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PSYCHIATRIC NEWS

The First and Last Word in Psychiatry

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APA's 2013 annual meeting is being held in San Francisco May 18 to 22. Among the meeting highlights are lectures by Nobel laureates and a special track of sessions sponsored by the National Institute on Drug Abuse. More information on these sessions appears on pages 20 and 21.

More Graduates Choose Psychiatry In 2013 Match

A new "all in" policy for this year's match, along with an increase in the number of medical students, contributes to the increase in graduates choosing psychiatry.

BY MARK MORAN

A total of 681 U.S. medical student seniors "matched" into psychiatry residencies in this year's National Resident Matching Program (NRMP).

This is an increase from 616 in 2012, or from 3.9 percent to 4.2 percent of seniors selecting careers in psychiatry. The uptick in graduates entering the profession is good news for psychiatry, reversing a trend of several years in which the numbers were dropping. Last year's figure of 616 was a decrease from 640 the year before and 670 in 2010 (see chart on page 24).

The annual match, in which the choices of graduating medical students are paired with those of residency programs, is typically watched as an indicator of workforce size and makeup of the various medical specialties for the coming years. But a new wrinkle in the match program makes this year's numbers harder to interpret—and may point to a significant problem for many medical school graduates.

This year the NRMP instituted an "all in" policy whereby residencies were required to enter all of their residency slots in the match. In past years, programs could participate in the NRMP by registering and filling some available

see ***Match*** *on page 24*

States' Decision on Expanding Medicaid Will Impact Inpatient Psychiatric Care

The percentage of a hospital's indigent patients is likely to be much higher on psychiatric wards; thus diminished DSH payments next year will disproportionately affect psychiatric care in states that don't expand Medicaid rolls.

BY MARK MORAN

States that opt not to expand their Medicaid rolls when that option becomes available next year under the Affordable Care Act may be courting disaster.

That's because beginning next year at the same time the Medicaid expansion becomes an option, the federal government will begin to reduce—ultimately by 50 percent—what are known as Disproportionate Share Hospital (DSH) payments that general hospitals receive for care of the uninsured.

States that do not expand their Medicaid rolls to those earning 133 percent of the federal poverty level will continue to bear the burden of care for the uninsured, but with substantially less federal DSH support. And since a great many of those uninsured are psychiatric patients, the funding shortfall is likely to fall heavily on the care of mentally ill individuals.

Joseph Parks, M.D., medical director of the Missouri Department of Mental Health, is raising alarms about this little-discussed provision in the ACA that he believes could dramatically affect state mental health budgets in ways that will affect patient care. Parks contacted *Psychiatric News* and began raising red flags with colleagues in other states after a study undertaken at the direction of Missouri Gov. Jay Nixon (D) looked at the pros and cons of Medicaid expansion on four Missouri hospitals—CoxHealth-Springfield; St. Joseph Health Center-St. Charles/Wentzville; Truman Medical Center-Lakewood; and Twin Rivers

see ***Medicaid*** *on page 22*

PERIODICALS: TIME SENSITIVE MATERIALS

INSIDE

Treatment refusals rise as more patients enter the criminal justice system.

Nora Volkow, M.D., will be a lecturer in the annual meeting NIDA track.

THERE ARE GOOD REASONS AMERICAN PROFESSIONAL AGENCY IS A LEADER IN PROVIDING MALPRACTICE INSURANCE FOR PSYCHIATRISTS HERE ARE TWO OF THEM.

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ANNUAL MEETING

Be the First to Get *DSM-5*

Attendees at APA's 2013 annual meeting are invited to attend a special event at the American Psychiatric Publishing (APP) Bookstore on Saturday, May 18, from 4 p.m. to 5 p.m. Attendees will have an exclusive opportunity to purchase *DSM-5* before it goes on sale to the public, receive a free gift with purchase, and meet the chairs of the *DSM-5* Task Force. And APA members are eligible to make their purchases at a discount. To register for the meeting, see box on page 21.

Departments

FROM THE PRESIDENT

Mindful Exercises and Meditation: Neurobiological Effects

BY DILIP JESTE, M.D.

There is a tendency to divide psychiatric interventions into two distinct groups: pharmacological/biological and psychosocial/behavioral. Such a classification implies that pharmaceuticals work through biologic mechanisms, while psychosocial ones act through mental/behavioral processes. This notion is simplistic and erroneous. Many studies have shown that at least a part of the effect of medications is probably placebo effect by virtue of a patient's expectations that a drug prescribed by an expert physician must be effective.

At the same time, a growing number of investigations have demonstrated biological changes, not just in function but also in the structure of the brain, produced by psychotherapeutic and social interventions. For example, cognition enhancement therapy has been shown to increase gray matter in specific regions of the brain on MRIs in people with schizophrenia. Similar research has recently expanded to integrative medicine—formerly called complementary and alternative medicine. Interventions such as meditation, Tai Chi, and yoga, which once were considered unscientific, have been found to be useful in some people with mental illness and to have significant effects on brain-based as well as blood-based biomarkers.

I invited Helen Lavretsky, M.D., M.S., who has been doing interesting and important research in this field, to discuss the psychological and biological effects of mindful exercises and meditation in people with mental illness. Dr. Lavretsky is a professor of psychiatry and director of the late-life mood, stress, and wellness research program at the UCLA Semel Insitute for Neuroscience and Human Behavior at the UCLA David Geffen School of Medicine.

Mind-Body Interventions Produce Positive Biopsychosocial Outcomes

BY HELEN LAVRETSKY, M.D., M.S.

Patients with mental disorders increasingly turn to integrative medicine for relief of symptoms of anxiety, mood, insomnia, impaired cognition, and perceived stress. Given widespread use of integrative, or mind-body, medicine among our patients, there is a need for greater awareness of and familiarity with the applications and biopsychosocial outcomes of commonly used mind-body interventions.

Mind-body medicine encompasses a number of techniques collectively known as mindful exercise (for example, yoga, Qi Gong, and Tai Chi), or meditation. Mindful physical exercise has become an increasingly used approach for improving psychological well-being and is defined as "physical exercise executed with a profound inwardly directed contemplative focus."

In general, mindful physical exercise contains the following key elements: (1) a noncompetitive, nonjudgmental meditative component, (2) mental focus on muscular movement and proprioceptive awareness combined with a low to moderate level of muscular activity, (3) centered breathing, (4) a focus on anatomic alignment (that is, spine, trunk, and pelvis) and proper physical form, and (5) energy-centric awareness of individual flow of intrinsic body energy, otherwise known as prana, life force, qi, or Kundalini. Mindful exercise seems to provide an immediate source of relaxation and mental quiescence. Scientific evidence has shown that medical conditions such as hypertension, cardiovascular disease, insulin resistance, depression, and anxiety disorders respond favorably to mindful exercises.

There is a growing database on physiological effects of mindful exercise and meditation. Tai Chi and Qi Gong have been shown to promote relaxation and decrease sympathetic output and to benefit anxiety, depression, hypertension, and immunity-mediated diseases. Tai Chi and Qi Gong have been reported to improve immune function and vaccine response. These practices also have been found to increase blood levels of endorphins and baroreflex sensitivity and to reduce levels of inflammatory markers (C-reactive protein), adrenocorticotrophic hormone (ACTH), and cortisol, implicating the hypothalamic-pituitary-adrenal axis as a mediator of stress and anxiety reduction. Electroencephalopathy studies of participants undergoing Tai Chi and Qi Gong exercise have shown increased frontal EEG alpha, beta, and theta wave activity, suggesting increased relaxation and attentiveness. These changes were not seen in comparison subjects who practiced aerobic exercise.

Our recent study of brief daily yogic meditation (Kirtan Kriya) for stressed family dementia caregivers found that meditation resulted in lower levels of depressive symptoms and improvements in mental health and cognitive functioning. Participants in the yogic meditation group showed a 43 percent improvement in telomerase activity after 12 minutes of daily practice for eight weeks, compared with 3.7 percent improvement in relaxation-music control participants. This suggests that brief daily meditation practices can benefit stress-induced cellular aging. Kirtan Kriya reversed the pattern of increased NF-κB-related transcription of pro-inflammatory cytokines and decreased IRF1-related transcription of innate antiviral response genes in distressed dementia caregivers. This reinforces the relationship between stress reduction and beneficial immune response. In the same study, nine caregivers received brain FDG-PET scans at baseline and postintervention. Significant group differences over time were found in various patterns of regional cerebral metabolism, suggesting brain-fitness effects different from those of passive relaxation.

Studies of meditation also show decreased sympathetic nervous activity and increased parasympathetic activity associated with decreased heart rate and blood pressure, decreased respiratory rate, and reduced oxygen metabolism. Functional neuroimaging studies have corroborated these subjective experiences by demonstrating the up-regulation in brain regions of internalized attention and emotion processing with meditation. In a systematic review of neurobiological and clinical features of mindfulness meditation in the August 2012 *Psychological Medicine*, Chiesa and Serretti provided evidence on the neurobiological changes related to mindfulness meditation practice in psychiatric disorders. Meditation practices that focus on concentration of an object or mantra seem to elicit the activation of

see ***From the President*** *on page 21*

PROFESSIONAL NEWS

Gambling Disorder to Be Included in Addictions Chapter

Research indicates that gambling and substance-related and addictive disorders share a common reward-system neurocircuitry and behavioral patterns.

BY MARK MORAN

Gambling disorder will take its place among substance-related and addictive disorders in *DSM-5,* which will be published next month.

The new disorder replaces what was previously called pathological gambling in the "Impulse-Control Disorders Not Elsewhere Classified" section of earlier editions. While the criteria are nearly identical, the inclusion of the disorder with substance-related disorders reflects evidence showing the similarity of reward-related neurocircuitry and behavior patterns of addictive gambling to those of other substance-related addictions.

"The idea of a non-substance-related addiction may be new to some people, but those of us who are studying the mechanisms of addiction find strong evidence from animal and human research that addiction is a disorder of the brain reward system, and it doesn't matter whether the system is repeatedly activated by gambling or alcohol or another substance," said Charles O'Brien, M.D., chair of the *DSM-5* Work Group on Substance-Related and Addictive Disorders. "In functional brain imaging—whether with gamblers or drug addicts—when they are showed video or photograph cues associated with their addiction, the same brain areas are activated," he explained.

The addition of gambling disorder and its inclusion with substance-related disorders is the most prominent change to the 16th chapter that will appear in Section II of the new *DSM*. The multiaxial system of previous editions has been eliminated, and chapters are now arranged according to a "lifespan," or developmental, approach—disorders affecting children appearing first and those more common in older individuals appearing later.

DSM-5 consists of three sections: Section I gives an introduction with instructions on how to use the manual; Section II outlines the categorical diagnoses according to a revised chapter organization that eliminates the multiaxial system; and Section III includes conditions that require further research before their consideration as formal diagnoses, as well as cultural formulations and other information.

In an interview with *Psychiatric News*, O'Brien said clinicians will see two important changes to the criteria for all disorders listed in the chapter—the inclusion of "craving" as a symptom, and the elimination of "recurrent legal problems" as a criterion.

More generally, the criteria in the chapter no longer include "dependence" and "abuse" as separate entities. "Dependence is a normal physiological reaction that can occur with many medications or substances in which the effect diminishes with time and repetition," he said. "It's been the cause of problems because sometimes pain medications or antidepressants have been withheld from patients because they were told they were—or believed themselves to be—'dependent.'"

And O'Brien said the term "abuse" is clinically meaningless, noting that "abuse, dependence, and addiction are all one continuous variable."

Rather, severity is rated in *DSM-5* on the number of criteria endorsed: two or three criteria indicate a mild disorder; four or five criteria, a moderate disorder; and six or more, a severe disorder. (The threshold for diagnosis of all the substance-related and addictive disorders is two or more criteria, in contrast to a threshold of one or more criteria for a diagnosis of *DSM-IV* substance abuse and three or more for *DSM-IV* substance dependence.)

Cannabis withdrawal is a new diagnosis in *DSM-5*, as is caffeine withdrawal (which in *DSM-IV* was in Appendix B, "Criteria Sets and Axes Provided for Further Study"). Early remission from a *DSM-5* substance use disorder is defined as at least three but less than 12 months without substance use disorder criteria (except craving), and sustained remission is defined as at least 12 months without criteria (except craving).

Other new *DSM-5* specifiers include "in a controlled environment" and "on maintenance therapy." O'Brien said these are to designate individuals whose addiction is in remission in a treatment setting or who are on methadone or other maintenance therapy.

Finally, the *DSM-IV* specifier for a physiological subtype has been eliminated, as has the *DSM-IV* diagnosis of polysubstance dependence. "Polysubstance dependence wasn't clinically useful," O'Brien said. "So many substance abusers use more than one substance, and gamblers often have accompanying problems with alcohol or drugs." PN

Additional information is posted at http://www.psychiatry.org/dsm5, including a fact sheet and video on substance use disorder and videos on how to diagnose substance use disorder and the impact of the new criteria on the number of people diagnosed with a substance use disorder.

Key Points

- Gambling disorder is included in *DSM-5,* replacing pathological gambling in the "Impulse-Control Disorders Not Elsewhere Classified" section of earlier editions.
- Inclusion of gambling with substance-related disorders reflects research evidence showing that reward-related neurocircuitry and behavior patterns of addictive gambling are similar to those of substance-related addictions.
- Craving has been added to criteria, and recurrent legal difficulties has been eliminated.
- Criteria in the chapter no longer include dependence and abuse as separate entities; abuse, dependence, and addiction are viewed as one continuous variable.
- The threshold for diagnosis of substance-related and addictive disorders is two or more criteria, in contrast to a threshold of one or more criteria for a diagnosis of *DSM-IV* substance abuse and three or more for *DSM-IV* substance dependence.
- The *DSM-IV* specifier for a physiological subtype has been eliminated, as has the diagnosis of polysubstance dependence.

Preorder Your *DSM-5* Now!

DSM-5 and related titles may be preordered at http://www.appi.org/SearchCenter/Pages/default.aspx?k=2555. Also, attendees at the 2013 annual meeting in May will have an exclusive opportunity to purchase *DSM-5* before it goes on sale to the public. The manual will be available in the American Psychiatric Publishing Bookstore in the Exhibit Hall in the Moscone Convention Center. Those who come to the bookstore on Saturday, May 18, from 4 p.m. to 5 p.m. can meet the *DSM-5* Task Force chairs and receive a free gift with purchase. (See the box on page 21 for meeting registration information.) Whether buying online or in person, APA members are eligible for a discount.

DSM-5 SELF-EXAM

Substance-Related and Addictive Disorders

An important departure from past diagnostic manuals is that in *DSM-5*, the substance-related and addictive disorders chapter has been expanded to include gambling disorder. This reflects the increasing and consistent evidence that some behaviors, such as gambling, also activate the same reward system with effects similar to those of drugs of abuse.

DSM-5 does not include the diagnoses of substance abuse and dependence as utilized in *DSM-IV.* Rather, criteria are provided for substance use disorder, accompanied by criteria for intoxication, withdrawal, substance induced-disorders, and unspecified substance-related disorders, where relevant.

These questions are from *DSM-5 Self-Exam Questions: Test Questions for the Diagnostic Criteria,* which may be preordered at http://www.appi.org/SearchCenter/Pages/SearchDetail.aspx?ItemId=62467 from American Psychiatric Publishing. The answers are posted at http://www.psychnews.org/pdfs/DSM-5_Self_Examination_QandA_3.pdf. The questions were developed under the leadership of Philip Muskin, M.D., a professor of clinical psychiatry at Columbia University College of Physicians and Surgeons. The book, available in August, contains 500 questions for all the categories of psychiatric disorders and includes Section III.

1. Which one of these is not a recognized alcohol-related disorder in *DSM-5*?

a) Alcohol dependence
b) Alcohol use disorder
c) Alcohol intoxication
d) Alcohol withdrawal
e) Alcohol-induced sexual disorder

2. The criteria for hallucinogen use disorder are the same as for other substance use disorders, with one exception. Which of the following is *not* a recognized symptom or consequence

see ***Self-Exam*** *on page 22*

PROFESSIONAL NEWS

FDA Said to Miss Adverse Events Caused by Dietary Supplements

Contrary to common perception, dietary supplements are not always safe, but the FDA is hampered by a lack of money to collect useful data and monitor safety problems.

BY JUN YAN

When it comes to protecting the public from the side effects and toxicities of dietary supplements, the Food and Drug Administration's (FDA) current adverse-event reporting system is missing a substantial chunk of the complaints that consumers have registered, according to a Government Accountability Office (GAO) report released March 18.

Dietary supplements, which include vitamins, minerals, and herbal products, constitute a $30-billion annual business in the United States, and the demand for these products is increasing, according to 2011 estimates published by *Nutrition Business Journal*. The FDA estimated that about 55,000 dietary supplement products were on the market in 2009.

Dietary supplements are primarily regulated by the FDA's Center for Food Safety and Applied Nutrition (CFSAN), and the agency's total regulatory activities in this area, ranging from inspections to safety surveillance, had a budget of $18.9 million in 2012, the GAO noted.

Unlike prescription drugs, however, dietary supplements can be marketed without the manufacturer having to prove their efficacy and safety. The burden of proof is on the FDA to demonstrate that a product is unsafe or harmful before actions can be taken. To date, one herbal ingredient, ephedrine alkaloids, which was used in weight-loss supplements, has been banned because of its link to several deaths.

For less-grave risks, the FDA can issue warning letters, seek court injunctions, block importation, or issue recalls for supplement products that fail inspections, contain adulterated ingredients, or pose other safety risks. In 2011, the agency issued about 90 warning letters related to dietary supplements and 30 voluntary-recall requests.

If consumers suffer adverse effects from a dietary supplement, they can report the problem directly to the FDA's MedWatch program, an online reporting portal (see URL at end of article). These reports are then transferred to CFSAN for evaluation. Consumers can also file a complaint with a local FDA field office or with the supplement's manufacturer or distributor, whose telephone number is required on the package. Starting in 2008, manufacturers or distributors were required to submit adverse-event reports to the FDA if the event is deemed serious. If the event is not considered serious, the manufacturer is not obligated but can voluntarily report it.

(The FDA defines a serious event as one that results "in a death, life-threatening experience, inpatient hospitalization, or birth defect or . . . require[s] a medical or surgical intervention to prevent the above-cited serious outcomes.")

From 2008 to 2011, the FDA received 6,307 adverse-event reports for dietary supplements, 71 percent of which came

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from the industry, reported as serious adverse events, according to the GAO audit. The GAO also found that from 2008 to 2010, 57 U.S. poison centers received 4,863 calls about adverse events related to dietary supplements, which was about 1,000 more reports than the FDA received in the same three-year period. These reports were generally not shared with the FDA, the GAO found.

Although the GAO recommends that the FDA obtain comprehensive adverse-event data from poison centers, CFSAN officials told the GAO that purchasing poison-center data would be cost prohibitive, as the CFSAN annual budget for adverse-event surveillance is about $400,000, far less than the price poison centers want to charge for the data.

Underreporting of adverse events is a constant concern. The GAO report cited reasons for underreporting supplement-related adverse events, in particular that "consumers, health care professionals, and others may not recognize the chronic or cumulative toxic effects of a dietary supplement, or . . . assume dietary supplements to be safe and not attribute negative effects to them." PN

FDA-issued product recalls are posted at www.fda.gov/Safety/MedWatch/default.htm.

PROFESSIONAL NEWS

DB's Mentorship Program Celebrates Anniversary

The Washington Psychiatric Society's Career, Leadership, and Mentorship Program celebrated its fifth anniversary recently. Program participants talked about what they've gained from it.

BY JOAN AREHART-TREICHEL

Five years ago, the Washington (D.C.) Psychiatric Society launched a Career, Leadership, and Mentorship (CLM) Program for young psychiatrists in the Washington area. It was funded by APA's Area 3 Council.

The CLM program's mission includes mentoring young psychiatrists, "engaging at local, regional, national, and international levels," and contributing to the development of future APA leaders. The program has tackled topics such as the benefits of APA membership, how to

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set up a private practice, pursuit of an academic research track, and leadership opportunities for APA members-in-training and early-career psychiatrists.

On February 28, several young psychiatrists who have participated in this program, as well as other interested psychiatrists, got together for a celebratory fifth anniversary party at a Washington, D.C., restaurant.

During the gathering, program participants discussed what they have gained from it.

For example, Urooj Saeed, M.D., who comes from St. Lucia in the West Indies and who is a second-year psychiatry resident at Howard University, has had Eliot Sorel, M.D., one of the founders of the CLM program, as a mentor. His help has been invaluable, she said. Currently the two of them are working on a project involving depression screening in primary care settings.

She also described her desire to become an APA member-in-training deputy representative from Area 3 to the APA Assembly. "I got lucky and was thrilled when I was elected," she said, adding that her message to other young psychiatrists is that it's important to become involved in organized psychiatry. "You are the future voice of psychiatry!" she declared.

"The CLM program is a wonderful opportunity to network with other psychiatrists and to learn about changes in our field," Veronica Slootsky, M.D., originally from Ukraine and a second-year psychiatry resident at George

see ***Mentorship Program*** *on page 15*

GOVERNMENT NEWS

APA Backs Training of School Staff to Monitor Student Mental Health

Students spend more than 16,000 hours a year in classrooms. Proposed legislation would teach the teacher and other school staff to recognize signs of mental health concerns in students.

BY LESLIE SINCLAIR

U.S. Sen. Amy Klobuchar (D-Minn.) has introduced a bill to provide support for teachers so they can learn about the key warning signs of mental health problems in students as well as the impact that mental health conditions can have on a student's ability to learn and behave in the classroom.

Sponsored by Klobuchar and Sen. Susan Collins (R-Maine), the Helping Educators Support All Students Act (S.648) is designed to amend the Elementary and Secondary Education Act of 1965 to add

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support for teachers and other school professionals to receive training on how to recognize signs that indicate that a student may have mental health problems.

The bill would create a four-year discretionary grant for state education agencies to provide training for teachers and other school staff in recognizing mental health issues. That training could be provided by qualified specialized instructional school personnel or in partnership with a community mental health program.

Klobuchar and Collins modeled the proposed legislation on the "Minnesota Approach." For the past several years, licensed teachers in Minnesota have been required, as part of renewing their licenses, to participate in in-service training sessions on the key warning signs of early-onset mental health conditions in children and adolescents. A follow-up survey showed that all participants improved their understanding of how the family of individuals with mental illness are affected, and 97 percent of participants indicated that after the program, they were better equipped to respond to the needs of both children and adults with mental illness.

APA expressed support for the bill in a March 22 letter to Klobuchar in which APA Medical Director James H. Scully Jr., M.D., said the initiative "paves the way for highly successful and evidence-based training initiatives . . . to empower more of these professionals with the knowledge of mental illness, the ability to detect warning signs, and the abil-

*see **Training** on page 19*

Possible risk factors for leukopenia/neutropenia include preexisting low white blood cell count (WBC) and history of drug induced leukopenia/neutropenia. Patients with a pre-existing low WBC or a history of drug induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and should discontinue FANAPT at the first sign of a decline in WBC in the absence of other causative factors.

Patients with neutropenia should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or signs occur. Patients with severe neutropenia (absolute neutrophil count <1000/mm^3) should discontinue FANAPT and have their WBC followed until recovery.

5.9 Hyperprolactinemia

As with other drugs that antagonize dopamine D2 receptors, FANAPT elevates prolactin levels.

Hyperprolactinemia may suppress hypothalamic GnRH, resulting in reduced pituitary gonadotropin secretion. This, in turn, may inhibit reproductive function by impairing gonadalsteroidogenesis in both female and male patients. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported with prolactin-elevating compounds. Long-standing hyperprolactinemia when associated with hypogonadism may lead to decreased bone density in both female and male patients.

Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin-dependent *in vitro*, a factor of potential importance if the prescription of these drugs is contemplated in a patient with previously detected breast cancer. Mammary gland proliferative changes and increases in serum prolactin were seen in mice and rats treated with FANAPT *[see Nonclinical Toxicology (13.1) in the full prescribing information]*. Neither clinical studies nor epidemiologic studies conducted to date have shown an association between chronic administration of this class of drugs and tumorigenesis in humans; the available evidence is considered too limited to be conclusive at this time.

In a short-term placebo-controlled trial (4-weeks), the mean change from baseline to endpoint in plasma prolactin levels for the FANAPT 24 mg/day-treated group was an increase of 2.6 ng/mL compared to a decrease of 6.3 ng/mL in the placebo-group. In this trial, elevated plasma prolactin levels were observed in 26% of adults treated with FANAPT compared to 12% in the placebo group. In the short-term trials, FANAPT was associated with modest levels of prolactin elevation compared to greater prolactin elevations observed with some other antipsychotic agents. In pooled analysis from clinical studies including longer term trials, in 3210 adults treated with iloperidone, gynecomastia was reported in 2 male subjects (0.1%) compared to 0% in placebo-treated patients, and galactorrhea was reported in 8 female subjects (0.2%) compared to 3 female subjects (0.5%) in placebo-treated patients.

5.10 Body Temperature Regulation

Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Appropriate care is advised when prescribing FANAPT for patients who will be experiencing conditions which may contribute to an elevation in core body temperature, e.g., exercising strenuously, exposure to extreme heat, receiving concomitant medication with anticholinergic activity, or being subject to dehydration.

5.11 Dysphagia

Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in elderly patients, in particular those with advanced Alzheimer's dementia. FANAPT and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia *[see Boxed Warning]*.

5.12 Suicide

The possibility of a suicide attempt is inherent in psychotic illness, and close supervision of high-risk patients should accompany drug therapy. Prescriptions for FANAPT should be written for the smallest quantity of tablets consistent with good patient management in order to reduce the risk of overdose.

5.13 Priapism

Three cases of priapism were reported in the pre-marketing FANAPT program. Drugs with alpha-adrenergic blocking effects have been reported to induce priapism. FANAPT shares this pharmacologic activity. Severe priapism may require surgical intervention.

5.14 Potential for Cognitive and Motor Impairment

FANAPT, like other antipsychotics, has the potential to impair judgment, thinking or motor skills. In short-term, placebo-controlled trials, somnolence (including sedation) was reported in 11.9% (104/874) of adult patients treated with FANAPT at doses of 10 mg/day or greater versus 5.3% (31/587) treated with placebo. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that therapy with FANAPT does not affect them adversely.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trial of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. The information below is derived from a clinical trial database for FANAPT consisting of 2070 patients exposed to FANAPT at doses of 10 mg/day or greater, for the treatment of schizophrenia. All of these patients who received FANAPT were participating in multiple-dose clinical trials. The conditions and duration of treatment with FANAPT varied greatly and included (in overlapping categories), open-label and double-blind phases of studies, inpatients and outpatients, fixed-dose and flexible-dose studies, and short-term and longer-term exposure.

Adverse reactions during exposure were obtained by general inquiry and recorded by clinical investigators using their own terminology. Consequently, to provide a meaningful estimate of the proportion of individuals experiencing adverse reactions, reactions were grouped in standardized categories using MedDRA terminology.

The stated frequencies of adverse reactions represent the proportions of individuals who experienced a treatment-emergent adverse reaction of the type listed. A reaction was considered treatment emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation.

The information presented in these sections was derived from pooled data from four placebo-controlled, 4- or 6-week, fixed- or flexible-dose studies in patients who received FANAPT at daily doses within a range of 10 to 24 mg (n=874).

Adverse Reactions Occurring at an Incidence of 2% or More among FANAPT-Treated Patients and More Frequent than Placebo

Table 7 enumerates the pooled incidences of treatment-emergent adverse reactions that were spontaneously reported in four placebo-controlled, 4- or 6-week, fixed- or flexible-dose studies, listing those reactions that occurred in 2% or more of patients treated with FANAPT in any of the dose groups, and for which the incidence in FANAPT-treated patients in any dose group was greater than the incidence in patients treated with placebo.

