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The First and Last Word in Psychiatry

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AP Photo/Andrew Gombert, Pool

A woman comforts a young girl during a vigil service for victims of the Sandy Hook Elementary School shooting in Newtown, Conn., on December 14. Connecticut Psychiatric Society members were among those who offered their services to the grieving community.

Psychiatrists Provide Help, Advice Following Newtown School Murders

Local psychiatrists volunteer to help Newtown, Conn., residents recover from last month's shooting tragedy.

BY AARON LEVIN

The Connecticut Psychiatric Society (CPS) reacted swiftly to the tragic shooting at Sandy Hook Elementary School in Newtown, Conn., on Friday, December 14.

Society President John Santopietro, M.D., and Disaster Committee Chair Shaukat Khan, M.D., consulted that afternoon with APA experts including members of APA's Committee on the Psychiatric Dimensions of Disasters.

Within hours, 100 society members responded to Santopietro's e-mail requesting volunteers to help in the stricken town.

Meanwhile, Khan contacted the Red Cross and the Connecticut State Medical Society to let them know about the CPS volunteers. Khan was already registered with the Red Cross as a mental health volunteer.

By coincidence, the CPS had conducted a disaster-response training session for members just a month earlier. That course was led by Frederick Stoddard, M.D., a clinical professor of psychiatry at Harvard Medical School and a psychiatrist at Massachusetts General Hospital. Stoddard is coauthor with Anand Pandya, M.D., and Craig Katz, M.D., of *Disaster Psychiatry Readiness, Evaluation, and Treatment* (American Psychiatric Publishing).

The class covered such points as the psychiatric impact of disasters, grief and resilience, psychological first aid, and the postacute stages of a disaster.

"The training helped prepare us for the situation at Newtown, but, of course, not entirely," said Khan, a psychiatrist at the VA Connecticut Health System

see ***Psychiatrists*** *on page 28*

Resilience, No Depression Best Predict Successful Aging

Community-dwelling older adults who have resilience and have been free from depression report "successful aging" even in the face of physical and cognitive decline.

BY MARK MORAN

Individuals who score high on a resilience scale and who did not suffer from clinical depression also reported high rates of "successful aging" even in the face of worsening physical and/or cognitive functioning.

And—even more surprising—the older the adult, the more likely he or she was to report a high degree of successful aging. In fact, older age was associated with a higher rating of successful aging, despite worsening physical and cognitive functioning, according to a report appearing online in the December 7, 2012, *AJP in Advance*.

The findings from a survey of community-dwelling older adults upend the stereotype of old age as an unhappy experience. "It was clear to us that, even in the midst of physical or cognitive decline, individuals in our study reported feeling that their well-being had improved with age," lead author and APA President Dilip Jeste, M.D., told *Psychiatric News*. "This counterintuitive increase in well-being with aging persisted even after accounting for variables like income, education, and marriage."

In the Successful Aging Evaluation

see ***Aging*** *on page 30*

PERIODICALS: TIME SENSITIVE MATERIALS

INSIDE

NOW AVAILABLE

Keep It Simple

New Forfivo™ XL provides a once-daily, bupropion 450 mg dose in a single tablet:

- Indicated for the treatment of major depressive disorder
- Forfivo XL is bioequivalent to three 150 mg tablets of Wellbutrin XL®[1]
- Rx Savings Program will automatically limit 30-day Rx cost to $28 for most commercial drug plan patients[2]

Do not initiate bupropion therapy with Forfivo XL because the 450 mg tablet is the only available dosage strength. Use a lower-dose bupropion product for therapy initiation and dose titration.

NEW! ONCE-DAILY **450 MG**

Forfivo™ XL

(bupropion hydrochloride extended-release tablets)

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IMPORTANT SAFETY INFORMATION FOR FORFIVO XL

WARNING: SUICIDALITY and ANTIDEPRESSANT DRUGS; PSYCHIATRIC EVENTS and SMOKING CESSATION
SUICIDALITY and ANTIDEPRESSANT DRUGS: Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. FORFIVO XL is not approved for use in pediatric patients.
PSYCHIATRIC EVENTS and SMOKING CESSATION: FORFIVO XL is not approved for smoking cessation treatment, but bupropion under the name ZYBAN® is approved for this use. Serious neuropsychiatric events, including but not limited to depression, suicidal ideation, suicide attempt, and completed suicide have been reported in patients taking bupropion for smoking cessation. Advise patients and caregivers that the patient using bupropion for smoking cessation should stop taking bupropion and contact a healthcare provider immediately if agitation, hostility, depressed mood, or changes in thinking or behavior that are not typical for the patient are observed, or if the patient develops suicidal ideation or suicidal behavior.

CONTRAINDICATIONS

FORFIVO XL is contraindicated in:

- **Seizure disorder, because these patients may have a lower seizure threshold**
- **Patients treated currently with other bupropion products, because seizure incidence is dose-dependent**
- **A current or prior diagnosis of bulimia or anorexia nervosa**
- **Patients undergoing abrupt discontinuation of alcohol or sedatives**
- **Concurrent administration of monoamine oxidase (MAO) inhibitors.** At least 14 days should elapse between discontinuation of an MAO inhibitor and initiation of treatment with FORFIVO XL.
- **Known hypersensitivity to bupropion or the other ingredients of FORFIVO XL**

WARNINGS AND PRECAUTIONS

Activation of Mania/Hypomania A major depressive episode may be the initial presentation of bipolar disorder. 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 FORFIVO XL is not approved for use in treating bipolar depression. **Seizures** Bupropion is associated with a dose-related risk of seizures. The risk of seizures is also related to patient factors, clinical situations, and concomitant medications, which must be considered in selection of patients for therapy with FORFIVO XL. FORFIVO XL should be discontinued and not restarted in patients who experience a seizure while on treatment. Retrospective analysis of clinical experience gained during the development of bupropion suggests that the risk of seizure may be minimized if the total daily dose of bupropion does not exceed 450 mg and the rate of incrementation of the bupropion dose is gradual. **Psychosis and Other Neuropsychiatric Events** Depressed patients treated with bupropion have been reported to show a variety of neuropsychiatric signs and symptoms, including delusions, hallucinations, psychosis, concentration disturbance, paranoia, and confusion. In some cases, these symptoms abated upon dose reduction and/or withdrawal of treatment. It is recommended stopping bupropion when the symptoms occur. **Severe Hypertension** In clinical practice, hypertension, in some cases severe, requiring acute treatment, has been reported in patients receiving bupropion alone and in combination with nicotine replacement therapy. These reactions have been observed in both patients with and without evidence of preexisting hypertension. Monitoring of blood pressure is recommended in patients who receive the combination of bupropion and nicotine replacement. **Agitation and Insomnia** Increased restlessness, agitation, anxiety, and insomnia, especially shortly after initiation of treatment, have been associated with treatment with bupropion. In clinical studies of MDD, these symptoms (see **Table 2** of the full prescribing information) were sometimes of sufficient magnitude to require treatment with sedative/hypnotic drugs. Symptoms in these studies were sufficiently severe to require discontinuation of treatment in 1% and 2.6% of patients treated with 300 and 400 mg/day, respectively, of bupropion hydrochloride sustained-release tablets and 0.8% of patients treated with placebo. **Altered Appetite and Weight** In placebo-controlled short-term studies of MDD using the sustained-release formulation of bupropion hydrochloride, patients experienced weight gain or weight loss (see **Table 3** of the full prescribing information). In studies conducted with the immediate-release formulation of bupropion hydrochloride, 35% of patients receiving tricyclic antidepressants gained weight, compared to 9% of patients treated with the immediate-release formulation of bupropion hydrochloride. If weight loss is a major presenting sign of a patient's depressive illness, the anorectic and/or weight-reducing potential of FORFIVO XL tablets should be considered. **Hypersensitivity Reactions** Anaphylactoid/anaphylactic reactions characterized by symptoms such as pruritus, urticaria, angioedema, and dyspnea requiring medical treatment have been reported in clinical trials with bupropion. In addition, there have been rare spontaneous postmarketing reports of erythema multiforme, Stevens-Johnson syndrome, and anaphylactic shock associated with bupropion. A patient should stop taking FORFIVO XL and consult a doctor if experiencing allergic or anaphylactoid/anaphylactic reactions (e.g., skin rash, pruritus, hives, chest pain, edema, and shortness of breath) during treatment. Arthralgia, myalgia, and fever with rash and other symptoms suggestive of delayed hypersensitivity have been reported in association with bupropion. These symptoms may resemble serum sickness [see ***Contraindications*** in the full prescribing information].

ADVERSE REACTIONS

Clinical Trials Experience: Commonly Observed Adverse Reactions in Controlled Clinical Trials The most common adverse reactions were (incidence ≥ 5%; ≥ 2 times placebo rate): Dry mouth, nausea, insomnia, dizziness, pharyngitis, abdominal pain, agitation, anxiety, tremor, palpitation, sweating, tinnitus, myalgia, anorexia, urinary frequency, and rash.

Please see brief summary of Prescribing Information, including complete Boxed Warnings, on the following pages.

[1]Wellbutrin XL is a registered trademark of GlaxoSmithKline.

[2]Maximum savings benefit per Rx is $35. Certain patient groups are not eligible for this Rx Savings Program (e.g., federal healthcare programs, including Medicare or Medicaid, Medicare Part D prescription drug plans, or by any similar federal or state program, including a state pharmaceutical assistance program, etc.). Cash-paying patients and Massachusetts patients are eligible but will require a physical Rx savings card.

EDGEMONT® PHARMACEUTICALS

FF0070_JA

FORFIVO XL (bupropion hydrochloride extended-release tablets), for oral use
Brief Summary: Consult package insert for full prescribing information

WARNING: SUICIDALITY and ANTIDEPRESSANT DRUGS; PSYCHIATRIC EVENTS and SMOKING CESSATION

SUICIDALITY and ANTIDEPRESSANT DRUGS: Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of FORFIVO XL or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. 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 in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. FORFIVO XL is not approved for use in pediatric patients *[see Warnings and Precautions]*.

PSYCHIATRIC EVENTS and SMOKING CESSATION: FORFIVO XL is not approved for smoking cessation treatment, but bupropion under the name ZYBAN® is approved for this use. Serious neuropsychiatric events, including but not limited to depression, suicidal ideation, suicide attempt, and completed suicide have been reported in patients taking bupropion for smoking cessation. Some cases may have been complicated by the symptoms of nicotine withdrawal in patients who stopped smoking. Depressed mood may be a symptom of nicotine withdrawal. Depression, rarely including suicidal ideation, has been reported in smokers undergoing a smoking cessation attempt without medication. However, some of these symptoms have occurred in patients taking bupropion who continued to smoke. All patients being treated with bupropion for smoking cessation treatment should be observed for neuropsychiatric symptoms including changes in behavior, hostility, agitation, depressed mood, and suicide-related events, including ideation, behavior, and attempted suicide. These symptoms, as well as worsening of pre-existing psychiatric illness and completed suicide have been reported in some patients attempting to quit smoking while taking ZYBAN in the postmarketing experience. When symptoms were reported, most were during treatment with ZYBAN, but some were following discontinuation of treatment with ZYBAN. These events have occurred in patients with and without pre-existing psychiatric disease; some have experienced worsening of their psychiatric illnesses. Patients with serious psychiatric illness such as schizophrenia, bipolar disorder, and major depressive disorder did not participate in the premarketing studies of ZYBAN. Advise patients and caregivers that the patient using bupropion for smoking cessation should stop taking bupropion and contact a healthcare provider immediately if agitation, hostility, depressed mood, or changes in thinking or behavior that are not typical for the patient are observed, or if the patient develops suicidal ideation or suicidal behavior. In many postmarketing cases, resolution of symptoms after discontinuation of ZYBAN was reported, although in some cases the symptoms persisted; therefore, ongoing monitoring and supportive care should be provided until symptoms resolve. The risks of using bupropion for smoking cessation should be weighed against the benefits of its use. ZYBAN has been demonstrated to increase the likelihood of abstinence from smoking for as long as 6 months compared to treatment with placebo. The health benefits of quitting smoking are immediate and substantial *[see Warnings and Precautions and Patient Counseling Information]*.

INDICATIONS AND USAGE: FORFIVO XL (bupropion hydrochloride extended-release tablets) is indicated for the treatment of major depressive disorder (MDD). The efficacy in the treatment of MDD was established in two 4-week and one 6-week and one maintenance trial in adult patients whose diagnoses corresponded most closely to the Major Depression category of the APA Diagnostic and Statistical Manual (DSM) *[see Clinical Studies]*. A major depressive episode (DSM-IV) implies the presence of 1) depressed mood or 2) loss of interest or pleasure; in addition, at least 5 of the following symptoms have been present during the same 2-week period and represent a change from previous functioning: depressed mood, markedly diminished interest or pleasure in usual activities, significant change in weight and/or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, a suicide attempt, or suicidal ideation. The efficacy of bupropion in pediatric population has not been established. The physician who elects to use FORFIVO XL for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient. **CONTRAINDICATIONS:** FORFIVO XL is contraindicated in patients with the following: seizure disorder because these patients may have a lower seizure threshold; patients treated currently with other bupropion products because the incidence of seizure is dose dependent; a current or prior diagnosis of bulimia or anorexia nervosa because of a higher incidence of seizures noted in patients treated for bulimia with the immediate-release formulation of bupropion in a pre-marketing clinical trial; patients undergoing abrupt discontinuation of alcohol or sedatives because of a lower seizure threshold in these conditions; concurrent administration of monoamine oxidase (MAO) inhibitors because MAOIs potentially can enhance the CNS toxicity, at least 14 days should elapse between discontinuation of an MAO inhibitor and initiation of treatment with FORFIVO XL; and known hypersensitivity to bupropion or the other ingredients of FORFIVO XL tablets. Anaphylactoid/anaphylactic reactions and Stevens-Johnson syndrome have been reported *[see Warnings and Precautions]*.

WARNINGS AND PRECAUTIONS: Clinical Worsening and Suicide Risk in Treating Psychiatric Disorder Patients with 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 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 trials of antidepressant drugs (SSRIs and others) show that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with 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 trials in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4,400 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (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) are provided in Table 1.

Table 1. Drug-Placebo Difference in Number of Cases of Suicidality per 1000 Patients Treated

Age Range	
Increases Compared to Placebo	
<18	14 additional cases
18–24	5 additional cases
Decreases Compared to Placebo	
25–64	1 fewer case
≥65	6 fewer cases

No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, 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 trials 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 *[see Boxed Warning and Use in Specific Populations]*. 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 MDD 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. Families and caregivers of patients being treated with antidepressants for MDD 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 health care providers. Such monitoring should include daily observation by families and caregivers *[see Patient Counseling Information]*. Prescriptions for FORFIVO XL should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. **Neuropsychiatric Symptoms and Suicide Risk in Smoking Cessation Treatment** FORFIVO XL is not approved for smoking cessation treatment, but bupropion under the name ZYBAN is approved for this use. Serious neuropsychiatric symptoms have been reported in patients taking bupropion for smoking cessation *[see Boxed Warning and Adverse Reactions]*. These have included changes in mood (including depression and mania), psychosis, hallucinations, paranoia, delusions, homicidal ideation, hostility, agitation, aggression, anxiety, and panic, as well as suicidal ideation, suicide attempt, and completed suicide *[see Patient Counseling Information]*. **Activation of Mania/Hypomania** A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) 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. 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 FORFIVO XL is not approved for use in treating bipolar depression. **Seizures** Bupropion is associated with a dose-related risk of seizures. The risk of seizures is also related to patient factors, clinical situations, and concomitant medications, which must be considered in selection of patients for therapy with FORFIVO XL. FORFIVO XL should be discontinued and not restarted in patients who experience a seizure while on treatment. Dose: At doses up to 300 mg/day of the sustained-release formulation of bupropion hydrochloride (WELLBUTRIN SR®), the incidence of seizure is approximately 0.1% (1/1,000). Data for the immediate-release formulation of bupropion hydrochloride revealed a seizure incidence of approximately 0.4% (i.e., 13 of 3,200 patients followed prospectively) in patients treated at doses in a range of 300 to 450 mg/day. This seizure incidence (0.4%) may exceed that of some other marketed antidepressants. Additional data accumulated for the immediate-release formulation of bupropion hydrochloride suggested that the estimated seizure incidence increases almost tenfold between 450 and 600 mg/day. The 600 mg dose is twice the usual adult dose and one and one-third the maximum recommended daily dose (450 mg) of FORFIVO XL. This disproportionate increase in seizure incidence with dose incrementation calls for caution in dosing. Patient Factors: Predisposing factors that may increase the risk of seizure with bupropion use include history of head trauma or prior seizure, central nervous system (CNS) tumor, the presence of severe hepatic cirrhosis, and concomitant medications that lower seizure threshold. Clinical Situations: Circumstances associated with an increased seizure risk include, among others, excessive use of alcohol or sedatives; addiction to opiates, cocaine, or stimulants; use of over-the-counter stimulants and anorectics; and diabetes treated with oral hypoglycemics or insulin. Concomitant Medications: Many medications (e.g., antipsychotics, antidepressants, theophylline, and systemic steroids) are known to lower seizure threshold. Recommendations for Reducing the Risk of Seizure: Retrospective analysis of clinical experience gained during the development of bupropion suggests that the risk of seizure may be minimized if the total daily dose of bupropion does not exceed 450 mg, the rate of incrementation of the bupropion dose is gradual. **Psychosis and Other Neuropsychiatric Events** Depressed patients treated with bupropion have been reported to show a variety of neuropsychiatric signs and symptoms, including delusions, hallucinations, psychosis, concentration disturbance, paranoia, and confusion. In some cases, these symptoms abated upon dose reduction and/or withdrawal of treatment. It is recommended stopping bupropion when the symptoms occurred. **Severe Hypertension** In clinical practice, hypertension, in some cases severe, requiring acute treatment, has been reported in patients receiving bupropion alone and in combination with nicotine replacement therapy. These reactions have been observed in both patients with and without evidence of preexisting hypertension. Data from a comparative study of the sustained-release formulation of bupropion hydrochloride (ZYBAN® Sustained-Release Tablets), nicotine transdermal system (NTS), the combination of sustained-release bupropion hydrochloride plus NTS, and placebo as an aid to smoking cessation suggest a higher incidence of treatment-emergent hypertension in patients treated with the combination of sustained-release bupropion hydrochloride and NTS. Monitoring of blood pressure is recommended in patients who receive the combination of bupropion and nicotine replacement. There is no clinical experience establishing the safety of FORFIVO XL tablets in patients with a recent history of myocardial infarction or unstable heart disease. Therefore, care should be exercised if it is used in these groups. Bupropion was well tolerated in depressed patients who had previously developed orthostatic hypotension while receiving tricyclic antidepressants, and was also generally well tolerated in a group of 36 depressed inpatients with stable congestive heart failure (CHF). However, bupropion was associated with a rise in supine blood pressure in the study of patients with CHF, resulting in discontinuation of treatment in 2 patients for exacerbation of baseline hypertension. **Agitation and Insomnia** Increased restlessness, agitation, anxiety, and insomnia, especially shortly after initiation of treatment, have been associated with treatment with bupropion. Patients in placebo-controlled trials of MDD with sustained-release formulation of bupropion hydrochloride, experienced agitation, anxiety, and insomnia as shown in Table 2.

