose mothers reported depressive symptoms at 2 to 4 months (OR = 1.44, CI = 1.17 to 1.76). These children also had decreased receipt of preventive services including age-appropriate well-child visits (e.g., at 12 months [OR = 0.80, CI = 0.67 to 0.95]) and up-to-date vaccinations at 24 months for 4 doses of diphtheria, tetanus, pertussis, 3 doses of polio vaccine, and 1 dose of measles-mumps-rubella (OR = 0.79, CI = 0.68 to 0.93). No association was found between maternal depressive symptoms at 30 to 33 months and children's preceding use of care.

Conclusions: Maternal depressive symptoms in early infancy contribute to unfavorable patterns of health care seeking for children. Options for enhancing the receipt of health care among young children include increased provider training for recognizing maternal depressive symptoms in office settings, more effective systems of referral, and development of partnerships between adult and pediatric providers.

Prevention and Treatment of Poststroke Depression With Mirtazapine in Patients With Acute Stroke

Niedermaier N, Bohrer E, Kerstin Schulte K, et al.

J Clin Psychiatry 2004;65:1619–1623

Background and objective: Poststroke depression is one of the most frequent complications of stroke, affecting approximately 20% to 40% of all patients. In spite of the importance of this neuropsychiatric disorder, little attention has been given to the prevention of poststroke depression. The purpose of this study was to examine whether prophylactic treatment with the antidepressant mirtazapine in patients with acute stroke given from day 1 after the incidence prevents poststroke depression.

Method: Patients with ischemic stroke received either 30 mg mirtazapine or no antidepressant medication from day 1 after the stroke in an open, randomized study design. Data were collected from August 2001 to December 2002. Seventy patients were enrolled in the study and were reexamined on days 7, 44, 90, 180, 270, and 360 using neurologic, functional, and depression rating scales. Those poststroke patients who developed depression (DSM-IV criteria) but had been randomly assigned to the nontreatment group were given the antidepressant mirtazapine after the diagnosis of depression had been established.

Results: Forty percent (14/35) of the nontreated patients and only 5.7% (2/35) of the patients who were treated with mirtazapine developed poststroke depression. Altogether, 16 patients developed poststroke depression, 15 of whom remitted after initiation of treatment with mirtazapine.

Conclusion: Mirtazapine significantly reduced the rate of poststroke depression in patients with acute stroke. The study also demonstrated that this antidepressant was highly effective in treating poststroke depression.

A Randomized Effectiveness Trial of Cognitive-Behavioral Therapy and Medication for Primary Care Panic Disorder

Roy-Byrne PP, Craske MG, Stein MB, et al.

Arch Gen Psychiatry 2005;62:290–298

Background: Panic disorder is prevalent and often disabling among primary care patients. Many studies have assessed effective treatments for depression in primary care, but few have been conducted for panic disorder.

Objective: To implement and evaluate a combined pharmacotherapy and cognitive-behavioral intervention for panic designed for the primary care setting.

Design: Randomized controlled study comparing intervention to treatment as usual.

Setting: 6 primary care clinics, associated with 3 university medical schools, serving an ethnically and socioeconomically diverse patient population.

Participants: Primary care patients with DSM-IV panic disorder (N = 232). Only those comorbid mental and physical disorders that did not contraindicate the treatment to be provided and were not acutely life threatening were permitted.

Intervention: Patients were randomly assigned to the treatment-as-usual group or an intervention group that received a combination of up to 6 sessions (across 12 weeks) of cognitive-behavioral therapy (CBT) modified for the primary care setting, with up to 6 follow-up telephone contacts during the next 9 months, and algorithm-based pharmacotherapy provided by the primary care physician with guidance from a psychiatrist. Behavioral health specialists, the majority inexperienced in CBT for panic disorder, were trained to deliver the CBT and coordinated overall care, including pharmacotherapy.

Main Outcomes Measures: Proportion of subjects achieving remission, defined as no panic attacks in the past month, minimal anticipatory anxiety, and Fear Questionnaire agoraphobia subscale score < 10; proportion of patients achieving response, defined as an Anxiety Sensitivity Index score < 20; and change over time in scores on the World Health Organization Disability Scale and Short Form 12.

Results: Patients in the combined CBT and pharmacotherapy group experienced sustained and gradually increasing improvement relative to those in the treatment-as-usual group. Significantly higher rates of subjects achieving remission

(3 months: 20% vs. 12%; 12 months: 29% vs. 16%) and response (3 months: 46% vs. 27%; 12 months: 63% vs. 38%) were seen at all points. Scores on the World Health Organization Disability Scale (all points) and the Short Form 12 (3 and 6 months) were also significantly improved in the combined intervention group. These effects were obtained in spite of similar rates of delivery of guideline-concordant pharmacotherapy to the 2 groups.

Conclusion: Use of the collaborative care model and a CBT-naïve, midlevel health specialist to deliver combined evidence-based CBT and medication is feasible and significantly more effective than usual care for panic disorder in the primary care setting.