Table 7: Treatment-Emergent Adverse Reactions in Short-Term, Fixed- or Flexible-Dose, Placebo-Controlled Trials in Adult Patients*

Body System or Organ Class Dictionary-derived Term	Percentage of Patients Reporting Reaction Placebo (N=587)	 FANAPT 10-16 mg/day (N=483)	 FANAPT 20-24 mg/day (N=391)
Body as a Whole			
Arthralgia	2	3	3
Fatigue	3	4	6
Musculoskeletal Stiffness	1	1	3
Weight Increased	1	1	9
Cardiac Disorders			
Tachycardia	1	3	12
Eye Disorders			
Vision Blurred	2	3	1
Gastrointestinal Disorders			
Nausea	8	7	10
Dry Mouth	1	8	10
Diarrhea	4	5	7
Abdominal Discomfort	1	1	3
Infections			
Nasopharyngitis	3	4	3
Upper Respiratory Tract Infection	1	2	3
Nervous System Disorders			
Dizziness	7	10	20
Somnolence	5	9	15
Extrapyramidal Disorder	4	5	4
Tremor	2	3	3
Lethargy	1	3	1
Reproductive System			
Ejaculation Failure	<1	2	2
Respiratory			
Nasal Congestion	2	5	8
Dyspnea	<1	2	2
Skin			
Rash	2	3	2
Vascular Disorders			
Orthostatic Hypotension	1	3	5
Hypotension	<1	<1	3

*Table includes adverse reactions that were reported in 2% or more of patients in any of the FANAPT dose groups and which occurred at greater incidence than in the placebo group. Figures rounded to the nearest integer.

Dose-Related Adverse Reactions in Clinical Trials

Based on the pooled data from four placebo-controlled, 4- or 6-week, fixed- or flexible-dose studies, adverse reactions that occurred with a greater than 2% incidence in the patients treated with FANAPT, and for which the incidence in patients treated with FANAPT 20-24 mg/day were twice than the incidence in patients treated with FANAPT 10-16 mg/day were: abdominal discomfort, dizziness, hypotension, musculoskeletal stiffness, tachycardia, and weight increased.

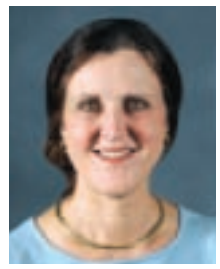
Common and Drug-Related Adverse Reactions in Clinical Trials

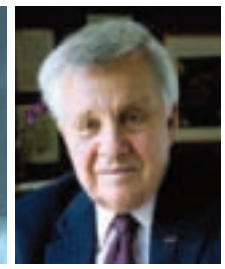
Based on the pooled data from four placebo-controlled, 4- or 6-week, fixed- or flexible-dose studies, the following adverse reactions occurred in ≥5% incidence in the patients treated with FANAPT and at least twice the placebo rate for at least one dose: dizziness, dry mouth, fatigue, nasal congestion,

VIEWPOINTS

Psychiatrists Have Obligation to Counter Stigmatizing Remarks

BY CATHERINE MAY, M.D., AND JERROLD POST, M.D.





Gun violence has made public policy concerning mentally ill individuals a topic for debate in the popular media. Unfortunately cynical and politically expedient solutions often predominate in this forum. In a particularly egregious example, immediately after the Newtown school shooting, the National Rifle Association's Wayne LaPierre attempted to deflect limits on guns by calling for a national registry individuals with mental illness.

On February 3, he appeared on Fox News calling for reinstitutionalization

somnolence, tachycardia, orthostatic hypotension, and weight increased. Dizziness, tachycardia, and weight increased were at least twice as common on 20-24 mg/day as on 10-16 mg/day.

Extrapyramidal Symptoms (EPS) in Clinical Trials

Pooled data from the four placebo-controlled, 4- or 6-week, fixed- or flexible-dose studies provided information regarding treatment-emergent EPS. Adverse event data collected from those trials showed the following rates of EPS-related adverse events as shown in Table 8.

Table 8: Percentage of EPS Compared to Placebo

Adverse Event Term	Placebo (%) (N=587)	FANAPT 10-16 mg/day (%) (N=483)	FANAPT 20-24 mg/day (%) (N=391)
All EPS events	**11.6**	**13.5**	**15.1**
Akathisia	2.7	1.7	2.3
Bradykinesia	0	0.6	0.5
Dyskinesia	1.5	1.7	1.0
Dystonia	0.7	1.0	0.8
Parkinsonism	0	0.2	0.3
Tremor	1.9	2.5	3.1

Adverse Reactions Associated with Discontinuation of Treatment in Clinical Trials

Based on the pooled data from four placebo-controlled, 4- or 6-week, fixed- or flexible-dose studies, there was no difference in the incidence of discontinuation due to adverse events between FANAPT-treated (5%) and placebo-treated (5%) patients. The types of adverse events that led to discontinuation were similar for the FANAPT- and placebo-treated patients.

Demographic Differences in Adverse Reactions in Clinical Trials

An examination of population subgroups in the four placebo-controlled, 4- or 6-week, fixed- or flexible-dose studies did not reveal any evidence of differences in safety on the basis of age, gender or race *[see Warnings and Precautions (5.1)]*.

Laboratory Test Abnormalities in Clinical Trials

There were no differences between FANAPT and placebo in the incidence of discontinuation due to changes in hematology, urinalysis, or serum chemistry.

In short-term placebo-controlled trials (4- to 6-weeks), there were 1.0% (13/1342) iloperidone-treated patients with hematocrit at least one time below the extended normal range during post-randomization treatment, compared to 0.3% (2/585) on placebo. The extended normal range for lowered hematocrit was defined in each of these trials as the value 15% below the normal range for the centralized laboratory that was used in the trial.

Other Reactions During the Pre-marketing Evaluation of FANAPT

The following is a list of MedDRA terms that reflect treatment-emergent adverse reactions in patients treated with FANAPT at multiple doses ≥4 mg/day during any phase of a trial with the database of 3210 FANAPT-treated patients. All reported reactions are included except those already listed in Table 7, or other parts of the *Adverse Reactions (6)* section, those considered in the *Warnings and Precautions (5)*, those reaction terms which were so general as to be uninformative, reactions reported in fewer than 3 patients and which were neither serious nor life-threatening, reactions that are otherwise common as background reactions, and reactions considered unlikely to be drug related. It is important to emphasize that, although the reactions reported occurred during treatment with FANAPT, they were not necessarily caused by it.

Reactions are further categorized by MedDRA system organ class and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring in at least 1/100 patients (only those not listed in Table 7 appear in this listing); infrequent adverse reactions are those occurring in 1/100 to 1/1000 patients; rare events are those occurring in fewer than 1/1000 patients.

Blood and Lymphatic Disorders: Infrequent – anemia, iron deficiency anemia; *Rare* – leukopenia

Cardiac Disorders: Frequent – palpitations; *Rare* – arrhythmia, atrioventricular block first degree, cardiac failure (including congestive and acute)

Ear and Labyrinth Disorders: Infrequent – vertigo, tinnitus

Endocrine Disorders: Infrequent – hypothyroidism

Eye Disorders: Frequent – conjunctivitis (including allergic); *Infrequent* – dry eye, blepharitis, eyelid edema, eye swelling, lenticular opacities, cataract, hyperemia (including conjunctival)

Gastrointestinal Disorders: Infrequent – gastritis, salivary hypersecretion, fecal incontinence, mouth ulceration; *Rare* – aphthous stomatitis, duodenal ulcer, hiatus hernia, hyperchlorhydria, lip ulceration, reflux esophagitis, stomatitis

General Disorders and Administrative Site Conditions: Infrequent – edema (general, pitting, due to cardiac disease), difficulty in walking, thirst; *Rare* – hyperthermia

Hepatobiliary Disorders: Infrequent – cholelithiasis

Investigations: Frequent: weight decreased; *Infrequent* – hemoglobin decreased, neutrophil count increased, hematocrit decreased

Metabolism and Nutrition Disorders: Infrequent – increased appetite, dehydration, hypokalemia, fluid retention

Musculoskeletal and Connective Tissue Disorders: Frequent – myalgia, muscle spasms; *Rare* – torticollis

Nervous System Disorders: Infrequent – paresthesia, psychomotor hyperactivity, restlessness, amnesia, nystagmus; *Rare* – restless legs syndrome

Psychiatric Disorders: Frequent – restlessness, aggression, delusion; *Infrequent* – hostility, libido decreased, paranoia, anorgasmia, confusional state, mania, catatonia, mood swings, panic attack, obsessive-compulsive disorder, bulimia nervosa, delirium, polydipsia psychogenic, impulse-control disorder, major depression

Renal and Urinary Disorders: Frequent – urinary incontinence; *Infrequent* – dysuria, pollakiuria, enuresis, nephrolithiasis; *Rare* – urinary retention, renal failure acute

Reproductive System and Breast Disorders: Frequent – erectile dysfunction; *Infrequent* – testicular pain, amenorrhea, breast pain; *Rare* – menstruation irregular, gynecomastia, menorrhagia, metrorrhagia, postmenopausal hemorrhage, prostatitis.

Respiratory, Thoracic and Mediastinal Disorders: Infrequent – epistaxis, asthma, rhinorrhea, sinus congestion, nasal dryness; *Rare* – dry throat, sleep apnea syndrome, dyspnea exertional

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of Fanapt: retrograde ejaculation. Because these reactions were reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

7 DRUG INTERACTIONS

Given the primary CNS effects of FANAPT, caution should be used when it is taken in combination with other centrally acting drugs and alcohol. Due to its α1-adrenergic receptor antagonism, FANAPT has the potential to enhance the effect of certain antihypertensive agents.

7.1 Potential for Other Drugs to Affect FANAPT

Iloperidone is not a substrate for CYP1A1, CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP2E1 enzymes. This suggests that an interaction of iloperidone with inhibitors or inducers of these enzymes, or other factors, like smoking, is unlikely.

Both CYP3A4 and CYP2D6 are responsible for iloperidone metabolism. Inhibitors of CYP3A4 (e.g., ketoconazole) or CYP2D6 (e.g., fluoxetine, paroxetine) can inhibit iloperidone elimination and cause increased blood levels.

Ketoconazole: Co-administration of ketoconazole (200 mg twice daily for 4 days), a potent inhibitor of CYP3A4, with a 3 mg single dose of iloperidone to 19 healthy volunteers, ages 18-45, increased the AUC of iloperidone and its metabolites P88 and P95 by 57%, 55% and 35%, respectively. Iloperidone doses should be reduced by about one-half when administered with ketoconazole or other strong inhibitors of CYP3A4 (e.g., itraconazole). Weaker inhibitors (e.g., erythromycin, grapefruit juice) have not been studied. When the CYP3A4 inhibitor is withdrawn from the combination therapy, the iloperidone dose should be returned to the previous level.

Fluoxetine: Co-administration of fluoxetine (20 mg twice daily for 21 days), a potent inhibitor of CYP2D6, with a single 3 mg dose of iloperidone to 23 healthy volunteers, ages 29-44, who were classified as CYP2D6 extensive metabolizers, increased the AUC of iloperidone and its metabolite P88, by about 2-3 fold, and decreased the AUC of its metabolite P95 by one-half. Iloperidone doses should be reduced by one-half when administered with fluoxetine. When fluoxetine is withdrawn from the combination therapy, the iloperidone dose should be returned to the previous level. Other strong inhibitors of CYP2D6 would be expected to have similar effects and would need appropriate dose reductions. When the CYP2D6 inhibitor is withdrawn from the combination therapy, iloperidone dose could then be increased to the previous level.

Paroxetine: Co-administration of paroxetine (20 mg/day for 5-8 days), a potent inhibitor of CYP2D6, with multiple doses of iloperidone (8 or 12 mg twice daily) to patients with schizophrenia ages 18-65 resulted in increased mean steady-state peak concentrations of iloperidone and its metabolite P88, by about 1.6 fold, and decreased mean steady-state peak concentrations of its metabolite P95 by one-half. Iloperidone doses should be reduced by one-half when administered with paroxetine. When paroxetine is withdrawn from the combination therapy, the iloperidone dose should be returned to the previous level. Other strong inhibitors of CYP2D6 would be expected to have similar effects and would need appropriate dose reductions. When the CYP2D6 inhibitor is withdrawn from the combination therapy, iloperidone dose could then be increased to previous levels.

Paroxetine and Ketoconazole: Co-administration of paroxetine (20 mg once daily for 10 days), a CYP2D6 inhibitor, and ketoconazole (200 mg twice daily) with multiple doses of iloperidone (8 or 12 mg twice daily) to patients with schizophrenia ages 18-65 resulted in a 1.4 fold increase in steady-state concentrations of iloperidone and its metabolite P88 and a 1.4 fold decrease in the P95 in the presence of paroxetine. So giving iloperidone with inhibitors of both of its metabolic pathways did not add to the effect of either inhibitor given alone. Iloperidone doses should therefore be reduced by about one-half if administered concomitantly with both a CYP2D6 and CYP3A4 inhibitor.

7.2 Potential for FANAPT to Affect Other Drugs

In vitro studies in human liver microsomes showed that iloperidone does not substantially inhibit the metabolism of drugs metabolized by the following cytochrome P450 isozymes: CYP1A1, CYP1A2, CYP2A6, CYP2B6,

of people with mental illness. In each instance, there was no psychiatrist on the set to rebut his misinformed and stigmatizing rhetoric. Left unchallenged, he had a solo platform from which to shape public opinion.

Not that psychiatry has been silent. Through press releases and testimony, APA has opposed the notion that the solution to gun violence is greater regulation of people with mental illness. For example, former APA President Paul Appelbaum, M.D., testified before Vice President Joseph Biden's Task Force on Gun Violence that 96 percent of violence in the U.S. is not committed by people with mental illness, and only 7 percent of individuals with schizophrenia commit any act of violence, including pushing and shoving (*Psychiatric News,* March 1).

These public statements are extremely important, but the question remains, why is psychiatry relatively silent in the broader public forum—the talk shows, network news, and cable TV, where public opinion is formed?

We suspect the silence is self-imposed. As a profession, our public engagement is guided by Section 7 of the *Principles of Medical Ethics With Annotations Especially Applicable to Psychiatry* (posted on APA's Web site at http://www.psych.org/practice/ethics). Unfortunately this principle is plagued by internal contradiction and may go too far in trying to serve its original intent.

Subsections 1 and 2 exhort psychiatrists to "serve society" and "share with the public their expertise." News releases and testimony are good and important examples of this. Subsection 3, known as the Goldwater Rule, is the key. It was prompted by controversy that arose during the 1964 presidential campaign. *Fact Magazine* surveyed APA members asking whether the Republican candidate, Barry Goldwater, was fit for office. The front-page story under the headline "1189 Psychiatrists Say Goldwater Is Psychologically Unfit to be President" was a major embarrassment for American psychiatry.

Section 7.3 of the ethics code, which states, "It is unethical for a psychiatrist to offer a professional opinion unless he/she has conducted an examination and has been granted proper authorization," was adopted to avoid such wild analysis of an individual's mental state.

Unfortunately, it restricts the ability of a psychiatrist to offer opinions in a public forum. But like it or not, public opinion forms in reaction to highly publicized individual cases that are the staple of the popular media. When we shy away from the debate, we lose the opportunity to educate the public, inform policy, and counter the stigmatization of people living with mental illness. By failing to offer an opinion, operating under a "better safe than sorry" interpretation of professional opinion, we in some ways undermine the integrity of the profession rather than preserve it.

Unless we address the issues raised by the case currently seizing the public attention, the opportunity to inform and influence the debate will be lost. In an op-ed piece in the *New York Times* concerning the Newtown shootings, Dr. Paul Steinberg noted "the chilling effect of the Goldwater Rule" in his effort to frame and qualify his comments. We believe that disproportionate concern about the "chilling" effect of Section 7.3 prevents more psychiatrists from engaging in arenas where sharing their expertise might educate the public and lead to a more reasoned approach to curbing gun violence.

Many psychiatrists choose to remain silent when their voices need to be heard so that psychiatric patients are not casually depicted as unpredictable and violent. In an effort to avoid a sin of commission, we have adopted a rule that now leads to a sin of omission. This suggests revisiting Section 7. One solution would be making 7.3 more specific, prohibiting a specific clinical diagnosis rather than

see ***Viewpoints*** *on page 22*

CLINICAL & RESEARCH NEWS

ADHD Meds May Not Cut Risk For Drug Abuse in Teens

Children with ADHD are at increased risk of substance use, particularly of tobacco and marijuana, and despite anecdotal reports to the contrary, ADHD treatments may not counter that risk.

BY LESLIE SINCLAIR

Researchers from the University of Pittsburgh and six other medical centers say that contrary to previous findings, medications for attention-deficit/hyperactivity disorder (ADHD) do not counter the risk for substance use and abuse among teenagers.

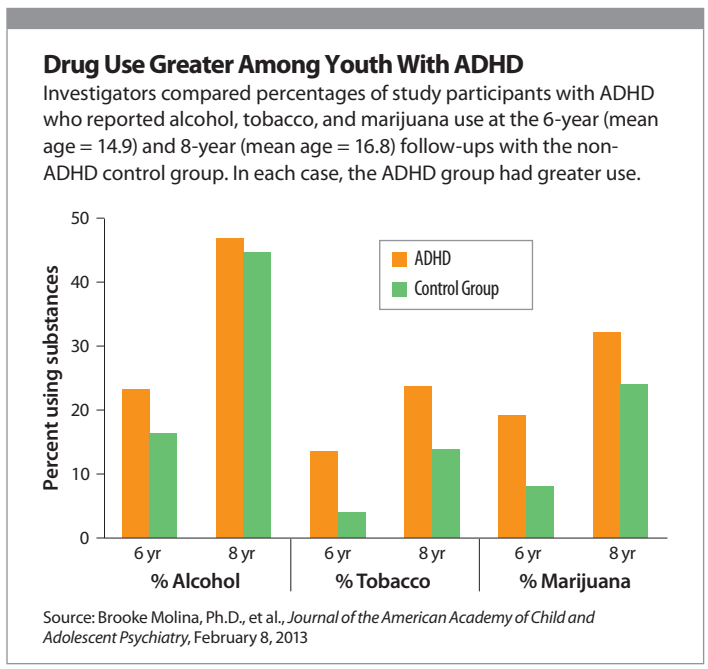
The study's lead author, Brooke Molina, Ph.D., a professor of psychiatry and psychology at the University of Pittsburgh School of Medicine, and colleagues said theirs is the first study to examine teenage substance abuse and treatment for ADHD in a large multisite sample and the first to recognize that increased use of cigarettes in teenagers with ADHD histories commonly occurs with use of other substances such as alcohol and marijuana. Their findings are published in the March *Journal of the American Academy of Child and Adolescent Psychiatry*.

The study participants were the nearly 600 youngsters in the Multimodal Treatment Study of ADHD (MTA), who were recruited in childhood, treated for ADHD for 14 months in a randomized clinical trial, and then followed up with substance use assessments through adolescence. Although the first published MTA report of substance use at the three-year mark (when participants were aged 10 to 13) showed no protective or predisposing associations between substance use and medication, the current study details the eight-year follow-up, when the participants were at a mean age of 16.8.

And this time, the results were different. They found a significantly higher prevalence of substance abuse and cigarette use by adolescents with ADHD histories than by those without ADHD.

Among the findings:

- When the adolescents were an average of 15 years old, 35 percent of those with ADHD histories reported using one or more substances, compared with only 20 percent of their peers without ADHD histories.
- Ten percent of those with ADHD met criteria for a substance abuse or dependence disorder, which means they experienced significant problems from their substance use; only 3 percent of the non-ADHD group did.
- When the adolescents were an average age of 17, marijuana was especially problematic, with 13 percent versus 7 percent of the ADHD and non-ADHD groups, respectively, indicating marijuana abuse or dependence.
- Daily cigarette smoking was very high at 17 percent in the ADHD group; the smoking rate of non-ADHD teens was only 8 percent.
- Alcohol use was high in both groups, highlighting its common occurrence in teenagers



see **ADHD** on page 23

How Do Abused Drugs Affect Fetus, Newborn?

When it comes to the effects of prenatal exposure on the fetus, drugs of abuse pose various types of risk to the baby.

BY AARON LEVIN

Several commonly abused drugs, both legal and illegal, can have serious effects on a fetus, two pediatricians cautioned their colleagues in the March *Pediatrics*.

"Alcohol can have pretty profound teratogenic, neurobehavioral, and anatomic effects," said lead researcher Marylou Behnke, M.D., a professor of pediatrics at the University of Florida, in an interview with *Psychiatric News*. "We don't see the same somatic changes with other drugs, but you can see subtle neurobehavioral changes that can be hard to tease out because they don't show up until the children grow older."

Behnke and coauthor Vincent Smith, M.D., M.P.H., both neonatologists, presented a technical report on the short- and long-term effects of prenatal substance abuse on the exposed fetus. They covered the most common substances used by pregnant women: nicotine, alcohol, marijuana, opiates, cocaine, and methamphetamine.

Some health messages may be getting through to this cohort. For a start, only 4.4 percent of pregnant women aged 15 to 44 acknowledge use of any illicit drugs, 10.8 percent drink alcohol, and 16.3 percent smoke cigarettes, according to data from the National Survey on Drug Use and Health, sponsored by the Substance Abuse and Mental Health Services Administration. Rates are significantly higher among nonpregnant women (see chart).

Furthermore, drug use by a pregnant woman does not automatically lead to problems in the offspring, but it does increase the baby's risks, Behnke pointed out.

From a population perspective, the effects of these drugs on a baby may seem subtle but they should not be ignored.

"Biologically and socially, drug addiction is not a good atmosphere to grow up in," she said. Aside from its biological effects, addiction can change maternal behavior in ways that can affect the fetus by leading to poor nutrition or health care, or exposure to violence or infection.

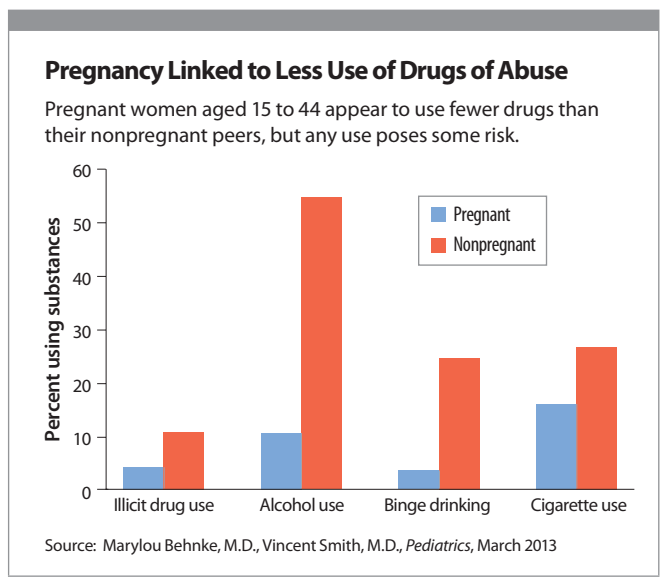
In addition, a mother's use of more than one drug at a time only complicates effects on the child, said Behnke.

Recent research indicates that the effects of drugs other than tobacco are less severe than was anticipated a couple of decades ago, when a nation obsessed with "crack babies" figured that children would be horribly damaged by maternal cocaine use, she said.

The effects of each of these drugs vary. Nicotine is a risk factor for low birth weight and is associated with decreased weight gain in the infant, possibly because the fetus is actually exposed to more nicotine than the mother is. However, infants experience no serious withdrawal effects. The effects on long-term growth are not clear, but problems with impulsivity, concentration, language development, and learning and memory have been highlighted by other researchers.

Alcohol is the best-studied of the drugs used by pregnant women. It has strong effects on fetal growth and anomalies, as well as influencing longer-term effects on growth, behavior, cognition, and academic achievement.

Marijuana has minor effects on infant neurobehavioral responses but has longer-term effects on behavior,



see **Fetus** on page 22

Three Key Factors Interact To Increase PTSD Risk

Combat exposure, prewar vulnerability, and harming civilians have additive effects on risk and long-term course of posttraumatic stress disorder among Vietnam vets.

BY AARON LEVIN

An intensive reanalysis of a subsample of the National Vietnam Veterans Readjustment Study (NVVRS) reinforces the central role of combat trauma for the onset of posttraumatic stress symptoms but also finds complex interactions between that experience, prewar vulnerabilities, and causing harm to civilians or enemy prisoners.

The relative significance of combat and prior vulnerabilities has sparked debate for years, noted Bruce Dohrenwend, Ph.D., a professor of epidemiology at Columbia University's Mailman School of Public Health and a professor of psychiatry at the College of Physicians and Surgeons at Columbia. The study by Dohrenwend and colleagues appeared online February 15 in *Clinical Psychological Science.*

Combat exposure is more important than vulnerability factors in the onset of posttraumatic stress disorder (PTSD), but vulnerability factors have a greater influence on the persistence of the disorder over time, they concluded. In addition, soldiers who harmed civilians or prisoners faced increased risk for PTSD.

"This is the first study to bring together these three factors," John Fairbank, Ph.D., a professor of psychiatry and behavioral sciences at Duke University, told *Psychiatric News.* Fairbank worked on the original NVVRS study, but was not involved with the current reanalysis. "It adds to the growing literature over the last decade showing that there's a complex interaction, and an additive effect, of risk factors."

The NVVRS studied 1,200 men in 1986 and 1987 who had served in Vietnam from 1965 to 1975. The current study covered a subsample of 248 men who had received a diagnostic examination using the Structured Clinical Interview for *DSM-III-R* (SCID). Measures of combat exposure were based on both unit military records and personal self-report, covering life-threatening experiences, witnessing the death of a friend, and killing enemy personnel. The men were also asked about involvement in harming or killing Vietnamese civilians or prisoners.

Dose-Dependent Effect Found

Dohrenwend and colleagues found that 32 percent of the veterans who experienced SCID Criterion A combat stressors developed PTSD symptom syndrome (PSS)—the co-occurrence of intrusive, avoidance/numbing, and arousal symptoms for at least one month.

The researchers distinguished between PTSD and PSS in order to "assess the presence or absence of PSS independently of the presence of Criterion A as stressors that are needed for the full PTSD analysis."

The effect of combat was dose dependent. Veterans with very severe combat exposure had an increasingly higher likelihood of both onset and current (prior six months in 1986-1987) PSS.

"PSS can occur in individuals who show little personal vulnerability when stressor exposure is especially severe," said the researchers. But that stressor was essential for development of posttraumatic symptoms: "[A]t most, 2 percent of the veterans had onsets of PSS in the absence of Criterion A."

This leads Dohrenwend to support a narrow definition of Criterion A, limiting it to life-threatening stressors such as combat exposure, rape, or child abuse rather than less-severe stressors of daily life such as divorce or unemployment, as others have suggested.

Four prewar vulnerability factors were found to have the highest statistical risk for PTSD onset: childhood physical abuse (39 percent), conduct disorder (39 percent), pre-Vietnam psychiatric disorders (34 percent), and family members with arrest records (38 percent). Younger age was also a risk factor.

Harming Civilians Raises PTSD Risk

The researchers initially hypothesized an inverse relationship between vulnerability and posttraumatic stress—that more vulnerable soldiers would develop PTSD at lower combat thresholds.

But in fact, the more severe the soldier's combat experience, the greater the effect of vulnerability was on the presence of current PSS. "[V]ulnerability makes a huge difference for those with the highest level of combat exposure," they noted.

One way to reduce the prevalence of chronic disorders related to posttraumatic stress would be to avoid placing the more-vulnerable soldiers into the most-stressful combat settings, suggested Dohrenwend.

Finally, about 13 percent of respondents reported some personal involvement in harming civilians or prisoners, acts that sharply increased their likelihood of PSS onset.

"Almost two-thirds of the harmers (62 percent) had onset, compared with only 15 percent of the nonharmers," said the authors. A dozen years after the war, 40 percent of the harmers had PTSD versus 6 percent of the nonharmers. Harming was more strongly associated with combat exposure than with vulnerability.

The three factors had a strong additive effect. The combination of high combat severity, high vulnerability, and harming produced a 97 percent chance of PSS onset.

"This study underscores that the onset and longitudinal course of PTSD is complex," said Fairbank.