Table 2. Incidence of Agitation, Anxiety, and Insomnia in Placebo-Controlled Trials of Bupropion HCl Sustained-release Tablets for Major Depressive Disorder

Adverse Reactions Term	Bupropion HCl 300 mg/day (n = 376)	Bupropion HCl 400 mg/day (n = 114)	Placebo (n = 385)
Agitation	3%	9%	2%
Anxiety	5%	6%	3%
Insomnia	11%	16%	6%

In clinical studies of MDD, these symptoms were sometimes of sufficient magnitude to require treatment with sedative/hypnotic drugs. Symptoms in these studies were sufficiently severe to require discontinuation of treatment in 1% and 2.6% of patients treated with 300 and 400 mg/day, respectively, of bupropion hydrochloride sustained-release tablets and 0.8% of patients treated with placebo. **Altered Appetite and Weight** In placebo-controlled short-term studies of MDD using the sustained-release formulation of bupropion hydrochloride, patients experienced weight gain or weight loss as shown in Table 3.

Table 3. Incidence of Weight Gain and Weight Loss in Placebo-Controlled Trials of Bupropion Hydrochloride Sustained-release tablets for Major Depressive Disorder

Weight Change	Bupropion HCl 300 mg/day (n = 339)	Bupropion HCl 400 mg/day (n = 112)	Placebo (n = 347)
Gained >5 lbs	3%	2%	4%
Lost >5 lbs	14%	19%	6%

In studies conducted with the immediate-release formulation of bupropion hydrochloride, 35% of patients receiving tricyclic antidepressants gained weight, compared to 9% of patients treated with the immediate-release formulation of bupropion hydrochloride. If weight loss is a major presenting sign of a patient's depressive illness, the anorectic and/or weight-reducing potential of FORFIVO XL tablets should be considered. **Hypersensitivity Reactions** Anaphylactoid/anaphylactic reactions characterized by symptoms such as pruritus, urticaria, angioedema, and dyspnea requiring medical treatment have been reported in clinical trials with bupropion. In addition, there have been rare spontaneous postmarketing reports of erythema multiforme, Stevens-Johnson syndrome, and anaphylactic shock associated with bupropion. A patient should stop taking FORFIVO XL and consult a doctor if experiencing allergic or anaphylactoid/anaphylactic reactions (e.g., skin rash, pruritus, hives, chest pain, edema, and shortness of breath) during treatment. Arthralgia, myalgia, and fever with rash and other symptoms suggestive of delayed hypersensitivity have been reported in association with bupropion. These symptoms may resemble serum sickness *[see Contraindications]*.

ADVERSE REACTIONS: The following risks are discussed in greater detail in other sections of the full prescribing information *[see Warnings and Precautions]*: clinical worsening and suicide risk, neuropsychiatric symptoms and suicide risk in smoking cessation treatment, activation of mania or hypomania, seizures, psychosis, and other neuropsychiatric events, severe hypertension, agitation and insomnia, altered appetite and weight, hypersensitivity reactions. **Clinical Trials Experience** Commonly Observed Adverse Reactions in Controlled Clinical Trials. 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 clinical practice. Adverse reactions from Table 5 occurring in at least 5% of patients treated with the sustained-release formulation of bupropion hydrochloride and at a rate at least twice the placebo rate are listed below for the 300- and 400-mg/day dose groups. 300 mg/day of bupropion sustained release: anorexia, dry mouth, rash, sweating, tinnitus, and tremor. 400 mg/day of bupropion sustained release: abdominal pain, agitation, anxiety, dizziness, dry mouth, insomnia, myalgia, nausea, palpitation, pharyngitis, sweating, tinnitus, and urinary frequency. FORFIVO XL is bioequivalent to three 150 mg tablets of WELLBUTRIN XL®, which has been demonstrated to have similar bioavailability both to the immediate-release formulation of bupropion and to the sustained-release formulation of bupropion. The information included under this subsection and under subsections 6.2 and 6.3 of the full prescribing information is based primarily on data from controlled clinical trials with the sustained-release formulation of bupropion hydrochloride. Adverse Reactions Leading to Discontinuation of Treatment with Bupropion Immediate Release or Bupropion Sustained Release. In placebo-controlled clinical trials, 9% and 11% of patients treated with 300 and 400 mg/day, respectively, of the sustained-release formulation of bupropion hydrochloride and 4% of patients treated with placebo discontinued treatment due to adverse reactions. The specific adverse reactions in these trials that led to discontinuation in at least 1% of patients treated with either 300 mg/day or 400 mg/day of the sustained-release formulation of bupropion hydrochloride, and at a rate at least twice the placebo rate are listed in Table 4.

Table 4. Treatment Discontinuations Due to Adverse Reactions in Placebo-Controlled Trials for Major Depressive Disorder using Bupropion Hydrochloride Sustained Release Formulation

Adverse Reaction	Bupropion HCl 300 mg/day (n = 376)	Bupropion HCl 400 mg/day (n = 114)	Placebo (n = 385)
Rash	2.4%	0.9%	0.0%
Nausea	0.8%	1.8%	0.3%
Agitation	0.3%	1.8%	0.3%
Migraine	0.0%	1.8%	0.3%

In clinical trials with the immediate-release formulation of bupropion, 10% of patients and volunteers discontinued due to an adverse reaction. Reactions resulting in discontinuation, in addition to those listed above for the sustained-release formulation of bupropion hydrochloride, include vomiting, seizures, and sleep disturbances. Adverse Reactions Occurring at an Incidence of 1% or More Among Patients Treated With Bupropion Immediate Release or Bupropion Sustained Release. Table 5 enumerates adverse reactions that occurred among patients treated with 300 and 400 mg/day of the sustained-release formulation of bupropion hydrochloride and with placebo in controlled trials. Reactions that occurred in either the 300- or 400-mg/day group at an incidence of 1% or more and were more frequent than in the placebo group are included. Reported adverse reactions were classified using a COSTART-based Dictionary. Accurate estimates of the incidence of adverse reactions associated with the use of any drug are difficult to obtain. Estimates are influenced by drug dose, detection technique, setting, physician judgments, etc. The figures cited cannot be used to predict precisely the incidence of untoward reactions in the course of usual medical practice where patient characteristics and other factors differ from those that prevailed in the clinical trials. These incidence figures also cannot be compared with those obtained from other clinical studies involving related drug products as each group of drug trials is conducted under a different set of conditions. Finally, it is important to emphasize that the tabulation does not reflect the relative severity and/or clinical importance of the reactions. A better perspective on the serious adverse reactions associated with the use of bupropion is provided in the **Warnings and Precautions**.

Table 5. Adverse Reactions in Placebo-Controlled Trials* for Major Depressive Disorder

Body System/Adverse Reaction	Bupropion HCl 300 mg/day (n = 376)	Bupropion HCl 400 mg/day (n = 114)	Placebo (n = 385)
Body (General)			
Headache	26%	25%	23%
Infection	8%	9%	6%
Abdominal pain	3%	9%	2%
Asthenia	2%	4%	2%

Chest pain	3%	4%	1%
Pain	2%	3%	2%
Fever	1%	2%	–
Cardiovascular			
Palpitation	2%	6%	2%
Flushing	1%	4%	–
Migraine	1%	4%	1%
Hot flashes	1%	3%	1%
Digestive			
Dry mouth	17%	24%	7%
Nausea	13%	18%	8%
Constipation	10%	5%	7%
Diarrhea	5%	7%	6%
Anorexia	5%	3%	2%
Vomiting	4%	2%	2%
Dysphagia	0%	2%	0%
Musculoskeletal			
Myalgia	2%	6%	3%
Arthralgia	1%	4%	1%
Arthritis	0%	2%	0%
Twitch	1%	2%	–
Nervous System			
Insomnia	11%	16%	6%
Dizziness	7%	11%	5%
Agitation	3%	9%	2%
Anxiety	5%	6%	3%
Tremor	6%	3%	1%
Nervousness	5%	3%	3%
Somnolence	2%	3%	2%
Irritability	3%	2%	2%
Memory decreased	–	3%	1%
Paresthesia	1%	2%	1%
Central nervous system stimulation	2%	1%	1%
Respiratory			
Pharyngitis	3%	11%	2%
Sinusitis	3%	1%	2%
Increased cough	1%	2%	1%
Skin			
Sweating	6%	5%	2%
Rash	5%	4%	1%
Pruritus	2%	4%	2%
Urticaria	2%	1%	0%
Special Senses			
Tinnitus	6%	6%	2%
Taste perversion	2%	4%	–
Blurred vision or diplopia	3%	2%	2%
Urogenital			
Urinary frequency	2%	5%	2%
Urinary urgency	–	2%	0%
Vaginal hemorrhage†	0%	2%	–
Urinary tract infection	1%	0%	–

* Adverse reactions that occurred in at least 1% of patients treated with either 300 or 400 mg/day of the sustained-release formulation of bupropion hydrochloride, but equally or more frequently in the placebo group, were: abnormal dreams, accidental injury, acne, appetite increased, back pain, bronchitis, dysmenorrhea, dyspepsia, flatulence, flu syndrome, hypertension, neck pain, respiratory disorder, rhinitis, and tooth disorder.

† Incidence based on the number of female patients.

— Hyphen denotes adverse reactions occurring in greater than 0 but less than 0.5% of patients.

Additional reactions to those listed in Table 5 that occurred at an incidence of at least 1% in controlled clinical trials of the immediate-release formulation of bupropion hydrochloride (300 to 600 mg/day) and that were numerically more frequent than placebo were: cardiac arrhythmias (5% vs. 4%), hypertension (4% vs. 2%), hypotension (3% vs. 2%), tachycardia (11% vs. 9%), appetite increase (4% vs. 2%), dyspepsia (3% vs. 2%), menstrual complaints (5% vs. 1%), akathisia (2% vs. 1%), impaired sleep quality (4% vs. 2%), sensory disturbance (4% vs. 3%), confusion (8% vs. 5%), decreased libido (3% vs. 2%), hostility (6% vs. 4%), auditory disturbance (5% vs. 3%), and gustatory disturbance (3% vs. 1%). Other adverse reactions occurring < 1% in clinical trials: Chills, facial edema, postural hypotension, stroke, syncope, bruxism, gastric reflux, gingivitis, glossitis, increased salivation, mouth ulcers, stomatitis, edema of tongue, ecchymosis, edema, abnormal coordination, decreased libido, depersonalization, emotional lability, hyperkinesia, hypertonia, hypesthesia, ataxia, and derealization, bronchospasm, accommodation abnormality, dry eye, impotence, and prostate disorder. **Postmarketing Experience** The following adverse reactions have been identified during post-approval use of bupropion hydrochloride. 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. Only those adverse reactions not previously listed for bupropion are included. The extent to which these reactions may be associated with FORFIVO XL is unknown. **Cardiovascular**—complete atrioventricular block, extrasystoles, myocardial infarction, phlebitis, and pulmonary embolism. **Gastrointestinal**—colitis, esophagitis, gastrointestinal hemorrhage, gum hemorrhage, intestinal perforation, pancreatitis, and stomach ulcer. **Endocrine**—hyperglycemia, hypoglycemia, and syndrome of inappropriate antidiuretic hormone. **Hemic and Lymphatic**—anemia, leukocytosis, leukopenia, lymphadenopathy, pancytopenia, and thrombocytopenia. **Metabolic and Nutritional**—glycosuria. **Musculoskeletal**—muscle rigidity/fever/rhabdomyolysis and muscle weakness. **Nervous System**—abnormal electroencephalogram (EEG), aggression, akinesia, aphasia, coma, delirium, dysarthria, dyskinesia, dystonia, extrapyramidal syndrome, hypokinesia, increased libido, neuralgia, neuropathy, and unmasking tardive dyskinesia. **Skin**—alopecia, exfoliative dermatitis, and hirsutism. **Eye**—mydriasis. **Urogenital**—abnormal ejaculation, cystitis, dyspareunia, dysuria, gynecomastia, painful erection, salpingitis, urinary incontinence, and urinary retention.

DRUG INTERACTIONS: Few systemic data have been collected on the metabolism of bupropion following concomitant administration with other drugs or, alternatively, the effect of concomitant administration of bupropion on the metabolism of other drugs. **Potential for Other Drugs to Affect FORFIVO XL** Because bupropion is extensively metabolized, the coadministration of other drugs may affect its clinical activity. Substrates or Inhibitors/Inducers of Cytochrome P450IIB6 (CYP2B6): In vitro studies indicate that bupropion is primarily metabolized to hydroxybupropion by the CYP2B6 isoenzyme. Therefore, the potential exists for a drug interaction between FORFIVO XL and drugs that are substrates or inhibitors/inducers of the CYP2B6 isoenzyme (e.g., orphenadrine, thiotepa, cyclophosphamide, ticlopidine and clopidogrel). In addition, in vitro studies suggest that paroxetine, sertraline, norfluoxetine, and fluvoxamine as well as nelfinavir, inhibit the hydroxylation of bupropion. *Ticlopidine, Clopidogrel:* In a study in healthy male volunteers, 75 mg clopidogrel once daily or 250 mg ticlopidine twice daily increased exposures (C_{max} and AUC) of bupropion by 40% and 60% for clopidogrel, by 38% and 85% for ticlopidine, respectively. The exposures of hydroxybupropion were decreased. This effect is thought to be due to the inhibition of the CYP2B6-catalyzed bupropion hydroxylation. Coadministration of FORFIVO XL with ticlopidine or clopidogrel is not recommended. *Prasugrel:* Prasugrel is a weak inhibitor of CYP2B6. In healthy subjects, prasugrel increased C_{max} and AUC values of bupropion by 14% and 18%, respectively, and decreased C_{max} and AUC values of hydroxybupropion, an active metabolite of bupropion, by 32% and 24%, respectively. The inhibition of prasugrel on bupropion metabolism is not considered clinically significant. *Ritonavir, Lopinavir, Efavirenz:* In a series of studies in healthy volunteers, ritonavir (100 mg twice daily or 600 mg twice daily) or ritonavir 100 mg plus lopinavir (KALETRA) 400 mg twice daily reduced the exposure of bupropion and its major metabolites in a dose dependent manner by approximately 20% to 80%. Similarly, efavirenz 600 mg once daily for 2 weeks reduced the exposure of bupropion by approximately 55%. This effect is thought to be due to the induction of bupropion metabolism. Patients receiving any of these drugs with bupropion may need increased doses of bupropion, but the maximum recommended dose of bupropion should not be exceeded *[see Clinical Pharmacology]*. *Cimetidine:* The threohydrobupropion metabolite of bupropion does not appear to be produced by the cytochrome P450 isoenzymes. The effects of concomitant administration of cimetidine on the pharmacokinetics of bupropion and its active metabolites were studied in 24 healthy young male volunteers. Following oral administration of two 150-mg tablets of the sustained-release formulation of bupropion hydrochloride with and without 800 mg of cimetidine, the pharmacokinetics of bupropion and hydroxybupropion were unaffected. However, there were 16% and 32% increases in the AUC and C_{max}, respectively, of the combined moieties of threohydrobupropion and erythrohydrobupropion. *Carbamazepine, Phenobarbital, Phenytoin:* While not systematically studied, these drugs may induce the metabolism of bupropion. **Potential for FORFIVO XL to Affect Other Drugs** Animal data indicated that bupropion may be an inducer of drug-metabolizing enzymes in humans. In one study, following chronic administration of bupropion hydrochloride, 100 mg 3 times daily to 8 healthy male volunteers for 14 days, there was no evidence of induction of its own metabolism. Nevertheless, there may be the potential for clinically important alterations of blood levels of coadministered drugs. Lamotrigine: Multiple oral doses of bupropion had no statistically significant effects on the single dose pharmacokinetics of lamotrigine in 12 healthy volunteers. Drugs Metabolized by Cytochrome P450IID6 (CYP2D6). Many drugs, including most antidepressants (SSRIs, many tricyclics), beta-blockers, antiarrhythmics, and antipsychotics are metabolized by the CYP2D6 isoenzyme. Although bupropion is not metabolized by this isoenzyme, bupropion and hydroxybupropion are inhibitors of the CYP2D6 isoenzyme in vitro. In a study of 15 male subjects (ages 19 to 35 years) who were extensive metabolizers of the CYP2D6 isoenzyme, daily doses of bupropion hydrochloride given as 150 mg twice daily followed by a single dose of 50 mg desipramine increased the C_{max}, AUC, and $t_{1/2}$ of desipramine by an average of approximately 2-, 5-, and 2-fold, respectively. The effect was present for at least 7 days after the last dose of bupropion. Concomitant use of bupropion with other drugs metabolized by CYP2D6 has not been formally studied. Therefore, coadministration of bupropion with drugs that are metabolized by the CYP2D6 isoenzyme including certain antidepressants (e.g., venlafaxine, nortriptyline, imipramine, desipramine, paroxetine, fluoxetine, and sertraline), antipsychotics (e.g., haloperidol, risperidone, and thioridazine), beta-blockers (e.g., metoprolol), and Type 1C antiarrhythmics (e.g., propafenone and flecainide), should be approached with caution and should be initiated at the lower end of the dose range of the concomitant medication. If bupropion is added to the treatment regimen of a patient already receiving a drug metabolized by CYP2D6, the need to decrease the dose of the original medication should be considered, particularly for those concomitant medications with a narrow therapeutic index. CYP2D6 in order to be effective (e.g., tamoxifen) theoretically could have reduced efficacy when administered concomitantly with inhibitors of CYP2D6 such as bupropion. Although citalopram is not primarily metabolized by CYP2D6, in one study bupropion increased the C_{max} and AUC of citalopram by 30% and 40%, respectively. Citalopram did not affect the pharmacokinetics of bupropion and its three metabolites. **Nicotine Transdermal System** Data from a smoking cessation study suggest that a higher incidence of hypertension in patients who received the combination of sustained-release bupropion hydrochloride and NTS. Monitoring of blood pressure is recommended in patients who receive the combination of bupropion and nicotine replacement *[see Warnings and Precautions]*. **Drug Laboratory Test Interactions** False-positive urine immunoassay screening tests for amphetamines have been reported in patients taking bupropion. This is due to lack of specificity of some screening tests. False-positive test results may result even following discontinuation of bupropion therapy. Confirmatory test such as gas chromatography/mass spectrometry, will distinguish bupropion from amphetamines. **MAO Inhibitors** Studies in animals demonstrate that the acute toxicity of bupropion is enhanced by the MAO inhibitor phenelzine *[see Contraindications]*. **Drugs that Lower Seizure Threshold** Since there is no lower strength for FORFIVO XL, concurrent administration of FORFIVO XL tablets and agents (e.g., antipsychotics, other antidepressants, theophylline, systemic steroids, etc.) that lower seizure threshold should be undertaken only with caution *[see Warnings and Precautions]*. **Alcohol** In postmarketing experience, there have been rare reports of adverse neuropsychiatric events or reduced alcohol tolerance in patients who were drinking alcohol during treatment with bupropion. Alcohol increased the release rate of FORFIVO XL in vitro. The consumption of alcohol during treatment with FORFIVO XL should be avoided. **Levodopa and Amantadine** Limited clinical data suggest a higher incidence of adverse experiences in patients receiving bupropion concurrently with either levodopa or amantadine. Since there is no lower strength for FORFIVO XL, administration of FORFIVO XL tablets to patients receiving either levodopa or amantadine concurrently should be undertaken with caution.