Detecting Depression in Alzheimer's Disease: Evaluation of Four Different Scales

Muller-Thomsen T, Arlt S, Mann U, et al.

Arch Clin Neuropsychol 2005;20:271-276

Background: Depression is frequent in Alzheimer's disease (AD). The prevalence of depressive symptoms depends on the severity of dementia and the instruments used to evaluate it.

Objective and Method: To assess the prevalence of depression according to severity of dementia by 4 different scales: the 15-point Geriatric Depression Scale (GDS), the Montgomery-Asberg Depression Rating Scale (MADRS), the Cornell Scale for Depression in Dementia (CSDD), and the Nurses Observation Scale for Geriatric Patients (NOSGER). The study population consisted of 316 patients with AD from a psychiatric outpatients memory clinic, which was divided into 2 groups: mild AD (Mini-Mental Status Examination [MMSE] score \geq 18) and moderate to severe AD (MMSE score $<$ 18). Internal consistency and correlation of these scales were also calculated.

Results: The prevalence of depression ranged between 27.5% and 53.4% in mild AD and between 36.3% and 68.4% in moderate to severe AD. For all scales, internal consistency was good (Cronbach alpha = 0.63-0.85). For the MADRS and CSDD, internal consistency was independent of the stage of AD, whereas for the GDS and NOSGER, internal consistency decreased with severity of dementia. Correlation between the scales was better in mild AD than in moderate to severe AD; the best results were obtained for the correlation between CSDD and MADRS in both groups.

Conclusion: In this study population, the CSDD and MADRS were the most consistent tools for detecting depression in AD independently of the severity of dementia.

Neuropsychological Test Performance in Healthy Elderly Volunteers Before and After Donepezil Administration: A Randomized, Controlled Study

Beglinger LJ, Tangphao-Daniels O, Kareken DA, et al.

J Clin Psychopharmacol 2005;25:159-165

Background: Neuropsychological performance was examined after administration of donepezil in healthy elderly participants. The primary objective was to determine the sensitivity of a series of neuropsychological measures to detect cognitive changes after drug administration using typical phase I research parameters (e.g., a small sample over a short treatment period).

Method: The double-blind parallel study was conducted over a period of 6 weeks. Twenty-six healthy participants aged

55 to 75 years were randomly assigned to donepezil, 5 mg twice a day, (N = 14) or placebo twice a day (N = 12) for 14 days. Neuropsychological tests were administered on days 0, 14 (prerandomization), 28 (end of treatment), and 42 (washout).

Results: Subjects in the donepezil group performed significantly worse on 2 tests of speed, attention, and short-term memory ($p < .05$) after 14 days of treatment (day 28) compared with the placebo group. During treatment with donepezil, no significant improvement in performance on any test was seen.

Conclusion: Results were consistent with a previous study in healthy young participants and should be considered when designing clinical development plans for putative cognitive-enhancing drugs. These results also raise the question of when the optimal time to begin treatment is in patients who do not yet meet criteria for dementia.

Treatment Guidelines for Children and Adolescents With Bipolar Disorder

Kowatch RA, Fristad M, Birmaher B, et al;

the Child Psychiatric Workgroup on Bipolar Disorder

J Am Acad Child Adolesc Psychiatry 2005;44:213-235

Background: Clinicians need current treatment guidelines for children and adolescents with bipolar disorder.

Method: Guidelines were developed by expert consensus and a review of the existing literature about the diagnosis and treatment of pediatric bipolar disorders.

Results: The guidelines consist of 4 sections that include information on diagnosis, comorbidity, acute treatment, and maintenance treatment.

Conclusion: These guidelines should not serve as an absolute standard of medical or psychological care but rather as a clinically useful guide for evaluation and treatment of children and adolescents with bipolar disorder. As our evidence base increases and practice patterns evolve, these guidelines are subject to change.

A Large, Double-Blind, Randomized Clinical Trial of Methylphenidate in the Treatment of Adults With Attention-Deficit/Hyperactivity Disorder

Spencer T, Biederman J, Wilens T, et al.

Biol Psychiatry 2005;57:456-463

Background: There are few controlled studies of methylphenidate in adults with attention-deficit/hyperactivity disorder (ADHD), and none have reported clear results. One previous, pilot study has suggested that these results were the result of inadequate dosing.

Method: 146 adults with DSM-IV ADHD participated in a randomized, 6-week, placebo-controlled, parallel study of methylphenidate. Standardized instruments were used for diagnosis; separate assessments were made for ADHD, depressive, and anxiety symptoms; and the average oral daily dose was 1.1 mg/kg/day.

Results: A marked therapeutic response was seen for ADHD symptoms in the methylphenidate treatment group compared with the placebo group (76% vs. 19%). Treatment was safe and well tolerated. Response to methylphenidate was independent of socioeconomic status, gender, and lifetime history of psychiatric comorbidity.

Conclusions: Robust doses of methylphenidate are effective in the treatment of adult ADHD.