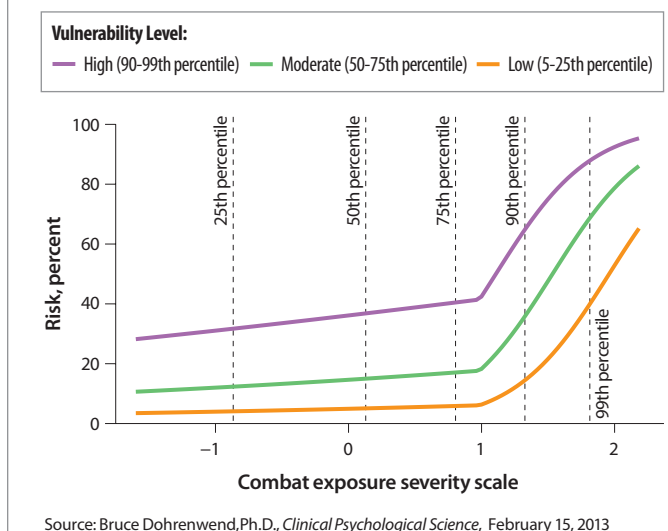
The lessons of a war four decades in the past may offer insights into present conflicts. For U.S. forces, the Vietnam War was a "war amongst the people," concluded Dohrenwend and colleagues. "So, more recently, have been the conflicts in Iraq and Afghanistan."

"When the original NVVRS study was completed in 1986-88, people were barely aware of PTSD," recalled Fairbank. "Now PTSD is part of everyday language. The country as a whole is more attentive to how men and women who have served [in the military] are doing, in both physical and psychological well-being." PN

"The Roles of Combat Exposure, Personal Vulnerability, and Involvement in Vietnam War–Related Posttraumatic Stress Disorder" is posted at http://cpx.sagepub.com/content/early/2013/02/25/2167702612469335.full.

Vulnerability a Factor Only With Intense Combat

The effect of pre-Vietnam War vulnerability is greatest at highest levels of combat exposure, reports Columbia University's Bruce Dohrenwend, Ph.D.



Source: Bruce Dohrenwend,Ph.D., *Clinical Psychological Science,* February 15, 2013

Mentorship Program

continued from page 9

Washington University, remarked.

Mona Thapa, M.D., who comes from Nepal and who is a third-year resident at Howard University, did a grand-rounds presentation at Howard University Hospital in collaboration with the CLM program. The title was "Global Mental Health With a Focus on Nepal."

Several of the speakers also proposed subjects that might be tackled during future CLM program events.

For instance, someone could address policy administration and telemedicine, Thapa suggested. Or perhaps each psychiatrist who is participating in the program could lecture on a topic in clinical care—for example, delirium, Saeed suggested.

Sorel, who organized the CLM anniversary celebration, commented on the current state of health care and psychiatry research in the United States. For example, he said, even though universal health insurance is becoming a reality in the United States, "it is shaky; it is not a done deal," he ventured. He noted as well that President Obama has proposed a big mission—mapping the human brain—and if that comes to pass, the possibilities for psychiatry, when added to what is being learned from the mapping of the human genome, are enormous.

Addressing the young psychiatrists at the dinner, Sorel said, "Health is a human right," according to a recently passed United Nations resolution. The United States signed this resolution in December 2012. "So we need optimistic, persistent young people such as yourselves in this game." PN

More information about the CLM program can be obtained from Sorel at esorel@gmail.com.

CLINICAL & RESEARCH NEWS

justasc/Shutterstock

The strong risk for homicidal death among those with mental illness does not seem to be explained by comorbid substance use and warrants further investigation.

Mental Disorders Increase Vulnerability to Homicide

More effective prevention of violent death among people with mental illness requires a better understanding of the risks of homicidal death, in addition to suicide and accidents.

BY LESLIE SINCLAIR

The perpetration of homicide and other violence by people with mental disorders has been studied for decades, but the risk of such people being victims of homicide has received little attention. Researchers at Stanford University recently teamed with the Center for Primary Health Care Research at Lund University in Malmö, Sweden, to determine whether people with mental disorders are at an increased risk of being victims of homicide.

Casey Crump, M.D., Ph.D., lead author of the study and a clinical assistant professor in the Department of Medicine at Stanford School of Medicine, and colleagues performed a nationwide cohort study of all people aged 17 or older who were living in Sweden on January 1, 2001 (n=7,253,516), identifying 615 homicide deaths during eight years of follow-up, including 141 among people who had been diagnosed with a mental illness.

After adjusting for gender and age, having been diagnosed with any mental disorder was associated with more than a sevenfold risk of being a victim of homicidal death, compared with people without a mental disorder. The risk of homicidal death was strongest (approximately 16-fold higher risk) among those with substance use disorders, but it was also increased among those with personality disorders, depression, anxiety disorders, or schizophrenia and did not seem to be explained by comorbid substance use, the researchers noted.

Men had twice the risk of being victims of homicide, and the risk was more than twice as high among people who were divorced or never married, compared with those who were married or cohabitating. Other independent risk factors included low education level, low income, being unemployed, and living in large cities rather than in medium-sized cities or small towns.

The researchers noted that the homicide rate in Sweden (1.1 per 100,000 person years) is much lower than that of the United States (7.0 per 100,000 person years), and it is in the United States, they said, "where our findings are likely to have a larger public-health impact."

In an accompanying editorial, a group from the Centre for Mental Health and Risk, part of the Institute of Brain, Behaviour, and Mental Health at the University of Manchester in Manchester, U.K., noted that the study had much valuable information to offer to clinicians. "A key implication of these new findings is that clinicians should assess risk for the full array of adverse outcomes that may befall people with mental health problems. This would include being a victim of violence as well as committing it, abuse and bullying, suicidal behavior, accidental drug overdoses, and other major adverse events linked with intoxication or impulsivity. These risks go together, and people with mental illness, as well as their families, should receive advice on avoiding various types of harm," wrote Roger Webb, Ph.D., Jenny Shaw, Ph.D., and Louis Appleby, F.R.C.Psych. Webb is a senior research fellow in psychiatric epidemiology, Shaw is a professor of forensic psychiatry, and Appleby is a professor of psychiatry at the center.

Their editorial also pointed out future directions for further study, calling for direct comparison of patients' risk of committing homicide with the risk of being a victim of it, as well as evaluation of how much of the risk of being a victim is a consequence of illness itself and therefore has the potential for prevention by mental health treatment. They also noted the need for analysis of the role hospitalization might play, saying "we know that discharged psychiatric patients and released prisoners are especially likely to take their own lives immediately after their return to the community. We need to know whether this heightened vulnerability on leaving institutional settings relates to being at risk from other people."

The study was supported by grants from the National Institute on Drug Abuse, the Swedish Research Council, and the Anna Lindh Foundation. PN

"Mental Disorders and Vulnerability to Homicidal Death: Swedish Nationwide Cohort Study" is posted at http://www.bmj.com/content/346/bmj.f557.

Rulings Guide Psychiatrists on Forced-Treatment Limits

A conference at historic St. Elizabeths Hospital sheds light on the current status of involuntary treatment of people in the criminal justice system.

BY AARON LEVIN

Arguments over whether individuals in the criminal justice system can be medicated against their will are unlikely to disappear soon, said two speakers at the first annual forensic psychiatry conference at St. Elizabeths Hospital in Washington, D.C.

"Right-to-refuse-treatment issues are likely to increase as more people [with mental illness] are diverted into the criminal justice system," said Charles Scott, M.D., a professor and chief of the Division of Psychiatry and the Law at the University of California, Davis. "With that, there will be more competency cases and more decisions about medication use."

Scott appeared with Howard Zonana, M.D., a professor of psychiatry and an adjunct clinical professor of law at Yale University.

The controversy over who in the criminal justice system can and cannot be medicated is hardly new, said Scott, the immediate past president of the American Academy of Psychiatry and the Law. The right to refuse treatment has its roots in the 19th century with cases involving standards for involuntary civil commitment.

Individuals have the right to refuse any medical treatment, but that right is not absolute, he said. The state may mandate treatment to protect others from "the dangerous mentally ill," in the case of mentally incompetent adults, or to maintain security in a state institution such as a prison or

see ***Forced Treatment*** *on page 24*

Aaron Levin

Howard Zonana, M.D.: Restoration of competency to stand trial raises numerous issues in law and medicine.

Aaron Levin

Charles Scott, M.D.: How and when defendants or prisoners can be forcibly medicated is a complex problem.

CLINICAL & RESEARCH NEWS

Threat Delusions Linked to Violence In First-Episode Psychosis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Delusion-provoked anger in individuals can contribute to serious violence. But is the anger a reaction to the delusion or part of it?

BY JOAN AREHART-TREICHEL

There is ample evidence that delusions sometimes lead to violent behavior. But when and why they do so has not been clear.

Now a new study appears to shed light on this complex subject. It looks as if delusions can trigger serious violence when the delusions imply threat and when the threat then leads to anger. The study was conducted by Simone Ullrich, Ph.D., of Queen Mary University of London and colleagues and published March 6 in *JAMA Psychiatry*.

"That anger induced by certain types of delusional thoughts is a causal link in the chain that leads to violence is theoretically plausible and in accordance with clinical experience," Paul Appelbaum, M.D., said during an interview. Appelbaum, the Dollard Professor of Psychiatry, Medicine, and Law and director of the Division of Law, Ethics, and Psychiatry at Columbia University and chair of the APA Committee on Judicial Action, has also researched the relationship between delusions and violence.

The study included 458 subjects with first-episode psychosis who were from an economically deprived inner-city area. The researchers used several instruments to learn what percentage of the subjects had engaged in violence during the year prior to the subjects' first contact with mental health services; whether subjects' delusions during that period had been linked with violence; and if so, whether any particular affect or intervention had mediated the delusion-violence link.

Thirty-eight percent of the cohort had engaged in violence during the year preceding their first contact with mental health services, and 12 percent had engaged in serious violence during that period. Among the seriously violent subgroup, significantly more were male, younger, had comorbid antisocial personality disorder, and used drugs.

Three types of delusions demonstrated significant associations with serious violence—those whose content involved being spied on, persecuted, and the object of a conspiracy. Moreover, anger due to such threatening delusions was significantly associated with serious violence. No significant associations were found, however, between violent behavior and the affective states of anxiety, fear, or elation due to delusional beliefs; depression actually had a protective effect against violence.

"Anger due to delusions appeared to constitute the main drive to serious violence," Ullrich and her colleagues concluded. "However, no currently available instrument can differentiate between anger due to a delusion and anger as part of the delusion itself. This differentiation would have testable implications for treatment interventions aimed to prevent future violence among deluded patients. If the anger is reactive to the delusional belief, it may be modifiable by treatment that specifically targets the anger. However, if it is part of the delusion itself, this would imply that treatment must simultaneously target the delusion and the associated anger."

"The authors suggest that treatment directed at angry thoughts could reduce violent outcomes, and that's certainly worth testing," Appelbaum commented. "But we shouldn't lose focus in reducing the strength of the delusions themselves."

The study was funded by St. Bartholomew's Hospital, the Royal London Hospital Special Trustees, the East London NHS Foundation Trust Research and Development, and the U.K. National Institute for Health Research. PN

"The Relationship Between Delusions and Violence: Findings From the East London First-Episode Psychosis Study" is posted at http://archpsyc.jamanetwork.com/article.aspx?articleid=1660586.

KEY POINTS

- Delusions of threat were significantly associated with serious violence in first-episode psychosis subjects.
- Moreover, anger due to such threatening delusions was significantly associated with serious violence in the study cohort.
- Thus anger due to delusions appears to constitute a drive to serious violence.
- If the anger is a reaction to the delusional belief, it may be modifiable by treatment that specifically targets the anger. However, if it is part of the delusion itself, then the treatment would have to simultaneously target the delusion and the associated anger.

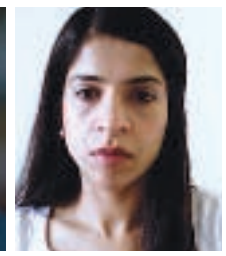
RESIDENTS' FORUM

Helping Residents Navigate Their C-L Experience

BY MICHAEL ASCHER, M.D., AND RENU MARIA CULAS, M.D..

As we reflect on our time supervising junior residents and medical students on our hospital's consultation-liaison (C-L) psychiatry service, we have developed a profound appreciation for the challenges of working in the space in which psychiatry and the rest of medicine intersect. As consulting psychiatrists on a busy medical service, we are asked to provide treatment recommendations that may include assessing a patient's capacity to make life-and-death decisions such as refusing medical interventions.

Our role is also to serve as advocates for mentally ill patients while educating the medical staff on critical issues of transference and countertransference that can influence both the care of the patient and the morale of the medical team. Younger trainees often feel less than adequately prepared to deal with the complex and mentally demanding nature of the rotation, which may lead to myriad emotions, including fear, anger, anxiety, sadness, and guilt. In this column we outline some of

these potential difficulties and offer recommendations that we hope will help optimize the learning environment.

When medical teams ask a psychiatrist to evaluate a patient, it can be difficult for the consulting psychiatrist to extract a specific question from the medical team. Often the medical team will ask broad questions, and it is up to the psychiatrist to distill the specific question and concern that needs to be addressed. Clarifying the question requires skill, experience, a high level of distress tolerance, and reflective functioning on the part of the psychiatrist. Supervisors can model effective ways of engaging with the medical team to better facilitate this process.

Psychiatry residents frequently hear the phrase "medically stable" during their C-L rotation. The concept of medical stability can be complex, especially if the plan is to transfer the patient to a psychiatric floor. The medical stability of a patient depends on many contextual factors including the potential for developing an acute medical emergency and the ability of mental health care providers to treat the patient on an inpatient unit. Communicating these factors to the medical team may be met with resistance because they have their own internal and external forces that guide the determination of how stable a patient is for transfer. Moreover, the medical team may have preconceived ideas about the ability of psychiatrists to manage a certain level of medical acuity, without appreciating the unique risks of inpatient psychiatric care.

The frustration experienced by the medical team can often translate into disparaging statements directed to psychiatric trainees such as "aren't you a doctor?" Supervisors can play a vital role in helping the trainee understand the

*see **Residents' Forum** on page 19*

Michael Ascher, M.D., is a PGY-4 resident at Beth Israel Medical Center. Renu Maria Culas, M.D., is a fellow in psychosomatic medicine at Beth Israel.

JOURNAL DIGEST

BY LESLIE SINCLAIR

Vision Loss Leads to Depression

Researchers at the National Institutes of Health said that self-reported loss of visual function was associated with depression in a study whose data came from a national survey of U.S. adults. The study analyzed data from the National Health and Nutrition Examination Survey (NHANES 2005-2008) and included 10,480 adults aged 20 or older. The estimated prevalence of depression was 11.3 percent among adults with self-reported visual function loss and 4.8 percent among adults without. The estimated prevalence of depression was 10.7 percent among adults with presenting visual acuity impairment compared with 6.8 percent among adults with normal visual acuity.

After controlling for age, sex, and general health status, self-reported visual function loss remained significantly associated with depression, whereas the association between presenting visual acuity impairment and depression was no longer statistically significant, according to the results.

"This study provides further evidence from a national sample to generalize the relationship between depression and vision loss to adults across the age spectrum. Better recognition of depression among people reporting reduced ability to perform routine activities of daily living due to vision loss is warranted," the researchers said.

The study was supported by the National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC).

Zhang X, Bullard K, Cotch M, et al. "Association Between Depression and Functional Vision Loss in Persons 20 Years of Age or Older in the United States, NHANES 2005-2008." JAMA Ophthalmol. 2013. March 7 [Epub ahead of print]. http://www.ncbi.nlm.nih.gov/pubmed/23471505

Black, Asian Women Most Affected by PTSD After Cancer Diagnosis

Nearly one-fourth of women newly diagnosed with breast cancer report symptoms consistent with posttraumatic stress disorder (PTSD), with increased risk among black and Asian women. Researchers at Columbia University recruited women with newly diagnosed nonmetastatic breast cancer from three U.S. sites. Telephone interviews were conducted within two to three months after diagnosis, and again at four and six months after diagnosis. Traumatic stress was measured in each interview using the Impact of Event Scale.

Of 1,139 participants, 23 percent reported symptoms consistent with a diagnosis of PTSD at baseline, 16.5 percent at the first follow-up, and 12.6 percent at the second follow-up. Persistent PTSD, defined as having PTSD at two consecutive interviews, was observed among 12.1 percent of participants. Younger age at diagnosis and being black or Asian had a stronger association with PTSD.

The researchers hoped that their findings would foster identification of potential risk factors for PTSD at the time of diagnosis and present an opportunity to provide early prevention and intervention to minimize PTSD symptomatology. "This approach may improve the quality of patients' lives and may also have an indirect impact on the observed racial disparity in breast cancer survival," they wrote.

The study was supported by the Department of Defense, the National Cancer Institute, and the Environmental Health Foundation.

Vin-Raviv N, Clarke Hillyer G, Hershman D, et al. "Racial Disparities in Posttraumatic Stress After Diagnosis of Localized Breast Cancer: The BQUAL Study." J Natl Cancer Inst. 2013. February 21 [Epub ahead of print]. http://www.ncbi.nlm.nih.gov/pubmed/23434900

Study Links Firearm Laws With Fewer Fatalities

Researchers from Boston Children's Hospital and Harvard Medical School and School of Public Health found that a higher number of firearm-control laws in a state are associated with a lower rate of firearm fatalities, both overall and for suicides and homicides individually. The group retrospectively analyzed all firearm-related deaths reported to the CDC's Injury Statistics Query and Reporting System from 2007 through 2010.

Their outcome measures were state-level firearm-related fatalities per 100,000 individuals per year overall, for suicide, and for homicide. They controlled for age, sex, race/ethnicity, poverty, unemployment, college education, population density, nonfirearm violence-related deaths, and household firearm ownership.

The researchers said their study could not determine cause-and-effect relationships and that further studies are necessary to define the nature of the association.

Fleegler E, Lee L, Monuteaux MC, et al. "Firearm Legislation and Firearm-Related Fatalities in the United States." JAMA Intern Med. 2013. March 6 [Epub ahead of print]. http://www.ncbi.nlm.nih.gov/pubmed/23467753

Marijuana Exposure May Lead to Nicotine Addiction

Researchers from the National Institute on Drug Abuse have reported that rats previously exposed to tetrahydrocannabinol (THC), the main active ingredient in marijuana, found nicotine more rewarding than did rats not exposed to THC. Although the doses of THC used in the study were high, the researchers said their results suggest that marijuana use may increase the risk for nicotine dependence.

The study was part of a series of studies on "gateway drug" effects in animal models of drug abuse. Rats were exposed to THC, receiving two intraperitoneal injections a day for three days. Beginning one week later, they were allowed to self-administer nicotine intravenously. THC exposure increased the likelihood of acquiring the nicotine self-administration response from 65 percent in rats that did not receive THC, to 94 percent in THC-exposed rats. When the "price" of nicotine was manipulated by increasing the response requirement, THC-exposed rats maintained higher levels of intake than nonexposed rats, indicating that THC exposure increased the value of nicotine reward.

"These results contrast sharply with our earlier findings that prior THC exposure did not increase the likelihood of rats acquiring either heroin or cocaine by self-administration, nor did it increase the reward value of these drugs," wrote the researchers, who said their findings suggest that a history of cannabis exposure might have lasting effects that increase the risk of becoming addicted to nicotine.

Panlilio L, Zanettini C, Barnes C, et al. "Prior Exposure to THC Increases the Addictive Effects of Nicotine in Rats." Neuropsychopharmacology. 2013. February 6 [Epub ahead of print]. http://www.nature.com/npp/journal/vaop/ncurrent/full/npp201316a.html

Escitalopram Appears To Reduce Symptoms of Night Eating Disorder

An open-label trial of escitalopram to treat night eating syndrome (NES) showed significant reduction in symptoms, according to researchers at the Perelman School of Medicine at the University of Pennsylvania. Thirty-one adults with NES participated in a 12-week trial in which outcome measures included the Night Eating Symptom Scale, percent of daily intake after the evening meal, number of nocturnal ingestions per week, weight, total awakenings a week, mood, and quality of life. Dosing of escitalopram began at 10 mg, with the dose cut to 5 mg for participants who experienced significant side effects and increased to 20 mg for participants whose symptoms were still present at week 4 of the study.

In addition to results that indicated significant decrease in all primary measures of NES by the end of the 12-week trial, the researchers reported that 58 percent of the participants were in remission at treatment end. The researchers said their results point to the need for a larger controlled trial to further test the efficacy of escitalopram for NES, given that the evidence for effective treatments for NES is still quite limited.

The study was supported by an investigator-initiated grant from Forest Laboratories.

Allison K, Studt S, Berkowitz R, et al. "An Open-Label Efficacy Trial of Escitalopram for Night Eating Syndrome." Eating Behaviors. 2013. 14(2): 199-203. http://www.sciencedirect.com/science/article/pii/S1471015313000172

mangostock/Shutterstock

Race of cancer surivors may be a factor in their development of PTSD.

2013 APA ANNUAL MEETING

KEYNOTE SPEECH BY PRESIDENT BILL CLINTON

NEW DATE
SUNDAY, MAY 19, 5:30 PM TO 6:30 PM
SAN FRANCISCO, CA
MOSCONE CENTER, HALL D

After leaving the White House, President Bill Clinton established the William J. Clinton Foundation with the mission to improve global health, strengthen economies, promote healthier childhoods, and protect the environment by fostering partnerships among governments, businesses, nongovernmental organizations (NGOs), and private citizens to turn good intentions into measurable results. Today the Foundation has staff and volunteers around the world working to improve lives through several initiatives, including the Clinton Health Access Initiative, which is helping 4.5 million people living with HIV/AIDS access lifesaving drugs. The Clinton Climate Initiative, the Clinton Development Initiative, and the Clinton Giustra Sustainable Growth Initiative – are applying a business-oriented approach to fight climate change worldwide and to promote sustainable economic growth in Africa and Latin America. In the U.S., the Foundation is working to combat the alarming rise in childhood obesity through the Alliance for a Healthier Generation, and is helping individuals and families succeed and to increase small business growth in underserved communities through the Clinton Economic Opportunity Initiative. Established in 2005, the Clinton Global Initiative brings together global leaders to devise and implement innovative solutions to some of the world's most pressing issues. So far, more than 2,100 Clinton Global Initiative commitments have improved the lives of 400 million people in 180 nations.

INTERNATIONALLY RENOWNED LECTURERS

NORA VOLKOW, M.D. • ELIZABETH BLACKBURN, Ph.D. • STANLEY PRUSINER, M.D.
ANDREW SCHALLY, M.D. • IRVIN YALOM, M.D. • AND OTHERS

annualmeeting.psychiatry.org

INDICATION and IMPORTANT SAFETY INFORMATION for Abilify Maintena™ (aripiprazole) for extended-release injectable suspension

INDICATION

Abilify Maintena is an atypical antipsychotic indicated for the treatment of schizophrenia.

- Efficacy was demonstrated in a placebo-controlled, randomized-withdrawal maintenance trial in patients with schizophrenia and additional support for efficacy was derived from oral aripiprazole trials.

IMPORTANT SAFETY INFORMATION

Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk (1.6 to 1.7 times) of death compared to placebo (4.5% vs 2.6%, respectively). Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Abilify Maintena is not approved for the treatment of patients with dementia-related psychosis.

Contraindication: Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Cerebrovascular Adverse Events, Including Stroke: Increased incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, have been reported in clinical trials of elderly patients with dementia-related psychosis treated with oral aripiprazole.

IMPORTANT SAFETY INFORMATION [*continued*]

Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as NMS may occur with administration of antipsychotic drugs, including Abilify Maintena. Rare cases of NMS occurred during aripiprazole treatment. Signs and symptoms of NMS include hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (e.g., irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.

Tardive Dyskinesia (TD): The risk of developing TD (a syndrome of abnormal, involuntary movements) and the potential for it to become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. Prescribing should be consistent with the need to minimize TD. There is no known treatment for established TD, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn.

Continued on next page.

Please see IMPORTANT SAFETY INFORMATION continued, and BRIEF SUMMARY of FULL PRESCRIBING INFORMATION, including **Boxed WARNING**, on the following pages.

NEW

400MG ONCE-MONTHLY

Abilify Maintena™

(aripiprazole) for extended release injectable suspension

IMPORTANT SAFETY INFORMATION for Abilify Maintena™ (aripiprazole) for extended-release injectable suspension [*continued*]

Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that include:

- **Hyperglycemia/Diabetes Mellitus:** Hyperglycemia, in some cases extreme and associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics including aripiprazole. Patients with diabetes should be regularly monitored for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.
- **Dyslipidemia:** Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics. There were no significant differences between aripiprazole- and placebo-treated patients in the proportion with changes from normal to clinically significant levels for fasting/nonfasting total cholesterol, fasting triglycerides, fasting low-density lipoproteins (LDLs), and fasting/nonfasting high-density lipoproteins (HDLs).
- **Weight Gain:** Weight gain has been observed. Clinical monitoring of weight is recommended.

Orthostatic Hypotension: Aripiprazole may cause orthostatic hypotension. Abilify Maintena should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or conditions which would predispose them to hypotension.

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia, neutropenia, and agranulocytosis have been reported. Patients with a history of clinically significant low white blood cell (WBC) count or drug-induced leukopenia/neutropenia should have their complete blood count monitored frequently during the first few months of therapy while receiving Abilify Maintena. In such patients, consider discontinuation of Abilify Maintena at the first sign of a clinically significant decline in WBC count in the absence of other causative factors.

Seizures/Convulsions: Abilify Maintena should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: Abilify Maintena may impair judgment, thinking, or motor skills. Instruct patients to avoid operating hazardous machinery including automobiles until they are certain Abilify Maintena does not affect them adversely.

Body Temperature Regulation: Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Advise patients regarding appropriate care in avoiding overheating and dehydration. Appropriate care is advised for patients who may exercise strenuously, may be exposed to extreme heat, receive concomitant medication with anticholinergic activity, or are subject to dehydration.

Dysphagia: Esophageal dysmotility and aspiration have been associated with Abilify Maintena; use caution in patients at risk for aspiration pneumonia.

Alcohol: Advise patients to avoid alcohol while taking Abilify Maintena.

Concomitant Medication: Dosage adjustments are recommended in patients who are CYP2D6 poor metabolizers and in patients taking concomitant CYP3A4 inhibitors or CYP2D6 inhibitors for greater than 14 days. If the CYP3A4 inhibitor or CYP2D6 inhibitor is withdrawn, the Abilify Maintena dosage may need to be increased. Avoid the concomitant use of CYP3A4 inducers with Abilify Maintena for greater than 14 days because the blood levels of aripiprazole are decreased and may be below the effective levels. Dosage adjustments are not recommended for patients with concomitant use of CYP3A4 inhibitors, CYP2D6 inhibitors or CYP3A4 inducers for less than 14 days.

Most commonly observed adverse reaction: The safety profile of Abilify Maintena is expected to be similar to that of oral aripiprazole. In patients who tolerated and responded to oral aripiprazole and single-blind Abilify Maintena and were then randomized to receive Abilify Maintena or placebo injections, the incidence of adverse reactions was similar between the two treatment groups. The adverse reaction ≥ 5% incidence and at least twice the rate of placebo for oral aripiprazole vs. placebo, respectively, was:

- Akathisia (8% vs 4%) in adult patients with schizophrenia.

Injection Site Reactions: In the open-label, stabilization phase of a study with Abilify Maintena in patients with schizophrenia, the percent of patients reporting any injection site-related adverse reaction was 6.3% for Abilify Maintena-treated patients.

Dystonia is a class effect of antipsychotic drugs. Symptoms of dystonia may occur in susceptible individuals during the first days of treatment and at low doses.

Pregnancy/Nursing: Based on animal data, may cause fetal harm. Abilify Maintena should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Aripiprazole is excreted in human breast milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Please see brief summary of FULL PRESCRIBING INFORMATION, including **Boxed WARNING**, on adjacent pages.