USE IN SPECIFIC POPULATIONS: Pregnancy Teratogenic Effects: **Pregnancy Category C**. In studies conducted in rats and rabbits, bupropion hydrochloride was administered orally at doses up to 450 and 150 mg/kg/day, respectively (approximately 11 and 7 times the maximum recommended human dose [MRHD], respectively, on a mg/m^2 basis), during the period of organogenesis. No clear evidence of teratogenic activity was found in either species; however, in rabbits, slightly increased incidences of fetal malformations and skeletal variations were observed at the lowest dose tested (25 mg/kg/day, approximately equal to the MRHD on a mg/m^2 basis) and greater. Decreased fetal weights were seen at 50 mg/kg and greater. When rats were administered bupropion hydrochloride at oral doses of up to 300 mg/kg/day (approximately 7 times the MRHD on a mg/m^2 basis) prior to mating and throughout pregnancy and lactation, there were no apparent adverse effects on offspring development. One study has been conducted in pregnant women. This retrospective, managed-care database study assessed the risk of congenital malformations overall, and cardiovascular malformations specifically, following exposure to bupropion in the first trimester compared to the risk of these malformations following exposure to other antidepressants in the first trimester and bupropion outside of the first trimester. This study included 7,005 infants with antidepressant exposure during pregnancy, 1,213 of whom were exposed to bupropion in the first trimester. The study showed no greater risk for congenital malformations overall, or cardiovascular malformations specifically, following first trimester bupropion exposure compared to exposure to all other antidepressants in the first trimester, or bupropion outside of the first trimester. The results of this study have not been corroborated. FORFIVO XL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nursing Mothers** Like many other drugs, bupropion and its metabolites are secreted in human milk. Because of the potential for serious adverse reactions in nursing infants from FORFIVO XL tablets, 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. Anyone considering the use of FORFIVO XL in a child or adolescent must balance the potential risks with the clinical need. **Geriatric Use** Of the approximately 6,000 patients who participated in clinical trials with bupropion hydrochloride sustained-release tablets (depression and smoking cessation studies), 275 were 65 years old and over and 47 were 75 years old and over. In addition, several hundred patients 65 and over participated in clinical trials using the immediate-release formulation of bupropion hydrochloride (depression studies). No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. A single-dose pharmacokinetic study demonstrated that the disposition of bupropion and its metabolites in elderly subjects was similar to that of younger subjects; however, another pharmacokinetic study, single and multiple dose, has suggested that the elderly are at increased risk for accumulation of bupropion and its metabolites *[see Clinical Pharmacology]*. Bupropion is extensively metabolized in the liver to active metabolites, which are further metabolized and excreted by the kidneys. The risk of toxic reaction to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function *[see Dosage and Administration and Use in Specific Populations]*. **Renal Impairment** Since there is no lower dose strength for FORFIVO XL, FORFIVO XL is not recommended in patients with renal impairment *[see Clinical Pharmacology]*. **Hepatic Impairment** Since there is no lower dose strength for FORFIVO XL, FORFIVO XL is not recommended in patients with hepatic impairment *[see Clinical Pharmacology]*.

DRUG ABUSE AND DEPENDENCE: Controlled Substance Bupropion is not a controlled substance. **Abuse** Humans: Controlled clinical studies of bupropion hydrochloride (immediate-release formulation) conducted in normal volunteers, in subjects with a history of multiple drug abuse, and in depressed patients showed some increase in motor activity and agitation/excitement. In a population of individuals experienced with drugs of abuse, a single dose of 400 mg of bupropion hydrochloride produced mild amphetamine-like activity as compared to placebo on the Morphine-Benzedrine Subscale of the Addiction Research Center Inventories (ARCI), and a score intermediate between placebo and amphetamine on the Liking Scale of the ARCI. These scales measure general feelings of euphoria and drug desirability. Findings in clinical trials, however, are not known to reliably predict the abuse potential of drugs. Nonetheless, evidence from single-dose studies does suggest that the recommended daily dosage of bupropion when administered in divided doses is not likely to be especially reinforcing to amphetamine or stimulant abusers. However, higher doses that could not be tested because of the risk of seizure might be modestly attractive to those who abuse stimulant drugs. Animals: Studies in rodents and primates have shown that bupropion exhibits some pharmacologic actions common to psychostimulants. In rodents, it has been shown to increase locomotor activity, elicit a mild stereotyped behavioral response, and increase rates of responding in several schedule-controlled behavior paradigms. In primate models to assess the positive reinforcing effects of psychoactive drugs, bupropion was self-administered intravenously. In rats, bupropion produced amphetamine-like and cocaine-like discriminative stimulus effects in drug discrimination paradigms used to characterize the subjective effects of psychoactive drugs.

OVERDOSAGE: Human Overdose Experience Overdoses of up to 30 g or more of bupropion have been reported. Seizure was reported in approximately one third of all cases. Other serious reactions reported with overdoses of bupropion alone included hallucinations, loss of consciousness, sinus tachycardia, and ECG changes such as conduction disturbances or arrhythmias. Fever, muscle rigidity, rhabdomyolysis, hypotension, stupor, coma, and respiratory failure have been reported mainly when bupropion was part of multiple drug overdoses. Although most patients recovered without sequelae, deaths associated with overdoses of bupropion alone have been reported in patients ingesting large doses of the drug. Multiple uncontrolled seizures, bradycardia, cardiac failure, and cardiac arrest prior to death were reported in these patients. **Overdosage Management** Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. EEG monitoring is also recommended for the first 48 hours post-ingestion. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. Gastric lavage with a large-bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal should be administered. There is no experience with the use of forced diuresis, dialysis, hemoperfusion, or exchange transfusion in the management of bupropion overdoses. No specific antidotes for bupropion are known. Due to the dose-related risk of seizures with FORFIVO XL, hospitalization following suspected overdose should be considered. Based on studies in animals, it is recommended that seizures be treated with intravenous benzodiazepine administration and other supportive measures, as appropriate. In managing overdosage, consider the possibility of multiple drug involvement. The physician should consider contacting a poison control center for additional information on the treatment of any overdose. Telephone numbers for certified poison control centers are listed in the Physicians' Desk Reference (PDR).

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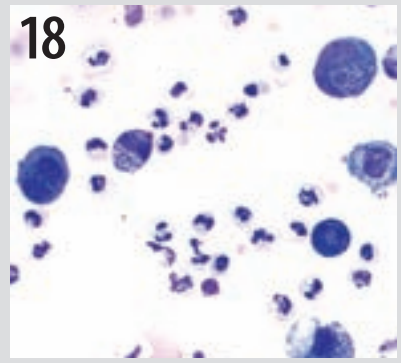

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Register for APA's 2013 annual meeting in San Francisco and and save on fees! Early-bird registration rates apply until January 24. To register, go to http://annualmeeting.psychiatry.org; you will need your log-in information to receive member rates. (If you do not have this information, call [703] 907-7300.) To receive the best hotel rates near the Moscone Convention Center, contact Travel Planners, the official APA housing bureau, at (800) 221-3531 or (212) 532-1660.

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Departments

FROM THE PRESIDENT

Canadian Psychiatry and Health Care System

BY DILIP JESTE, M.D.

APA has had a special relationship with our Canadian colleagues for decades. Psychiatrists trained and practicing in Canada are regular members of APA. APA has three district branches in Canada: Ontario, Quebec and Eastern Canada, and Western Canada. To date, 9 percent of APA's annual meetings have been held in Canada (Montreal, Niagara Falls, Quebec, and Toronto). Seven APA presidents lived/worked in Canada at the time they held office: Drs. Daniel Clark (1891-92), Richard Bucke (1897-98), Thomas Burgess (1904-05), James Anglin (1917-18), Walter English (1930-31), George Stevenson (1940-41), and Ewen Cameron (1952-53). Three APA presidents were born in Canada but lived or worked in the United States: Drs. Alexander MacDonald (1903-04), William Russell (1931-32), and Harold Eist (1996-97).

One of the most striking differences between our two countries is in our health care systems. Canada has universal health insurance, while the system in the United States has been largely based on employer-covered health insurance, except for government-funded Medicare and Medicaid. The U.S. system is undergoing major transformation at this time. The Affordable Care Act, supported by President Obama, has brought significant changes that are particularly helpful for people with mental illness. For example, it eliminates lifetime dollar limits on insurance coverage, allows single individuals younger than 26 to remain on their parents' insurance, and provides access to insurance for uninsured individuals with preexisting conditions (in 2014, the law will prohibit coverage denial due to preexisting conditions). These measures will help provide access to health care for many people who do not currently have it. Nonetheless, the U.S. system will continue to be markedly different from its Canadian counterpart.

I invited Suzane Renaud, M.D., president of the Canadian Psychiatric Association (CPA), and Fiona McGregor, M.D., immediate past president of the CPA, to describe the Canadian health care system from a psychiatric perspective. Below are their comments.

Why Canadians Value Our Universal Health Care System

BY SUZANE RENAUD, M.D., AND FIONA MCGREGOR, M.D.

One of us (Dr. Renaud), a Quebec psychiatrist who trained in the United States, has been involved at the APA district branch level and served as a representative to the APA Assembly for a decade. The other (Dr. McGregor) is a Scottish-trained psychiatrist who came to Canada 22 years ago. Thus, coming from disparate backgrounds, we are excellent models of integrative practice.

In Canada, everyone enjoys the benefits of universal health insurance that Canadians regard as their birthright. Over 90 percent of Canadians in repeated polls believe this is an essential part of the government's responsibilities. How did our two countries develop such different health care systems? Canada separated from the United Kingdom 90 years after the U.S. Declaration of Independence. Canada's Constitution Act of 1867 carried provisions for legislating health care and divided the jurisdiction of health between the provinces and federal government. In 1957 the Canadian government entered into an agreement with the provinces to establish a comprehensive universal plan.

Because of alarm over provincial spending on health care, which the federal government met dollar for dollar, the Canada Health Act was passed in 1984. This defines the principles—but not the practice—of how health care is delivered. The principles are

- **Public administration of health insurance by an accountable nonprofit agency:** This has kept costs far below those of the United States.
- **Comprehensiveness:** All insured services must be covered.
- **Universality:** All citizens living within a province are covered.
- **Portability:** Insurance is portable across Canada.
- **Accessibility:** Access time to necessary services should be reasonable.

Currently our federal government covers only 26 percent of all health care costs, leaving itself in a weak position to advocate for national standards. Our current government is not interested in standards, to the dismay of 90 percent of Canadians, according to a recent poll by the Canadian Medical Association.

Health care spending has not increased dramatically, apart from the cost of pharmaceuticals, and so far our government has been deaf to the lobby calling for a national "pharmacare" strategy that would enormously reduce costs.

How does the Canada Health Act affect us as psychiatrists? One of the joys of this system as physicians is the lower cost and reduced time spent on administrative tasks such as billing, not having to choose which patients can be seen, not having to justify treatment strategies, and having access to medications that patients can afford. The downside is that since the system is public, the workload is heavy and accompanied by the pressure to respond to all needs.

Generally the first port of call for those with mental illness is the primary care system, as self-referral to a psychiatrist is becoming a rarity. Secondary care is delivered in different ways, depending on the province.

The culture of private-practice psychiatry is declining as psychiatrists see the benefits of working as part of multidisciplinary teams. There is usually good collaboration with other professionals in the mental health field as all belong to a unique public-system network.

The issue of wait lists in Canada is often misrepresented, but most patients say that once they are in the system, the quality of care is good. The hallmark of this single-payor system is that the security of payment allows Canadian psychiatrists to give attention to the treatment of patients without discrimination over which patients they can see. Continuity of care is guaranteed as psychiatrists are responsible and control treatment plans, including the frequency of follow-up or transfer back to first-line services (usually family doctors). The physician is responsible for finding appropriate care, but limited numbers of inpatient beds can present a challenge. The CPA is constantly advocating for greater parity of health care funding for mental health (a current goal is to increase funding from 7 percent to 9 percent of total budget).

The CPA has 4,354 members, comprising 52 percent of Canadian psychiatrists. The smaller size of our organization necessitates, as well as allows for, more flexibility in decision making. There is no counterpart to the APA Assembly. Rather, volunteers work on committees onto which they are delegated by their provincial associations. Both associations publish a journal, develop position papers, and have working committees and an annual conference.

The CPA collaborates with the provincial organizations and lobbies on federal health responsibilities. The CPA continues to state the need for appropriate psychiatric care and fight against stigma, similar to APA.

It is fascinating to observe how our two countries, with similar mental health care concerns, deal so differently with issues as a result of differences in the two cultures. Our two countries now have similar family incomes; however, the Canadian health care system protects individuals at a low cost for the same health issues. Since the risk of encountering a mental illness in a lifetime is high, universal health insurance continues to be a good idea according to the Canadian point of view. PN

Suzane Renaud, M.D., is president of the Canadian Psychiatric Association, and Fiona McGregor, M.D., is immediate past president.

Eating-Disorders Guideline Still Current and Valid, Panel Finds

A review of the 2006 APA practice guideline on eating disorders finds that it is substantially current and is not affected by changes in diagnostic criteria in *DSM-5*.

BY MARK MORAN

The APA practice guideline on the treatment of eating disorders, originally issued in 2006, is still current and can be regarded by clinicians as valid.

That was the determination of an expert panel led by Joel Yager, M.D., chair of the APA Steering Committee on Practice Guidelines. Their review of the practice guideline and recent treatment research are available on APA's Web site under the title "Guideline Watch: Practice Guideline for Treatment of Patients With Eating Disorders–Third Edition."

Yager's coauthors are Michael Devlin, M.D., Katherine Halmi, M.D., David Herzog, M.D., James Mitchell III, M.D., Pauline Powers, M.D., and Katherine Zerbe, M.D.

The sole problem in the guideline is a recommendation for use of sibutramine for the treatment of binge-eating disorder. But since the guideline was issued, the Food and Drug Administration has withdrawn approval for sibutramine because clinical trials showed increased risk of heart attack and stroke. Also, the manufacturer, Abbott Laboratories, subsequently withdrew this medication from the U.S. market, Yager said.

Guideline watches summarize significant developments in practice that have occurred since publication of an APA practice guideline. Watches may be written and reviewed by experts associated with the original guideline development and are approved for publication by APA's Executive Committee on Practice Guidelines. Thus, watches represent the opinion of the authors and have the approval of the Executive Committee but are not APA policy.

Yager added that in their review of the practice guideline, he and fellow authors anticipated changes in criteria that were proposed for eating disorders in the new *DSM-5* and that have since been approved by the APA Board of Trustees—and found that the changes in diagnostic criteria do not affect the validity of the practice guideline.

For the practice guideline watch, Yager and colleagues searched MEDLINE, using PubMed, for randomized, controlled trials and meta-analyses published from 2003 through December 13, 2011, searching on words related to eating disorders. The search yielded 1,346 articles; of these, 693 were rejected as not relating to treatment of eating disorders.

They retained and reviewed 91 articles pertaining to anorexia nervosa, 84 to bulimia nervosa, 95 to binge eating, 12 to osteoporosis treatment in eating disorders, and 60 to miscellaneous topics, most of which covered more than one eating disorder. The watch reviews literature pertaining to anorexia, bulimia, binge-eating disorder, and eating disorders in middle age and later life.

Yager said other practice-guideline watches that are being readied for publication include reviews of guidelines for obsessive-compulsive disorder and for Alzheimer's and related disorders.

"The purpose of the guideline watch is to review evolving literature related to a guideline and to bring to the attention of clinicians the advances that have been made in the field," Yager said. "We want to examine how a practice guideline has stood the test of time and to provide clinicians with important updates." PN

"Guideline Watch: Practice Guideline for Treatment of Patients With Eating Disorders, Third Edition" is posted at http://www.psychiatry.org/File%20Library/Practice/ED_PG_Watch_August_2012.pdf.

Project Will Prepare ECP Members for Leadership

Two APA Assembly members launch an early career psychiatrist (ECP) initiative they hope will inspire ECPs to not just remain APA members, but to become APA leaders.

BY JOAN AREHART-TREICHEL

There is talk about young people not joining organizations the way their predecessors did. Whether or not that is true, at APA there has been a decline in the number of early career psychiatrists (ECPs) joining and remaining members over the past few years.

Thus, a few months ago, APA Assembly Speaker Scott Benson, M.D., pondered how to use Assembly funds allocated for new initiatives to address this situation and encourage ECPs to remain APA members and even become leaders of the Association. He discussed the issue with members of the Assembly Executive Committee and then proposed a project to provide leadership training opportunities for some ECPs.

The project they envisioned would consist of "pairing some ECPs with rising leaders in district branches or APA Areas," Benson explained to *Psychiatric News*. "By connecting these psychiatrists there would be opportunities to more effectively use the resources of the district branches to guarantee the project's success."

The Assembly Executive Committee endorsed the proposal and enlisted the help of Steve Koh, M.D., to begin the process of finding ECPs who would be appropriate for the project. Koh, who is on the clinical faculty of the Naval Hospital in San Diego, is the ECP representative to the APA Assembly Executive Committee. (He noted that he does his work for APA as an individual, not representing the Navy.)

The Assembly Committee of Early Career Psychiatrists is made up of ECP leaders from APA's seven geographic-based Areas. Koh asked each of these leaders to find in their Area both an ECP and a general member who were involved in organized psychiatry at the local level, but not nationally. The general member was also to have indicated an interest in ECP issues and be, as Koh explained in a recent interview, "committed to making sure that organized psychiatry has a strong younger-generation component."

Altogether 14 individuals—one ECP and one general member from each of the seven Areas—were recruited.

David Hathcox

Steve Koh, M.D.: "We hope that these seven ECPs will become leaders of psychiatry not only in their local areas, but nationally."

Then last September, these 14 psychiatrists were brought to Washington, D.C., for APA's annual components meeting. During their day and a half together, they were given a crash course in what APA is all about. Some APA staff taught them how to talk to the media. Other staff reviewed legislative issues and what is happening on Capitol Hill. Still other speakers described the structure of APA and how the different pieces fit together to accomplish APA's mission and goals.

The participants also met with several APA leaders. For example, "Jeffrey Borenstein, M.D., editor in chief of *Psychiatric News* and chair of the Council on Communications, was there to talk about *Psychiatric News* as well as his thoughts on electronic media and his vision for electronic communication for APA," Koh said. "APA President Dilip Jeste, M.D., and APA President-elect Jeffrey Lieberman, M.D., stopped by to say hello. We had a trustee-at-large talk to the participants about state-level legislative issues." The hope was that the seven ECPs would become infected with their senior colleagues' passion and want to become APA leaders in their own right.

Finally the ECPs and their general-member partners were asked to come up with one or more projects to entice ECPs to remain members of APA after completing their residency, during which they paid lower APA dues, but to stay committed to the Association. One key initiative on which they are working, Koh said, is putting easy-to-access maintenance of certification (MOC) content on the APA Web site. Another is developing a membership recruitment tool.

"We are eager to see how these projects develop during the coming year," Koh stated. "We hope that these seven ECPs will become leaders of psychiatry not only in their local areas, but nationally. They can then pass on what they have learned to other ECPs and convince them that involvement with APA is part of our professional responsibility."

Members can contact Koh about the APA ECP initiative by e-mail at Shkoh77@yahoo.com. PN

PROFESSIONAL NEWS

NIMH Tries to Jumpstart Drug Innovations

Researchers and NIMH hope a series of "FAST" clinical trials will foster breakthroughs in new drugs and improve clinical trial methods and tools for future psychiatric research.

BY JUN YAN

The National Institute of Mental Health (NIMH) has made a major investment in short, early-stage clinical trials with the hope of jumpstarting psychiatric drug discovery in the next three years.

In late September, NIMH announced that it has awarded contracts, each amounting to $9 million over three years, to three academic institutions to conduct clinical trials in psychotic spectrum disorders, mood and anxiety disorders, and autism spectrum disorders. The three programs are named FAST-PS, FAST-MAS, and FAST-AS, respectively.