Otsuka Lundbeck

ABILIFY MAINTENA™ (aripiprazole) for extended-release injectable suspension, for intramuscular use

BRIEF SUMMARY OF PRESCRIBING INFORMATION (For complete details, please *see Full Prescribing Information and Medication Guide.)*

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

See full prescribing information for complete boxed warning.

- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death
- ABILIFY MAINTENA is not approved for the treatment of patients with dementia-related psychosis

INDICATIONS AND USAGE: ABILIFY MAINTENA (aripiprazole) is indicated for the treatment of schizophrenia. Efficacy was demonstrated in a placebo-controlled, randomized-withdrawal maintenance trial in patients with schizophrenia and additional support for efficacy was derived from oral aripiprazole trials.

CONTRAINDICATIONS: ABILIFY MAINTENA is contraindicated in patients with a known hypersensitivity to aripiprazole. Hypersensitivity reactions ranging from pruritus/urticaria to anaphylaxis have been reported in patients receiving aripiprazole.

WARNINGS AND PRECAUTIONS: Increased Mortality in Elderly Patients with Dementia-Related Psychosis: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group.

Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. ABILIFY MAINTENA is not approved for the treatment of patients with dementia-related psychosis.

Cerebrovascular Adverse Reactions, Including Stroke in Elderly Patients with Dementia-Related Psychosis: In placebo-controlled clinical studies (two flexible dose and one fixed dose study) of dementia-related psychosis, there was an increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack), including fatalities, in oral aripiprazole-treated patients (mean age: 84 years; range: 78-88 years). In the fixed-dose study, there was a statistically significant dose response relationship for cerebrovascular adverse reactions in patients treated with oral aripiprazole. ABILIFY MAINTENA is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome: A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) may occur with administration of antipsychotic drugs, including ABILIFY MAINTENA. Rare cases of NMS occurred during aripiprazole treatment in the worldwide clinical database.

Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to exclude cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system pathology.

The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

Tardive Dyskinesia: A syndrome of potentially irreversible, involuntary, dyskinetic movements, may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

The risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and, thereby, may possibly mask the underlying process. The effect of symptomatic suppression on the long-term course of the syndrome is unknown.

Given these considerations, ABILIFY MAINTENA should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who suffer from a chronic illness that 1) is known to respond to antipsychotic drugs and 2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient treated with ABILIFY MAINTENA drug discontinuation should be considered. However, some patients may require treatment with ABILIFY MAINTENA despite the presence of the syndrome.

Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that include hyperglycemia/diabetes mellitus, dyslipidemia, and weight gain. While all drugs in the class have been shown to produce some metabolic changes, each drug has its own specific risk profile. Although the following metabolic data were collected in patients treated with oral formulations of aripiprazole, the findings pertain to patients receiving ABILIFY MAINTENA as well.

- **Hyperglycemia/Diabetes Mellitus:** Hyperglycemia, in some cases extreme and associated with diabetic ketoacidosis, hyperosmolar coma, or death, has been reported in patients treated with atypical antipsychotics. There have been reports of hyperglycemia in patients treated with aripiprazole. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse reactions is not completely understood. However, epidemiological studies suggest an increased risk of hyperglycemia-related adverse reactions in patients treated with atypical antipsychotics. Because aripiprazole was not marketed at the time these studies were performed, it is not known if aripiprazole is associated with this increased risk. Precise risk estimates for hyperglycemia-related adverse reactions in patients treated with atypical antipsychotics are not available. Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes), who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the atypical antipsychotic drug.

  In an analysis of 13 placebo-controlled monotherapy trials in adults, primarily with schizophrenia or bipolar disorder, the mean change in fasting glucose in aripiprazole-treated patients (+4.4 mg/dL; median exposure 25 days; N=1057) was not significantly different than in placebo-treated patients (+2.5 mg/dL; median exposure 22 days; N=799). Table 1 shows the proportion of aripiprazole-treated patients with normal and borderline fasting glucose at baseline (median exposure 25 days) that had high fasting glucose measurements compared to placebo-treated patients (median exposure 22 days).

Table 1: Changes in Fasting Glucose From Placebo-controlled Monotherapy Trials in Adult Patients

	Category Change (at least once) from Baseline	Treatment Arm	n/N	%
Fasting Glucose	Normal to High (<100 mg/dL to ≥126 mg/dL)	Aripiprazole	31/822	3.8
		Placebo	22/605	3.6
	Borderline to High (≥100 mg/dL and <126 mg/dL to ≥126 mg/dL)	Aripiprazole	31/176	17.6
		Placebo	13/142	9.2

  At 24 weeks, the mean change in fasting glucose in aripiprazole-treated patients was not significantly different than in placebo-treated patients [+2.2 mg/dL (n=42) and +9.6 mg/dL (n=28), respectively].

- **Dyslipidemia:** Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics.

  There were no significant differences between aripiprazole- and placebo-treated patients in the proportion with changes from normal to clinically significant levels for fasting/nonfasting total cholesterol, fasting triglycerides, fasting LDLs, and fasting/nonfasting HDLs. Analyses of patients with at least 12 or 24 weeks of exposure were limited by small numbers of patients.

  Table 2 shows the proportion of adult patients, primarily from pooled schizophrenia and bipolar disorder monotherapy placebo-controlled trials, with changes in total cholesterol (pooled from 17 trials; median exposure 21 to 25 days), fasting triglycerides (pooled from eight trials; median exposure 42 days), fasting LDL cholesterol (pooled from eight trials; median exposure 39 to 45 days, except for placebo-treated patients with baseline normal fasting LDL measurements, who had median treatment exposure of 24 days) and HDL cholesterol (pooled from nine trials; median exposure 40 to 42 days).

Table 2: Changes in Blood Lipid Parameters From Placebo-controlled Monotherapy Trials in Adults

	Treatment Arm	n/N	%
Total Cholesterol Normal to High (<200 mg/dL to ≥240 mg/dL)	Aripiprazole	34/1357	2.5
	Placebo	27/973	2.8
Fasting Triglycerides Normal to High (<150 mg/dL to ≥200 mg/dL)	Aripiprazole	40/539	7.4
	Placebo	30/431	7.0
Fasting LDL Cholesterol Normal to High (<100 mg/dL to ≥160 mg/dL)	Aripiprazole	2/332	0.6
	Placebo	2/268	0.7
HDL Cholesterol Normal to Low (≥40 mg/dL to <40 mg/dL)	Aripiprazole	121/1066	11.4
	Placebo	99/794	12.5

In monotherapy trials in adults, the proportion of patients at 12 weeks and 24 weeks with changes from Normal to High in total cholesterol (fasting/nonfasting), fasting triglycerides, and fasting LDL cholesterol were similar between aripiprazole- and placebo-treated patients: at 12 weeks, Total Cholesterol (fasting/nonfasting), 1/71 (1.4%) vs. 3/74 (4.1%); Fasting Triglycerides, 8/62 (12.9%) vs. 5/37 (13.5%); Fasting LDL Cholesterol, 0/34 (0%) vs. 1/25 (4.0%), respectively; and at 24 weeks, Total Cholesterol (fasting/nonfasting), 1/42 (2.4%) vs. 3/37 (8.1%); Fasting Triglycerides, 5/34 (14.7%) vs. 5/20 (25%); Fasting LDL Cholesterol, 0/22 (0%) vs. 1/18 (5.6%), respectively.

- **Weight Gain:** Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended. In an analysis of 13 placebo-controlled monotherapy trials, primarily from pooled schizophrenia and bipolar disorder, with a median exposure of 21 to 25 days, the mean change in body weight in aripiprazole-treated patients was +0.3 kg (N=1673) compared to –0.1 kg (N=1100) in placebo-controlled patients. At 24 weeks, the mean change from baseline in body weight in aripiprazole-treated patients was –1.5 kg (n=73) compared to –0.2 kg (n=46) in placebo-treated patients.

  Table 3 shows the percentage of adult patients with weight gain ≥7% of body weight in the 13 pooled placebo-controlled monotherapy trials.

Table 3: Percentage of Patients From Placebo-controlled Trials in Adult Patients with Weight Gain ≥7% of Body Weight

	Indication	Treatment Arm	N	n (%)
Weight gain ≥7% of body weight	Schizophrenia[a]	Aripiprazole	852	69 (8.1)
		Placebo	379	12 (3.2)
	Bipolar Mania[b]	Aripiprazole	719	16 (2.2)
		Placebo	598	16 (2.7)

[a]4-6 weeks' duration. [b]3 weeks' duration.

Orthostatic Hypotension: Aripiprazole may cause orthostatic hypotension, perhaps due to its α_1-adrenergic receptor antagonism. Orthostasis occurred in 4/576 (0.7%) patients treated with ABILIFY MAINTENA during the stabilization phase, including abnormal orthostatic blood pressure (1/576, 0.2%), postural dizziness (1/576, 0.2%), presyncope (1/576, 0.2%) and orthostatic hypotension (1/576, 0.2%).

In the stabilization phase, the incidence of significant orthostatic change in blood pressure (defined as a decrease in systolic blood pressure ≥20 mmHg accompanied by an increase in heart rate ≥25 when comparing standing to supine values) was 0.2% (1/575).

Leukopenia, Neutropenia, and Agranulocytosis: *Class Effect:* In clinical trials and post-marketing experience, leukopenia and neutropenia have been reported temporally related to antipsychotic agents, including oral aripiprazole. Agranulocytosis has also been reported.

Possible risk factors for leukopenia/neutropenia include pre-existing low white blood cell count (WBC) and history of drug-induced leukopenia/neutropenia. In patients with a history of a clinically significant low WBC or drug-induced leukopenia/neutropenia perform a complete blood count (CBC) frequently during the first few months of therapy. In such patients, consider discontinuation of ABILIFY MAINTENA at the first sign of a clinically significant decline in WBC in the absence of other causative factors.

Monitor patients with clinically significant neutropenia for fever or other symptoms or signs of infection and treat promptly if such symptoms or signs occur. Discontinue ABILIFY MAINTENA in patients with severe neutropenia (absolute neutrophil count <1000/mm^3) and follow their WBC counts until recovery.

Seizures: As with other antipsychotic drugs, use ABILIFY MAINTENA cautiously in patients with a history of seizures or with conditions that lower the seizure threshold. Conditions that lower the seizure threshold may be more prevalent in a population of 65 years or older.

Potential for Cognitive and Motor Impairment: ABILIFY MAINTENA, like other antipsychotics, may impair judgment, thinking, or motor skills. Instruct patients to avoid operating hazardous machinery, including automobiles, until they are reasonably certain that therapy with ABILIFY MAINTENA does not affect them adversely.

Body Temperature Regulation: Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Appropriate care is advised when prescribing ABILIFY MAINTENA for patients who will be experiencing conditions which may contribute to an elevation in core body temperature, (e.g., exercising strenuously, exposure to extreme heat, receiving concomitant medication with anticholinergic activity, or being subject to dehydration).

Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotic drug use, including ABILIFY MAINTENA. ABILIFY MAINTENA and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

ADVERSE REACTIONS: The following adverse reactions are discussed in more detail in other sections of the labeling in the *Full Prescribing Information:*

- Increased Mortality in Elderly Patients with Dementia-Related Psychosis *[see Boxed Warning and Warnings and Precautions (5.1)]*
- Cerebrovascular Adverse Reactions, Including Stroke in Elderly Patients with Dementia-Related Psychosis *[see Boxed Warning and Warnings and Precautions (5.2)]*
- Neuroleptic Malignant Syndrome *[see Warnings and Precautions (5.3)]*
- Tardive Dyskinesia *[see Warnings and Precautions (5.4)]*
- Metabolic Changes *[see Warnings and Precautions (5.5)]*
- Orthostatic Hypotension *[see Warnings and Precautions (5.6)]*
- Leukopenia, Neutropenia, and Agranulocytosis *[see Warnings and Precautions (5.7)]*
- Seizures *[see Warnings and Precautions (5.8)]*
- Potential for Cognitive and Motor Impairment *[see Warnings and Precautions (5.9)]*
- Body Temperature Regulation *[see Warnings and Precautions (5.10)]*
- Dysphagia *[see Warnings and Precautions (5.11)]*

Clinical Trials Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Safety Database of ABILIFY MAINTENA and Oral Aripiprazole: Aripiprazole has been evaluated for safety in 16,114 adult patients who participated in multiple-dose, clinical trials in schizophrenia and other indications, and who had approximately 8,578 patient-years of exposure to oral aripiprazole. A total of 3,901 patients were treated with oral aripiprazole for at least 180 days, 2,259 patients were treated with oral aripiprazole for at least 360 days, and 933 patients continuing aripiprazole treatment for at least 720 days.

ABILIFY MAINTENA 300-400 mg every 4 weeks has been evaluated for safety in 1,287 adult patients in clinical trials in schizophrenia, with approximately 1,281 patient-years of exposure to ABILIFY MAINTENA. A total of 832 patients were treated with ABILIFY MAINTENA for at least 180 days (at least 7 consecutive injections) and 630 patients treated with ABILIFY MAINTENA had at least 1 year of exposure (at least 13 consecutive injections).

The conditions and duration of treatment with ABILIFY MAINTENA included double-blind and open-label studies. The safety profile of ABILIFY MAINTENA is expected to be similar to that of oral aripiprazole. Therefore, most of the safety data presented below are derived from trials with the oral formulation. In patients who tolerated and responded to treatment with oral aripiprazole and single-blind ABILIFY MAINTENA and were then randomized to receive ABILIFY MAINTENA or placebo injections under double-blind conditions, the incidence of adverse reactions was similar between the two treatment groups.

Adverse Reactions of ABILIFY MAINTENA and Oral Aripiprazole: *Adverse Reactions Associated with Discontinuation of Oral Aripiprazole:* Based on a pool of five placebo-controlled trials (four 4-week and one 6-week) in which oral aripiprazole was administered to adults with schizophrenia in doses ranging from 2 mg/day to 30 mg/day, the incidence of discontinuation due to adverse reactions was 7% in oral aripiprazole-treated and 9% in placebo-treated patients. The types of adverse reactions that led to discontinuation were similar for the aripiprazole-treated and placebo-treated patients.

Commonly Observed Adverse Reactions of Oral Aripiprazole: Based on a pool of five placebo-controlled trials (four 4-week and one 6-week) in which oral aripiprazole was administered to adults with schizophrenia in doses ranging from 2 mg/day to 30 mg/day, the only commonly observed adverse reaction associated with the use of oral aripiprazole in patients with schizophrenia (incidence of 5% or greater and aripiprazole incidence at least twice that for placebo) was akathisia (aripiprazole 8%; placebo 4%).

Less Common Adverse Reactions in Adults Treated with Oral Aripiprazole: Table 4 enumerates the pooled incidence, rounded to the nearest percent, of adverse reactions that occurred during acute therapy (up to 6 weeks in schizophrenia and up to 3 weeks in bipolar mania), including only those reactions that occurred in 2% or more of patients treated with oral aripiprazole (doses ≥2 mg/day) and for which the incidence in patients treated with aripiprazole was greater than the incidence in patients treated with placebo in the combined dataset.

Table 4: Adverse Reactions in Short-term, Placebo-controlled Trials in Adult Patients Treated with Oral Aripiprazole

	Percentage of Patients Reporting Reaction[a]	
System Organ Class Preferred Term	**Oral Aripiprazole (n=1843)**	**Placebo (n=1166)**
Eye Disorders		
Blurred Vision	3	1
Gastrointestinal Disorders		
Nausea	15	11
Constipation	11	7
Vomiting	11	6
Dyspepsia	9	7
Dry Mouth	5	4
Toothache	4	3
Abdominal Discomfort	3	2
Stomach Discomfort	3	2
General Disorders and Administration Site Conditions		
Fatigue	6	4
Pain	3	2
Musculoskeletal and Connective Tissue Disorders		
Musculoskeletal Stiffness	4	3
Pain in Extremity	4	2
Myalgia	2	1
Muscle Spasms	2	1
Nervous System Disorders		
Headache	27	23
Dizziness	10	7
Akathisia	10	4
Sedation	7	4
Extrapyramidal Disorder	5	3
Tremor	5	3
Somnolence	5	3
Psychiatric Disorders		
Agitation	19	17
Insomnia	18	13
Anxiety	17	13
Restlessness	5	3
Respiratory, Thoracic, and Mediastinal Disorders		
Pharyngolaryngeal Pain	3	2
Cough	3	2

[a]Adverse reactions reported by at least 2% of patients treated with oral aripiprazole, except adverse reactions which had an incidence equal to or less than placebo.

An examination of population subgroups did not reveal any clear evidence of differential adverse reaction incidence on the basis of age, gender, or race.

Dose-Related Adverse Reactions of Oral Aripiprazole: Dose response relationships for the incidence of treatment-emergent adverse events were evaluated from four trials in adult patients with schizophrenia comparing various fixed oral doses of aripiprazole (2 mg/day, 5 mg/day, 10 mg/day, 15 mg/day, 20 mg/day, and 30 mg/day) to placebo. This analysis, stratified by study, indicated that the only adverse reaction to have a possible dose response relationship, and then most prominent only with 30 mg, was somnolence [including sedation]; (incidences were placebo, 7.1%; 10 mg, 8.5%; 15 mg, 8.7%; 20 mg, 7.5%; 30 mg, 12.6%).

Injection Site Reactions of ABILIFY MAINTENA: In the open-label, stabilization phase of a study with ABILIFY MAINTENA in patients with schizophrenia, the percent of patients reporting any injection site-related adverse reaction was 6.3% for ABILIFY MAINTENA-treated patients. The mean intensity of injection pain reported by subjects using a visual analog scale (0=no pain to 100=unbearably painful) was minimal and improved in subjects receiving ABILIFY MAINTENA from the first to the last injection in the open-label, stabilization phase (6.1 to 4.9).

Investigator evaluation of the injection site for pain, swelling, redness and induration following injections of ABILIFY MAINTENA in the open-label, stabilization phase were rated as absent for 74%-96% of subjects following the first injection and 77%-96% of subjects following the last injection.

Extrapyramidal Symptoms of Oral Aripiprazole: In short-term, placebo-controlled trials in schizophrenia, the incidence of reported EPS-related events, excluding events related to akathisia, for oral aripiprazole-treated patients was 13% vs. 12% for placebo; and the incidence of akathisia-related events for aripiprazole-treated patients was 8% vs. 4% for placebo.

Objectively collected data from those trials was collected on the Simpson Angus Rating Scale (for EPS), the Barnes Akathisia Scale (for akathisia), and the Abnormal Involuntary Movement Scale (for dyskinesias). In the schizophrenia trials, the objectively collected data did not show a difference between aripiprazole and placebo, with the exception of the Barnes Akathisia Scale (aripiprazole, 0.08; placebo, –0.05).

Similarly, in a long-term (26-week), placebo-controlled trial of schizophrenia in adults, objectively collected data on the Simpson Angus Rating Scale (for EPS), the Barnes Akathisia Scale (for akathisia), and the Abnormal Involuntary Movement Scale (for dyskinesias) did not show a difference between aripiprazole and placebo.

Dystonia: Class Effect: Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first few days of treatment. Dystonic symptoms include: spasm of the neck muscles, sometimes progressing to tightness of the throat, swallowing difficulty, difficulty breathing, and/or protrusion of the tongue. While these symptoms can occur at low doses, they occur more frequently and with greater severity with high potency and at higher doses of first generation antipsychotic drugs. An elevated risk of acute dystonia is observed in males and younger age groups.

Adverse Reactions in Long-Term, Double-Blind, Placebo-Controlled Trials of Oral Aripiprazole: The adverse reactions reported in a 26-week, double-blind trial comparing oral aripiprazole and placebo in patients with schizophrenia were generally consistent with those reported in the short-term, placebo-controlled trials, except for a higher incidence of tremor [8% (12/153) for oral aripiprazole vs. 2% (3/153) for placebo]. In this study, the majority of the cases of tremor were of mild intensity (8/12 mild and 4/12 moderate), occurred early in therapy (9/12 ≤49 days), and were of limited duration (7/12 ≤10 days). Tremor infrequently led to discontinuation (<1%) of oral aripiprazole. In addition, in a long-term, active-controlled study, the incidence of tremor was 5% (40/859) for oral aripiprazole.

Other Adverse Reactions Observed During the Premarketing Evaluation of Oral Aripiprazole: Following is a list of MedDRA terms that reflect adverse reactions reported by patients treated with oral aripiprazole at multiple doses ≥2 mg/day during any phase of a trial within the database of 13,543 adult patients. All events assessed as possible adverse drug reactions have been included with the exception of more commonly occurring events. In addition, medically/clinically meaningful adverse reactions, particularly those that are likely to be useful to the prescriber or that have pharmacologic plausibility, have been included. Events already listed in other parts of *Adverse Reactions (6),* or those considered in *Warnings and Precautions (5) or Overdosage (10)* have been excluded. Although the reactions reported occurred during treatment with aripiprazole, they were not necessarily caused by it.

Events are further categorized by MedDRA system organ class and listed in order of decreasing frequency according to the following definitions: those occurring in at least 1/100 patients (only those not already listed in the tabulated results from placebo-controlled trials appear in this listing); those occurring in 1/100 to 1/1000 patients; and those occurring in fewer than 1/1000 patients.

Blood and Lymphatic System Disorders: ≥1/1000 patients and <1/100 patients - thrombocytopenia; *Cardiac Disorders:* ≥1/1000 patients and <1/100 patients - palpitations, cardiopulmonary failure, myocardial infarction, cardio-respiratory arrest, atrioventricular block, extrasystoles, angina pectoris, myocardial ischemia; <1/1000 patients - atrial flutter, supraventricular tachycardia, ventricular tachycardia; *Eye Disorders:* ≥1/1000 patients and <1/100 patients - photophobia, diplopia, eyelid edema, photopsia; *Gastrointestinal Disorders:* ≥1/1000 patients and <1/100 patients - gastroesophageal reflux disease, swollen tongue, esophagitis; <1/1000 patients - pancreatitis; *General Disorders and Administration Site Conditions:* ≥1/100 patients - asthenia, peripheral edema, chest pain; ≥1/1000 patients and <1/100 patients - face edema, angioedema; <1/1000 patients - hypothermia; *Hepatobiliary Disorders:* <1/1000 patients - hepatitis, jaundice; *Immune System Disorders:* ≥1/1000 patients and <1/100 patients - hypersensitivity; *Injury, Poisoning, and Procedural Complications:* ≥1/100 patients - fall; <1/1000 patients - heat stroke; *Investigations:* ≥1/1000 patients and <1/100 patients - blood prolactin increased, blood urea increased, blood creatinine increased, blood bilirubin increased; <1/1000 patients - blood lactate dehydrogenase increased, glycosylated hemoglobin increased; *Metabolism and Nutrition Disorders:* ≥1/1000 patients and <1/100 patients - anorexia, hyponatremia, hypoglycemia, polydipsia; <1/1000 patients - diabetic ketoacidosis; *Musculoskeletal and Connective Tissue Disorders:* ≥1/1000 patients and <1/100 patients - muscle rigidity, muscular weakness, muscle tightness, mobility decreased; <1/1000 patients - rhabdomyolysis; *Nervous System Disorders:* ≥1/100 patients - coordination abnormal; ≥1/1000 patients and <1/100 patients - speech disorder, hypokinesia, hypotonia, myoclonus, akinesia, bradykinesia; <1/1000 patients - choreoathetosis; *Psychiatric Disorders:* ≥1/100 patients - suicidal ideation; ≥1/1000 patients and <1/100 patients - loss of libido, suicide attempt, hostility, libido increased, anger, anorgasmia, delirium, intentional self injury, completed suicide, tic, homicidal ideation; <1/1000 patients - catatonia, sleepwalking; *Renal and Urinary Disorders:* ≥1/1000 patients and <1/100 patients - urinary retention, polyuria, nocturia; *Reproductive System and Breast Disorders:* ≥1/1000 patients and <1/100 patients - menstruation irregular, erectile dysfunction, amenorrhea, breast pain; <1/1000 patients - gynecomastia, priapism; *Respiratory, Thoracic, and Mediastinal Disorders:* ≥1/100 patients - nasal congestion, dyspnea; *Skin and Subcutaneous Tissue Disorders:* ≥1/100 patients - rash (including erythematous, exfoliative, generalized, macular, maculopapular, papular rash; acneiform, allergic, contact, exfoliative, seborrheic dermatitis, neurodermatitis, and drug eruption), hyperhydrosis; ≥1/1000 patients and <1/100 patients - pruritus, photosensitivity reaction, alopecia, urticaria.

Postmarketing Experience: The following adverse reactions have been identified during post-approval use of oral aripiprazole. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: rare occurrences of allergic reaction (anaphylactic reaction, angioedema, laryngospasm, pruritus/urticaria, or oropharyngeal spasm).

DRUG INTERACTIONS: Carbamazepine or Other CYP3A4 Inducers: Concomitant use of ABILIFY MAINTENA with carbamazepine or other CYP3A4 inducers decreases the concentrations of aripiprazole. Avoid use of ABILIFY MAINTENA in combination with carbamazepine and other inducers of CYP3A4 for greater than 14 days *[see Indications and Usage, Dosage and Administration (2.3) and Clinical Pharmacology (12.3)].*

Ketoconazole or Other Strong CYP3A4 Inhibitors: Concomitant use of ABILIFY MAINTENA with ketoconazole or other CYP3A4 inhibitors for more than 14 days increases the concentrations of aripiprazole and reduction of the ABILIFY MAINTENA dose is recommended *[see Dosage and Administration (2.3) and Clinical Pharmacology (12.3)].* Due to prolonged-release characteristics of ABILIFY MAINTENA, short-term co-administration of ketoconazole or other inhibitors of CYP3A4 with ABILIFY MAINTENA does not require a dose adjustment.

Quinidine or Other Strong CYP2D6 Inhibitors: Concomitant use of ABILIFY MAINTENA with quinidine or other CYP2D6 inhibitors increases the concentrations of aripiprazole after longer-term use (i.e., over 14 days) and reduction of the ABILIFY MAINTENA dose is recommended *[see Dosage and Administration (2.3) and Clinical Pharmacology (12.3)].* Due to prolonged-release characteristics of ABILIFY MAINTENA, short-term co-administration of quinidine or other CYP2D6 inhibitors with ABILIFY MAINTENA does not require a dose adjustment.

CNS Depressants: Given the CNS depressant effects of aripiprazole, use caution when ABILIFY MAINTENA is taken in combination with other centrally-acting drugs or alcohol.

Anti-Hypertensive Agents: Due to its α_1-adrenergic antagonism, aripiprazole has the potential to enhance the effect of certain antihypertensive agents.

USE IN SPECIFIC POPULATIONS: Pregnancy: *Pregnancy Category C: Risk Summary:* Adequate and well controlled studies with aripiprazole have not been conducted in pregnant women. Neonates exposed to antipsychotic drugs (including ABILIFY MAINTENA) during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. In animal studies, aripiprazole demonstrated developmental toxicity, including possible teratogenic effects in rats and rabbits at doses 1-10 times the oral maximum recommended human dose [MRHD] of 30 mg/day based on a mg/m^2 body surface area. ABILIFY MAINTENA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Clinical Considerations: Fetal/Neonatal Adverse Reactions: Monitor neonates exhibiting extrapyramidal or withdrawal symptoms. Some neonates recover within hours or days without specific treatment; others may require prolonged hospitalization.

Animal Data: Pregnant rats were treated with oral doses of 3 mg/kg/day, 10 mg/kg/day, and 30 mg/kg/day (1 times, 3 times, and 10 times the oral maximum recommended human dose [MRHD] of 30 mg/day on a mg/m^2 body surface area) of aripiprazole during the period of organogenesis. Gestation was slightly prolonged at 30 mg/kg. Treatment caused a slight delay in fetal development, as evidenced by decreased fetal weight (30 mg/kg), undescended testes (30 mg/kg), and delayed skeletal ossification (10 mg/kg and 30 mg/kg). There were no adverse effects on embryofetal or pup survival. Delivered offspring had decreased body weights (10 mg/kg and 30 mg/kg), and increased incidences of hepatodiaphragmatic nodules and diaphragmatic hernia at 30 mg/kg (the other dose groups were not examined for these findings). A low incidence of diaphragmatic hernia was also seen in the fetuses exposed to 30 mg/kg. Postnatally, delayed vaginal opening was seen at 10 mg/kg and 30 mg/kg and impaired reproductive performance (decreased fertility rate, corpora lutea, implants, live fetuses, and increased post-implantation loss, likely mediated through effects on female offspring) was seen at 30 mg/kg. Some maternal toxicity was seen at 30 mg/kg; however, there was no evidence to suggest that these developmental effects were secondary to maternal toxicity.