The FAST-PS program will be led by Jeffrey Lieberman, M.D., chair of the Department of Psychiatry at Columbia University, director of the New York State Psychiatric Institute, and president-elect of APA. The principal investigator of FAST-MAS is Andrew Krystal, M.D., a professor of psychiatry and behavioral sciences at Duke University School of Medicine. The principal investigator of FAST-AS is James McCracken, M.D., a professor of child psychiatry at the NPI-Semel Institute for Neuroscience and Human Behavior at the University of California, Los Angeles. The principal investigators will coordinate with several research sites around the country to carry out three to five clinical trials in each program.

Jeffrey Lieberman, M.D.

"These [programs] are contracts rather than grants, so that NIMH is closely involved in how the trials are conducted," Jill Heemskerk, Ph.D., deputy director of the Division of Adult Translational Research at NIMH, told *Psychiatric News*.

Promising Drugs Tested

NIMH has convened a committee of experts, along with the investigators, to choose candidate drugs that will be tested in the clinical trials. The candidate drugs will include a mixture of novel compounds that have not been approved for clinical use and repurposed drugs that have been used for other indications.

One source for the novel compounds is a set of 58 compounds made available through collaboration between pharmaceutical companies and the National Institutes of Health's newly established National Center for Advancing Translational Sciences (NCATS). These compounds have already been tested for safety in humans, and their pharmacological properties have been studied in laboratories. The companies still own their patents but are not actively developing them for marketing approval.

NIMH will make public announcements soon to solicit suggestions on selecting promising candidate drugs.

Each FAST program hopes to conduct several phase 1 or phase 2a studies, according to the three investigators who will lead the programs. The study designs

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will depend on the properties of each selected drug, the scope of the research, and nature of the disease studied.

The studies will take a "fast-fail" experimental approach, seeking early physiological evidence of whether a drug is likely to be effective. Some of these studies will be as short as "one or two doses of the treatment, or at most one to four weeks," said Lieberman. The sample size in each study will range from a handful of volunteers to dozens.

Biomarkers Allow Fast Studies

Although conventional clinical trials tend to last for weeks or months, researchers leading the rapid trials for these programs expect to observe rapid response to a drug in the living human brain by using cutting-edge technologies and biomarkers, thus directly connecting molecular manipulations in the brain to observed changes in brain activities in particular regions and to clinical symptoms.

"We plan to use PET scan, functional MRI [fMRI], magnetic resonance spectroscopy, and radioactive ligands, which will show [molecular] binding to target sites," said Lieberman. For example, the FAST-PS program will study the effects of some drugs on cognitive impairment by observing changes in blood flood to the prefrontal cortex. Also, the antipsychotic effects of certain drugs may be reflected in brain scans as reduced glutamate bind-

*see **NIMH** on page 10*

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NIMH

continued from page 9

ing, as glutamate is a neurotransmitter implicated in psychotic symptoms.

In the FAST-MAS program, Krystal and colleagues plan to use EEG and fMRI to study changes in the brain's capacity to inhibit or regulate emotional responses such as fear and negative mood. They believe that this neurological pathway is a key aspect in both mood and anxiety disorders.

Autistism spectrum disorders could be more difficult to study than psychotic or mood disorders, McCracken acknowledged, as the biomarkers and neurocircuits are less defined. The FAST-AS program will focus on the neurological effects of drugs acting on the GABA system using tools such as magnetic resonance spectroscopy. Correlations between autism symptoms and the brain's reward system in ventral striatum will also be studied.

In all three areas, the studies will help validate or establish biomarkers to help scientists "look inside the brain" and quantitatively measure neuropsychiatric dysfunctions.

Given the high rate of failures in psychotropic drug development, it is possible that none of the candidate drugs will "make it" into an effective new treatment for any of the disorders studied, Heemskerk acknowledged. However, even fail-

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ures will generate valuable knowledge to advance research. If a drug fails, the results from brain scans and biomarker measurements will provide some direct explanation for why it fails, and the same goes for success. From this knowledge, researchers will have a clear idea about how to proceed.

In addition, the investigators noted that the studies will apply NIMH's research domain criteria (RDoc) to focus on specific functional impairments that may cross-cut psychiatric diagnosis but share common neurocircuitry or genetic bases.

Beyond looking for promising new drugs, the FAST programs could "help the field improve methodology…and establish new ways to evaluate treatment in general," said Krsytal. For the FAST-MAS studies, his team has proposed using adaptive design, which allows researchers to determine whether to continue with a study or terminate early in the middle of a trial.

"This is a unique investment by NIMH in the high-risk, high-reward type of research…and explore the edge of our knowledge," McCracken commented.

"We will generate examples of how these clinical trials should be conducted to guide future NIMH-funded trials," said Heemskerk. The initiative can potentially establish a faster and more efficient drug discovery model that will benefit psychiatric research for years to come. PN

PROFESSIONAL NEWS

Norway Addresses Mental Health Needs of War Vets

A top Norwegian army psychiatrist elaborates on his country's approach to caring for military troops after war-zone action.

BY AARON LEVIN

The United States isn't the only nation concerned about the mental health of soldiers once they return home from dangerous duty abroad.

Norway has deployed its soldiers on peacekeeping missions to the former Yugoslavia and Lebanon. More than 10,000 Norwegian troops have served in Afghanistan as well.

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

5.5 Metabolic Changes

Atypical antipsychotic drugs have been associated with metabolic changes that may increase cardiovascular/cerebrovascular risk. These metabolic changes include hyperglycemia, dyslipidemia, and body weight gain *[see Patient Counseling Information (17.3) in the full prescribing information]*. While all atypical antipsychotic drugs have been shown to produce some metabolic changes, each drug in the class has its own specific risk profile.

Hyperglycemia and Diabetes Mellitus

Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including FANAPT. 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 events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics included in these studies. Because FANAPT was not marketed at the time these studies were performed, it is not known if FANAPT is associated with this increased risk.

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 antidiabetic treatment despite discontinuation of the suspect drug.

Data from a 4-week, fixed-dose study in adult subjects with schizophrenia, in which fasting blood samples were drawn, are presented in Table 1.

Table 1. Change in Fasting Glucose

	Placebo	FANAPT® 24 mg/day
	Mean Change from Baseline (mg/dL)	
	n=114	n=228
Serum Glucose Change from Baseline	-0.5	6.6
	Proportion of Patients with Shifts	
Serum Glucose Normal to High (<100 mg/dL to ≥126 mg/dL)	2.5% (2/80)	10.7% (18/169)

Pooled analyses of glucose data from clinical studies including longer term trials are shown in Table 2.

Table 2: Change in Glucose

	Mean Change from Baseline (mg/dL)		
	3-6 months	6-12 months	>12 months
FANAPT 10-16 mg/day	1.8 (N=773)	5.4 (N=723)	5.4 (N=425)
FANAPT 20-24 mg/day	-3.6 (N=34)	-9.0 (N=31)	-18.0 (N=20)

Dyslipidemia

Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics.

Data from a placebo-controlled, 4-week, fixed-dose study, in which fasting blood samples were drawn, in adult subjects with schizophrenia are presented in Table 3.

Table 3. Change in Fasting Lipids

	Placebo	FANAPT® 24 mg/day
	Mean Change from Baseline (mg/dL)	
Cholesterol	n=114	n=228
Change from baseline	-2.17	8.18
LDL	n= 109	n=217
Change from baseline	-1.41	9.03
HDL	n= 114	n=228
Change from baseline	-3.35	0.55
Triglycerides	n= 114	n=228
Change from baseline	16.47	-0.83

(continued)

Table 3. Change in Fasting Lipids (cont)

	Placebo	FANAPT® 24 mg/day
	Proportion of Patients with Shifts	
Cholesterol		
Normal to High (<200 mg/dL to ≥240 mg/dL)	1.4% (1/72)	3.6% (5/141)
LDL		
Normal to High (<100 mg/dL to ≥160 mg/dL)	2.4% (1/42)	1.1% (1/90)
HDL		
Normal to Low (≥40 mg/dL to <40 mg/dL)	23.8% (19/80)	12.1% (20/166)
Triglycerides		
Normal to High (<150 mg/dL to ≥200 mg/dL)	8.3% (6/72)	10.1% (15/148)

Pooled analyses of cholesterol and triglyceride data from clinical studies including longer term trials are shown in Tables 4 and 5.

Table 4: Change in Cholesterol

	Mean Change from Baseline (mg/dL)		
	3-6 months	6-12 months	>12 months
FANAPT 10-16 mg/day	-3.9 (N=783)	-3.9 (N=726)	-7.7 (N=428)
FANAPT 20-24 mg/day	-19.4 (N=34)	-23.2 (N=31)	-19.4 (N=20)

Table 5: Change in Triglycerides

	Mean Change from Baseline (mg/dL)		
	3-6 months	6-12 months	>12 months
FANAPT 10-16 mg/day	-8.9 (N=783)	-8.9 (N=726)	-17.7 (N=428)
FANAPT 20-24 mg/day	-26.6 (N=34)	-35.4 (N=31)	-17.7 (N=20)

Weight Gain

Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

Across all short- and long-term studies, the overall mean change from baseline at endpoint was 2.1 kg.

Changes in body weight (kg) and the proportion of subjects with ≥7% gain in body weight from four placebo-controlled, 4- or 6-week, fixed- or flexible-dose studies in adult subjects are presented in Table 6.

Table 6. Change in Body Weight

	Placebo	FANAPT 10-16 mg/day	FANAPT 20-24 mg/day
	n=576	n=481	n=391
Weight (kg) Change from Baseline	-0.1	2.0	2.7
Weight Gain ≥7% increase from Baseline	4%	12%	18%

5.6 Seizures

In short-term placebo-controlled trials (4- to 6-weeks), seizures occurred in 0.1% (1/1344) of patients treated with FANAPT compared to 0.3% (2/587) on placebo. As with other antipsychotics, FANAPT should be used cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold, e.g., Alzheimer's dementia. Conditions that lower the seizure threshold may be more prevalent in a population of 65 years or older.

5.7 Orthostatic Hypotension and Syncope

FANAPT can induce orthostatic hypotension associated with dizziness, tachycardia, and syncope. This reflects its alpha1-adrenergic antagonist properties. In double-blind placebo-controlled short-term studies, where the dose was increased slowly, as recommended above, syncope was reported in 0.4% (5/1344) of patients treated with FANAPT, compared with 0.2% (1/587) on placebo. Orthostatic hypotension was reported in 5% of patients given 20-24 mg/day, 3% of patients given 10-16 mg/day, and 1% of patients given placebo. More rapid titration would be expected to increase the rate of orthostatic hypotension and syncope.

FANAPT should be used with caution in patients with known cardiovascular disease (e.g., heart failure, history of myocardial infarction, ischemia, or conduction abnormalities), cerebrovascular disease, or conditions that predispose the patient to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications). Monitoring of orthostatic vital signs should be considered in patients who are vulnerable to hypotension.

5.8 Leukopenia, Neutropenia and Agranulocytosis

In clinical trial and postmarketing experience, events of leukopenia/neutropenia have been reported temporally related to antipsychotic agents. Agranulocytosis (including fatal cases) has also been reported.

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Øyvind Erik Jensen, M.D.

The Norwegian approach to military psychiatry grew out of decades of experience after those military involvements, explained Maj. Øyvind Erik Jensen, M.D., in a recent interview in Montreal with *Psychiatric News.*

"Psychiatrists help train the troops before they go, but we do not deploy with them," because the units are too small to warrant a full-time clinician, said Jensen. Overall responsibility for soldiers' welfare always lies with their commanding officers. "We are just their advisors."

However, two psychiatrists or psychologists are on duty 24 hours a day in Norway during deployment of its troops and can fly out to the unit if some major traumatic event, like a roadside bomb blast with casualties, occurs.

Jensen did serve two six-month tours of duty in Kosovo and Afghanistan but as a general medical officer, not a psychiatrist.

One major difference between U.S. and Norwegian soldiers is that Americans spend a year in battle zones while the Norwegians serve only six months away. (U.S. Marines serve shorter deployments.) The Norwegians also get two two-week home leaves during that time.

"We are only borrowing the soldier

see ***Norway*** *on page 30*

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,

PROFESSIONAL NEWS

College Discontinuity (1a9) XXXXReplace

College students who experience symptoms of depression or seek treatment for depression might be at risk of dropping out.

BY AARON LEVIN

Emotional problems can interfere with academic progress and temporarily derail a student's college career. Dropping out is also problematic for college administrators, who want to keep classroom seats filled and graduation rates high.

However, students who first develop symptoms of depression during their early years in college have a higher risk of discontinuing their education that other students—even those who were diagnosed in high school and were already in treatment, according to a study by epidemiologist Amelia Arria, Ph.D., director of the Center on Young

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,

PROFESSIONAL NEWS

Health and Development in the University of Maryland School of Public Health in College Park, and colleagues. Their report appeared online December 3, 2012, in *Psychiatric Services in Advance*.

Most prior studies have focused on college graduation rates, but dropping out for one or more semesters is a much more subtle outcome, wrote Arria and colleagues.

"A student's struggles with emotional problems will have an impact on academic success," commented Victor Schwartz, M.D., medical director of the Jed Foundation and co-editor of *Mental Health Care in the College Community* (Wiley. 2010), in an interview. Schwartz was not involved with the present study, although he has collaborated with Arria in the past. "It's important to watch the transition points, like the transition from high school to college, and provide support by continuing or adjusting treatment, if needed."

The study's findings suggest that "depressive symptoms—but not necessarily depressive disorders—predict increased risk of college noncompletion," said the researchers. Dropping out of college in the first year or two thus is not always due solely to difficulties adjusting to a new learning environment.

Arria and colleagues used data from the College Life Study, an ongoing investigation of students who arrived at the University of Maryland as freshman beginning in 2004. The final sample covered 1,145 young people who completed assessments in year 3 or 4 of the study.

By year 4, 14 percent of the students had been diagnosed with depression, 13 percent with anxiety, and 10 percent with attention-deficit/hyperactivity disorder (ADHD). Rates of diagnosis before and during college were roughly similar for the three disorders. After adjustment, a depression diagnosis in college was associated with twice the increased risk of discontinuation of the student's college career. Freshman with high levels of depressive symptoms were at increased risk of dropping out for one or more semesters during their freshman or sophomore years.

However, said the authors, "students entering college with a prior diagnosis of depression, anxiety, or ADHD were not at increased risk of interruptions in enrollment over four years."

"Students who are diagnosed early, get into treatment, and are symptomatically stable will do as well as their classmates," said Schwartz. "It's not the diagnosis but the extent to which the person is symptomatic."

Each 1-point increase in the Beck Depression Inventory score increased risk by 7 percent for dropping out during the first two years. Cannabis use frequency and number of alcoholic drinks per drinking day predicted discontinuity in the junior and senior years.

"This is an important paper because it addresses the interlocking need for both intellectual and emotional tools to succeed in college," said Schwartz.

"Screening for drug use, heavy drinking, and depressive symptoms, especially during the first year of college, might be useful for identifying students at risk of temporary withdrawal or dropout," concluded Arria and colleagues.

"Students need to know that treatment helps," said Schwartz. "They pay a price for stigma, for not seeking help, so that's a self-defeating strategy. They should take advantage of the resources offered by the college counseling services. PN

An abstract of "Discontinuous College Enrollment: Associations With Substance Use and Mental Health" is posted at http://ps.psychiatryonline.org/Article.aspx?ArticleID=1471075.

PROFESSIONAL NEWS

Biographer Explores Character, Pathology, and Achievement

Biographer Joshua Kendall explores the interplay between character—and character pathology—and achievement.

BY MARK MORAN

"Obsessive: excessive, often to an unreasonable degree."

—Merriam Webster's Collegiate Dictionary, 11th Edition.

The polymath who was father of today's *Merriam-Webster's Dictionary*—originally *Webster's American Dictionary of the English Language*, first published in 1828—may be one of the most underrecognized but influential figures from America's revolutionary and post-revolutionary period. Noah Webster, confidant of George Washington and Alexander Hamilton, was editor during the republic's early years of *American Minerva*, New York City's first daily newspaper. He served as a state representative from Connecticut and Massachusetts, was a founder and early president of Amherst College, and was the author and publisher of a grade-school "speller" that well into the 19th century was teaching school-age Americans to read.

To the extent that he is remembered at all, Webster is remembered best for his dictionary, the focus of his life's effort and the fruit of one large idea that Webster nurtured and travelled the towns of 18th-century America to propagate: that America needed to assert not only its political and economic independence from Britain, but its cultural independence as well by codifying a uniquely American idiom of the English language.

An accomplished fellow, by anyone's standard. But according to Webster biographer Joshua Kendall, Webster was also a problem—to others and, one suspects, to himself. Widely regarded in his own time as vain, arrogant, and self-regarding, Webster had little capacity for connecting with others, and the drivenness and need for order that propelled his success may have been considered by others to be "excessive to an unreasonable degree."

Joshua Kendall

Joshua Kendall writes about how obsessive features of some personalities in history have helped them achieve success.

In *The Forgotten Father: Noah Webster's Obsession and the Creation of an American Culture* (published by G.P. Putnam's Sons), Kendall argues that Webster may have had what today would be called obsessive-compulsive personality disorder. "For this order lover who came close to a complete breakdown on several occasions, defining became his ruling obsession," Kendall wrote. "The 30-year quest to complete the dictionary was inextricably linked to the fight to maintain his own sanity."

Webster is not the only high-achieving obsessive that has caught Kendall's attention. In 2008 he published *The Man Who Made Lists: Love, Madness, and the Creation of Roget's Thesaurus*, which psychiatrist Peter Kramer, M.D., called a "fascinating account of the transformation of obsession into inspiration."

"Going from Roget to Webster was kind of a natural," Kendall told *Psychiatric News* in an interview. "Roget was a great British dictionary maker who was obsessed with lists and words, and when I looked to our own soil, I found in Webster a kindred spirit."

Next year Kendall will publish *America's Obsessives: The Compulsive Energy*

see **Biographer** on page 27

APA to Survey Members About EHR Use

The survey should help inform the design of future electronic health record (EHR) systems for psychiatrists and minimize or avoid pitfalls associated with EHRs.

BY MARK MORAN

Are you using an electronic health record (EHR), and if so what kind? APA wants to know and will be surveying its members early this year to find out.

In conjunction with AmericanEHR Partners and the American College of Physicians (ACP), APA is participating in a nationwide survey of physicians from every major specialty group. The survey, which is being e-mailed to members this month, is designed to ascertain the extent to which physicians are using electronic health records, the kinds of products they use, and their opinions about them.

Members who complete the survey will be entered into a drawing for a new Apple mini-tablet computer.

Robert Plovnick, M.D., M.S., director of APA's Office of Quality Improvement and Psychiatric Services, said the survey will take approximately 50 minutes to complete. It consists of a set of questions that every physician, regardless of specialty, will be asked; a second set of questions targeting those who are currently using some kind of EHR product; and a third set of questions specifically for psychiatrists.

Responses to the survey will be confidential, and physician identities will not be used in reporting survey results.

"The goal is to get a sense of EHR usage and collect detailed information on the products currently used by psychiatrists," Plovnick told *Psychiatric News*. "This is directly responsive to requests we have received from all areas of the organization. Everyone wants to know which EHRs psychiatrists are using and what they think of them, so we can have a sense of the state of the EHR market and help our members make their own purchasing decisions.

"So far we have had to rely on anecdotal evidence, so the survey is an opportunity to provide more-robust information about available EHR products to our members," he said. "The more feedback we get, the more useful it will be to the field."