In pregnant rats receiving aripiprazole injection intravenously (3 mg/kg/day, 9 mg/kg/day, and 27 mg/kg/day) during the period of organogenesis, decreased fetal weight and delayed skeletal ossification were seen at the highest dose, which also caused some maternal toxicity.

Pregnant rabbits were treated with oral doses of 10 mg/kg/day, 30 mg/kg/day, and 100 mg/kg/day (2 times, 3 times, and 11 times human exposure at the oral MRHD of 30 mg/day based on AUC and 6 times, 19 times, and 65 times the oral MRHD of 30 mg/day based on mg/m^2 body surface area) of aripiprazole during the period of organogenesis. Decreased maternal food consumption and increased abortions were seen at 100 mg/kg. Treatment caused increased fetal mortality (100 mg/kg), decreased fetal weight (30 mg/kg and 100 mg/kg), increased incidence of a skeletal abnormality (fused sternebrae at 30 mg/kg and 100 mg/kg), and minor skeletal variations (100 mg/kg).

In pregnant rabbits receiving aripiprazole injection intravenously (3 mg/kg/day, 10 mg/kg/day, and 30 mg/kg/day) during the period of organogenesis, the highest dose, which caused pronounced maternal toxicity, resulted in decreased fetal weight, increased fetal abnormalities (primarily skeletal), and decreased fetal skeletal ossification. The fetal no-effect dose was 10 mg/kg, which produced 5 times the human exposure at the oral MRHD based on AUC and is 6 times the oral MRHD of 30 mg/day based on mg/m^2 body surface area.

In a study in which rats were treated with oral doses of 3 mg/kg/day, 10 mg/kg/day, and 30 mg/kg/day (1 times, 3 times, and 10 times the oral MRHD of 30 mg/day on a mg/m^2 body surface area) of aripiprazole perinatally and postnatally (from day 17 of gestation through day 21 postpartum), slight maternal toxicity and slightly prolonged gestation were seen at 30 mg/kg. An increase in stillbirths and decreases in pup weight (persisting into adulthood) and survival were seen at this dose.

In rats receiving aripiprazole injection intravenously (3 mg/kg/day, 8 mg/kg/day, and 20 mg/kg/day) from day 6 of gestation through day 20 postpartum, an increase in stillbirths was seen at 8 mg/kg and 20 mg/kg, and decreases in early postnatal pup weights and survival were seen at 20 mg/kg. These doses produced some maternal toxicity. There were no effects on postnatal behavioral and reproductive development.

Nursing Mothers: Aripiprazole is excreted in human breast milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

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CYP2D6 Poor Metabolizers: Approximately 8% of Caucasians and 3–8% of Black/African Americans cannot metabolize CYP2D6 substrates and are classified as poor metabolizers (PM). Dosage adjustment is recommended in CYP2D6 poor metabolizers due to high aripiprazole concentrations *[see Dosage and Administration (2.3), Clinical Pharmacology (12.3)].*

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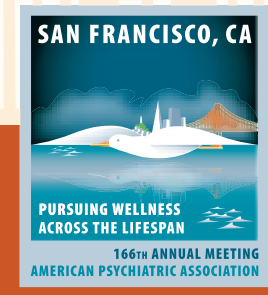

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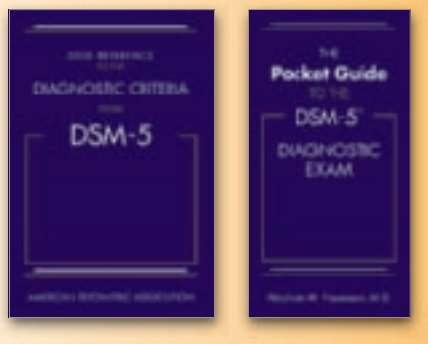

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COMMUNITY NEWS

Volunteer Clinicians Ensure That Uninsured Get Needed MH Care

A pro-bono mental health program is seeking psychiatrists to volunteer their clinical expertise to help uninsured New Yorkers seeking mental health services.

BY EVE BENDER

An innovative, nonprofit program based in New York City has created a unique opportunity for psychiatrists to collaborate in an effort to provide free mental health services to those who are in need of help but do not have access to these services due to financial hardship.

MilestonesNYC operates on a private-practice model and hinges on the psychiatrists, psychologists, and social workers who donate their time and clinical services to treat patients in their own offices at no cost.

Psychiatrist Scott Shapiro, M.D., who launched the program in 2009, told *Psychiatric News* that during his time in medical school and residency, he realized how many people lacked access to basic mental health care. "Many people I treated needlessly suffered unwanted pregnancies, job losses, or contracted HIV, perhaps related to untreated mental illnesses such as bipolar disorder, depression, and posttraumatic stress disorder," he said. Thus, providing people with access to mental health care would vastly improve the lives of individuals and families and go a long way toward preventing such social problems, he reasoned.

Shapiro is an assistant clinical professor of psychiatry and medicine at New York Medical College and has a private practice in Manhattan. He previously served as director of HIV psychiatry at St. Vincent's Hospital and Mount Sinai Hospital.

Here's how the program works: When those who need mental health services reach out to MilestonesNYC, local graduate students volunteering as senior care coordinators assess callers for program eligibility. If eligibility requirements are met, the care coordinators match them with one of the provider volunteers based on specialty and location. If eligibility is not met, care coordinators refer callers to appropriate agencies or hospitals in the New York area.

To be eligible to receive services through MilestonesNYC, potential clients must earn no more than $44,000 annually, be uninsured or underinsured, and must not be in crisis or have chronic mental health issues that may require immediate hospitalization or specialized treatment.

"While we wish we could serve everyone, we do not have the resources to be able to do so," Shapiro said. Most of the patients benefitting from the pro-bono services are struggling with symptoms of mood or anxiety disorders, he noted, and may have had problems obtaining or keeping jobs due to untreated symptoms.

The program fills a gap not covered by local free mental health clinics, which are established to serve indigent patients with severe and persistent mental illness.

Scott Shapiro, M.D., realized as a medical student and resident the extent to which people from "all walks of life" lacked access to mental health services.

Before launching MilestonesNYC, Shapiro said he researched the structure and operations of similar programs, such as Give an Hour, a Washington, D.C.-based organization offering free mental health services to U.S. military personnel and their families, and the Pro Bono Counseling Project, a nonprofit mental health referral network based in Baltimore serving low-income and uninsured families. After consulting with the heads of those programs, Shapiro obtained 501(c)3 legal status and then launched a pilot version of the program and successfully matched eight patients with providers offering pro-bono services.

MilestonesNYC also has a psychoeducation component—some providers may not be able to donate their clinical services, but can instead volunteer by presenting workshops in the community on a variety of mental health topics. For instance, Shapiro presented a workshop on cognitive-behavioral therapy at a church in Brooklyn to an audience of more than 50 community members. Another volunteer gave a lecture on stress management, according to Shapiro.

Clients can see MilestonesNYC providers for up to a year and are then referred to a clinician in the community if they need continuing services, or they may stay with the provider if the provider so chooses, Shapiro said.

He sees numerous benefits deriving from participation in the MilestonesNYC network. "This is a convenient way to give back to the community without ever having to leave the office," he noted. He also sees the experience as an opportunity to broaden one's scope of practice in terms of the diversity of patients.

"MilestonesNYC enabled me to use my expertise in addiction treatment to give back to New York City," Mark Edison, Ph.D., told *Psychiatric News*. He noted that he didn't have to travel to see patients, which helped in terms of convenience and scheduling.

MilestonesNYC also accepts donations and maintains an annual budget of approximately $50,000 to $75,000, which supports marketing materials, provider recruitment strategies, and outreach to potential recipients of its free services. "The return on the investment is projected at $15 for every $1 donated," Shapiro said, "meaning that a donation of $1,000 would provide $15,000 worth of care," due to the fact that overhead is greatly reduced by providers using their own offices to see clients. PN

More information about MilestonesNYC is posted at www.milestonesnyc.org. A donation may be made by sending a check made out to MilestonesNYC to MilestonesNYC, 286 Fifth Avenue, Suite 10H, New York, N.Y. 10001.

Residents' Forum

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dynamics at play. They can, for example, use role playing to help teach trainees on the C-L service the art of diplomacy in dealing with other physicians while being respectful and assertive. The supervisor can help reframe potentially negative interactions as learning exercises that can help foster competency in professionalism, conflict resolution, collaborative care, and teaching.

Assessing safety issues and the patient's risk of harm to self or others can be complicated for trainees. The space needs to be created for them to discuss concerns openly with supervisors, especially when they feel conflicted about decisions affecting patient care. Supervisors should carve out weekly time for trainees to be able to process their own thoughts, feelings, and emotions about the C-L clinical experience.

Trainees should also learn how to advocate for patients and become a source of support, education, and understanding. Embracing a patient's autonomy also includes eliciting his or her own wishes, values, morals, and spiritual or religious beliefs. Some of the decisions our patients choose to make can be strikingly at odds with our own feelings about what is best for the patient. Our goal should be to move away from any type of conversation with the patient that appears paternalistic or authoritarian. In some cases, trainees should encourage patients to bring in their spouses, partners, and other loved ones for family sessions, especially when there is conflict within the family stemming from patient choices and/or the symptoms of mental illness. Families can also be an important resource for a psychiatrist who is trying to establish the baseline cognitive status of a patient.

A wonderful book that we recommend for both trainees and practicing psychiatrists is *Manual of Psychiatric Care for the Medically Ill* by Antoinette Ambrosino Wyszynski and Bernard Wyszynski, which is available from American Psychiatric Publishing (http://www.appi.org/SearchCenter/Pages/SearchDetail.aspx?ItemId=62118).

Finally, supervisors should emphasize the importance of good self-care with practices such as mindfulness. We have found that introducing trainees to basic mindfulness exercises can provide the catalyst for more meaningful engagement and therapeutic communication with other health care providers and patients. PN

Training

continued from page 11

ity to take appropriate action in linking children and adolescents to the services they need."

Such an initiative would pave the way, Scully said, for highly successful and evidence-based training initiatives, such as the American Psychiatric Foundation's "Typical or Troubled?" school program.

The bill has been referred to the Senate Committee on Health, Education, Labor, and Pensions. PN

The text of S.648, the Helping Educators Support All Students Act is posted at http://beta.congress.gov/bill/113th-congress/senate-bill/648/text. APA's letter to Klobuchar is posted at http://www.psychnews.org/pdfs/Senator_Klobuchar_letter.pdf.

ANNUAL MEETING

Addiction-Related Issues to Be Focus Of Special NIDA Track

An extensive update on prescription opioid abuse and treatment options will be featured in NIDA's track of symposia at the APA annual meeting.

BY LESLIE SINCLAIR

The National Institute on Drug Abuse (NIDA) will present a five-day track of symposia addressing the latest clinical and research knowledge in addiction psychiatry at the APA annual meeting in San Francisco.

It will begin Saturday, May 18, when Petra Jacobs, M.D., an associate director for program development, and Udi Ghitza, Ph.D., a health scientist administrator, both of NIDA's Center for Clinical Trials Network, will chair the session "Smoking Cessation in Patients With Severe Mental Illness: New Research Findings and Clinical Implications." This symposium will feature recent findings on safety and efficacy of varenicline in patients with severe mental illness, as well as the impact of concurrent smoking-cessation and stimulant-dependence treatment on outcomes. New technologies used for delivery of smoking-cessation interventions will also be discussed.

On Sunday May 19, Yu Lin, M.D., Ph.D., a program director of NIDA's Division of Clinical Neuroscience and Behavior Research, and Scott Kollins, Ph.D., an associate professor of psychiatry at Duke University Medical Center, will co-chair "Smoking and ADHD Comorbidity: Mechanisms and Clinical Implications." Presenters will describe the association between a diagnosis of attention-deficit/hyperactivity disorder (ADHD) and risk for cigarette smoking, identify mechanisms that underlie the link between ADHD and smoking, and discuss evidence-based treatments for patients with comorbid ADHD and nicotine dependence.

The track continues on Monday, May 20, when Wilson Compton, M.D., M.P.E., director of the Division of Epidemiology, Services, and Prevention Research at NIDA, and Meyer Glantz, Ph.D., an associate director for science in that division, will co-chair a session titled "Comorbid Psychiatric and Substance Use Disorders: Common and Specific Influences and Implications for Early Identification and Treatment." They will discuss the impact of psychiatric disorders on development of substance use disorders and discuss how to apply behavioral genetics research findings to the diagnosis and treatment of comorbid psychopathologies and substance use disorders.

NIDA

NIDA Director Nora Volkow, M.D., will present an APA Frontiers of Science Lecture at the annual meeting.

A second symposium on Monday, May 20, "Advances in Pharmacotherapies for Substance Use Disorders," will be co-chaired by Phil Skolnick, Ph.D., director of the Division of Pharmacotherapies and Medical Consequences of Drug Abuse, and Ivan Montoya, M.D., M.P.H., a deputy director in that division. They will discuss medications and biologic therapeutics recently evaluated in clinical trials for substance use disorders, including depot naltrexone, implantable buprenorphine, and an engineered butyrylcholinesterase.

The addiction psychiatry track will continue on Tuesday, May 21, with "Cannabis Use and Youth: Updates on Risk, Assessment, and Treatment,"

*see **NIDA Track** on facing page*

ANNUAL MEETING

Nobel Prize Winners To Lecture at Meeting

Three Nobel laureates will talk about their groundbreaking research and what their discoveries could mean for the future of psychiatric treatment.

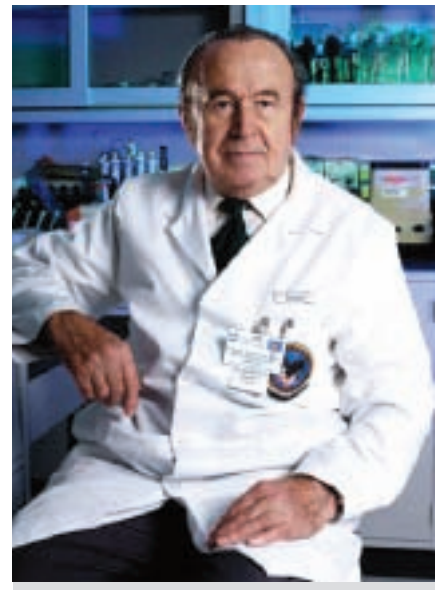
Among the many accomplished researchers who will be delivering lectures at next month's APA annual meeting in San Francisco are three Nobel Prize laureates, all of whom were honored in the category Physiology or Medicine.

Elizabeth Blackburn, Ph.D., won a 2009 Nobel Prize for her discoveries in telomere biology that have solved many of the mysteries surrounding normal cell functioning. She is the Morris Herzstein Endowed Chair in Biology and Physiology in the Department of Biochemistry and Biophysics at the University of California, San Francisco (UCSF). The Nobel is only one of the multiple prestigious awards Blackburn has won—in 2006 she was presented with the Albert Lasker Award for Basic Medical Research, and the following year *Time* magazine named her one of the 100 most influential people in the world.

On Monday, May 20, Blackburn will discuss "Telomeres and Telomerase: Their Relation to Stress and Human Disease."

Elizabeth Blackburn, Ph.D.

Stanley Prusiner, M.D.



Andrew Schally, Ph.D., M.D.H.C.

Another UCSF faculty member and Nobel Prize winner on the annual meeting program is Stanley Prusiner, M.D., who won the award in 1997. In addition to being a professor of neurology, he heads the UCSF Institute for Neurodegenerative Diseases. Among his contributions is discovering a class of pathogens called prions. These infectious proteins cause degenerative diseases in humans and animals. He is currently involved in research to develop a drug that he hopes will retard neurodegeneration in Alzheimer's, Parkinson's, and prion diseases as well as in frontotemporal dementias. Prusiner, who in 2009 won the National Medal of Science, will lecture on "Prion Biology: New Interface Between Psychiatry and Neurology" on Sunday, May 19.

Andrew Schally, Ph.D., M.D.H.C., is another Nobel laureate who will lecture at the annual meeting. He is the Distinguished Leonard M. Miller Professor of Pathology at the University of Miami Miller School of Medicine and Director of the Endocrine, Polypeptide, and Cancer Institute. Schally's talk, which will be on Sunday, May 19, is titled "Beneficial Effects of Novel Antagonists of GHRH in Different Models of Alzheimer's Disease." Schally, an expert in hypothalamic hormones, has written or cowritten more than 2,300 scientific publications on endocrinology and oncology. He has pioneered treatments for various types of cancer and other diseases and spends considerable time in Miami and abroad helping clinicians implement these treatments. PN

NIDA Track

continued from facing page

co-chaired by Geetha Subramaniam, M.D., a team leader of the Behavior and Social Science Team of NIDA's Center for Clinical Trials Network, and Kevin Gray, M.D., an associate professor of psychiatry at the Medical University of South Carolina. Topics will include the neurocognitive effects of cannabis use on youth, as well as interventions and pharmacological treatments for youth who abuse cannabis.

Also on Tuesday, NIDA Director Nora Volkow, M.D., will present "Substance Use Disorders: New Scientific Findings and Therapeutic Opportunities," part of the APA Frontiers of Science Lecture Series.

Wrapping up the track on Wednesday, May 22, Richard Denisco, M.D., M.P.H., a medical officer in NIDA's Services Research Branch, and Will Aklin, Ph.D., a program official in NIDA's Behavioral and Integrative Treatment Branch, will co-chair "Update on Prescription Opioid Abuse and Treatment Options for the Psychiatrist," which will focus on epidemiological trends in prescription drug abuse, as well as diagnostic and treatment options for patients with chronic pain and co-occurring psychiatric disorders including addiction.

Meeting goers will once again have the opportunity to view NIDA's popular Addiction Performance Project, which will be held Sunday, May 19. It is part of NIDA's outreach to practicing health professionals and trainees and consists of a dramatic reading of Act III of Eugene O'Neill's "Long Day's Journey Into Night," followed by an expert panel presentation and audience discussion on caring for drug-addicted patients. The part of Mary Tyrone will be played by Kate Burton, whose television credits include Dr. Ellis Grey on "Grey's Anatomy" and Vice President Sally Langston on "Scandal." (The actor playing James Tyrone has not yet been announced.) The project was developed and produced by Outside the Wire (www.outsidethewirellc.com), which uses theater and other media to address pressing public health issues. Registration for the annual meeting is required to attend this event. Students may attend for free. PN

From the President

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fronto-parietal networks of internalized attention, while meditation techniques that focus on breathing may elicit additional activation of paralimbic regions of insula and anterior cingulate, and meditation techniques that focus on emotions may elicit fronto-limbic activation. Future studies can help disentangle the brain-activation patterns related to different meditation traditions.

Given the noninvasive nature of mindful exercise and meditation, these exercises may be recommended to patients with psychiatric disorders that have been studied in randomized, controlled trials. Significant evidence supports the assertion that Tai Chi, Qi Gong, yoga, and meditation can improve health-related quality of life and mental health. However, ethical considerations should be taken into account when recommending spiritual interventions to respect individual patients' religious or other personal beliefs in choosing mind-body interventions. PN

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Additional annual meeting information can be accessed at http://annualmeeting.psychiatry.org/.

Medicaid

continued from page 1

Regional Medical Center-Kennett.

Following are major findings of the report:

- Under the ACA, Missouri hospitals will lose about $250 million in federal reimbursements for the charity care they provide, regardless of whether the state extends eligibility.

- The hospitals included in this study will lose between $1.0 million and $10.6 million in federal indigent care reimbursements annually under the DSH reduction, depending on the hospital's size. Since 24 percent to 58 percent of charity care that these hospitals provide annually occurs on their inpatient psychiatric units, the hospitals will be forced to cut adult acute psychiatric beds as the DSH cuts take effect.

- If community hospital psychiatric beds close, there will be increasing pressure on elected officials to open state acute psychiatric beds. The operating costs for state-operated acute beds would average approximately $850 a day, or about $31 million a year for every 100 beds, not including capital costs.

In an interview with *Psychiatric News*, Parks noted that there will be downstream effects on patients in the community. He said individuals who are seriously mentally ill and in crisis are often involuntarily committed to acute inpatient care for diagnosis and treatment by Missouri's courts.

"The additional loss of acute psychiatric beds will create even greater problems for county sheriffs and city law-enforcement departments that must transport these patients, often for long distances, in search of a psychiatric inpatient bed," he said. "Local law-enforcement officers already stay at the hospital emergency rooms and inpatient units for many hours as these patients are admitted to care. This situation will worsen."

Parks said states that rely heavily on DSH payments will be the most dramatically affected next year if they do not expand their Medicaid rolls to cover the uninsured. The DSH payment reduction will begin next year regardless of a state's decision regarding expansion; in the first years of expansion a state would receive full federal matching funds but be liable for 10 percent of costs by 2020. While a dollar-for-dollar comparison is difficult, in most instances the net effect of expansion would be an increase in funding, while in states that have relied very heavily on DSH payments, the effect of not expanding could be devastating.

Irvin "Sam" Muszynski, J.D., director of APA's Department of Healthcare Systems and Financing, said his analysis of the ACA confirms that the effects Parks has found in Missouri could be felt nationwide in states that opt not to expand Medicaid rolls.

Howard Goldman, M.D., editor of the APA journal *Psychiatric Services* and an expert on mental health parity and Medicaid policy, concurred. "The loss of DSH payments for uninsured patients creates a strong incentive for states to elect to participate in the Medicaid expansion under the ACA," Goldman told *Psychiatric News*. "Failing to expand Medicaid, however, will make it difficult to reduce the reliance on state psychiatric hospitals for uninsured individuals. In many states, uninsured patients will not be admitted to general hospitals and will continue to be admitted to state-operated facilities. States will have to pay for the care with state dollars without the federal participation for Medicaid and without the cost-offset from federal DSH payments for individuals who have no insurance at all."

Joel Miller, senior director of policy and health care reform for the National Association of State Mental Health Program Directors (NASMHPD), went further, saying the reduction in DSH payments along with other factors affecting mental health funding—such as sequestration and the continuing exclusion from Medicaid payment of Institutions of Mental Disorders—could create a "perfect storm" of a crisis in public mental health.

"We believe it's going to be the worst of all worlds if several states that rely heavily on DSH payments choose not to participate in the Medicaid expansion," Miller told *Psychiatric News*. "States that do not opt into the expansion are really going to be caught in a very tight payment vise as they try to provide care to the uninsured with psychiatric conditions because they are going to be getting little or no compensation from federal agencies."

Miller said the effects will not be confined to inpatient psychiatric beds because many states also use the DSH payments to shore up resources for residential and outpatient services. He said NASMHPD has been alerting policymakers at the federal and state levels to pay attention to what may have major public health consequences.

Parks agreed. "I think we should make sure that the legislators making decisions about Medicaid expansion are fully informed about this potential disaster for access to psychiatric inpatient care and emergency rooms," he told *Psychiatric News*. "I have not seen this particular issue discussed in the individual state dialogues around whether or not to expand Medicaid, but it certainly needs serious consideration." PN

Key Points

- Beginning next year when the option to expand Medicaid rolls to 133 percent of the federal poverty level becomes available under the ACA, federal Disproportionate Share Hospital (DSH) payments will be reduced.
- States that opt not to expand Medicaid rolls will still be burdened with care of the uninsured, but with substantially less DSH funding support.
- Lower DSH payments could result in closure of psychiatric beds, as well as effects on residential and outpatient services.

Bottom Line: Diminished DSH payments could dramatically affect state mental health budgets, and states that rely heavily on DSH payments should weigh this consideration when deciding whether to expand Medicaid rolls.

Fetus

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cognition, and achievement, said Behnke and Smith.

"The most significant effect of prenatal opiate exposure is neonatal abstinence syndrome," they noted. Behavior is affected, but there is either no consensus or a lack of data regarding cognition, language development, and academic achievement.

Cocaine has long-term effects on behavior and possibly language, as well as on fetal growth and infant neurobehavior.

"Studies of prenatal methamphetamine exposure are still in their infancy," Behnke and Smith pointed out. Some effects have been noted on fetal growth and infant neurobehavior, but evidence is insufficient regarding most other outcomes.

Behnke said that a full spectrum of medical professionals must intervene when needed to lessen the risk to the fetus and the developing child.

"Whether we are ob/gyns, pediatricians, or psychiatrists, we as physicians have the opportunity to interact with patients at various points along the lifespan," she said. "We should be in the business of trying to diagnose people and refer them to treatment. We may not have all the information yet, but we should state what we know and what we don't know and develop therapies and places to refer our patients." PN

"Prenatal Substance Abuse: Short and Long-Term Effects on the Exposed Fetus" is posted at http://pediatrics.aappublications.org/content/131/3/e1009.long.

Self-Exam

continued from page 5

of hallucinogen use?

a) Withdrawal
b) Tolerance
c) Desire or efforts to cut down or stop use
d) Use in situations in which it is physically hazardous
e) Craving or a strong desire or urge to use the drug

3. Which of the following is the only non-substance-related addictive disorder to be included in the *DSM-5* chapter on addictive disorders?

a) Gambling disorder
b) Internet gaming disorder
c) Electronic communication addiction disorder
d) Compulsive computer gaming
e) Compulsive shopping

4. All of the substances listed in *DSM-5* are associated with a substance use disorder with the exception of one class. Which substance or class of substances is not associated with a substance use disorder diagnosis in the "Substance Related and Addictive Disorders" section of *DSM-5*?

a) Caffeine
b) Hallucinogens
c) Inhalants
d) Stimulants
e) Tobacco PN

Viewpoints

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stating it is "unethical for psychiatrists to offer a professional opinion," which is indeed so broad as to be chilling. This will permit informed discussion of issues arising from specific cases without offering a diagnosis.

The loosening of this prohibition would enable APA members to step forward to inject science and experience into the debate and counter the demonization of our patients. This requires not just testifying before commissions and publishing in the print media. It requires a more vigorous and proactive public-relations effort and a presence on the Sunday talk shows and electronic media so that the spokesmen for extremism are never again given a solo platform. PN

Catherine May, M.D., is chair of the Ethics Committee of the Washington Psychiatric Society and an associate clinical professor of psychiatry at George Washington University (GW) School of Medicine. Jerrold Post, M.D., is a professor of psychiatry, political psychology, and international affairs at GW.

ADHD

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in general.

- Substance abuse rates did not differ between children who were still being treated with ADHD medication and those who were not. Cumulative stimulant treatment also had no effect on rates.

"This study underscores the significance of the substance abuse risk for both boys and girls with childhood ADHD," said Molina, in a statement coinciding with the study's publication. "These findings also are the strongest test to date of the association between medication for ADHD and teenage substance abuse."

The authors noted in particular the finding that substance abuse rates were the same in teens still taking ADHD medication and those no longer doing so and said that their findings point to a need to identify alternative approaches to substance abuse prevention and treatment for youth with ADHD.

"We are working hard to understand the reasons why children with ADHD have increased risk of drug abuse. Our hypotheses, partly supported by our research and that of others, is that impulsive decision making, poor school performance, and difficulty making healthy friendships all contribute," Molina said.

"Some of this is biologically driven, because we know that ADHD runs in families. However, similar to managing high blood pressure or obesity, there are nonmedical things we can do to decrease the risk of a bad outcome. As researchers and practitioners, we need to do a better job of helping parents and schools address these risk factors that are so common for children with ADHD."