(According to its Web site, AmericanEHR Partners has been developed by Cientis Technologies and ACP; it provides physicians, state and federal agencies, vendors, and funding organizations with tools to identify, implement, and effectively use electronic health records and other health care technologies.)

The psychiatry-specific questions gauge clinician satisfaction with the ability of an EHR to use *DSM* diagnoses and coding; ability to create or customize templates for psychiatry specific documentation; ability to manage separate psychotherapy notes; ability to create and share records with members of a treatment team, including other physicians, psychologists, and social workers; and ability to record substance use, among other issues.

Psychiatrist Daniel Balog, M.D., a member of APA's Committee on Electronic Health Records, said psychiatrist participation in the survey can also help influence the design of EHR products in the future.

"The majority of current EHR systems were designed with a predominance of medical input, so APA's involvement in this clinical survey provides member psychiatrists a platform to share their EHR experiences," Balog told *Psychiatric News*. "The survey includes specialty questions designed by the APA EHR Committee to target information relevant to member psychiatrists who are shopping for EHR systems or who are in a position to influence purchasing decisions made by larger organizations." PN

More information about EHRs is posted on the APA Web site at www.psychiatry.org/ehr. Information about American EHR Partners, including information about EHR products derived from responses from physicians who have completed the survey, is posted at http://www.americanehr.com.

ASSOCIATION NEWS

Board Votes New Caucuses, Backs Workforce Legislation

Caucuses will be established for members-in training and psychiatrists interested in college mental health issues, and the Council on Research and Quality Care will be divided into two councils.

BY KEN HAUSMAN

While its vote to approve the diagnostic categories and criteria for the next edition of APA's *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)* was the most newsworthy action the Board of Trustees took at its meeting last month (*Psychiatric News*, December 21, 2012), Board members voted on several other issues as well.

Among the proposals that won Board approval at the December meeting was one from a group of members-in-training (MITs) who are active in APA urging formation of a caucus that would make it easier and more efficient for them to organize and conduct their business. As their proposal stated, "Our efforts to advocate within APA, to raise policy issues, and to promote APA to nonmembers [are] fragmented and sometimes are not well-coordinated. . . . We believe that it is appropriate to bring these activities formally under APA's umbrella" through establishment of a caucus. The new Caucus of Members-in-Training will be placed under the auspices of the Council on Medical Education and Lifelong Learning.

The Board also agreed to the formation of a second new caucus, this one composed of members who are interested in issues related to mental health on college and university campuses. The College Mental Health Caucus will be a component of the Council on Children, Adolescents, and Their Families.

The Trustees also voted to approve dividing the Council on Research and Quality Care into separate councils to deal with the current council's complex agenda in which issues fall into one of its two primary focuses. Separate councils were combined into one several years ago during a major restructuring of APA's components. Council Chair Joel Yager, M.D., pointed out that it is difficult to manage "the many important areas under the limited time and resources of a single council." The new Council on Research will focus on areas such as clinical diagnosis and assessment, treatment research, prevention research, and ECT, as well other electromagnetic therapies. Among issues under the purview of the new Council on Quality Care will be quality indicators and the federal program promoting their use, standards and survey procedures, psychotherapy by psychiatrists, HIV/AIDS, practice-guideline development, and electronic health records.

In addition, the Board voted to change the name of the Caucus of Psychiatrists Treating Persons With Mental Retardation and Developmental Disabilities to the Caucus of Psychiatrists Treating Persons With Intellectual Disabilities. The proposal for the name change noted that "the term mental retardation has taken on negative connotations and is demeaning, hurtful, and humiliating. Since the term was coined years ago, attitudes about people with disabilities have changed to focus on abilities, personal growth and independence."

see ***Board*** *on page 29*

CLINICAL & RESEARCH NEWS

Link Between Parasite, Suicide Remains a Mystery

A third of the people in the world are positive for the parasite *Toxoplasma gondii*. So why is there a link between the parasite and suicidal behavior?

BY JOAN AREHART-TREICHEL

The parasite *Toxoplasma gondii*, which was previously linked with suicidal attempts in a small clinical sample, has also been linked with such attempts in a large prospective study.

The study's senior researcher was Teodor Postolache, M.D., director of the mood and anxiety program at the University of Maryland. The results appeared in the November 2012 *Archives of General Psychiatry*.

The study included some 46,000 Danish women whose infants had been tested for *T. gondii* antibody levels at childbirth. Twenty-seven percent of the newborns were found to have a *T. gondii* infection, which reflected the same rate as in their mothers. The researchers then looked to see whether during subsequent years any of the women had attempted suicide. Almost 1,000 had, seven of whom completed a suicide. Finally the researchers assessed whether there was a connection between women's *T. gondii* infection at the time of childbirth and later suicide attempts or completions.

There was, the researchers found. *T. gondii*-infected mothers had a relative risk of attempted suicide of 1.53 compared with noninfected mothers, and the risk appeared to increase as *T. gondii* antibody levels increased. For violent suicide attempts, the relative risk was 1.81, and for completed suicide, 2.05.

"This study is very interesting, and the prospective cohort design makes the findings . . . robust," Paul Links, M.D., a professor of psychiatry at Western University in London, Ontario, Canada, and a suicide expert, told *Psychiatric News*.

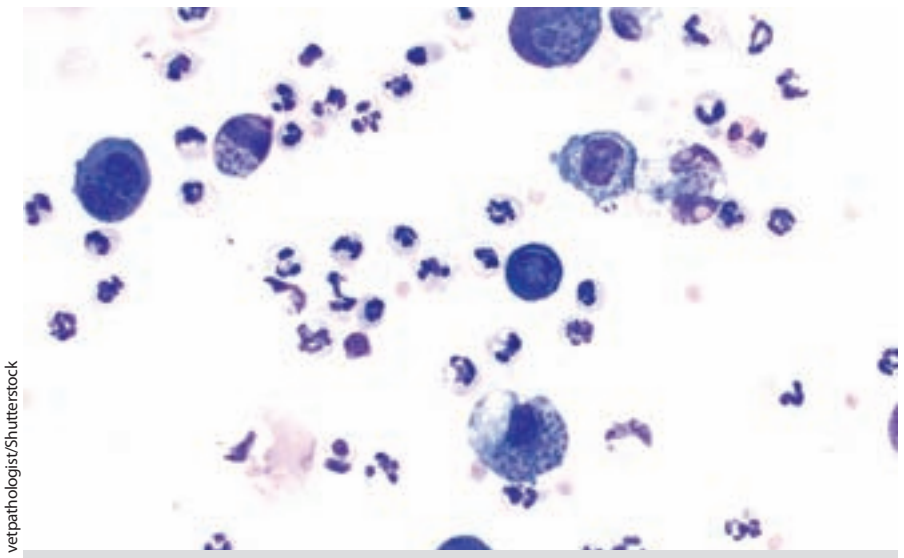
But what does the association between *T. gondii* and suicidal behavior actually mean? "Association does not necessarily mean that there is a causal relationship."

During an interview, Postolache concurred with Links. "We obviously hypothesized that *T. gondii* can affect the brain and lead to suicide attempts. But we did not rule out the possibility that somehow people at risk for suicide may have an increased risk of becoming *T. gondii*-positive. The most common risk factor for *T. gondii* in developed countries is undercooked meat. It could be that people who are impulsive [and thus prone to suicidal attempts] may also be more prone to eating a steak that is rare rather than well done."

The results "also had an element of surprise," Postolache said. "We thought that the relationship between *T. gondii* and suicidal behavior would have been stronger in those patients diagnosed with schizophrenia or bipolar disorder [since schizophrenia and bipolar disorder have been linked with *T. gondii* in the past]. In fact, what we did find was that those who had such illnesses were, to a certain degree, protected from the association. So the question is why."

Unfortunately, until such questions are answered, the link between *T. gondii* and suicidal behavior will probably have little impact on day-to-day clinical psychiatry practice, Postolache pointed out.

The study was funded by the American Foundation for Suicide Prevention; the Stanley Medical Research Institute; and the VA Capitol Health Care Network Mental Illness Research, Education, and Clinical Center. PN



vetpathologist/Shutterstock

Clusters of *Toxoplasma gondii* parasites can be seen within macrophages from a cytology smear.

An abstract of "Toxoplasma Gondii Infection and Self-Directed Violence in Mothers" is posted at http://archpsyc.jamanetwork.com/article.aspx?articleid=1206779.

Teens' Psychotic Symptoms Strongly Associated With Suicidal Behavior

Adolescents with symptoms of psychosis were 10 times more likely to report suicidal behavior than were nonpsychotic peers.

BY MARK MORAN

Psychotic symptoms are strongly associated with increased risk for suicidal behavior in the general adolescent population and in adolescents with nonpsychotic psychiatric disorders, according to a report of two independently conducted case-control clinical interview studies from Ireland.

In both studies, an absolute majority of adolescents with more severe suicidal behavior (including ideation, suicidal plans and acts) reported psychotic symptoms when directly questioned about this as part of a psychiatric interview.

The report was published in the December 2012 *Archives of General Psychiatry*.

"The immediate clinical relevance of these findings is that all patients presenting at risk for suicidal behavior should receive a thorough assessment of psychotic symptoms and not just a screening to rule out psychotic disorder," write Ian Kelleher, Ph.D., and colleagues at the Royal College of Surgeons in Ireland. "Research has shown that the largest increase in suicide risk in the general population occurs after there has already been contact with mental health services and that approximately half of patients who complete suicide have contact with primary care providers in the month preceding their death."

The two independently conducted case-control clinical interview studies included one with 212 adolescents aged 11 to 13 and a second with 211 adolescents aged 13 to 15.

Participants were recruited from schools, and suicidal behavior and psychotic symptoms were assessed by semi-structured diagnostic clinical interview.

The researchers found that psychotic symptoms were associated with a 10-fold increased odds of any suicidal behavior (including ideation, plans, or acts) in both the early- and middle-adolescence studies.

Adolescents with depressive disorders who also experienced psychotic symptoms were at a nearly 14-fold increased odds of more severe suicidal behavior (suicide plans and suicide acts) compared with adolescents with depressive disorders who did not experience psychotic symptoms. Among all adolescents with suicidal ideation, those who also reported psychotic symptoms had a nearly 20-fold increased odds of suicide plans and suicide acts compared with adolescents with suicidal ideation who did not report psychotic symptoms.

The researchers suggest several possible explanations as to the mechanisms underlying the strong relationship between psychotic symptoms and suicidal behavior. "The most obvious is that hallucinations may direct the individual to harm or kill themselves," they wrote. "In fact, a post hoc analysis of the type of psychotic symptoms reported by adolescents with suicidal behavior demonstrated that all included auditory hallucinations. However, only one of the participants in either of the studies reported command hallucinations to harm or kill themselves. It is possible, however, that psychotic symptoms may impact suicidal behavior via indirect cognitive mechanisms. Changes in the subjective sense of self, for example, are among the earliest recognizable symptoms of psychosis, and a sense of disintegration and fragmentation of the self resulting from intrusive voices or thoughts has been linked to suicidal thinking." PN

Teens Not Overmedicated, NIMH Study Finds

Despite some claims to the contrary, NIMH says that rates of psychotropic medication prescription among adolescents are "appropriate."

BY AARON LEVIN

Too much, too little, or just right? Are American adolescents with psychiatric disorders over- or under-prescribed psychotropic medications? The controversy flares up frequently in the professional and lay media, but a new National Institute of Mental Health (NIMH) study says that these medications are "prescribed appropriately."

"There was no compelling evidence for either misuse or overuse of psychotropic medications," wrote Kathleen Merikangas, Ph.D., chief of the Genetic Epidemiology Research Branch in the Intramural Research Program at NIMH, and colleagues, online December 3, 2012, in the *Archives of Pediatric and Adolescent Medicine.*

The study, which was funded by NIMH, "very clearly refutes the prejudicial view that youth are overmedicated," said Joseph Biederman, M.D., chief of the clinical and research programs in pediatric psychopharmacology and adult ADHD at Massachusetts General Hospital and a professor of psychiatry at Harvard Medical School. "In fact, the rates of disorders way exceed the rates of treatment." Biederman was not involved with the NIMH study.

The researchers collected data from 10,123 adolescents aged 13 to 18 from 2001 to 2004 as part of the National Comorbidity Survey—Adolescent Supplement (NCS-A). Besides gathering demographic and medication information, trained lay interviewers used a version of the World Health Organization's Composite International Diagnostic Interview to assess the presence of mood, anxiety, substance use, eating, and behavior disorders. Stated medication use was checked against prescription bottles, when possible.

The research builds on earlier reports from the NCS-A that found a high frequency of psychiatric disorders but only modest levels of treatment for them (*Psychiatric News,* April 15, 2011).

About 24.9 percent of the young people assessed received mental health services in the prior year, and 14.2 percent of those with a mental disorder said they were treated with a psychotropic medication, Merikangas noted.

Just 2.5 percent of those receiving such drugs did not have a 12-month *DSM-IV* disorder, but 78 percent of those adolescents had a lifetime history of psychiatric or developmental impairment.

Patients receiving psychotropic medications were also more likely to be treated in mental health specialty settings than in primary care settings.

Because the survey did not include questions about schizophrenia or obsessive-compulsive disorder, said Merikangas, "it is likely that an even smaller percentage of adolescents would be found to have no objective mental health need for psychotropic treatment."

Less than half of young people diagnosed with either depression or attention-deficit/hyperactivity disorder (ADHD) received antidepressants or stimulants, respectively, suggesting to Biederman a pattern of under- rather than over-treatment.

Ethnic-minority youth recorded lower prevalence rates of medication use compared with white youth. Family income was inversely associated with antidepressant use, while children of parents who did not finish high school reported more prescribed stimulant use than did those with better-educated parents.

Antipsychotic use was rare, most often found among youth with neurodevelopmental or bipolar disorders, plus some with ADHD and behavioral disorders.

Only 15 percent of the NCS-A respondents fell below the poverty line, and that may have skewed the results, noted an accompanying editorial by David Rubin, M.D., M.S.C.E., codirector of PolicyLab at Children's Hospital of Philadelphia and an associate professor of pediatrics at the Perelman School of Medicine at the University of Pennsylvania.

He suggested that publicly insured patients may be quickly moved onto drug therapy rather than into hard-to-find psychotherapy.

"The investments in nonpharmacological treatment options, in workforce development, and in better models of engaging families are simply lacking," said Rubin. PN

An abstract of "Medication Use in US Youth With Mental Disorders'" is posted at http://archpedi.jamanetwork.com/article.aspx?articleid=1465762#Abstract.

Some Binge-Eating Patients Benefit From Experimental Drug

An opioid-receptor antagonist can temper appetite, especially for sweet and fatty foods, in obese binge eaters. Can it also lead to long-term weight loss?

BY JOAN AREHART-TREICHEL

An experimental antagonist of the mu-opioid receptor in the brain has been found to reduce appetite, especially for sweet and fatty foods, in obese people with binge-eating disorder.

This finding was reported by Hisham Ziauddeen, a doctoral student in psychiatry at the University of Cambridge in England, and colleagues online November 13, 2012, in *Molecular Psychiatry.*

Previous studies have found that between 25 percent and 50 percent of people with binge-eating disorder seeking weight-loss treatment are obese. Since there is a paucity of effective and safe pharmacological treatments for binge eating and/or obesity and since the mu-opioid receptor has been implicated in binge eating, Ziauddeen and his team decided to see what effects an antagonist of the mu-opioid receptor might have on binge eating and weight in obese binge eaters.

Sixty-three obese binge eaters were randomized to three groups for a 28-day period. One group received 2 mg/day of an experimental mu-opioid receptor antagonist called GSK1521498. A second group received 5 mg/day of the experimental antagonist, and the third group received a placebo.

Alexander Oriov/Shutterstock

Compared with the placebo group, the 2 mg/day antagonist group experienced no significant changes in eating behavior or weight. However, the 5 mg/day group did show a change. Subjects in that group experienced a significant reduction in hedonic responses to sweetened dairy products and reduced their caloric intake, especially of high-fat desserts, during unrestricted buffet dining.

Moreover, the antagonist was found to be safe according to the Profile of Mood States–Brief, the Beck's Anxiety and Depression Inventory, the Columbia Suicide Severity Rating Scale, cardiovascular parameters, liver-function tests, and standard lab measures. The antagonist was also generally well tolerated, although diarrhea and abdominal discomfort tended to be more commonly reported by the antagonist groups than by the placebo group.

But the effects of the 5 mg/day antagonist on eating behavior did not translate into weight reduction. One possible explanation for this, the researchers suggested, is that it might have taken longer than 28 days for the antagonist's influence on eating behavior to bring about weight loss. Another possibility, they noted, is that outside of the lab experiments, subjects could eat whatever they wanted.

In any event, even though "the study did not show drug effects on body weight in the sample as a whole, the pharmacogenetic analyses showed that patients with the less-common form of the opioid receptor gene did have significantly greater weight reduction," Ziauddeen told *Psychiatric News.* "As far as we know, this is the first time it has been shown that genetic variation in the opioid receptor gene can modify a drug's effects on body weight."

Also intriguingly, he pointed out, "the same genetic variant can modify the effects of similar opioid-receptor-antagonist drugs used in the treatment of alcohol dependence." So in the future, he said, it might be possible to personalize treatments for binge eating and alcohol dependence based on individual differences in the mu-opioid receptor gene. Indeed, he and his colleagues "are currently in the process of examining the role of mu-opioid antagonism on eating behavior… in genetically stratified groups."

These are "provocative" findings and "a promising area for future research, including determining whether these findings will lead to useful clinical appli-

see ***Experimental Drug*** *on page 30*

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Early Intervention Offers Hope For Preventing PTSD

Stephen Finn/Shutterstock

Measures to prevent posttraumatic stress disorder remain elusive in the emergency room, though exposure therapy is one intervention being studied.

BY AARON LEVIN

Clinicians have searched with mixed success for interventions that are useful shortly after trauma occurs to prevent later development of posttraumatic stress disorder (PTSD).

Now Emory University researchers add to that complex record with a study of the effects of prolonged exposure therapy in the emergency department on trauma survivors. They found that the intervention helped some trauma survivors but not others.

"Exposure therapy has received more empirical support than any other intervention for ASD [acute stress disorder] and PTSD but has never been attempted within hours of the traumatic event," wrote Barbara Rothbaum, Ph.D., a professor in the Department of Psychiatry and Behavioral Sciences and director of the Trauma and Anxiety Recovery Program at Emory University School of Medicine, and colleagues in the December 1, 2012, *Biological Psychiatry*.

The study's outcomes are encouraging but still leave unanswered the question of how—or if—PTSD can be prevented by some action in the emergency department, said Arieh Shalev, M.D., a professor of psychiatry at Hadassah Medical Center in Jerusalem, Israel, and a visiting professor at New York University. Shalev, a PTSD expert, was not involved with the Emory study.

The 137 participants were randomized to receive three one-hour sessions of a modified prolonged exposure intervention. The first session took place during the initial visit to the emergency room, within 12 hours of the trauma, on average. The other sessions were held one and two weeks later. Procedures included imaginal exposure and processing, guided by a trained therapist, as well as homework. Blinded assessors used several methods to evaluate symptoms of PTSD at four and 12 weeks and depression at four weeks.

"[T]he modified prolonged exposure intervention presented here may be able to prevent the development of PTSD . . . by encouraging engagement with the trauma memory and providing an opportunity for fear habituation and processing of unhelpful cognitions, thus modifying the memory before it is consolidated," wrote Rothbaum.

Studies by other researchers indicate that early extinction training may prevent the effects of traumatic fear memories, she noted.

The differences in PTSD symptoms between the intervention and control groups were significant at week 4 for accident victims and for victims of sexual assault at both weeks 4 and 12. However, differences in PTSD severity at weeks 4 and 12 were not significant for patients who experienced physical assault or at week 12 for those who survived road accidents.

Other work based on the fear-conditioning model of PTSD has tested early interventions with treatments ranging from cognitive-behavioral therapy to propranolol, SSRIs, or cortisol to prevent the consolidation of memory, said Shalev, in an interview with *Psychiatric News*. However, no one has found the emergency-department key to preventing PTSD.

Complicating theory and practice in responding to trauma may be that trauma survivors who come to the emergency department may still be in the midst of the trauma, said Shalev.

"Some may still be within the trauma experience," he explained. "They may be upset, can't concentrate, feel out of control, have financial distress, or be facing surgery."

The presence of one or more of these factors means that prolonged exposure therapy at that stressful moment may work for some people but not for others. More needs to be done to understand what drives early responses to trauma, he said.

Also, it is difficult to sort out early on who will or won't develop PTSD. In the Emory study, many trauma survivors who were eligible for the study intervention chose not to participate, a finding similar to that observed by Shalev in a study he conducted in Jerusalem several years ago (*Psychiatric News*, November 18, 2011).

"There is a total overlap in the experience of people who go on to develop PTSD and those who don't," said Shalev. "Most people expect things to improve, and 85 percent of them do improve. But we are not able to tell in the first hours who is at the highest risk."

If some treatment were truly effective during the consolidation window—about six to eight hours after the trauma—then additional treatment would not be necessary, he suggested.

More research is needed into this aspect of trauma care, Rothbaum and colleagues agree, "particularly to determine who requires early intervention and who will recover naturally without using valuable resources unnecessarily, what is the optimal window for intervention, how many sessions are needed, and what types of treatment are needed for what patients." PN

FROM THE EXPERTS

Repurposed Medications Show Promise in Stimulant Dependence

BY THOMAS KOSTEN, M.D., AND COLIN HAILE, M.D., PH.D.

Stimulant dependence is a substance use disorder (SUD) that continues to affect society on many levels. The economic temptation of producing or bringing stimulants or their precursors (methamphetamine and cocaine) across the U.S. border to sell is continuing as certain South American countries now allow full-fledged coca plant cultivation. Containing the flow of illicit drugs within state lines and across U.S. borders is an insurmountable task for any agency, and demand reduction from effective treatments is desperately needed.

Research for these addiction treatments has benefited greatly from neuroimaging studies and "repurposed" medications.

Neuroimaging studies have been essential to understanding central deficits and altered neurotransmission linked to stimulant dependence. For example, recent evidence dispels the widely held misconception that stimulant-dependent individuals are more sensitive to these drugs than the average person, and this is why they become dependent. In fact, the opposite is true. They are less sensitive to the positive euphoric effects of stimulants. This also extends to natural rewards such as food. In contrast, these same individuals are often hypersensitive to stress and overly influenced by environmental cues associated with drug taking that can trigger relapse. Environmental cues that control behavior are influenced by usurped memory circuits. SUDs are often accompanied by comorbid negative mood states that may also contribute to continued drug use through self-medication.

Neuroimaging has revealed that abnormally low dopaminergic neurotransmission is paired with orbitofrontal hypoactivation in stimulant dependence and limits impulse control, executive functioning, and working memory. Medications that modulate dopamine, glutamate, and norepinephrine (NE) neurotransmission

see ***From the Experts*** *on page 30*

Thomas Kosten, M.D., is the J.H. Waggoner Professor of Psychiatry, Pharmacology and Neuroscience, vice chair for psychiatry, and codirector of the Institute for Clinical and Translational Research at Baylor College of Medicine. Colin Haile, M.D., Ph.D., is an assistant professor at Baylor College of Medicine, Menninger Department of Psychiatry and Michael E. DeBakey VA Medical Center. He and Kosten are the coauthors of *Cocaine and Methamphetamine Dependence: Advances in Treatment* from American Psychiatric Publishing. APA members may purchase the book at a discount at http://www.appi.org/SearchCenter/Pages/SearchDetail.aspx?ItemId=62407.

Schizophrenia can tear patients apart

For the treatment of schizophrenia

LATUDA can help put your patients back together

- Symptom improvement was established in several pivotal trials[1]
- The safety and tolerability of LATUDA were evaluated in pivotal trials and multiple studies up to 52 weeks[1]
- The recommended starting dose, 40 mg/day, is an effective dose with no initial dose titration required. The maximum recommended dose is 160 mg/day[1]
  - LATUDA should be taken with food (at least 350 calories)
  - Dose adjustment is recommended in moderate and severe renal and hepatic impairment patients. The recommended starting dose is 20 mg. The dose in moderate and severe renal impairment patients and in moderate hepatic impairment patients should not exceed 80 mg/day. The dose in severe hepatic impairment patients should not exceed 40 mg/day
  - LATUDA should not be used in combination with strong CYP3A4 inhibitors such as ketoconazole or strong CYP3A4 inducers such as rifampin. When coadministered with a moderate CYP3A4 inhibitor such as diltiazem, the recommended starting dose of LATUDA is 20 mg/day and the maximum recommended dose is 80 mg/day

INDICATIONS AND USAGE

LATUDA is an atypical antipsychotic indicated for the treatment of patients with schizophrenia. Efficacy was established in five 6-week controlled studies of adult patients with schizophrenia. The effectiveness of LATUDA for longer-term use, that is, for more than 6 weeks, has not been established in controlled studies. Therefore, the physician who elects to use LATUDA for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

IMPORTANT SAFETY INFORMATION FOR LATUDA

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.**
- **LATUDA is not approved for the treatment of patients with dementia-related psychosis.**

Please see additional Important Safety Information, including **Boxed Warning**, and Brief Summary of Prescribing Information on adjacent pages.

SUNOVION

Latuda®
(lurasidone HCl) tablets
20mg | 40mg | 80mg | 120mg

INDICATIONS AND USAGE

LATUDA is an atypical antipsychotic agent indicated for the treatment of patients with schizophrenia. Efficacy was established in five 6-week controlled studies of adult patients with schizophrenia. The effectiveness of LATUDA for longer-term use, that is, for more than 6 weeks, has not been established in controlled studies. Therefore, the physician who elects to use LATUDA for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

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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.**
- **LATUDA is not approved for the treatment of patients with dementia-related psychosis.**

CONTRAINDICATIONS

LATUDA is contraindicated in the following:

- Any patient with a known hypersensitivity to lurasidone HCl or any components in the formulation. Angioedema has been observed with lurasidone.
- Concomitant use with strong CYP3A4 inhibitors (e.g., ketoconazole).
- Concomitant use with strong CYP3A4 inducers (e.g., rifampin).

WARNINGS AND PRECAUTIONS

Cerebrovascular Adverse Reactions, Including Stroke: LATUDA is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS): NMS, a potentially fatal symptom complex, has been reported with administration of antipsychotic drugs, including LATUDA. NMS can cause 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 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 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. Given these considerations, LATUDA should be prescribed in a manner that is most likely to minimize the occurrence of TD. If signs and symptoms appear in a patient on LATUDA, drug discontinuation should be considered.

Metabolic Changes

Hyperglycemia and Diabetes Mellitus: Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. 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 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 suspect drug.

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

Weight Gain: Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

Hyperprolactinemia: As with other drugs that antagonize dopamine D2 receptors, LATUDA elevates prolactin levels. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported in patients receiving prolactin-elevating compounds.

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia/neutropenia has been reported during treatment with antipsychotic agents. Agranulocytosis (including fatal cases) has been reported with other agents in the class. Patients with a preexisting low white blood cell count (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 LATUDA should be discontinued at the first sign of a decline in WBC in the absence of other causative factors.

Orthostatic Hypotension and Syncope: LATUDA may cause orthostatic hypotension. Orthostatic vital signs should be monitored in patients who are vulnerable to hypotension and in patients with known cardiovascular disease or cerebrovascular disease.

Seizures: LATUDA should be used cautiously in patients with a history of seizures or with conditions that lower seizure threshold (e.g., Alzheimer's dementia).

Potential for Cognitive and Motor Impairment: In short-term, placebo-controlled trials, somnolence was reported in 17.0% (256/1508) of patients treated with LATUDA compared to 7.1% (50/708) of placebo patients, respectively. Patients should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that therapy with LATUDA 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 LATUDA for patients who will be experiencing conditions that 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.

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

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. LATUDA and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

ADVERSE REACTIONS

Commonly Observed Adverse Reactions: (incidence ≥5% and at least twice the rate of placebo) in patients treated with LATUDA were somnolence, akathisia, nausea and parkinsonism.

Please see brief summary of prescribing information on adjacent pages, including **Boxed Warning**.

Reference: 1. LATUDA prescribing information. Sunovion Pharmaceuticals Inc. May 2012.

FOR MORE INFORMATION, PLEASE CALL 1-888-394-7377 OR VISIT **www.LatudaHCP.com**.

Brief Summary (for Full Prescribing Information, see package insert)

WARNING: 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 *[see Warnings and Precautions (5.1)]*.**
- **LATUDA is not approved for use in patients with dementia-related psychosis *[see Warnings and Precautions 5.1)]*.**

1 INDICATIONS AND USAGE

LATUDA is indicated for the treatment of patients with schizophrenia.

The efficacy of LATUDA in schizophrenia was established in five 6-week controlled studies of adult patients with schizophrenia *[Clinical Studies (14.1)]*.

The effectiveness of LATUDA for longer-term use, that is, for more than 6 weeks, has not been established in controlled studies. Therefore, the physician who elects to use LATUDA for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient *[see Dosage and Administration (2)]*.

4 CONTRAINDICATIONS

LATUDA is contraindicated in the following:

- Any patient with a known hypersensitivity to lurasidone HCl or any components in the formulation. Angioedema has been observed with lurasidone *[see Adverse Reactions (6.1)]*.
- Concomitant use with strong CYP3A4 inhibitors (e.g., ketoconazole) *[see Drug Interactions (7.1)]*.
- Concomitant use with strong CYP3A4 inducers (e.g., rifampin) *[see Drug Interactions (7.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 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. LATUDA is not approved for the treatment of patients with dementia-related psychosis *[see Boxed Warning]*.

5.2 Cerebrovascular Adverse Reactions, Including Stroke in Elderly Patients with Dementia-Related Psychosis

In placebo-controlled trials with risperidone, aripiprazole, and olanzapine in elderly subjects with dementia, there was a higher incidence of cerebrovascular adverse reactions (cerebrovascular accidents and transient ischemic attacks), including fatalities, compared to placebo-treated subjects. LATUDA is not approved for the treatment of patients with dementia-related psychosis *[see also Boxed Warning and Warnings and Precautions (5.1)]*.

5.3 Neuroleptic Malignant Syndrome

A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with administration of antipsychotic drugs, including LATUDA.

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 creatinine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

The diagnostic evaluation of patients with this syndrome is complicated. 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 NMS.

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

5.4 Tardive Dyskinesia

Tardive dyskinesia is a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements that can 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 cases of 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 that symptomatic suppression has upon the long-term course of the syndrome is unknown.

Given these considerations, LATUDA 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 on LATUDA, drug discontinuation should be considered. However, some patients may require treatment with LATUDA despite the presence of the syndrome.

5.5 Metabolic Changes

Atypical antipsychotic drugs have been associated with metabolic changes that may increase cardiovascular/cerebrovascular risk. These metabolic changes include hyperglycemia, dyslipidemia, and body weight gain. While all of the drugs in the class have been shown to produce some metabolic changes, each drug has its own specific risk profile.

Hyperglycemia and Diabetes Mellitus

Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. 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 events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. Because LATUDA was not marketed at the time these studies were performed, it is not known if LATUDA is associated with this increased risk.

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 suspect drug.

Pooled data from short-term, placebo-controlled studies are presented in Table 1.

Table 1: Change in Fasting Glucose

		LATUDA				
	Placebo	20 mg/day	40 mg/day	80 mg/day	120 mg/day	160 mg/day
Mean Change from Baseline (mg/dL)						
	n=680	**n=71**	**n=478**	**n=508**	**n=283**	**n=113**
Serum Glucose	–0.0	–0.6	2.6	–0.4	2.5	2.5
Proportion of Patients with Shifts to ≥ 126 mg/dL						
Serum Glucose (≥ 126 mg/dL)	8.3% (52/628)	11.7% (7/60)	12.7% (57/449)	6.8% (32/472)	10.0% (26/260)	5.6% (6/108)

In the uncontrolled, longer-term studies (primarily open-label extension studies), LATUDA was associated with a mean change in glucose of +1.8 mg/dL at week 24 (n=355), +0.8 mg/dL at week 36 (n=299) and +2.3 mg/dL at week 52 (n=307).

Dyslipidemia

Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics. Pooled data from short-term, placebo-controlled studies are presented in Table 2.

Table 2: Change in Fasting Lipids

		LATUDA				
	Placebo	20 mg/day	40 mg/day	80 mg/day	120 mg/day	160 mg/day
Mean Change from Baseline (mg/dL)						
	n=660	**n=71**	**n=466**	**n=499**	**n=268**	**n=115**
Total cholesterol	–5.8	–12.3	–5.7	–6.2	–3.8	–6.9
Triglycerides	–13.4	–29.1	–5.1	–13.0	–3.1	–10.6
Proportion of Patients with Shifts						
Total Cholesterol (≥ 240 mg/dL)	5.3% (30/571)	13.8% (8/58)	6.2% (25/402)	5.3% (23/434)	3.8% (9/238)	4.0% (4/101)
Triglycerides (≥ 200 mg/dL)	10.1% (53/526)	14.3% (7/49)	10.8% (41/379)	6.3% (25/400)	10.5% (22/209)	7.0% (7/100)

In the uncontrolled, longer-term studies (primarily open-label extension studies), LATUDA was associated with a mean change in total cholesterol and triglycerides of –3.8 (n=356) and –15.1 (n=357) mg/dL at week 24, –3.1 (n=303) and –4.8 (n=303) mg/dL at week 36 and –2.5 (n=307) and –6.9 (n=307) mg/dL at week 52, respectively.

Weight Gain

Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

Pooled data from short-term, placebo-controlled studies are presented in Table 4. The mean weight gain was 0.43 kg for LATUDA-treated patients compared to –0.02 kg for placebo-treated patients. Change in weight from baseline for olanzapine was 4.15 kg and for quetiapine extended-release was 2.09 kg in Studies 3 and 5 *[see Clinical Studies (14.1)]*, respectively. The proportion of patients with a ≥ 7% increase in body weight (at Endpoint) was 4.8% for LATUDA-treated patients versus 3.3% for placebo-treated patients.

Table 3: Mean Change in Weight (kg) from Baseline

		LATUDA				
	Placebo (n=696)	20 mg/day (n=71)	40 mg/day (n=484)	80 mg/day (n=526)	120 mg/day (n=291)	160 mg/day (n=114)
All Patients	–0.02	–0.15	0.22	0.54	0.68	0.60

In the uncontrolled, longer-term studies (primarily open-label extension studies), LATUDA was associated with a mean change in weight of –0.69 kg at week 24 (n=755), –0.59 kg at week 36 (n=443) and –0.73 kg at week 52 (n=377).

5.6 Hyperprolactinemia

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

Hyperprolactinemia may suppress hypothalamic GnRH, resulting in reduced pituitary gonadotrophin secretion. This, in turn, may inhibit reproductive function by impairing gonadal steroidogenesis 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 *[see Adverse Reactions (6)]*.

In short-term, placebo-controlled studies, the median change from baseline to endpoint in prolactin levels for LATUDA-treated patients was 0.4 ng/mL and was –1.9 ng/mL in the placebo-treated patients. The median change from baseline to endpoint for males was 0.5 ng/mL and for females was –0.2 ng/mL. Median changes for prolactin by dose are shown in Table 5.

Table 4: Median Change in Prolactin (ng/mL) from Baseline

		LATUDA				
	Placebo	20 mg/day	40 mg/day	80 mg/day	120 mg/day	160 mg/day
All Patients	–1.9 (n=672)	–1.1 (n=70)	–1.4 (n=476)	–0.2 (n=495)	3.3 (n=284)	3.3 (n=115)
Females	–5.1 (n=200)	–0.7 (n=19)	–4.0 (n=149)	–0.2 (n=150)	6.7 (n=70)	7.1 (n=36)
Males	–1.3 (n=472)	–1.2 (n=51)	–0.7 (n=327)	–0.2 (n=345)	3.1 (n=214)	2.4 (n=79)

The proportion of patients with prolactin elevations ≥ 5× upper limit of normal (ULN) was 2.8% for LATUDA-treated patients versus 1.0% for placebo-treated patients. The proportion of female patients with prolactin elevations ≥ 5x ULN was 5.7% for LATUDA-treated patients versus 2.0% for placebo-treated female patients. The proportion of male patients with prolactin elevations > 5x ULN was 1.6% versus 0.6% for placebo-treated male patients.

In the uncontrolled longer-term studies (primarily open-label extension studies), LATUDA was associated with a median change in prolactin of –0.9 ng/mL at week 24 (n=357), –5.3 ng/mL at week 36 (n=190) and –2.2 ng/mL at week 52 (n=307).

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 considered in a patient with previously detected breast cancer. As is common with compounds which increase prolactin release, an increase in mammary gland neoplasia was observed in a LATUDA carcinogenicity study conducted in rats and mice *[see Nonclinical Toxicology (13)]*. 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, but the available evidence is too limited to be conclusive.

5.7 Leukopenia, Neutropenia and Agranulocytosis

Leukopenia/neutropenia has been reported during treatment with antipsychotic agents. Agranulocytosis (including fatal cases) has been reported with other agents in the class.

Possible risk factors for leukopenia/neutropenia include pre-existing 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 LATUDA should be discontinued at the first sign of 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 LATUDA and have their WBC followed until recovery.

5.8 Orthostatic Hypotension and Syncope

LATUDA may cause orthostatic hypotension, perhaps due to its α1-adrenergic receptor antagonism. The incidence of orthostatic hypotension and syncope events from short-term, placebo-controlled studies was (LATUDA incidence, placebo incidence): orthostatic hypotension [0.3% (5/1508), 0.1% (1/708)] and syncope [0.1% (2/1508), 0% (0/708)]. Assessment of orthostatic hypotension was defined by vital sign changes (≥ 20 mm Hg decrease in systolic blood pressure and ≥ 10 bpm increase in pulse from sitting to standing or supine to standing positions). In short-term clinical trials, orthostatic hypotension occurred with a frequency of 0.8% with LATUDA 40 mg, 2.1% with LATUDA 80 mg, 1.7% with LATUDA 120 mg and 0.8% with LATUDA 160 mg compared to 0.7% with placebo.

Orthostatic vital signs should be monitored in patients who are vulnerable to hypotension (e.g., dehydration, hypovolemia, and treatment with antihypertensive medications), and in patients with known cardiovascular disease (e.g., heart failure, history of myocardial infarction, ischemia, or conduction abnormalities), or cerebrovascular disease.

5.9 Seizures

As with other antipsychotic drugs, LATUDA should be used cautiously in patients with a history of seizures or with conditions that lower the seizure threshold, e.g., Alzheimer's dementia. Conditions that lower the seizure threshold may be more prevalent in patients 65 years or older.