In an editorial accompanying the study, Benjamin Goldstein, M.D., Ph.D., an assistant professor in the departments of psychiatry, pharmacology, and toxicology at the University of Toronto and director of the Youth Bipolar Disorder Program at Sunnybrook Health Sciences Center in Toronto, agreed that this new information is useful, if not definitive. "Based on the extant literature—bolstered by the current study—it would be inaccurate to characterize stimulants as a globally effective inoculation against substance misuse," he said. "Nonetheless, it remains likely that there is a subset of youth for whom ongoing stimulant treatment may prevent the academic impairment, peer difficulties, family conflict, and impulsive decisions that plant the seeds of substance misuse."

Commenting on the study for *Psychiatric News*, child and adolescent psychiatrist David Fassler, M.D., a clinical professor of psychiatry at the University of Vermont and treasurer of APA, said, "Consistent with previous findings, the authors report that ADHD was associated with an increased risk of substance use and substance use disorders in this age group; however, the prevalence was neither increased nor decreased as a result of treatment with medication. This result challenges the widely held belief that early and appropriate treatment of ADHD will reduce the risk of substance use during adolescence. As the authors noted, the finding underscores the importance of identifying effective approaches to the prevention and treatment of substance use disorders in adolescents with ADHD."

This research was supported by the National Institute of Mental Health and National Institute on Drug Abuse. PN

An abstract of "Adolescent Substance Use in the Multimodal Treatment Study of Attention-Deficit/Hyperactivity Disorder (ADHD) (MTA) as a Function of Childhood ADHD, Random Assignment to Childhood Treatments, and Subsequent Medication" is posted at http://www.jaacap.com/article/S0890-8567(12)01000-3/abstract.

Match

continued from page 1

residency positions, while also reserving some to be filled outside the match. In short, programs could decide which positions were "in" the match and which were "out."

So with the "all in" policy there were more slots offered in the match: in psychiatry, 1,360 positions were offered (compared with 1,118 in 2012). And of the 1,360 slots, 1,330 were filled. Positions not filled by U.S. graduates were filled by international medical graduates (including U.S. and non-U.S. citizens), Canadian students, graduates of osteopathic schools, and students who graduated from medical school in previous years.

Sidney Weissman, M.D., a former APA Trustee and president of the American Association of Directors of Psychiatric Residency Training, noted that the inclusion of all available slots in the Match does not necessarily reflect an actual increase in residency opportunities. Meanwhile, there has been an increase in U.S. seniors from 16,527 in 2012 to 17,856 in 2013.

Weissman noted that this has greatly increased competition for certain specialties without a corresponding increase in residency slots. So some students with high class standing who only ranked those highly competitive specialties may not have found positions through the match.

And he also said it's possible that some of the increase in U.S. graduates entering psychiatry is due to individuals choosing the field over more competitive specialties.

Weissman said that more than a 1,000 seniors did not find residency positions this year through the match. They then were able to compete for one of the 1,041 unfilled match positions, which are offered through the NRMP Supplemental Offer and Acceptance Program (SOAP). During SOAP, the NRMP makes available the locations of unfilled positions so that unmatched applicants can apply for them.

Weissman said reports indicate that after SOAP, some 500 U.S. seniors still did not have a position. He called attention to the reality that many of these students were more than $100,000 in debt.

The Association of American Medical Colleges (AAMC) has expressed concern about the reports of large numbers of unmatched graduates. Psychiatrist Darrell Kirch, M.D., president and CEO of the AAMC, said in a statement that the situation highlights the need for increased federal support of residency positions.

Kirch noted that there is a projected shortage of more than 90,000 doctors by 2020. "To avert the coming shortage, we need to begin today to increase the overall supply of physicians in this country by lifting the cap on residency training positions imposed in 1997 by the Balanced Budget Act," he said. "Inaction will only mean extensive shortages of both primary care physicians and a wide range of specialists."

AMA President Jeremy Lazarus, M.D., also cited the impending physician shortage and said that in light of the reports of graduates being unable to find residency training positions, the AMA had worked with Sens. Bill Nelson, Charles Schumer, and Harry Reid and Reps. Aaron Schock and Allyson Schwartz to introduce legislation to create additional positions.

"In keeping with the AMA's historic leadership in physician education at all levels, we are also working to strategically reshape physician education in the United States to meet current and future workforce needs," Lazarus said in a statement.

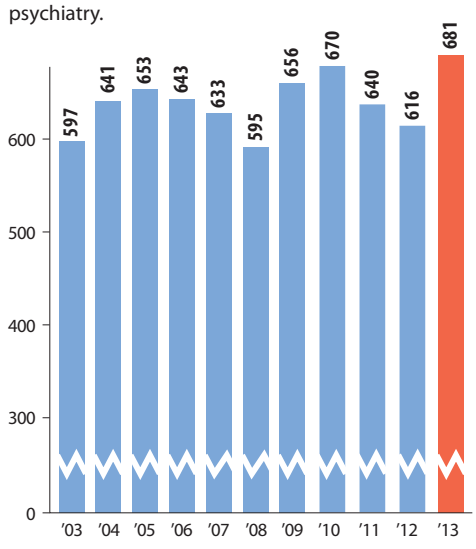
Weissman told *Psychiatric News* that while new factors may be affecting recruitment into psychiatry, this year's numbers offer reason to be hopeful about the appeal of psychiatry to medical school graduates.

"We've seen a stabilization of interest in psychiatry," he said. "With the naturally occurring fluctuations from year to year, we will continue to have to focus on varied recruitment strategies. We can use the implementation of the Affordable Care Act to demonstrate psychiatry's unique role in health care." PN

More information about the 2013 match is posted at http://www.nrmp.org/. Information about the new "all in" policy is posted at http://www.nrmp.org/allinpolicyexception.pdf.

More U.S. Grads Matching Into Psychiatry

The number of medical students entering psychiatry residencies this year increased substantially over last year. Increasing numbers of graduates and a new "all in" policy has increased competition for highly sought specialties—which may have benefitted psychiatry.



Source: National Resident Matching Program, 2013

Forced Treatment

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hospital.

Several cases in recent decades have delineated when and how patients can be held or forcibly treated, said Scott.

Washington v. Harper in 1990 found that inmates with a serious mental illness who refused treatment could be medicated against their will if they were deemed dangerous to self or others, provided that the state adhered to proper procedural due process. Under *Harper*, that includes a hearing board that includes a psychiatrist.

Time is important, too, said Scott. In 1992's *Jackson v. Indiana*, a developmentally disabled deaf-mute young man who stole $9 was committed to a state hospital until his competency to stand trial was restored. The U.S. Supreme Court found that Jackson's competency could *never* be restored and that his confinement amounted to a life sentence without a conviction. A patient could be held only for a "reasonable period of time" and only as long restoration was likely, said the Court.

Finally, in *Sell v. United States* in 2003, the Court enumerated the standards for involuntary administration of medication to criminal defendants to render them competent to stand trial.

These "Sell criteria" include a serious criminal act, the likelihood that competency will be restored without serious side effects, that medication is the best way to restore competency, that it is medically appropriate, and that alternate grounds for medicating (like dangerousness) be considered first, said Zonana.

In criminal law, competency is a defendant's ability to understand the proceedings in court and assist in his or her defense, Zonana noted. "But the need for competency goes beyond the necessity for a fair trial," he said. "Competency is also needed for the dignity of the criminal justice process, for accuracy and reliability in adjudication, and for the autonomy of the defendant, who has a right to decide matters about his case that can't be taken away from him."

Competency Rulings May Not Clarify Issue

However, court rulings on competency have proven hard to interpret, he said. "Courts want to hear conclusory opinions about a defendant's competency, not just a delineation of capacities."

Worse yet are policies that keep people in custody for indeterminate lengths of time while awaiting competency restoration. A defendant restored to competency will be sent back to jail to await trial, but if he stops his medications and symptoms return, he will be transferred back to the hospital for restoration, and the cycle continues.

The case of Jared Loughner, the gunman in the Tucson, Ariz., shooting in which he killed six people and wounded 11 others, including then-Rep. Gabrielle Giffords, is an example of how complex such cases can be, said Zonana.

Loughner was sent to a hospital to "see if he could be restored to competency." Because he had not yet been tried and was thus presumed innocent, he was entitled to greater constitutional protections than a convicted prisoner.

"But how is it possible to tell if someone responds to treatment if we don't administer medications?" asked Zonana. However, since Loughner's condition deteriorated when not taking medications, he was forcibly medicated on an emergency basis because he became violent.

Ultimately, in August 2012, Loughner was declared competent and pleaded guilty without entering an insanity plea, concluding the case, said Zonana.

Existing case law will increasingly come into play as more patients are committed involuntarily, said Scott. "You need to know your state's law relating to medication refusal for each legal classification," he said. "And always document dangerousness with the *Harper* and *Sell* cases in mind."

Scott concluded by reminding his listeners about the significance of their work in forensic psychiatry.

"You are dealing with legitimate individuals struggling with mental illness that sometimes impairs their insight," he said. "You're trying to move forward; you know there are a lot of people who are trying to get better." PN

Information about St. Elizabeths Hospital is posted at http://dmh.dc.gov/page/saint-elizabeths-hospital.

Director of Emergency Psychiatry

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Horizon Health seeks a Psychiatrist for our 10-bed Senior Adult, and 10-bed Adult, inpatient Behavioral Health programs our client hospital **St. Claire Regional Medical Center in Morehead, KY.** Experience with geriatric population preferred. Excellent salary, benefits and practice opportunity. For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com. EOE.

LOUISIANA

Tulane University Health Sciences Center (TUHSC) is recruiting an adult clinical psychologist and a child clinical psychologist to serve as inpatient attendings at Northlake Behavioral Health Systems. We are seeking candidates with experience in working with adults and children with severe mental illnesses in both inpatient and outpatient treatment settings. The persons selected for these positions must be professionally competent in clinical psychology and must be eligible for psychology licensure in the State of Louisiana. In addition, candidates must be eligible for clinical privileges at Tulane University Hospital and Clinic under the appropriate staff category and must agree to abide by those privileges as outlined by the current bylaws of the institution. The Department of Psychiatry and Behavioral Sciences has an active APA Accredited clinical psychology internship. Involvement in the teaching and supervision of interns and psychiatry residents is an integral part of these faculty positions. These are full-time faculty positions – rank and salary is commensurate with experience. A competitive benefits package is included. We will continue to accept applications until suitable qualified candidates are found. All qualified candidates who are interested in these positions should forward a copy of their updated curriculum vitae and the names and complete contact information of five references to Paula Zeanah, PhD, Director of the Division of Clinical Psychology, Tulane University School of Medicine, Department of Psychiatry and Behavioral Sciences TB52, 1440 Canal Street, New Orleans, LA 70112 or pzeanah@tulane.edu. Tulane is strongly committed to policies of non-discrimination and affirmative action in student admission and in employment.

The Department of Psychiatry and Behavioral Sciences at Tulane University School of Medicine is recruiting for a Training Program Director in Child and Adolescent Psychiatry, including the Tulane University Triple Board Training Program. This is a full-time faculty position with half-time devoted to the residency training program and half-time to other academic pursuits. An associate director is available to assist with program leadership and administration. The person selected for this position must be professionally competent and be board eligible/certified in general and child and adolescent psychiatry. She/he must be eligible for medical licensure in the State of Louisiana and have a current state and federal narcotics number. In addition, candidates must be eligible for clinical privileges at Tulane University Hospital and Clinic under the appropriate staff category and must agree to abide by those privileges as outlined by the current bylaws of the institution. This is a fully accredited child psychiatry program for 6 child and adolescent psychiatry residents and an additional 10 triple board residents. Salary will be competitive and commensurate with the level of the candidate's academic appointment. We will continue to accept applications for this position until a suitable qualified candidate is identified. Qualified applicants should send an email of interest, updated CV and list of references to Charles H. Zeanah MD, Sellars Polchow Professor and Vice Chair for Child and Adolescent Psychiatry, at czeanah@tulane.edu or a letter to the Section of Child and Adolescent Psychiatry, Tulane University School of Medicine, 1430 Tulane Avenue #8055, New Orleans LA 70112. Tulane is strongly committed to policies of non-discrimination and affirmative action in student admissions and in employment.

DEPARTMENT OF PSYCHIATRY AND BEHAVIORAL SCIENCES, TULANE UNIVERSITY SCHOOL OF MEDICINE in New Orleans, LA, is recruiting for several general and forensic psychiatrists (clinical track) for our growing department, at the Assistant/Associate Professor level, salary commensurate with experience. Candidates must have completed an approved general psychiatry residency and be board certified/eligible in general psychiatry and forensic psychiatry, respectively. Responsibilities will include direct patient care, teaching of medical students and house officers, and research (clinical and basic science) at various state hospitals, state correctional institutions, the Southeast Louisiana Veterans Health Care System (Biloxi, MS) and at Tulane University Health Sciences Center. Time allocations will be based upon individual situations. Applicants must be eligible to obtain a Louisiana medical license. In addition, candidates must be eligible for clinical privileges at Tulane University Hospital and Clinic under the appropriate staff category and must agree to abide by those privileges as outlined by the current bylaws of the institution. Applications will be accepted until suitable qualified candidates are found. Email (winstead@tulane.edu) or send CV and list of references to Daniel K. Winstead, MD, Heath Professor and Chair, Department of Psychiatry and Behavioral Sciences, Tulane University School of Medicine, 1440 Canal Street TB48, New Orleans, LA 70112. For further information, you may contact Dr. Winstead, at 504-988-5246 or winstead@tulane.edu. Tulane is strongly committed to policies of non-discrimination and affirmative action in student admission and in employment.

MAINE

Dorothea Dix Psychiatric Center in Bangor, Maine seeks to fill immediate opening for a full time Board eligible/board certified Psychiatrist. On call duties are minimal. For more information on salary/benefits, call Dr. Michelle Gardner@207-941-4038. DDPC is a free-standing, publicly funded psychiatric hospital in Bangor, Maine just miles from the beautiful Downeast coast.

EEO/AAE

MARYLAND

BOARD CERTIFIED
CLINICAL DIRECTOR
ASSOCIATE CLINICAL DIRECTOR
FORENSIC PSYCHIATRIST
STAFF PSYCHIATRIST

Spring Grove Hospital Center, a progressive, publicly funded, freestanding psychiatric hospital is currently seeking to hire several full-time board certified Psychiatrists. Spring Grove Hospital Center is a 388 bed complex that provides a broad spectrum of inpatient psychiatric services to adults and adolescents. The center is owned and operated by the State of Maryland and is under the governance of the Mental Hygiene Administration of the Department of Health and Mental Hygiene. Spring Grove was founded in 1797 and is the second oldest continuously operating psychiatric hospital in the United States, fully accredited and certified. We have an ongoing commitment to providing psychiatric care and treatment of the highest quality. We also maintain a number of student teaching programs and serve as a popular training site for many professional schools including the University of Maryland. We are located on a scenic 200 acre campus in Catonsville just outside of Baltimore, Maryland and conveniently located along the I-95 corridor between Baltimore and Washington, D.C. We offer competitive salary and excellent State of Maryland benefits, including generous vacation and retirement packages. For further clarification of job duties of the position, contact Dr. Krishnan and provide a curriculum vitae (CV), license, and board certification. Interested candidates also need to complete an electronic State application (MS-100) downloaded at www.dbm.maryland.gov) for Physician Clinical Specialist and include a valid State of Maryland license and board certification.

Devika Krishnan, M.D.
Clinical Director
Spring Grove Hospital Center
55 Wade Avenue
Catonsville, Maryland 21228
410-402-7595
410-402-7038 (fax)
EOE

CLASSIFIEDS

PSYCHIATRIST/MEDICAL DIRECTOR

BE/BC Child/Adolescent Psychiatrist/Medical Director needed 20-40 hours a week for outpatient community mental health facility on Maryland's scenic Eastern Shore, one hour, 15 minutes from Baltimore-Washington area. The clinic is located in a Professional Shortage Area, is a National Health Service Corps site and is eligible for loan repayment. Send resume/vitae with cover letter to Michael Campbell. LCSW-C, Director, Caroline Co. Mental Health Clinic, P.O. Box 10 Denton, Md. 21629, phone 410-479-3800, ext. 117, fax 410-479-0052 or e-mail mike.campbell@maryland.gov - EOE.

Springfield Hospital Center is seeking Board-certified or Board-eligible **general psychiatrists** for our 350-bed MHA adult inpatient facility. Salary is negotiable, within MHA guidelines. Our rural, tobacco-free campus is 22 miles west of Baltimore, convenient to the Chesapeake Bay, Washington, and a variety of cultural, historic, sports, and recreational venues. Benefits include 27 paid days off in the first year, subsidized health insurance, free parking, a generous retirement program, and a truly pleasant workplace. A Medical Services physician is always on campus to attend to patients' somatic needs. Staff psychiatrists are not expected to work after hours, but some choose to supplement their salary by providing evening and weekend/holiday coverage under contract. In addition, we offer after-hours coverage contracts to psychiatrists who are not full-time staff members. Please send CV to **Paramjit Agrawal, M.D., Clinical Director, SHC, 6655 Sykesville Road, Sykesville, MD 21784. For questions, call (410)970-7006 or e-mail paramjit.agrawal@dhmh.state.md.us.** EOE

MASSACHUSETTS

Berkshire Health Systems

Psychiatrist Opportunity in the Beautiful Berkshires. Top notch colleagues.

Berkshire Medical Center's Department of Psychiatry and Behavioral Science provides you the opportunity to become part of a stable, highly integrated clinical collaboration among Psychiatry, Primary Care, and Medical Specialty Services. Our Health System has an excellent opportunity for an Adult Psychiatrist to work in a highly integrated clinical collaborative at the interface of Primary Care and Behavioral Health. A clinical background in geriatric psychiatry is preferred. Our psychiatry residency program allows you to contribute to the education of the next generation of mental health specialists. Berkshire Medical Center is nationally recognized by HealthGrades and many other independent organizations for outstanding care.

Please contact Antoinette Lentine in the Physician Recruitment Department at 413-395-7866 or e-mail at mdrecruitment@bhs1.org.

CAPE COD HEALTHCARE
We're taking good care of you.™

Cape Cod Healthcare Out-Patient Psychiatrist Opportunity

Cape Cod Healthcare (www.capecodhealth.org) in Hyannis, MA is looking for a BC/BE psychiatrist. This opportunity allows the applicant to work weekdays-only in an outpatient setting and then enjoy the beaches, recreational activities, and beauty of Cape Cod each weekend. Boston and Providence are both an hour's drive away. Responsibilities include performing new evaluations and monitoring medications at the largest outpatient clinic on Cape Cod. Competitive salary and benefit package. For additional information, email Jolia Georges, Director of Physician Recruitment, jgeorges@capecodhealth.org, or call 508-862-5481.

UMass Memorial Seeks BC/BE Child and Adult Psychiatrists For Our Affiliated Community Mental Health Centers

Both full- and part-time physician leadership and staff physician opportunities are currently available in our community mental health center in Central MA.

Community Healthlink (CHL) is a dynamic, multi-service organization committed to establishing, maintaining and restoring the dignity, well being and overall mental health of individuals and families in Central MA. CHL psychiatrists receive competitive salaries and comprehensive benefits packages. Faculty appointments, commensurate with training and experience, are available as well, as is the opportunity to teach UMass Medical Students, Residents and Fellows.

For additional information about CHL, please visit our website: www.communityhealthlink.org. Interested candidates are encouraged to submit their CVs and letters of interest to: David DeLuca at: psychiatry-recruitment@umassmemorial.org.

Psychiatrist, Concord, Mass. Unique opportunity for board certified/eligible psychiatrist or psychiatric RNCS to join strong psychiatric service at Emerson Hospital. Provide moonlighter coverage between 4 pm Friday and 5 pm Sunday. In-hospital time varies based on number of admissions and consultation requests. Overnight call is home-call only, except for rare emergency visits to the hospital for seclusion/restraint. Continuous back up support provided by full-time psychiatrists who round on existing patients. Compensation is $108K/year without benefits. Position may be split between two qualified applicants who each agree to work two weekends per month. Please contact Robert Stern MD, Chair, department of Psychiatry, 978-287-3512 or rstern@emersonhosp.org.

NORTH SUFFOLK Mental Health Association

Mobilizing Communities Building Careers

North Suffolk Mental Health Association has a common vision for improving the communities we serve. For more than 50 years, we've been helping individuals with mental health, disability, substance abuse, and other daily challenges achieve independence and explore possibilities. A career here is a commitment to opportunity, with a focus on a future of progress and change. Join our dedicated employees to help shape the future of the community we care so deeply for.

The Medical Director is responsible for overall management of all medical matters for the North Suffolk Mental Health Association. Ensures continuous quality Improvement of all medical matters and standards for the Agency. The medical director reports to the Chief Executive Director (CEO) and works closely with the Chief Operating Officer (COO), Director of Compliance and Quality Improvement, all Senior Managers, Department of Mental Health Medical Director and the Massachusetts General Hospital Department of Psychiatry.

Qualified candidates will have a minimum of five years of professional experience, as well as current and valid registration as a physician under the Massachusetts Board of Registration in Medicine. Candidates must be board certified by the American Board of Psychiatry and licensed to practice medicine in the Commonwealth of Massachusetts; five years of clinical experience and prior demonstrated competency in management and administrative roles. Board certification in Psychiatry required. Experience in community mental health and mental retardation is highly desirable.

How to apply: North Suffolk offers a comprehensive benefit package which includes medical/dental insurance, 403(b), FSA, and generous paid time off.Interested candidates should send cover letter and resume to: North Suffolk Mental Health Association, Attn: Recruiter, 301 Broadway, Chelsea, MA 02150; Fax 617-912-7971, Email: gethired@northsuffolk.org.

Equal opportunity employer.

Medical Director – Psychiatrist Palmer, MA

Wing Memorial Behavioral Health Services is seeking a full-time Medical Director. Candidate must be a Board Certified Psychiatrist with leadership experience. Duties are divided as twenty hours of administrative time and twenty hours of outpatient clinical care. Administrative responsibilities include: committee work, policy development, implementation of the LEAN model of process improvement, oversight on quality in clinical practice both on the inpatient units and outpatient setting, supervision of clinical nurse specialists and medical student teaching.

Wing Memorial Hospital is an exciting venue for an interested candidate. Inpatient services include two thriving units: adult and geriatric. The outpatient division employs over twenty therapists and multiple psychopharmacologists. Support staff is extensive. Physical space is newly renovated. Behavioral Health Services at Wing Memorial Hospital boasts a truly collegial atmosphere. On call is 1/8 weekends. Compensation and Benefits are generous.

Join our experienced team as we continue to serve the highest quality of behavioral healthcare to the local community.

Please email resume to:
Michelle.Burnham@umassmemorial.org.

We embrace diversity in both our workforce and our approach to patient care. An Affirmative Action/Equal Opportunity Employer.

PSYCHIATRIC ATTENDING POSITIONS AVAILABLE AT MARLBOROUGH HOSPITAL, MEMBER HOSPITAL OF UMASS MEMORIAL HEALTH CARE

The Department of Psychiatry at UMass Memorial Health Care is actively seeking Attending Physicians for its affiliated program at Marlborough Hospital. The positions primarily involve the provision of inpatient psychiatric care, leading an interdisciplinary treatment team and participating in medical student education on the service. Both full and part-time employment is available for interested candidates. The ideal candidate will possess strong clinical abilities and a commitment to providing patient centered care in a collaborative environment. Physicians receive a highly competitive benefits package as part of our UMass Memorial Group Practice and academic appointment at the medical school commensurate with experience.

For consideration and/or additional details, or to learn about other opportunities affiliated with UMass, please send your CV and letter of introduction to: psychiatryrecruitment@umassmemorial.org. Applicants are also encouraged to visit the UMass Department of Psychiatry's web site: www.umassmed.edu/psychiatry.

CLASSIFIEDS

Medical Director–Boston/Cape Cod
Pembroke Hospital is seeking a full time Medical Director to join our 115-bed psychiatric facility's Leadership Team. The ideal candidate will be Board Certified with Medical Director level experience & 5 plus years experience in an inpatient behavioral health setting. The Medical Director will oversee the PI/Quality program, Utilization Review committee, and work with the CEO in new program development. The successful candidate will have strong interpersonal, written & verbal communication skills & a passion for providing excellent care in a cost effective, changing healthcare environment. The Medical Director will supervise Physician staff and have both administrative/clinical duties. Because we have physicians on site 24/7, **there is no routine weeknight or weekend call requirement.** The Medical Director position comes with a very competitive compensation package of salary & benefits including paid time off, CME, malpractice reimbursement & opportunities to earn additional income. Pembroke Hospital is part of the Arbour Health System & a subsidiary of Universal Health Services, Inc (UHS). We are located in Pembroke, MA only 8 miles from the coast in a beautiful suburban community within easy reach of Boston & Cape Cod. **Contact Will DeCuyper, In-house Recruiter @ 866-227-5415 OR email will.decuyper@uhsinc.com.**

The Department of Psychiatry at Mount Auburn Hospital, affiliated with Harvard Medical School, is recruiting for a full-time position as attending psychiatrist on our geriatric psychiatry inpatient unit. The 15 bed unit, fully accredited by DMH, provides acute treatment to geriatric patients with a variety of psychiatric disorders. The full medical resources of our general hospital are utilized in the care of our patients. Responsibilities include attending patients on the unit, consultation to the medical/surgical services of the hospital, and participation in the teaching activities of the Department. A clinical appointment in psychiatry at Harvard Medical School is anticipated.

Please send letter of interest and cv to: Joseph D'Afflitti, M.D., Chair, Department of Psychiatry, Mount Auburn Hospital, 330 Mount Auburn Street, Cambridge, MA 02138; tel: 617 499-5054; email:jdafflit@mah.harvard.edu.

MISSISSIPPI

Horizon Health seeks a **Medical Director** for a 19-bed Adult Inpatient Psychiatric Program in **Northern MS.** Well established, busy program with full complement of support staff and administration. $200K+ Salary, Full Benefits, CME, Relocation and more. For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

MISSOURI

FT, PT & Per Diem Psychiatrists needed in **Bowling Green, Farmington, St Joseph & Vandalia** with MHM Services, Inc. A leader in Correctional Mental Health, we offer highly competitive, guaranteed salaries, paid malpractice insurance & excellent benefits. NHSC loan repayment is available. Join the fastest-growing segment of behavioral health today. To apply, contact **Mark Hyde: 877-861-7993** or email CV to mark@mhmcareers.com. **No locums solicitations, please.**

Make An Income that Matches All the Work You Do –20 Minutes From St. Louis – 30 Minutes To Work – Seeking a Psychiatrist to join a very successful group practice in Festus. Work would be primarily inpatient work on adult & geropsych units in Farmington. Ideal opportunity for someone who wants the ability to make a very large income based on all your hard work. All billing and scheduling is done for you. Can also employ if preferred; H1 and J1 applicants welcome. Please **call Terry B. Good, Horizon Health, at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@horizonhealth.com. EOE

One of the Midwest's Best Kept Secrets - St. Joseph, MO – Close to Kansas City – Wonderful city to live and work, great schools, and so close to the metro area. Full-time salaried position with benefits & bonus on a 24-bed adult inpatient psychiatric unit based in a very impressive general hospital. Position is inpatient and outpatient. Offering attractive student loan repayment if needed. Come join our incredible behavioral health team on this growing psych service. This is a **"must see"** opportunity if you looking for a quality Psychiatry program; and the area is wonderful! Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

NEVADA and KANSAS CITY–Child Psychiatrists–Residential & Inpatient Services. Compensation package includes salary, benefits, bonus and more… Contact Joy Lankswert, In-house recruiter @ 866-227-5415; OR email joy.lankswert@uhsinc.com.

Did you know

APA members can access a collection of various **disaster psychiatry resources** prepared by the APA for use by mental health professionals and those involved with disaster preparedness? From a tool that links members to over 75 District Branch Disaster Liaisons and the Assembly Area Representative Disaster Network...to APA and other organizations' comprehensive disaster psychiatry resources, you can find more information at www.psychiatry.org/practice/professional-interests/disaster-psychiatry

NEW HAMPSHIRE

PARTNERSHIP FOR SUCCESSFUL LIVING

Come be a change agent in Nashua, NH – twice voted the country's best place to live. Harbor Homes, Inc., a non-profit health and human service agency, seeks:
- **Psychiatrists or**
- Psychiatric ARNPs

Help change the way behavioral health care is delivered in the community. Job responsibilities include medical consultations in acute care settings, initial evaluations, and coordination with community agencies, and collaboration with primary care physicians. Competitive salary, exceptional benefits, and excellent work/life balance offered.