In short-term, placebo-controlled trials, seizures/convulsions occurred in 0.1% (2/1508) of patients treated with LATUDA compared to 0.1% (1/708) placebo-treated patients.

5.10 Potential for Cognitive and Motor Impairment

LATUDA, like other antipsychotics, has the potential to impair judgment, thinking or motor skills.

In short-term, placebo-controlled trials, somnolence was reported by 17.0% (256/1508) of patients treated with LATUDA (15.5% LATUDA 20 mg, 15.6% LATUDA 40 mg, 15.2% LATUDA 80 mg, 26.5% LATUDA 120 mg and 8.3% LATUDA 160 mg/day) compared to 7.1% (50/708) of placebo patients. In these short-term trials, somnolence included: hypersomnia, hypersomnolence, sedation and somnolence.

Patients should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that therapy with LATUDA does not affect them adversely.

5.11 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 LATUDA for patients who will be experiencing conditions that

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 *[see Patient Counseling Information (17.9)]*.

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 LATUDA should be written for the smallest quantity of tablets consistent with good patient management in order to reduce the risk of overdose.

In short-term, placebo-controlled studies in patients with schizophrenia, the incidence of treatment-emergent suicidal ideation was 0.4% (6/1508) for LATUDA-treated patients compared to 0.8% (6/708) on placebo. No suicide attempts or completed suicides were reported in these studies.

5.13 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. LATUDA and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

5.14 Use in Patients with Concomitant Illness

Clinical experience with LATUDA in patients with certain concomitant illnesses is limited *[see Clinical Pharmacology (12.3)]*.

Patients with Parkinson's Disease or Dementia with Lewy Bodies are reported to have an increased sensitivity to antipsychotic medication. Manifestations of this increased sensitivity include confusion, obtundation, postural instability with frequent falls, extrapyramidal symptoms, and clinical features consistent with the neuroleptic malignant syndrome.

LATUDA has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were excluded from premarketing clinical trials. Because of the risk of orthostatic hypotension with LATUDA, caution should be observed in patients with known cardiovascular disease *[see Warnings and Precautions (5.8)]*.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in more detail in other sections of the labeling:

- Use in Elderly Patients with Dementia-Related Psychosis *[see Boxed Warning and Warnings and Precautions (5.1)]*
- Cerebrovascular Adverse Reactions, Including Stroke *[see Warnings and Precautions (5.2)]*
- Neuroleptic Malignant Syndrome *[see Warnings and Precautions (5.3)]*
- Tardive Dyskinesia *[see Warnings and Precautions (5.4)]*
- Hyperglycemia and Diabetes Mellitus *[see Warnings and Precautions (5.5)]*
- Hyperprolactinemia *[see Warnings and Precautions (5.6)]*
- Leukopenia, Neutropenia, and Agranulocytosis *[see Warnings and Precautions (5.7)]*
- Orthostatic Hypotension and Syncope *[see Warnings and Precautions (5.8)]*
- Seizures *[see Warnings and Precautions (5.9)]*
- Potential for Cognitive and Motor Impairment *[see Warnings and Precautions (5.10)]*
- Body Temperature Regulation *[see Warnings and Precautions (5.11)]*
- Suicide *[see Warnings and Precautions (5.12)]*
- Dysphagia *[see Warnings and Precautions (5.13)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in 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 clinical practice.

The information below is derived from a clinical study database for LATUDA consisting of 2905 patients with schizophrenia exposed to one or more doses with a total experience of 985.3 patient-years. Of these patients, 1508 participated in short-term, placebo-controlled schizophrenia studies with doses of 20 mg, 40 mg, 80 mg, 120 mg or 160 mg once daily. A total of 769 LATUDA-treated patients had at least 24 weeks and 371 LATUDA-treated patients had at least 52 weeks of exposure.

Adverse events during exposure to study treatment were obtained by general inquiry and voluntarily reported adverse experiences, as well as results from physical examinations, vital signs, ECGs, weights and laboratory investigations. Adverse experiences were recorded by clinical investigators using their own terminology. In order to provide a meaningful estimate of the proportion of individuals experiencing adverse events, events were grouped in standardized categories using MedDRA terminology.

The following findings are based on the short-term, placebo-controlled premarketing studies for schizophrenia in which LATUDA was administered at daily doses ranging from 20 to 160 mg (n=1508).

Commonly Observed Adverse Reactions: The most common adverse reactions (incidence ≥ 5% and at least twice the rate of placebo) in patients treated with LATUDA were somnolence, akathisia, nausea and parkinsonism.

Adverse Reactions Associated with Discontinuation of Treatment: A total of 9.5% (143/1508) LATUDA-treated patients and 9.3% (66/708) of placebo-treated patients discontinued due to adverse reactions. There were no adverse reactions associated with discontinuation in subjects treated with LATUDA that were at least 2% and at least twice the placebo rate.

Adverse Reactions Occurring at an Incidence of 2% or More in LATUDA-Treated Patients: Adverse reactions associated with the use of LATUDA (incidence of 2% or greater, rounded to the nearest percent and LATUDA incidence greater than placebo) that occurred during acute therapy (up to 6 weeks in patients with schizophrenia) are shown in Table 5.

Table 5: Adverse Reactions in 2% or More of LATUDA-Treated Patients and That Occurred at Greater Incidence than in the Placebo-Treated Patients in Short-term Schizophrenia Studies

	Percentage of Patients Reporting Reaction	
Body System or Organ Class Dictionary-derived Term	**Placebo (N=708)**	**All LATUDA (N=1508)**
Gastrointestinal Disorders		
Nausea	5	10
Vomiting	6	8
Dyspepsia	5	6
Salivary Hypersecretion	<1	2
Musculoskeletal and Connective Tissue Disorders		
Back Pain	2	3
Nervous System Disorders		
Somnolence*	7	17
Akathisia	3	13
Parkinsonism**	5	10
Dizziness	2	4
Dystonia***	<1	4
Psychiatric Disorders		
Insomnia	8	10
Agitation	4	5
Anxiety	4	5
Restlessness	1	2

Note: Figures rounded to the nearest integer
* Somnolence includes adverse event terms: hypersomnia, hypersomnolence, sedation, and somnolence
** Parkinsonism includes adverse event terms: bradykinesia, cogwheel rigidity, drooling, extrapyramidal disorder, hypokinesia, muscle rigidity, parkinsonism, psychomotor retardation, and tremor
*** Dystonia includes adverse event terms: dystonia, oculogyric crisis, oromandibular dystonia, tongue spasm, torticollis, and trismus

Dose-Related Adverse Reactions

In pooled data from the short-term, placebo-controlled, fixed-dose studies, there were no dose-related adverse reactions (greater than 5% incidence) in patients treated with LATUDA across the 20 mg/day to 160 mg/day dose range. However, the frequency of akathisia increased with dose up to 120 mg/day (5.6% LATUDA 20 mg, 10.7% LATUDA 40 mg, 12.3% LATUDA 80 mg, 22.0% LATUDA 120 mg); akathisia was reported by 7.4% (9/121) of patients receiving 160 mg/day. Akathisia occurred in 3.0% of subjects receiving placebo.

Extrapyramidal Symptoms

In the short-term, placebo-controlled schizophrenia studies, for LATUDA-treated patients, the incidence of reported events related to extrapyramidal symptoms (EPS), excluding akathisia and restlessness, was 13.5% versus 5.8% for placebo-treated patients. The incidence of akathisia for LATUDA-treated patients was 12.9% versus 3.0% for placebo-treated patients. Incidence of EPS by dose is provided in Table 7.

Table 6: Incidence of EPS Compared to Placebo

		LATUDA				
Adverse Event Term	**Placebo (N=709) (%)**	**20 mg/day (N=71) (%)**	**40 mg/day (N=487) (%)**	**80 mg/day (N=538) (%)**	**120 mg/day (N=291) (%)**	**160 mg/day (N=121) (%)**
All EPS events	**9**	**10**	**21**	**23**	**39**	**20**
All EPS events, excluding Akathisia/ Restlessness	**6**	**6**	**11**	**12**	**22**	**13**
Akathisia	3	6	11	12	22	7
Dystonia*	<1	0	4	5	7	2
Parkinsonism**	5	6	9	8	17	11
Restlessness	1	1	3	1	3	2

Note: Figures rounded to the nearest integer
* Dystonia includes adverse event terms: dystonia, oculogyric crisis, oromandibular dystonia, tongue spasm, torticollis, and trismus
** Parkinsonism includes adverse event terms: bradykinesia, cogwheel rigidity, drooling, extrapyramidal disorder, hypokinesia, muscle rigidity, parkinsonism, psychomotor retardation, and tremor

In the short-term, placebo-controlled schizophrenia studies, data was objectively collected on the Simpson Angus Rating Scale for extrapyramidal symptoms (EPS), the Barnes Akathisia Scale (for akathisia) and the Abnormal Involuntary Movement Scale (for dyskinesias). The mean change from baseline for LATUDA-treated patients was comparable to placebo-treated patients, with the exception of the Barnes Akathisia Scale global score (LATUDA, 0.1; placebo, 0.0). The percentage of patients who shifted from normal to abnormal was greater in LATUDA-treated patients versus placebo for the BAS (LATUDA, 14.4%; placebo, 7.1%) and the SAS (LATUDA, 5.0%; placebo, 2.3%).

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.

In the short-term, placebo-controlled clinical trials, dystonia occurred in 4.2% of LATUDA-treated subjects (0.0% LATUDA 20 mg, 3.5% LATUDA 40 mg, 4.5% LATUDA 80 mg, 6.5% LATUDA 120 mg and 2.5% LATUDA 160 mg) compared to 0.8% of subjects receiving placebo. Seven subjects (0.5%, 7/1508) discontinued clinical trials due to dystonic events – four were receiving LATUDA 80 mg/day and three were receiving LATUDA 120 mg/day.

Other Adverse Reactions Observed During the Premarketing Evaluation of LATUDA

Following is a list of adverse reactions reported by patients treated with LATUDA at multiple doses of ≥ 20 mg once daily during any phase of a study within the database of 2905 patients. The reactions listed are those that could be of clinical importance, as well as reactions that are plausibly drug-related on pharmacologic or other grounds. Reactions listed in Table 5 or those that appear elsewhere in the LATUDA label are not included. Although the reactions reported occurred during treatment with LATUDA, they were not necessarily caused by it.

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

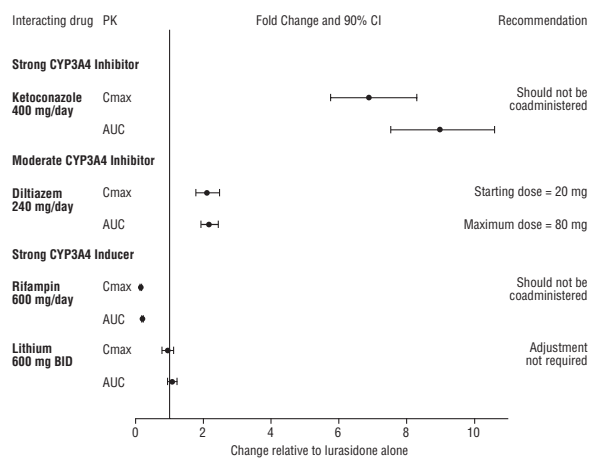
Blood and Lymphatic System Disorders: ***Infrequent:*** *anemia*
Cardiac Disorders: ***Frequent:*** *tachycardia;* ***Infrequent:*** *AV block 1st degree, angina pectoris, bradycardia*
Ear and Labyrinth Disorders: ***Infrequent:*** *vertigo*
Eye Disorders: ***Frequent:*** *blurred vision*
Gastrointestinal Disorders: ***Frequent:*** *abdominal pain, diarrhea;* ***Infrequent:*** *gastritis*
General Disorders and Administrative Site Conditions: ***Rare:*** *sudden death*
Investigations: ***Frequent:*** *CPK increased*
Metabolism and Nutritional System Disorders: ***Frequent:*** *decreased appetite*
Musculoskeletal and Connective Tissue Disorders: ***Rare:*** *rhabdomyolysis*
Nervous System Disorders: ***Infrequent:*** *cerebrovascular accident, dysarthria*
Psychiatric Disorders: ***Infrequent:*** *abnormal dreams, panic attack, sleep disorder;*
Renal and Urinary Disorders: ***Infrequent:*** *dysuria;* ***Rare:*** *renal failure*
Reproductive System and Breast Disorders: ***Infrequent:*** *amenorrhea, dysmenorrhea;* ***Rare:*** *breast enlargement, breast pain, galactorrhea, erectile dysfunction*
Skin and Subcutaneous Tissue Disorders: ***Frequent:*** *rash, pruritus;* ***Rare:*** *angioedema*
Vascular Disorders: ***Frequent:*** *hypertension*

7 DRUG INTERACTIONS

7.1 Potential for Other Drugs to Affect LATUDA

LATUDA is predominantly metabolized by CYP3A4. LATUDA should not be used in combination with strong inhibitors or inducers of this enzyme *[see Contraindications (4)]* and dose should be limited when used in combination with moderate inhibitors of CYP3A4 *[see Dosage and Administration (2.4)]*. No dose adjustment is needed with concomitant use of lithium (see Figure 1).

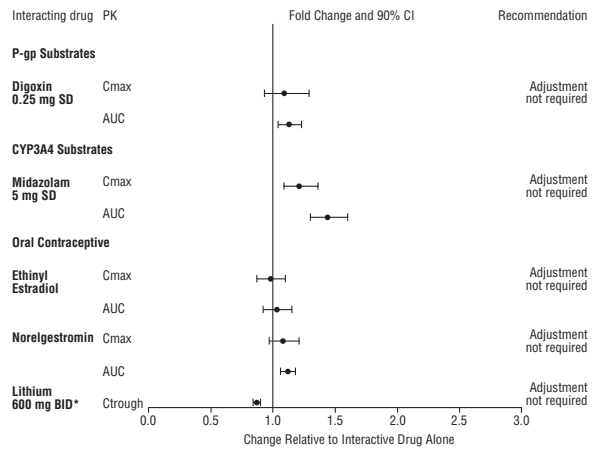
Figure 1: Impact of Other Drugs on LATUDA Pharmacokinetics



7.2 Potential for LATUDA to Affect Other Drugs

No adjustment is needed on the dose of lithium, or substrates of P-gp or CYP3A4 when coadministered with LATUDA (Figure 2).

Figure 2: Impact of LATUDA on Other Drugs



*Steady state lithium Ctrough on Day 4 vs Day 8 when lithium was coadministered with lurasidone at steady state

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects

Pregnancy Category B

LATUDA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Non-teratogenic Effects

Neonates exposed to antipsychotic drugs during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress and feeding disorder in these neonates. These complications have varied in severity; while in some cases symptoms have been self-limited, in other cases neonates have required intensive care unit support and prolonged hospitalization.

Safe use of LATUDA during pregnancy or lactation has not been established; therefore, use of LATUDA in pregnancy, in nursing mothers, or in women of childbearing potential requires that the benefits of treatment be weighed against the possible risks to mother and child.

Animal Data
No adverse developmental effects were seen in a study in which pregnant rats were given LATUDA during the period of organogenesis and continuing through weaning at doses up to 10 mg/kg/day; this dose is approximately half of the MRHD based on body surface area.

No teratogenic effects were seen in studies in which pregnant rats and rabbits were given LATUDA during the period of organogenesis at doses up to 25 and 50 mg/kg/day, respectively. These doses are 1.5- and 6- times, in rats and rabbits respectively, the maximum recommended human dose (MRHD) of 160 mg/day based on body surface area.

8.3 Nursing Mothers
LATUDA was excreted in milk of rats during lactation. It is not known whether LATUDA or its metabolites are excreted in human milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, considering risk of drug discontinuation to the mother.

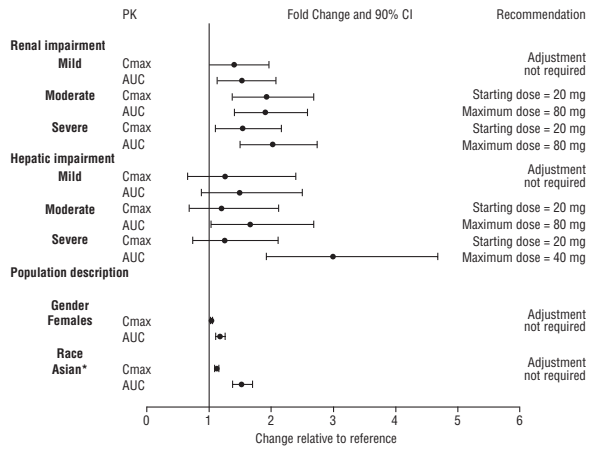
8.4 Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use
Clinical studies of LATUDA in the treatment of schizophrenia did not include sufficient numbers of patients aged 65 and older to determine whether or not they respond differently from younger patients. In elderly patients with psychosis (65 to 85), LATUDA concentrations (20 mg/day) were similar to those in young subjects *[see Clinical Pharmacology (12.3)]*. No dose adjustment is necessary in elderly patients (Figure 2).

Elderly patients with dementia-related psychosis treated with LATUDA are at an increased risk of death compared to placebo. LATUDA is not approved for the treatment of patients with dementia-related psychosis *[see Boxed Warning]*.

8.6 Other Patient Factors
The effect of intrinsic patient factors on the pharmacokinetics of LATUDA is presented in Figure 3.

Figure 3: Impact of Other Patient Factors on LATUDA Pharmacokinetics



*Compare to Caucasian

10 OVERDOSAGE

10.1 Human Experience
In premarketing clinical studies involving 2905 patients, accidental or intentional overdosage of LATUDA was identified in one patient who ingested an estimated 560 mg of LATUDA. This patient recovered without sequelae. This patient resumed LATUDA treatment for an additional two months.

10.2 Management of Overdosage
Consult a Certified Poison Control Center for up-to-date guidance and advice. There is no specific antidote to LATUDA, therefore, appropriate supportive measures should be instituted and close medical supervision and monitoring should continue until the patient recovers.

Cardiovascular monitoring should commence immediately, including continuous electrocardiographic monitoring for possible arrhythmias. If antiarrhythmic therapy is administered, disopyramide, procainamide, and quinidine carry a theoretical hazard of additive QT-prolonging effects when administered in patients with an acute overdose of LATUDA. Similarly, the alpha-blocking properties of bretylium might be additive to those of LATUDA, resulting in problematic hypotension.

Hypotension and circulatory collapse should be treated with appropriate measures. Epinephrine and dopamine should not be used, or other sympathomimetics with beta-agonist activity, since beta stimulation may worsen hypotension in the setting of LATUDA-induced alpha blockade. In case of severe extrapyramidal symptoms, anticholinergic medication should be administered.

Gastric lavage (after intubation if patient is unconscious) and administration of activated charcoal together with a laxative should be considered.

The possibility of obtundation, seizures, or dystonic reaction of the head and neck following overdose may create a risk of aspiration with induced emesis.