Qualified interested candidates please send resume and salary requirements to: Human Resources 45 High Street Nashua, NH 03060 or careers@nhpartnership.org

EOE-AAM

NEW JERSEY

CHILD & ADOLESCENT PSYCHIATRIST
Millburn and Cedar Knolls, NJ

Child/Adolescent Psychiatrist positions are available for our Millburn and Cedar Knolls, New Jersey locations, to join our private upscale fee-for-service comprehensive child, adolescent and adult therapy Center. Candidate will be part of a multi-disciplinary team and will provide psychiatric evaluation, medication management and, if desired, psychotherapy, in a supportive collegial atmosphere. Salary and benefit package are generous, and include excellent medical and dental insurance benefits, generous vacation and CME time, retirement plan and more. Opportunities for growth also exist. Candidate must be board certified or board eligible in child/adolescent psychiatry. **E-mail cv to abbazn@aol.com.**

Medical Director Position–Northern NJ-Seeking psychiatrist in private practice who wants to follow inpatients on adult psych unit in Jersey City. Administrative stipend available for PT admin work that can be done while the doctor is at the hospital. Can round in the mornings or afternoons and go to practice the rest of the time. Great opportunity to grow one's practice, increase revenue. Additional income to the psychiatrist such as being paid for weekend call plus additional revenue that I would be happy to discuss with you. Please contact **Terry B. Good at 1-804-684-5661,** Fax#: 804-684-5663; Email: terry.good@horizonhealth.com.

NEW YORK CITY & AREA

Child and Adolescent Psychiatrist
P/T - 10-15 hours per week (evenings and/or weekends) in a Child and Family Mental Health Center in Brooklyn. Excellent compensation. No call. Fax resume to (718) 553-6769, or email to clinicaldirector@nypcc.org.

Jamaica Hospital Medical Center is pleased to announce the opening of our Comprehensive Psychiatric Emergency Program in the near future. We are recruiting for the following positions: Psychiatrists, Program Coordinator, Social Workers, Creative Arts Therapists and an Executive Secretary. Please fax CV to Seeth Vivek, MD, Chairman, Department of Psychiatry to 718-206-7169 or email Svivek@jhmc.org.

NEW YORK STATE

St. Lawrence Psychiatric Center Psychiatrists
NYS Licensed or Limited Permit (Limited Permit option – see below)**
Salary based on experience**
Earn up to an additional $74,000/year through a voluntary on-call programFringe Benefits equal to 50.16% of your salary
Monday – Friday, 8:00A – 4:30P

St. Lawrence Psychiatric Center is seeking Licensed Psychiatrists for Adult, Children/Youth, and Sex Offender Treatment Inpatient Services and for Adult and Children/Youth Outpatient Services.
- National Health Services Corps (NHSC) student loan repayment may be available (Up to $60,000 for a 2-year FT commitment; up to $170,000 with a 5-year FT commitment, and possible total debt alleviation with 6 or more years of service)
- Doctors Across New York (DANY) loan repayment or sign-on bonuses may be available (applications are time limited and considered in the order in which they are received).
- Excellent NYS Benefits to include medical/dental/vision insurance, paid vacation, holiday and sick time, an excellent retirement plan, and educational and professional leaves.
- Our location offers quality housing prices, mild traffic, a regional airport, Clarkson University, St. Lawrence University, and 2 SUNY colleges; 1 hr drive to Ottawa; 2 hr drive to Montreal, Lake Placid, and Syracuse.

**Limited Permit Option: If you have finished your residency, but not the USLME, you may be appointed on limited permit, initially for 2 years, renewable for further 2 years.

Applications are available by calling
(315) 541-2179
or send resume to:
Personnel Office
St. Lawrence Psychiatric Center
1 Chimney Point Drive
Ogdensburg, NY 13669-2291
or to Angela Grant at
Angela.Grant@omh.ny.gov.

SLPC is a fully accredited Joint Commission program/AA/EEOE/Self-indemnified.**Affiliated with SUNY Upstate Medical University.**

CLASSIFIEDS

Western New York-Chautauqua Region: Jamestown Psychiatric PC is seeking a Psychiatrist to join our rapidly growing Adult and Child Psychiatric team. Competitive salary and flexible growth opportunities are offered. We will offer a starting bonus to eligible candidates. Loan repayment, J1 or H1 assistance available. Please contact Mrs. Linda Jones, office manager @ lj@psychwebmd.com or Phone 716-483-2603. Fax CV and qualifications to 716-483-2828.

ELMIRA PSYCHIATRIC CENTER
Adult and Adolescent Psychiatrists
Board Eligible/Board Certified
$148,421-$256,700*
Limited Permit eligible applicants will also be considered

- All positions **M-F 8-4:30**
- Student loan repayment available
- Excellent NYS benefits package
- Inpatient, Outpatient and Day Treatment services
- Our location offers: quality housing prices; little traffic; regional airport; Cornell University; 4hr drive to NYC, Toronto & Philadelphia; 5½ hr drive to Boston & DC; less than 1hr to Finger Lakes Wine Country; Watkins Glen International Racetrack.

*Includes voluntary low stress on-call at regular pay rate.

For further info contact: Patricia Santulli, Director of Human Resources, Elmira Psychiatric Center, 100 Washington Street, Elmira, NY 14901; e-mail: P.Santulli@omh.ny.gov; call: (607) 737-4726 or fax: (607) 737-4722. An AA/EOE Employer

NORTH CAROLINA

Four beautiful seasons in North Carolina!

Candidate sought for partnership or employment in a busy private practice. Adult, 80% outpatient psychiatry practice with 1:3 call. H1b Visa physicians will be considered.Location: I-95 corridor, northeastern NC. 2.5 hours to coast, centrally located 1.5 hours from Raleigh-Durham, NC, Richmond, VA, and Norfolk, Va. Fabulous water activities. Area population: 85K.

Send letter and CV to Pam Ballew
pballew@halifaxrmc.org
www.halifaxregional.org
www.visithalifax.com

Healthy Minds. Healthy Lives – a blog by the American Psychiatric Association – provides online resources and information on mental health issues.

To view this blog, visit: http://apahealthyminds.blogspot.com/

NORTH DAKOTA

Sanford Clinic North
Fargo, North Dakota
Seeking BC/BE Adult Psychiatrists

Medical Director, In-Patient and Partial Hospitalization Programs—Join a team of inpatient hospitalists covering a 24 bed inpatient unit and a partial hospitalization unit with a 16 bed capacity.

General Adult Psychiatrist—This position provides the opportunity to practice outpatient and in-patient psychiatry.

Sanford's Behavioral Health Sciences Department is staffed by more than 30 psychiatrists, clinical nurse specialists, doctorate-level psychologists and master's-level psychologists offering a continuum of care, from inpatient hospitalization and partial hospitalization programs, to outpatient individual and group therapy including eating disorders at the highly regarded Eating Disorders Institute. Responsibilities include teaching psychiatry resident and medical students through the University of North Dakota School of Medicine.

Sanford Health is the largest, rural, not-for-profit, health care system in the nation, serving 126 communities in seven states plus children's clinic services expanding into several countries.

Fargo, ND, a community of 190,000, offers excellent schools, a wonderful blend of cultural and recreational activities, low crime and affordable and upscale living.

Jean Keller, Physician Recruiter
Phone: (701) 280-4853
Email: Jean.Keller@sanfordhealth.org
www.sanfordhealth.org

OHIO

Southeast, Inc. Healthcare Services is seeking a **Psychiatrist** in our Columbus, Ohio outpatient office to perform psychiatric assessments, diagnosis and treatment; referrals for medical evaluations and follow-up; and consultation with a multi-disciplinary team of professionals. We offer many great benefits, including health, dental, vision, 401(k), an on-site fitness room, generous time off and no on-call or weekends. If you are interested in learning more about opportunities available at Southeast, Inc. **send CV to: Southeast Inc., HR Dept., 16 W. Long St., Columbus, OH 43215 or e-mail at creitha@southeastinc.com.**

Southern OH – Hospital Named 10th in the Top 100 Best Places to Work - Outpatient Position with some on-call duties for the geropsych unit. Enjoy small town living at its best; laid-back, wonderful quality of life. Great place to raise a family. Salaried position with production & performance bonuses; medical school loan repayment plan up to $200k. Join our top notch team at this truly impressive hospital and enjoy where you live & work every day. Please **call Terry B. Good, Horizon Health, at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

OKLAHOMA

Red Rock Behavioral Health Services is seeking a Psychiatrist to perform evaluations for treatment and management of patient's needs; prescribing medications and performing Telemedicine services to satellite offices. Red Rock BHS provides outpatient and crisis stabilization services for individuals and families throughout Oklahoma. Please submit current CV to Wanda Birdwell, wbirdwell@red-rock.com. Red Rock BHS offers an excellent salary and benefit package. EOE

PENNSYLVANIA

We have exciting full and part-time positions in our five-hospital system close to Philadelphia and Wilmington. There are immediate openings in our outpatient psychotherapy practice which includes the **Women's Behavioral Health Program, Child/Adolescent, and General Adult.** Psychiatrists provide both psychotherapy and medication management. We also seek psychiatric leadership of our Pain Management Program.

Excellent salaries and benefit package. Send CV to Kevin Caputo, MD, Chairman Department of Psychiatry, Crozer-Keystone Health System, One Medical Center Blvd., Upland, PA 19013 or call 610-874-5257.

MEDICAL DIRECTOR POSITION - Lancaster is a lovely area in eastern PA – Inpatient psychiatrist needed; adult and geriatric; offering employment or independent contractor arrangement if private practice is preferred. An easy drive to so many wonderful metro areas. Grow with this program in a great location. Please call Terry B. Good at 1-804-684-5661, Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

C/A Psychiatrist - 50 Minutes from Pittsburgh – Forbes' Top Ten "Best Places to Live Cheaply" because of the low cost of living, highly rated schools, low unemployment and low crime rate. Impressive general hospital with new Child/Adol. Pavilion; this is an inpatient and outpatient position; salaried with benefits and attractive bonus plan. Top-notch staff; great quality of life—truly a "must see" position when considering a new job in a new place. Contact **Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; terry.good@horizonhealth.com. EOE

SOUTH CAROLINA

Medical Director Position - Make A Difference in This Community/Hospital – Head up an 8-bed inpatient Geropsychiatric Unit; salaried with benefits or practice opportunity for those who prefer independent contract. Weekend call is 1 in 3 or 4. Rounding on weekends is not necessary unless there is an admission on Friday or Saturday which is rare. Fantastic group of people to work with; huge amount of support. Located in northeast SC, easy drive to Florence, SC and Fayetteville, NC; 2 hours from Columbia, Myrtle Beach, Charlotte, Raleigh, and Wilmington. Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

TENNESSEE

EAST TENNESSEE STATE UNIVERSITY
JAMES H. QUILLEN COLLEGE OF MEDICINE
DEPARTMENT OF PSYCHIATRY & BEHAVIORAL SCIENCES

ADULT PSYCHIATRIST, CHILD PSYCHIATRIST, GERIATRIC PSYCHIATRIST: Three full-time positions available for Adult Psychiatrist, Child Psychiatrist and Geriatric Psychiatrist. The department seeks Adult Psychiatrist who is BE/BC (at time of hire), Child Psychiatrist who is BE/BC (at the time of hire) in the subspecialty of Child and Adolescent Psychiatry, and Geriatric Psychiatrist who is BE/BC (at the time of hire) in the subspecialty of geriatric psychiatry and will become involved in the development of a Geriatric Psychiatry Fellowship. Positions may include inpatient and/or outpatient. Program activities include clinical care of patients combined with teaching and supervision of residents and medical students. Adult or Child position may be considered for Director of Outpatient Clinic Programs. Research is encouraged but not essential. Salary and academic rank are commensurate with experience and qualifications. Salary is competitive with funding available through the Medical School, faculty private practice and extramural contracts.

ETSU is located in Johnson City which is the perfect blend of four mild and beautiful seasons, gentle mountains and a symphony orchestra. Come explore this ideal family location of college/urban sophistication surrounded by national forests and serene pastures. No state income tax, low cost-of-living, low crime rate, lots of parks, golf courses, and lakes. Apply to this position at https://jobs.etsu.edu. Telephone inquiries should be made at (423) 439-2235 or e-mail at lovedayc@etsu.edu. AA/EOE.

Horizon Health, in partnership with **Livingston Regional Hospital** in **Livingston, TN**, near beautiful **Dale Hollow Lake,** has an exciting opportunity for a **Medical Director** at our 10-bed Geriatric Inpatient Psychiatric Program. Excellent income with great quality of life! 2 hours from Nashville and Knoxville and one of the lowest costs of living in the U.S. For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com. EOE

TEXAS

The Texas A&M Health Science Center College of Medicine, Department of Psychiatry & Behavioral Sciences is seeking a board certified Psychiatrist to establish a Residency Training Program in Psychiatry. Optimally, the applicant will have prior experience at the Training Director or Associate Training Director level. Interested applicants should send a curriculum vitae and letter of interest to: Joseph Sokal, MD, TAMHSC, 8441 State Hwy 47, Suite 1100, Bryan, TX 77807 or via email to sokal@medicine.tamhsc.edu. Applications will be accepted until the position is filled. Texas A&M University is an EEO Employer.

CLASSIFIEDS

PSYCHIATRISTS

The Mental Health Mental Retardation Authority of Harris County (MHMRA) in Houston, Texas is one of the largest mental health centers in the United States. In anticipation of expected growth in 2013 we are now recruiting for additional BE/BC psychiatrists throughout the Agency.

We will have needs in our
Crisis Services, IDD, Forensics and Outpatient Clinics
seeking both Child/Adolescent and Adult

Positions are full time and
may offer flex hours
Some positions have no on-call
and are M-F

Texas licensure is required for all positions.

Interviewing now for current open positions and near future start dates.

MHMRA offers competitive salary plus an excellent benefits package including generous retirement plans which match up to 10%. Houston offers excellent quality of life; lower than average cost of living, no state income tax and exciting cultural, entertainment, sporting and tourists venues.

Contact Charlotte Simmons at (713) 970-7397, or submit your C.V. to charlotte.simmons@mhmraharris.org, fax 713-970-3386 or apply online at www.mhmraharris.org.

The Department of Psychiatry and Behavioral Sciences of the University of Texas Medical School at Houston has an extraordinary opportunity for psychiatrists seeking to develop and implement new outpatient clinical and research initiatives in community based outpatient clinics within the Houston area with our partner Harris Health. We are also adding faculty to our 250 bed inpatient hospital, the Harris County Psychiatric Center. Our inpatient and outpatient services include unique and robust clinical and research initiatives. The Department is looking to expand clinical and research areas and is seeking general psychiatrists, child and adolescent psychiatrists and geriatric psychiatrists to join a growing academic department dedicated to excellence in training and education, and primacy in research and investigation. The Medical School is part of the University of Texas Health Science Center Houston, located in the Texas Medical Center – the largest medical center in the world. Individuals applying for these positions must be Board Certified in general psychiatry, child & adolescent psychiatry and geriatric psychiatry or have completed an accredited training in these specialty and subspecialty areas in the United States. Additionally, they must be licensed or be eligible for licensing in the State of Texas. Depending upon the applicant's qualification and credentials, faculty appointments at the level of Assistant Professor, Associate Professor or Professor will be offered. Salary levels are very competitive and also carry excellent fringe benefit packages. To find out more information about these unique academically driven positions or to apply for them, please write to Jair C. Soares, M.D., Professor and Chair, and include a copy of your curriculum vitae and a letter of interest to 1941 East Road, Houston, Texas 77054, e-mail: Jair.C.Soares@uth.tmc.edu phone 713-486-2507; fax 713-486-2553. The University of Texas Health Science Center at Houston is an EO/AA employer. M/F/D/V

UTAH

SALT LAKE CITY and OREM/PROVO: Inpatient & partial programs. General and Military specialty services. Staff and Directorship opportunities. Top salary, benefits and more. Contact Joy Lankswert, In-house recruiter @ 866-227-5415; OR email joy.lankswert@uhsinc.com.

VIRGINIA

VA BEACH: Addiction Psychiatrist – Inpatient Services. **PORTSMOUTH and KEMPSVILLE:** Child Psychiatrists for Residential Treatment and/or Inpatient Services. All positions are fulltime offering salary, benefits and bonus opportunity. Contact Tiffany Crawford, In-house recruiter @ 866-227-5415; OR email tiffany.crawford@uhsinc.com.

WEST VIRGINIA

Third Psychiatrist for outpatient position in multidisciplinary Community Health Center 90 minutes from DC/Baltimore. Behavioral Health department has 2 psychiatrists, 13 therapists. Experience/training in addictionology a plus. Salaried position, incentive compensation, standard benefits. Federal Loan Repayment site. Dynamic community rich in recreational & cultural resources. Contact Tina Burns 304-596-2610, ext 1066; tburns@svms.net FAX 304-263-0984. Visit our website www.svms.net.

C/A Psychiatrist - 50 Minutes from Pittsburgh – Forbes' Top Ten "Best Places to Live Cheaply" because of the low cost of living, highly rated schools, low unemployment and low crime rate. Impressive general hospital with new Child/Adol. Pavilion; this is an inpatient and outpatient position; salaried with benefits and attractive bonus plan. Top-notch staff; great quality of life—truly a "must see" position when considering a new job in a new place. Contact **Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; terry.good@horizonhealth.com. EOE

Excellent private practice opportunity for a adult/ or child-trained psychiatrist in Southern West Virginia to join a well-established practice. In-patient, out-patient, and consultation services. Exceptional salary and benefits. Good place to raise children. Easy drive to several big cities, heaven for outdoor lovers. Can help with visa conversion and sponsorship. Fax cv to (304) 252-1703 or email nafa2 @aol.com.

WISCONSIN

Milwaukee or Kenosha: Outpatient mental health and AODA clinic seeks part-time psychiatrists to provide clinical services at our Milwaukee and/or Kenosha locations. Hourly rate- $150.00, professional liability insurance provided. Must be licensed in State of Wisconsin and able to write RX for Suboxone. EOE. Email CV to jhutch@innovativehc.org, Fax to 877-904-2920 or call 847-410-8785 ext. 101.

Fellowships

Geriatric Psychiatry Fellowship Program: The University of Texas Health Science Center at San Antonio is currently accepting applications for 2013-2014. This one-year program offers training in a wide variety of outpatient, inpatient and consultative settings, as well as opportunities for research and teaching. Interested individuals should contact (210)567-5432.

Pristiq® desvenlafaxine Extended-Release Tablets

BRIEF SUMMARY. See package insert for full Prescribing Information. For further product information and current package insert, please visit www.pristiqhcp.com or call Pfizer US Medical Information toll-free at (800) 438-1985.

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term studies. These studies did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in patients over age 24; there was a reduction in risk with antidepressant use in patients aged 65 and older *[see Warnings and Precautions (5.1) in the full prescribing information]*.

In patients of all ages who are started on antidepressant therapy, monitor closely for worsening, and for emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber *[see Warnings and Precautions (5.1) in the full prescribing information]*.

PRISTIQ is not approved for use in pediatric patients *[see Use in Specific Populations (8.4) in the full prescribing information]*.

INDICATIONS AND USAGE: PRISTIQ, a serotonin and norepinephrine reuptake inhibitor (SNRI), is indicated for the treatment of major depressive disorder (MDD) *[see Clinical Studies (14) and Dosage and Administration (2.1) in the full prescribing information]*. The efficacy of PRISTIQ has been established in four short-term (8-week, placebo-controlled studies) and two maintenance studies in adult outpatients who met DSM-IV criteria for major depressive disorder.

CONTRAINDICATIONS: Hypersensitivity—Hypersensitivity to desvenlafaxine succinate, venlafaxine hydrochloride or to any excipients in the PRISTIQ formulation. Angioedema has been reported in patients treated with PRISTIQ *[see Adverse Reactions (6.1) in the full prescribing information]*. **Monoamine Oxidase Inhibitors**—The use of monoamine oxidase inhibitors (MAOIs) intended to treat psychiatric disorders with PRISTIQ or within 7 days of stopping treatment with PRISTIQ is contraindicated because of an increased risk of serotonin syndrome. The use of PRISTIQ within 14 days of stopping an MAOI intended to treat psychiatric disorders is also contraindicated *[see Dosage and Administration (2.6) and Warnings and Precautions (5.2) in the full prescribing information]*. Starting PRISTIQ in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue is also contraindicated because of an increased risk of serotonin syndrome *[see Dosage and Administration (2.6) and Warnings and Precautions (5.2) in the full prescribing information]*.

WARNINGS AND PRECAUTIONS: Suicidal Thoughts and Behaviors in Adolescents and Young Adults—Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled studies of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18 to 24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The pooled analyses of placebo-controlled studies in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term studies of 9 antidepressant drugs in over 4,400 patients. The pooled analyses of placebo-controlled studies in adults with MDD or other psychiatric disorders included a total of 295 short-term studies (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1,000 patients treated) included 14 additional cases of increases among those aged <18, 5 additional cases of increases among those aged 18 to 24, 1 fewer case of decrease among those aged 25 to 64, and 6 fewer cases of decrease among those aged ≥65.

No suicides occurred in any of the pediatric studies. There were suicides in the adult studies, but the number was not sufficient to reach any conclusion about drug effect on suicide. It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance studies in adults with depression that the use of antidepressants can delay the recurrence of depression. **All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.** The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms *[see Dosage and Administration (2.4) and Warnings and Precautions (5.7) in the full prescribing information for a description of the risks of discontinuation of PRISTIQ]*. **Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to healthcare providers. Such monitoring should include daily observation by families and caregivers.** Prescriptions for PRISTIQ should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. Screening patients for bipolar disorder—A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled studies) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that PRISTIQ is not approved for use in treating bipolar depression. **Serotonin Syndrome:** The development of a potentially life-threatening serotonin syndrome has been reported with SNRIs and SSRIs, including PRISTIQ, alone but particularly with concomitant use of other serotonergic drugs (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort), and with drugs that impair metabolism of serotonin (in particular, MAOIs, both those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue). Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Patients should be monitored for the emergence of serotonin syndrome. The concomitant use of PRISTIQ with MAOIs intended to treat psychiatric disorders is contraindicated. PRISTIQ should also not be started in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue. All reports with methylene blue that provided information on the route of administration involved intravenous administration in the dose range of 1 mg/kg to 8 mg/kg. No reports involved the administration of methylene blue by other routes (such as oral tablets or local tissue injection) or at lower doses. There may be circumstances when it is necessary to initiate treatment with a MAOI such as linezolid or intravenous methylene blue in a patient taking PRISTIQ. PRISTIQ should be discontinued before initiating treatment with the MAOI *[see Contraindications (4.2) and Dosage and Administration (2.6) in the full prescribing information]*. If concomitant use of PRISTIQ with other serotonergic drugs, including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, buspirone, tryptophan, and St. John's Wort is clinically warranted, patients should be made aware of a potential increased risk for serotonin syndrome, particularly during treatment initiation and dose increases. Treatment with PRISTIQ and any concomitant serotonergic agents should be discontinued immediately if the above events occur and supportive symptomatic treatment should be initiated. **Elevated Blood Pressure:** Patients receiving PRISTIQ should have regular monitoring of blood pressure since increases in blood pressure were observed in clinical studies *[see Adverse Reactions (6.1) in the full prescribing information]*. Pre-existing hypertension should be controlled before initiating treatment with PRISTIQ. Caution should be exercised in treating patients with pre-existing hypertension, cardiovascular, or cerebrovascular conditions that might be compromised by increases in blood pressure. Cases of elevated blood pressure requiring immediate treatment have been reported with PRISTIQ. Sustained blood pressure increases could have adverse consequences. For patients who experience a sustained increase in blood pressure while receiving PRISTIQ, either dose reduction or discontinuation should be considered *[see Adverse Reactions (6.1) in the full prescribing information]*. **Abnormal Bleeding:** SSRIs and SNRIs, including PRISTIQ, may increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs, warfarin, and other anticoagulants may add to this risk. Case reports and epidemiological studies (case-control and cohort design) have demonstrated an association between use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal bleeding. Bleeding events related to SSRIs and SNRIs have ranged from ecchymosis, hematoma, epistaxis, and petechiae to life-threatening hemorrhages. Patients should be cautioned about the risk of bleeding associated with the concomitant use of PRISTIQ and NSAIDs, aspirin, or other drugs that affect coagulation or bleeding. **Narrow-angle Glaucoma**: Mydriasis has been reported in association with PRISTIQ; therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma (angle-closure glaucoma) should be monitored. **Activation of Mania/Hypomania:** During all MDD phase 2 and phase 3 studies, mania was reported for approximately 0.02% of patients treated with PRISTIQ. Activation of mania/hypomania has also been reported in a small proportion of patients with major affective disorder who were treated with other marketed antidepressants. As with all antidepressants, PRISTIQ should be used cautiously in patients with a history or family history of mania or hypomania. **Discontinuation Syndrome:** Discontinuation symptoms have been systematically and prospectively evaluated in patients treated with PRISTIQ during clinical studies in Major Depressive Disorder. Abrupt discontinuation or dose reduction has been associated with the appearance of new symptoms that include dizziness, nausea, headache, irritability, insomnia, diarrhea, anxiety, fatigue, abnormal dreams, and hyperhidrosis. In general, discontinuation events occurred more frequently with longer duration of therapy. During marketing of SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors), and SSRIs (Selective Serotonin Reuptake Inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesia, such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment with PRISTIQ. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate *[see Dosage and Administration (2.4) and Adverse Reactions (6.1) in the full prescribing information]*. **Seizure:** Cases of seizure have been reported in pre-marketing clinical studies with PRISTIQ. PRISTIQ has not been systematically evaluated in patients with a seizure disorder. Patients with a history of seizures were excluded from pre-marketing clinical studies. PRISTIQ should be prescribed with caution in patients with a seizure disorder. **Hyponatremia:** Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including PRISTIQ. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Cases with serum sodium lower than 110 mmol/L have been reported. Elderly patients may be at greater risk of developing hyponatremia with SSRIs and SNRIs. Also, patients taking diuretics or who are otherwise volume depleted can be at greater risk *[see Use in Specific Populations (8.5) and Clinical Pharmacology (12.6) in the full prescribing information]*. Discontinuation of PRISTIQ should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted. Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which can lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death. **Interstitial Lung Disease and Eosinophilic Pneumonia:** Interstitial lung disease and eosinophilic pneumonia associated with venlafaxine (the parent drug of PRISTIQ) therapy have been rarely reported. The possibility of these adverse events should be considered in patients treated with PRISTIQ who present with progressive dyspnea, cough, or chest discomfort. Such patients should undergo a prompt medical evaluation, and discontinuation of PRISTIQ should be considered.

ADVERSE REACTIONS: The following adverse reactions are discussed in greater detail in other sections of the label: Hypersensitivity *[see Contraindications (4)]*, Suicidal Thoughts and Behaviors in Adolescents and Young Adults *[see Warnings and Precautions (5.1)]*, Serotonin Syndrome *[see Warnings and Precautions (5.2)]*, Elevated Blood Pressure *[see Warnings and Precautions (5.3)]*, Abnormal Bleeding *[see Warnings and Precautions (5.4)]*, Narrow-Angle Glaucoma *[see Warnings and Precautions (5.5)]*, Activation of Mania/Hypomania *[see Warnings and Precautions (5.6)]*, Discontinuation Syndrome *[see Warnings and Precautions (5.7)]*, Seizure *[see Warnings and Precautions (5.8)]*, Hyponatremia *[see Warnings and Precautions (5.9)]*, Interstitial Lung Disease and Eosinophilic Pneumonia *[see Warnings and Precautions (5.10)]*. **Clinical Studies Experience:** Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in clinical practice. Patient exposure—PRISTIQ was evaluated for safety in 4,158 patients diagnosed with major depressive disorder who participated in multiple-dose pre-marketing studies, representing 1,677 patient-years of exposure. Among these 4,158 PRISTIQ treated patients; 1,834 patients were exposed to PRISTIQ in 8-week, placebo-controlled studies at doses ranging from 50 to 400 mg/day. Out of the 1,834 patients, 687 PRISTIQ treated patients continued into a 10-month open-label study. Of the total 4,158 patients exposed to at least one dose of PRISTIQ; 1,320 were exposed to PRISTIQ for 6 months, representing 1,058 patient-years of exposure, and 274 were exposed for one year, representing 241 patient-years of exposure. Adverse reactions reported as reasons for discontinuation of treatment—In the pooled 8-week placebo-controlled studies in patients with MDD, 12% of the 1,834 patients who received PRISTIQ (50 to 400 mg) discontinued treatment due to an adverse reaction, compared with 3% of the 1,116 placebo-treated patients. At the recommended dose of 50 mg, the discontinuation rate due to an adverse reaction for PRISTIQ (4.1%) was similar to the rate for placebo (3.8%). For the 100 mg dose of PRISTIQ the discontinuation rate due to an adverse reaction was 8.7%. The most common adverse reactions leading to discontinuation in at least 2% and at a rate greater than placebo of the PRISTIQ treated patients in the short-term studies, up to 8 weeks, were: nausea (4%); dizziness, headache and vomiting (2% each); in the longer-term studies, up to 11 months, the most common was vomiting (2%). Common adverse reactions in placebo-controlled MDD studies—The most commonly observed adverse reactions in PRISTIQ treated MDD patients in short-term fixed-dose studies (incidence ≥ 5% and at least twice the rate of placebo in the 50 or 100 mg dose groups) were: nausea, dizziness, insomnia, hyperhidrosis, constipation, somnolence, decreased appetite, anxiety, and specific male sexual function disorders. The incidence of common adverse reactions that occurred in ≥2% of PRISTIQ-treated MDD patients and twice the rate of placebo at any dose in the pooled 8-week, placebo-controlled, fixed-dose clinical studies (placebo, n=636; PRISTIQ 50 mg, n=317; PRISTIQ 100 mg, n=424; PRISTIQ 200 mg, n=307; PRISTIQ 400 mg, n=317) included Cardiac disorders: Blood pressure increased (1% placebo, 1% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 2% PRISTIQ 200 mg, 2% PRISTIQ 400 mg); Gastrointestinal disorders: Nausea (10% placebo, 22% PRISTIQ 50 mg, 26% PRISTIQ 100 mg, 36% PRISTIQ 200 mg, 41% PRISTIQ 400 mg), Dry mouth (9% placebo, 11% PRISTIQ 50 mg, 17% PRISTIQ 100 mg, 21% PRISTIQ 200 mg, 25% PRISTIQ 400 mg), Constipation (4% placebo, 9% PRISTIQ 50 mg, 9% PRISTIQ 100 mg, 10% PRISTIQ 200 mg, 14% PRISTIQ 400 mg), Vomiting (3% placebo, 3% PRISTIQ 50 mg, 4% PRISTIQ 100 mg, 6% PRISTIQ 200 mg, 9% PRISTIQ 400 mg); General disorders and administration site conditions: Fatigue (4% placebo, 7% PRISTIQ 50 mg, 7% PRISTIQ 100 mg, 10% PRISTIQ 200 mg, 11% PRISTIQ 400 mg), Chills (1% placebo, 1% PRISTIQ 50 mg, <1% PRISTIQ 100 mg, 3% PRISTIQ 200 mg, 4% PRISTIQ 400 mg), Feeling jittery (1% placebo, 1% PRISTIQ 50 mg, 2% PRISTIQ 100 mg, 3% PRISTIQ 200 mg, 3% PRISTIQ 400 mg); Metabolism and nutrition disorders: Decreased appetite (2% placebo, 5% PRISTIQ 50 mg, 8% PRISTIQ 100 mg, 10% PRISTIQ 200 mg, 10% PRISTIQ 400 mg); Nervous system disorders: Dizziness (5% placebo, 13% PRISTIQ 50 mg, 10% PRISTIQ 100 mg, 15% PRISTIQ 200 mg, 16% PRISTIQ 400 mg), Somnolence (4% placebo, 4% PRISTIQ 50 mg, 9% PRISTIQ 100 mg, 12% PRISTIQ 200 mg, 12% PRISTIQ 400 mg), Tremor (2% placebo, 2% PRISTIQ 50 mg, 3% PRISTIQ 100 mg, 9% PRISTIQ 200 mg, 9% PRISTIQ 400 mg), Disturbance in attention (<1% placebo, <1% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 2% PRISTIQ 200 mg, 1% PRISTIQ 400 mg); Psychiatric disorders: Insomnia (6% placebo, 9% PRISTIQ 50 mg, 12% PRISTIQ 100 mg, 14% PRISTIQ 200 mg, 15% PRISTIQ 400 mg), Anxiety (2% placebo, 3% PRISTIQ 50 mg, 5% PRISTIQ 100 mg, 4% PRISTIQ 200 mg, 4% PRISTIQ 400 mg), Nervousness (1% placebo, <1% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 2% PRISTIQ 200 mg, 2% PRISTIQ 400 mg), Abnormal dreams (1% placebo, 2% PRISTIQ 50 mg, 3% PRISTIQ 100 mg, 2% PRISTIQ 200 mg, 4% PRISTIQ 400 mg); Renal and urinary disorders: Urinary hesitation (0% placebo, <1% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 2% PRISTIQ 200 mg, 2% PRISTIQ 400 mg); Respiratory, thoracic and mediastinal disorders: Yawning (<1% placebo, 1% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 4% PRISTIQ 200 mg, 3% PRISTIQ 400 mg); Skin and subcutaneous tissue disorders: Hyperhidrosis (4% placebo, 10% PRISTIQ 50 mg, 11% PRISTIQ 100 mg, 18% PRISTIQ 200 mg, 21% PRISTIQ 400 mg); Special Senses: Vision blurred (1% placebo, 3% PRISTIQ 50 mg, 4% PRISTIQ 100 mg, 4% PRISTIQ 200 mg, 4% PRISTIQ 400 mg), Mydriasis (<1% placebo, 2% PRISTIQ 50 mg, 2% PRISTIQ 100 mg, 6% PRISTIQ 200 mg, 6% PRISTIQ 400 mg), Vertigo (1% placebo, 2% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 5% PRISTIQ 200 mg, 3% PRISTIQ 400 mg), Tinnitus (1% placebo, 2% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 1% PRISTIQ 200 mg, 2% PRISTIQ 400 mg), Dysgeusia (1% placebo, 1% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 1% PRISTIQ 200 mg, 2% PRISTIQ 400 mg); Vascular disorders: Hot flush (<1% placebo, 1% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 2% PRISTIQ 200 mg, 2% PRISTIQ 400 mg).

Sexual function adverse reactions—The incidence of sexual function adverse reactions that occurred in ≥ 2% of PRISTIQ treated MDD patients in any fixed-dose group (pooled 8-week, placebo-controlled, fixed and flexible-dose, clinical studies) included Men only (placebo, n=239; PRISTIQ 50 mg, n=108; PRISTIQ 100 mg, n=157; PRISTIQ 200 mg, n=131; PRISTIQ 400 mg, n=154): Anorgasmia (0% placebo, 0% PRISTIQ 50 mg, 3% PRISTIQ 100 mg, 5% PRISTIQ 200 mg, 8% PRISTIQ 400 mg), Libido decreased (1% placebo, 4% PRISTIQ 50 mg, 5% PRISTIQ 100 mg, 6% PRISTIQ 200 mg, 3% PRISTIQ 400 mg), Orgasm abnormal (0% placebo, 0% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 2% PRISTIQ 200 mg, 3% PRISTIQ 400 mg), Ejaculation delayed (<1% placebo, 1% PRISTIQ 50 mg, 5% PRISTIQ 100 mg, 7% PRISTIQ 200 mg, 6% PRISTIQ 400 mg), Erectile dysfunction (1% placebo, 3% PRISTIQ 50 mg, 6% PRISTIQ 100 mg, 8% PRISTIQ 200 mg, 11% PRISTIQ 400 mg), Ejaculation disorder (0% placebo, 0% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 2% PRISTIQ 200 mg, 5% PRISTIQ 400 mg), Ejaculation failure (0% placebo, 1% PRISTIQ 50 mg, 0% PRISTIQ 100 mg, 2% PRISTIQ 200 mg, 2% PRISTIQ 400 mg), Sexual dysfunction (0% placebo, 1% PRISTIQ 50 mg, 0% PRISTIQ 100 mg, 0% PRISTIQ 200 mg, 2% PRISTIQ 400 mg); Women only (placebo, n=397; PRISTIQ 50 mg, n=209; PRISTIQ 100 mg, n=267; PRISTIQ 200 mg, n=176; PRISTIQ 400 mg, n=163): Anorgasmia (0% placebo, 1% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 0% PRISTIQ 200 mg, 3% PRISTIQ 400 mg).

Other adverse reactions observed in clinical studies: Other infrequent adverse reactions, not described elsewhere in the label, occurring at an incidence of <2% in MDD patients treated with PRISTIQ were: *Cardiac disorders*—Tachycardia; *General disorders and administration site conditions*—Asthenia; *Investigations*—Weight increased, liver function test abnormal, blood prolactin increased; *Musculoskeletal and connective tissue disorders*—Musculoskeletal stiffness; *Nervous system disorders*—Syncope, convulsion, dystonia; *Psychiatric disorders*—Depersonalization, bruxism; *Renal and urinary disorders*—Urinary retention; *Skin and subcutaneous tissue disorders*—Rash, alopecia, photosensitivity reaction, angioedema. In clinical studies, there were uncommon reports of ischemic cardiac adverse reactions, including myocardial ischemia, myocardial infarction, and coronary occlusion requiring revascularization; these patients had multiple underlying cardiac risk factors. More patients experienced these events during PRISTIQ treatment as compared to placebo.

Laboratory, ECG and vital sign changes observed in MDD clinical studies—The following changes were observed in placebo-controlled, short-term MDD studies with PRISTIQ. *Lipids*—Elevations in fasting serum total cholesterol, LDL (low density lipoproteins) cholesterol, and triglycerides occurred in the controlled studies. Some of these abnormalities were considered potentially clinically significant. The percentage of patients who exceeded a predetermined threshold value included: Total Cholesterol increase of ≥50 mg/dl and an absolute value of ≥261 mg/dl (2% placebo, 3% PRISTIQ 50 mg, 4% PRISTIQ 100 mg, 4% PRISTIQ 200 mg, 10% PRISTIQ 400 mg), LDL Cholesterol increase ≥50 mg/dl and an absolute value of ≥190 mg/dl (0% placebo, 1% PRISTIQ 50 mg, 0% PRISTIQ 100 mg, 1% PRISTIQ 200 mg, 2% PRISTIQ 400 mg), Triglycerides, fasting, ≥327 mg/dl (3% placebo, 2% PRISTIQ 50 mg, 1% PRISTIQ 100 mg, 4% PRISTIQ 200 mg, 6% PRISTIQ 400 mg).

Proteinuria—Proteinuria, greater than or equal to trace, was observed in the fixed-dose controlled studies. This proteinuria was not associated with increases in BUN or creatinine and was generally transient. The percentage of patients with proteinuria in the fixed-dose clinical studies were 4% placebo, 6% PRISTIQ 50 mg, 8% PRISTIQ 100 mg, 5% PRISTIQ 200 mg, 7% PRISTIQ 400 mg.

Vital sign changes—Mean changes observed in placebo-controlled, short-term, fixed-dose, pre-marketing, controlled studies with PRISTIQ in patients with MDD included Blood pressure: Supine systolic bp (-1.4 mm Hg placebo, 1.2 mm Hg PRISTIQ 50 mg, 2.0 mm Hg PRISTIQ 100 mg, 2.5 mm Hg PRISTIQ 200 mg, 2.1 mm Hg PRISTIQ 400 mg); Supine diastolic bp (-0.6 mm Hg placebo, 0.7 mm Hg PRISTIQ 50 mg, 0.8 mm Hg PRISTIQ 100 mg, 1.8 mm Hg PRISTIQ 200 mg, 2.3 mm Hg PRISTIQ 400 mg); Pulse rate: Supine pulse (-0.3 bpm placebo, 1.3 bpm PRISTIQ 50 mg, 1.3 bpm PRISTIQ 100 mg, 0.9 bpm PRISTIQ 200 mg, 4.1 bpm PRISTIQ 400 mg); Weight: (0.0 kg placebo, -0.4 kg PRISTIQ 50 mg, -0.6 kg PRISTIQ 100 mg, -0.9 kg PRISTIQ 200 mg, -1.1 kg PRISTIQ 400 mg).

Treatment with PRISTIQ at all doses from 50 mg/day to 400 mg/day in controlled studies was associated with sustained hypertension, defined as treatment-emergent supine diastolic blood pressure (SDBP) ≥90 mm Hg and ≥10 mm Hg above baseline for 3 consecutive on-therapy visits. The proportion of patients with sustained elevation of supine diastolic blood pressure included 0.5% placebo, 1.3% PRISTIQ 50 mg, 0.7% PRISTIQ 100 mg, 1.1% PRISTIQ 200 mg, 2.3% PRISTIQ 400 mg. Analyses of patients in PRISTIQ short-term controlled studies who met criteria for sustained hypertension revealed a consistent increase in the proportion of patients who developed sustained hypertension. This was seen at all doses with a suggestion of a higher rate at 400 mg/day.

Orthostatic hypotension—In the short-term, placebo-controlled clinical studies with doses of 50 to 400 mg, systolic orthostatic hypotension (decrease ≥30 mm Hg from supine to standing position) occurred more frequently in patients ≥65 years of age receiving PRISTIQ (8%, 7/87) versus placebo (2.5%, 1/40), compared to patients <65 years of age receiving PRISTIQ (0.9%, 18/1,937) versus placebo (0.7%, 8/1,218). **Postmarketing Experience**—The following adverse reaction has been identified during post-approval use of PRISTIQ. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: *Skin and subcutaneous tissue disorders*—Stevens-Johnson syndrome. **DRUG INTERACTIONS: Monoamine Oxidase Inhibitors (MAOI)**—*[see Dosage and Administration (2.6), Contraindications (4) and Warnings and Precautions (5.2) in the full prescribing information]*. **Serotonergic Drugs**—*[see Dosage and Administration (2.6), Contraindications (4) and Warnings and Precautions (5.2) in the full prescribing information]*. **Drugs that Interfere with Hemostasis (e.g., NSAIDs, Aspirin, and Warfarin)**—Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of case-control and cohort design that have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. These studies have also shown that concurrent use of an NSAID or aspirin may potentiate this risk of bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs and SNRIs are co-administered with warfarin. Patients receiving warfarin therapy should be carefully monitored when PRISTIQ is initiated or discontinued *[see Warnings and Precautions (5.4) in the full prescribing information]*. **Potential for Desvenlafaxine to Affect Other Drugs**—Clinical studies have shown that desvenlafaxine does not have a clinically relevant effect on CYP2D6 metabolism at the dose of 100 mg daily. Substrates primarily metabolized by CYP2D6 (e.g., desipramine, atomoxetine, dextromethorphan, metoprolol, nebivolol, perphenazine, tolterodine) should be dosed at the original level when co-administered with PRISTIQ 100 mg or lower. Reduce the dose of these substrates by one-half if co-administered with 400 mg of PRISTIQ. The substrate dose should be increased to the original level when 400 mg of PRISTIQ is discontinued. **Other Drugs Containing Desvenlafaxine or Venlafaxine**—Avoid use of PRISTIQ with other desvenlafaxine-containing products or venlafaxine products. The concomitant use of PRISTIQ with other desvenlafaxine-containing products or venlafaxine will increase desvenlafaxine blood levels and increase dose-related adverse reactions *[see Adverse Reactions (6) in the full prescribing information]*. **Ethanol**—A clinical study has shown that PRISTIQ does not increase the impairment of mental and motor skills caused by ethanol. However, as with all CNS-active drugs, patients should be advised to avoid alcohol consumption while taking PRISTIQ.

USE IN SPECIFIC POPULATIONS: Pregnancy—Pregnancy Category C: *Risk summary*—There are no adequate and well-controlled studies of PRISTIQ in pregnant women. In reproductive developmental studies in rats and rabbits with desvenlafaxine succinate, evidence of teratogenicity was not observed at doses up to 30 times a human dose of 100 mg/day (on a mg/m^2 basis) in rats, and up to 15 times a human dose of 100 mg/day (on a mg/m^2 basis) in rabbits. An increase in rat pup deaths was seen during the first 4 days of lactation when dosing occurred during gestation and lactation, at doses greater than 10 times a human dose of 100 mg/day (on a mg/m^2 basis). PRISTIQ should be used during pregnancy only if the potential benefits justify the potential risks to the fetus. *Clinical considerations*—A prospective longitudinal study of 201 women with history of major depression who were euthymic at the beginning of pregnancy, showed women who discontinued antidepressant medication during pregnancy were more likely to experience a relapse of major depression than women who continued antidepressant medication. *Human data*—Neonates exposed to SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors), or SSRIs (Selective Serotonin Reuptake Inhibitors), late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome *[see Warnings and Precautions (5.2) in the full prescribing information]*. *Animal data*—When desvenlafaxine succinate was administered orally to pregnant rats and rabbits during the period of organogenesis at doses up to 300 mg/kg/day and 75 mg/kg/day, respectively, no teratogenic effects were observed. These doses are 30 times a human dose of 100 mg/day (on a mg/m^2 basis) in rats and 15 times a human dose of 100 mg/day (on a mg/m^2 basis) in rabbits. However, fetal weights were decreased and skeletal ossification was delayed in rats in association with maternal toxicity at the highest dose, with a no-effect dose 10 times a human dose of 100 mg/day (on a mg/m^2 basis). **When desvenlafaxine succinate was administered orally to pregnant rats throughout gestation and lactation, there was a decrease in pup weights and an increase in pup deaths during the first four days of lactation at the highest dose of 300 mg/kg/day. The cause of these deaths is not known. The no-effect dose for rat pup mortality was 10 times a human dose of 100 mg/day (on a mg/m^2 basis). Post-weaning growth and reproductive performance of the progeny were not affected by maternal treatment with desvenlafaxine succinate at a dose 30 times a human dose of 100 mg/day (on a mg/m^2 basis).** **Nursing Mothers**—Desvenlafaxine (O-desmethylvenlafaxine) is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from PRISTIQ, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. **Pediatric Use**—Safety and effectiveness in pediatric patients have not been established *[see Boxed Warning and Warnings and Precautions (5.1) in the full prescribing information]*. Anyone considering the use of PRISTIQ in a child or adolescent must balance the potential risks with the clinical need. **Geriatric Use**—Of the 4,158 patients in clinical studies with PRISTIQ, 6% were 65 years of age or older. No overall differences in safety or efficacy were observed between these patients and younger patients; however, in the short-term placebo-controlled studies, there was a higher incidence of systolic orthostatic hypotension in patients ≥65 years of age compared to patients <65 years of age treated with PRISTIQ *[see Adverse Reactions (6) in the full prescribing information]*. For elderly patients, possible reduced renal clearance of PRISTIQ should be considered when determining dose *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.3) in the full prescribing information]*. SSRIs and SNRIs, including PRISTIQ, have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event *[see Warnings and Precautions (5.9) in the full prescribing information]*. **Renal Impairment**—In subjects with renal impairment the clearance of PRISTIQ was decreased. In subjects with severe renal impairment (24-hr CrCl <30 mL/min, Cockcroft-Gault) and end-stage renal disease, elimination half-lives were significantly prolonged, increasing exposures to PRISTIQ; therefore, dosage adjustment is recommended in these patients *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.3) in the full prescribing information]*. **Hepatic Impairment**—The mean terminal half life ($t_{1/2}$) changed from approximately 10 hours in healthy subjects and subjects with mild hepatic impairment to 13 and 14 hours in moderate and severe hepatic impairment, respectively. The recommended dose in patients with moderate to severe hepatic impairment is 50 mg/day. Dose escalation above 100 mg/day is not recommended *[see Clinical Pharmacology (12.3) in the full prescribing information]*.

DRUG ABUSE AND DEPENDENCE: Controlled Substance—PRISTIQ is not a controlled substance.

OVERDOSAGE: Human Experience with Overdosage—There is limited clinical trial experience with desvenlafaxine succinate overdosage in humans. However, desvenlafaxine (PRISTIQ) is the major active metabolite of venlafaxine. Overdose experience reported with venlafaxine (the parent drug of PRISTIQ) is presented below; the identical information can be found in the *Overdosage* section of the venlafaxine package insert. In postmarketing experience, overdose with venlafaxine (the parent drug of PRISTIQ) has occurred predominantly in combination with alcohol and/or other drugs. The most commonly reported events in overdosage include tachycardia, changes in level of consciousness (ranging from somnolence to coma), mydriasis, seizures, and vomiting. Electrocardiogram changes (e.g., prolongation of QT interval, bundle branch block, QRS prolongation), sinus and ventricular tachycardia, bradycardia, hypotension, rhabdomyolysis, vertigo, liver necrosis, serotonin syndrome, and death have been reported. Published retrospective studies report that venlafaxine overdosage may be associated with an increased risk of fatal outcomes compared to that observed with SSRI antidepressant products, but lower than that for tricyclic antidepressants. Epidemiological studies have shown that venlafaxine-treated patients have a higher pre-existing burden of suicide risk factors than SSRI-treated patients. The extent to which the finding of an increased risk of fatal outcomes can be attributed to the toxicity of venlafaxine in overdosage, as opposed to some characteristic(s) of venlafaxine-treated patients, is not clear. **Management of Overdosage**—No specific antidotes for PRISTIQ are known. In managing over dosage, consider the possibility of multiple drug involvement. In case of overdose, call Poison Control Center at 1-800-222-1222 for latest recommendations.

This brief summary is based on PRISTIQ Prescribing Information LAB-0452-8.0, revised February 2013.

Help your adult patients with Major Depressive Disorder (MDD) toward their treatment goals

GO forward with Pristiq® (desvenlafaxine)

Results from PRISTIQ 50 mg clinical studies:

- An SNRI with proven efficacy[1]
- Significant improvement in the Sheehan Disability Scale* total score vs placebo, comprising 3 domains: work, social life/leisure activities, and family life/home responsibilities[2]
- Discontinuation rate due to adverse reactions comparable to placebo (4.1% vs 3.8%, respectively)[3]
- The most commonly observed adverse reactions in patients taking PRISTIQ (incidence ≥5% and ≥2x the rate of placebo) were nausea, dizziness, hyperhidrosis, constipation, and decreased appetite

*A validated, self-rated measure of functional impairment.[4]

To learn more about PRISTIQ, go to www.pristiqhcp.com

PRISTIQ Extended-Release Tablets are indicated for the treatment of major depressive disorder in adults.

Important Safety Information for PRISTIQ

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term studies. These studies did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in patients over age 24; there was a reduction in risk with antidepressant use in patients aged 65 and older.

In patients of all ages who are started on antidepressant therapy, monitor closely for worsening, and for emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber.

PRISTIQ is not approved for use in pediatric patients.

Contraindications

- PRISTIQ is contraindicated in patients with a known hypersensitivity to PRISTIQ or venlafaxine. Angioedema has been reported in patients treated with PRISTIQ.
- **Serotonin syndrome and MAOIs:** Do not use MAOIs intended to treat psychiatric disorders with PRISTIQ or within 7 days of stopping treatment with PRISTIQ. Do not use PRISTIQ within 14 days of stopping an MAOI intended to treat psychiatric disorders. In addition, do not start PRISTIQ in a patient who is being treated with an MAOI such as linezolid or intravenous methylene blue.

Selected Warnings and Precautions

- **All patients treated with antidepressants should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the first few months of treatment and when changing the dose.** Consider changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse or includes symptoms of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, mania, or suicidality that are severe, abrupt in onset, or were not part of the patient's presenting symptoms. **Families and caregivers of patients being treated with antidepressants should be alerted about the need to monitor patients.**
- The development of a potentially life-threatening serotonin syndrome has been reported with SSRIs and SNRIs, including with PRISTIQ, both when taken alone, but especially when co-administered with other serotonergic agents (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort) and with drugs that impair metabolism of serotonin (in particular, MAOIs, both those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue). If such events occur, immediately discontinue PRISTIQ and any concomitant serotonergic agents, and initiate supportive treatment. If concomitant use of PRISTIQ with other serotonergic drugs is clinically warranted, patients should be made aware of a potential increased risk for serotonin syndrome, particularly during treatment initiation and dose increase.
- Patients receiving PRISTIQ should have regular monitoring of blood pressure, since increases in blood pressure were observed in clinical studies. Pre-existing hypertension should be controlled before starting PRISTIQ. Caution should be exercised in treating patients with pre-existing hypertension, cardiovascular or cerebrovascular conditions that might be compromised by increases in blood pressure. Cases of elevated blood pressure requiring immediate treatment have been reported. For patients who experience a sustained increase in blood pressure, either dose reduction or discontinuation should be considered.
- SSRIs and SNRIs, including PRISTIQ, may increase the risk of bleeding events. Concomitant use of aspirin, NSAIDs, warfarin, and other anticoagulants may add to this risk.
- Mydriasis has been reported in association with PRISTIQ; therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma (angle-closure glaucoma) should be monitored.
- PRISTIQ is not approved for use in bipolar depression. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine the risk of bipolar disorder.
- PRISTIQ should be used cautiously in patients with a history or family history of mania or hypomania or with a history of seizure disorder.
- On discontinuation, adverse events, some of which may be serious, have been reported with PRISTIQ and other SSRIs and SNRIs. Abrupt discontinuation of PRISTIQ has been associated with the appearance of new symptoms. Patients should be monitored for symptoms when discontinuing treatment. A gradual reduction in dose rather than abrupt cessation is recommended whenever possible.
- Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including PRISTIQ. Discontinuation of PRISTIQ should be considered in patients with symptomatic hyponatremia.
- Interstitial lung disease and eosinophilic pneumonia associated with venlafaxine (the parent drug of PRISTIQ) therapy have been rarely reported.

Adverse Reactions

- The most commonly observed adverse reactions in patients taking PRISTIQ vs placebo for MDD in short-term fixed-dose premarketing studies (incidence ≥5% and at least twice the rate of placebo in the 50-mg dose group) were nausea (22% vs 10%), dizziness (13% vs 5%), hyperhidrosis (10% vs 4%), constipation (9% vs 4%), and decreased appetite (5% vs 2%).

Pristiq® desvenlafaxine 50 mg
EXTENDED-RELEASE TABLETS

References: 1. Thase ME, Kornstein SG, Germain JM, Jiang Q, Guico-Pabia C, Ninan PT. An integrated analysis of the efficacy of desvenlafaxine compared with placebo in patients with major depressive disorder. *CNS Spectr.* 2009;14(3):144-154. **2.** Soares CN, Kornstein SG, Thase ME, Jiang Q, Guico-Pabia CJ. Assessing the efficacy of desvenlafaxine for improving functioning and well-being outcome measures in patients with major depressive disorder: a pooled analysis of 9 double-blind, placebo-controlled, 8-week clinical trials. *J Clin Psychiatry.* 2009;70(10):1365-1371. **3.** Clayton AH, Kornstein SG, Rosas G, Guico-Pabia C, Tourian KA. An integrated analysis of the safety and tolerability of desvenlafaxine compared with placebo in the treatment of major depressive disorder. *CNS Spectr.* 2009;14(4):183-195. **4.** Leon AC, Olfson M, Portera L, Farber L, Sheehan DV. Assessing psychiatric impairment in primary care with the Sheehan Disability Scale. *Int J Psychiatry Med.* 1997;27:93-105.

Please see brief summary of Prescribing Information on adjacent pages.