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☐ Early Career Psychiatrist
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What Is Your Primary Work Setting? ***(Check all that apply)***
☐ Private – Group
☐ Private – Solo
☐ Community Mental Health Center
☐ State Mental Health Hospital
☐ Academic Faculty
☐ VA/Federal Facility Other
☐ Hospital
☐ Academic Student

COURSE ENROLLMENT *Indicate course number found in the Course Brochure.*

Registrant

Saturday	First Choice(s) _____	Alternate(s) _____
Sunday	First Choice(s) _____	Alternate(s) _____
Monday	First Choice(s) _____	Alternate(s) _____
Tuesday	First Choice(s) _____	Alternate(s) _____
Wednesday	First Choice(s) _____	Alternate(s) _____

Spouse/Significant Other

Saturday	First Choice(s) _____	Alternate(s) _____
Sunday	First Choice(s) _____	Alternate(s) _____
Monday	First Choice(s) _____	Alternate(s) _____
Tuesday	First Choice(s) _____	Alternate(s) _____
Wednesday	First Choice(s) _____	Alternate(s) _____

PAYMENT INFORMATION

	FULL REGISTRATION	DAILY
Registrant Registration	$_____	$_____ ___ Sat ___ Sun ___ Mon ___ Tues ___ Wed
Registrant Courses	$_____	
Spouse/Significant Other Registration	$_____	$_____ ___ Sat ___ Sun ___ Mon ___ Tues ___ Wed
Spouse/Significant Other Courses	$_____	
Course Director	$ 0	I authorize charge of total payment:
APA Honorary Fellow	$ 0	
Medical Student	$ 0	
Donation to Mental Health Association of San Francisco	$_____	_____ SIGNATURE
Mail/Fax Fee	$10	_____ Exp. Date _____
TOTAL PAYMENT	$_____	CREDIT CARD NUMBER (American Express, MasterCard, or VISA only)

TRAVEL INFORMATION

MACNAIR TRAVEL MANAGEMENT

Travel Services Representative

For the **American Psychiatric Association's 2013 Annual Meeting** in San Francisco unique travel discounts are being offered on United, Delta, and American, as well as a variety of low-cost airline carriers, and web fares by **MacNair Travel Management/ American Express**, APA's official travel company. Contact MacNair via the communication channels listed below and secure the best value for your travel to and from the meeting, as well as any pre- or post- meeting travel arrangements you may require. Following are details of the United, Delta, and American discounted fare programs.

United – ***To be announced***

Delta – 5-10% off certain published fares on Delta, KLM or Air France

American – ***5% off***

Call **MacNair Travel Management** to make your travel arrangements:

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For residents of Virginia, Maryland, or the District of Columbia, or outside the U.S. or Canada, please call **202-496-9307, 8:30 a.m. - 7:00 p.m., EST,or you may fax** your request to (703) 879-7387. E-mail requests may be sent to apa@macnairtravel.com

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Or you may contact the following carriers directly:

United Airlines
1-800-521-4041
www.united.com
Meeting Code: ***To be announced***

Delta Air Lines
1-800-328-1111
Meeting ID Code: ***NMENK***

American Airlines
www.aa.com
Meeting Code: ***A4953BV***

REGISTRATION FORM

American Psychiatric Association • 166th Annual Meeting
May 18-22, 2013 • San Francisco, CA

EARLY BIRD REGISTRATION: Members: November 1, 2012 – January 24, 2013 **Nonmembers:** November 15, 2012 – January 24, 2013
ADVANCE REGISTRATION: January 25 – April 19, 2013

REGISTER ONLINE: www.psychiatry.org/learn/annual-meeting

Register by fax at **703-907-1097** or mail your registration form with payment (payable to APA) to:
American Psychiatric Association Annual Meeting • P.O. Box 418237 • Boston, MA 02241-8237
Mailed and faxed forms will not be accepted after April 19, 2013.
Written cancellations must be received in the APA office by May 8, 2013.

REGISTRATION INFORMATION ***(address may be published)***

First Name _____ APA Member # _____
Last Name _____ Degree _____
Address _____
Address _____
City _____ State/Prov _____ Zip Code _____-_____
Country (if outside U.S.) _____ Email* _____
*mandatory for confirmation and for meeting announcements
Day Phone _____ Cell Number _____
for meeting alerts
NPI Number _____ First time attendee? ☐ Yes ☐ No
SPOUSE/SIGNIFICANT OTHER (if registering) Hotel: _____
First Name _____ Last Name _____ Degree _____

What Is Your Discipline? ***(Check all that apply)***
☐ Psychiatrist
☐ Mental Health Advocate/Consumer
☐ Other MD/DO
☐ Resident – Year of graduation from residency _____
☐ Other Mental Health Professional
☐ Medical Student

Are you? ***(Check all that apply)***
☐ Early Career Psychiatrist
☐ International Medical Graduate

What Is Your Primary Work Setting? ***(Check all that apply)***
☐ Private – Group
☐ Private – Solo
☐ Community Mental Health Center
☐ State Mental Health Hospital
☐ Academic Faculty
☐ VA/Federal Facility Other
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☐ Academic Student

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Delta Air Lines
1-800-328-1111
Meeting ID Code: ***NMENK***

American Airlines
www.aa.com
Meeting Code: ***A4953BV***

HOTEL RESERVATION INFORMATION

HOTEL RESERVATION INFORMATION

- **Online:** www.psychiatry.org/learn/annual-meeting (click on the 2013 Annual Meeting logo, then housing information, then attendee or exhibitor information, and then on housing and travel)
- **Fax:** (nine (9) rooms or less) attached housing reservation form to (212) 779-6128
- **Fax:** (ten (10) rooms or more) attached housing reservation form to (212) 532-1556
- **Mailing Address:** Travel Planners, Inc., 381 Park Avenue South, Third Floor, New York, NY 10016
- **By phone:** dial (800) 221-3531 (USA, Caribbean, and Canada); internationally, dial (212) 532-1660

Deposit Policy: Reservations will only be accepted with a credit card guarantee or check deposit. Deposit checks and wire transfers must be received within ten (10) days of booking or by March 22, 2013, whichever is earlier. (Reservations will automatically be canceled if checks or wires are not received within this time frame.) After March 22, 2013, reservations will be accepted with a credit card guarantee only. Reservations and changes are subject to hotel availability. Please check your reservation confirmation for details.

Cancellation Policy: Cancellations of hotel reservations must be made directly with Travel Planners.

Additional Reservation Information:

1. Travel Planners will process requests on a first-come, first-served basis.
2. Group bookings will be based on previous room pick-up history and per APA guidelines for exhibitors.
3. Group rooming lists are due on March 15, 2013. On March 16, 2013, any unassigned room held for a group will be released if name is not provided and rooms are not guaranteed with a credit card or check deposit.
4. Reservations will be accepted with a credit card guarantee or check deposit only.
   a. If you are making more than one reservation, you will need to provide a credit card and billing address for each room to be charged.
   b. If one card is going to pay for all rooms (up to a maximum of 10 rooms) then only one card and address is necessary.
   c. A different credit card must be used for every ten (10) rooms.
5. The following credit cards can be used to make your reservation: Visa, MasterCard, or American Express.
6. Each credit card must be valid through the reservation dates of the stay. Should your card expire prior to the 2013 Annual Meeting, you may guarantee your block with a deposit by check.
7. To pay by check, make check payable to: Travel Planners, Inc., and mail to: Travel Planners, Inc., 381 Park Avenue South, Third Floor, New York, NY 10016.
8. Suites and function/meeting space are for approved affiliates only and requests must be approved by APA. Affiliate Meeting Space Request Forms are available through the APA website beginning November 15, 2012.
9. Individual policies for each hotel must be strictly adhered to. Most hotels impose fees for early departures. This policy is at the discretion of the individual hotel and the amount of the fee varies by hotel. Be sure to verify your actual date of departure at the time of check in.
10. For fax or group reservations (10 rooms or more), you will receive a confirmation within three business days.
11. For fax requests, please provide credit card information upon receipt of confirmation.
12. For individual online reservations, you will receive a confirmation immediately.

Travel Planners, Inc. makes no guarantee of any kind that the hotels and rates listed will be available at the time you make your reservation. Reservation requests and changes are subject to the availability and discretion of the hotels.

All information is as of September 5, 2012, and subject to change.

HOTEL REGISTRATION FORM

American Psychiatric Association • 166th Annual Meeting
May 18-22, 2013 • San Francisco, CA

Name: _____ Date: _____

Company Name: _____

Address: _____
(Street) (Suite/Floor)

_____
(City) (State) (Zip/Country Code) (Country)

Contact Name: _____

Phone: (_____) _____Ext._____Fax: (_____)_____Email:_____

HOTEL SELECTION (Please fill in all six choices)

1st: _____ 4th: _____
2nd: _____ 5th: _____
3rd: _____ 6th: _____

NO ADVANCE DEPOSIT REQUIRED

Use more than one row for different dates if necessary and indicate the number of rooms required for each room type.

Occupant Name (required)	Attendee, Exhibitor, or APA Member?	Check-In Date	Check-Out Date	# Single Rooms	# Double Rooms (2 ppl/1 bed)	# Twin Rooms (2 ppl/2 beds)

Total number of rooms needed: _____ SPECIAL REQUIREMENTS/REQUESTS: _____

Do you require an ADA-Compatible Room? _____ Smoking or Nonsmoking? _____

Other requirements/requests? _____

This form is to indicate preference only and submission does not guarantee confirmation. Notification of confirmed details will be faxed/emailed by Travel Planners, Inc. within three business days of receipt.

Cancellation policy: Until three business days prior to arrival, cancellations of reservations must be made directly with Travel Planners. Hotel's cancellation policies are strictly adhered to and may vary by hotel. Cancellation policies will be outlined on your confirmation. Travel Planners, Inc. makes no warranties of any kind that the hotels and rates listed will be available at the time you make your reservation. Reservation requests and changes are subject to the availability and discretion of the hotels.

Fax: (212) 779-6128
(9 rooms or less)

(212) 532-1556
(10 rooms or more)

Mail: Travel Planners, Inc. 381 Park Avenue South, Third Floor New York, NY 10016

If you do not receive confirmation receipt within three business days, please call Travel Planners, Inc.

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CLINICAL & RESEARCH NEWS

El-Branden Brazil

Many owned dogs, like this Akita mix named Sam, were left behind when their owners fled the post earthquake tsunami that hit Japan's eastern coast on March 11, 2011. Sam was later rescued from the exclusion zone near the Fukushima nuclear power plant, but untold numbers of companion animals remain abandoned and homeless in the aftermath of the disaster.

Extreme Stress After Quakes Not Limited to Humans

Dogs from Fukushima, Japan, exhibit deficits in attachment and learning ability, suggesting the depth of the stress they endured from the earthquake and its aftermath.

BY LESLIE SINCLAIR

Researchers in the Department of Animal Science and Biotechnology at Azabu University in Kanagawa, Japan, have reported that dogs abandoned in the aftermath of the March 11, 2011, earthquake that devastated the Tohoku coastline are exhibiting long-term signs of distress that mimic posttraumatic stress disorder (PTSD) in humans.

In the October 2012 *Nature*, lead author Miho Nagasawa, Ph.D., and his colleagues reported that the 340,000 people who are still living as refugees after the disaster are not the only ones seriously impacted by the tragedy—the earthquake also left many companion animals unintentionally abandoned.

"Many dogs have roamed or been chained and left alone for long periods, and some of them have been living in a semiferal state in the exclusion zone around the nuclear reactor," they said.

Students at Azabu University have conducted a program to place abandoned dogs with new owners after provision of psychosomatic care in a training facility at the university, and Nagasawa and his colleagues, in an effort to elucidate the consequences of stress from one of the highest-magnitude earthquakes recorded in history, compared behavior and urinary cortisol levels between some of the disaster-affected dogs from Fukushima Prefecture and dogs that had experienced abandonment in a nondisaster area, Kanagawa Prefecture.

They used the Canine Behavioral Assessment and Research Questionnaire (C-BARQ) to assess the dogs and found that the Fukushima dogs showed significantly lower aggression toward unfamiliar people, lower trainability, and lower attachment when evaluated one month after being transported from the training facility. After three months, the Fukushima dogs showed significantly lower separation anxiety and attachment than the Kanagawa dogs. Urinary cortisol levels were monitored in both groups of dogs for 70 days after their arrival at the facility, and the Fukushima dogs exhibited cortisol levels five to 10 times higher than those of the Kanagawa dogs, a trend that persisted throughout the 10-week period.

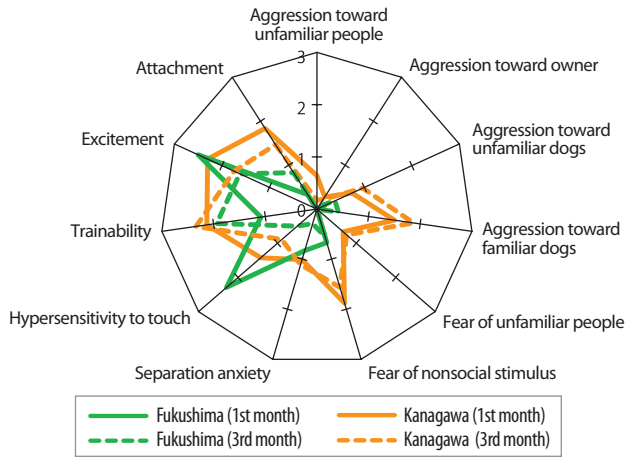
The researchers said their work has limitations, including a small sample and a difference in age between the Kanagawa and Fukushima dogs (although an analysis of the age effect was performed, with no significant findings).

"The low trainability and attachment scores among these dogs warrant special attention," said Nagasawa and his colleagues, who noted that impaired learning ability due to oversecretion of glucocorticoids is a core symptom in people who have experienced extreme stress, including those with PTSD. In addition, PTSD patients have been reported to show impaired ability with respect to attachment and bonding. "Similar results have been observed in experimental animals, and the disaster-affected dogs in this study appear to show signs of the same behavioral phenomenon. . . . Long-term care and concern regarding the psychological impact of disasters appears necessary in humans and companion animals," they concluded. PN

An abstract of "Continued Distress Among Abandoned Dogs in Fukushima" is posted at www.nature.com/srep/2012/121011/srep00724/full/srep00724.html.

Abandoned Earthquake Dogs Less Aggressive, but Aloof

Median scores for C-BARQ behavioral evaluation criteria at one month and three months after arrival in a training facility at Azabu University indicated significantly lowered aggression toward unfamiliar people and lowered trainability and attachment in the dogs from disaster-affected Fukushima than in a control group of dogs from the nondisaster area of Kanagawa.



Source: Miho Nagasawa, Ph.D., et al., *Scientific Reports*, October 11, 2012

Biographer

continued from page 16

That Built a Nation, cataloguing the obsessive traits of such high achievers as Thomas Jefferson, Melvil Dewey, Estee Lauder, and Ted Williams.

"The job of a biographer is to get inside of a subject's head," Kendall said. "I guess what fascinates me about obsessional types is that they are always pretty clear about what is on their minds."

In the telling of these personal American histories, Kendall is exploring the complex interplay between character—and character pathology—and human achievement. As such, his subject is one that also captures the attention of psychiatric diagnosticians and researchers, especially those interested in personality traits and disorders.

Past APA President and personality disorders expert John Oldham, M.D., was one of dozens of mental health professionals Kendall consulted in his research. In an interview with *Psychiatric News*, Oldham said he has not reviewed the texts of Kendall's work but consulted with the author in a general way about the emerging consensus among personality researchers: that a mix of personality traits is common to just about everyone and that the intensity of these traits may vary along a continuum from benign—even useful—to extremely disabling.

In a 1995 lay manual that Oldham co-wrote with Lois Morris titled *The New Personality Self-Portrait: Why You Think, Work, Love and Act the Way You Do*, he explored the ways in which personality traits that can be disabling in extreme cases can also be the keys to successful living when those traits are moderated.

"We took each category of personality disorder and conceptually 'turned the volume down' so that traits that are extreme in the case of a personality disorder might be looked at as healthy, adaptive styles."

So, for instance, the traits of obsessive-compulsive personality disorder with the "volume turned down" constitute a "conscientious style" personality when moderated: an individual always concerned with doing "the right thing" and doing it the "right way," with a knack for order and detail—the kind of fellow who might be very good at compiling a dictionary.

If the tangle of good and not-so-good traits that everyone displays is a conundrum for psychiatric diagnosticians, it is also a challenge for biographers striving to avoid the pitfalls of hagiography and the smear job. To capture the richness of a human life is to appreciate that troubled or even deeply flawed individuals may often accomplish great things.

"Biographers are tempted to either slime their subjects or idealize them," Kendall said. "But people are so much more complex." PN

COMMUNITY

Conn. Community Will Need Ongoing MH Vigilance, Say Experts

Disaster psychiatry experts map the long road ahead for a devastated Connecticut community.

BY AARON LEVIN

"I have seen trauma in many places but nothing ever struck me so hard as hearing about babies shot so many times," said Syed Arshad Husain, M.D.

Husain, a professor emeritus of psychiatry and child health at the University of Missouri-Columbia School of Medicine, has cared for children after war in Bosnia, earthquakes in Pakistan, and tornados in Joplin, Mo., but all that paled next to the horrors of Newtown, Conn., on a Friday morning in December.

The shooting deaths of 20 children and seven adults in Newtown, Conn., was an especially terrible reminder of the need to help survivors, families of victims, and an entire community cope with overwhelming tragedy.

Hard as it might have seemed in the days immediately after the massacre, redeveloping a sense of safety was the key to reducing the risk of deeper psychological trauma in the surviving children, said child psychiatrist Louis Kraus, M.D., chair of APA's Council on Children, Adolescents, and Their Families. Part of that effort means reestablishing the familiar routines of daily life.

"You have to get them back to school," said Kraus in an interview. "The longer they don't get back, the longer it will take them to recover."

By the Tuesday following the shooting, in fact, the other schools in Newtown were back in operation. At press time, however, the Sandy Hook students were scheduled to remain out of school until after winter break.

Through the Connecticut Psychiatric Society, Husain, a member of APA's Committee on the Psychiatric Dimensions of Disasters, volunteered to train Newtown teachers to recognize signs of psychiatric problems in students using a program developed by the International Center for Psychosocial Trauma, which he directs.

Parents also have to be aware of their own acute reactions to the event, said Kraus. "If they are not doing well, they can't take care of their children."

Caring for surviving classmates and siblings will be more complex because children respond to death differently depending on their developmental age, said Stephen Cozza, M.D., a professor of psychiatry at the Uniformed Services University of the Health Sciences. Cozza has studied and worked with children of military personnel who were killed or wounded.

Children younger than age 6 may reenact the event or complain of somatic symptoms, like headaches or stomachaches, he said in an interview.

"Others may exhibit magical thinking, believing they could have done something to prevent the event," said Cozza. "We have to relieve the child of that misguided sense of responsibility."

Some children may have symptoms of acute stress shortly after the event, but others may not exhibit serious psychopathology for a while, said Kraus. Still others may resolve initial symptoms only to have them reemerge months or years later.

Parents should also minimize their children's exposure to media stories about the event. Younger children may perceive replays on television as evidence that the event is not over and the danger continues, making it hard to reestablish the needed sense of safety, said Cozza.

Parents of the child victims have the extraordinary burden of living with their own grief while trying to care for their other children, said Cozza. They may feel guilt at their "failure" to protect their child and anger at the perpetrator. The effects on a child's body of fatal traumatic wounds, if seen by a parent, may add another excruciating level of emotional pain.

"Losing a child is one of the most horrific things someone can endure," said Carol North, M.D., M.P.E., a professor of psychiatry and surgery in the Division of Emergency Medicine at the University of Texas Southwestern Medical Center and director of the Program in Trauma and Disaster at the VA North Texas Health Care System in Dallas.

"People are permanently changed, but the psychological damage has a specific course," said North in an interview. "They may experience bereavement or traumatic grief or develop PTSD. Some may not develop psychiatric illness but can still be very distressed for a long time."

In North's studies of survivors of the 1995 Oklahoma City bombing seven years later, most people who had been diagnosed with PTSD, even if their cases remitted, still reported posttraumatic symptoms. However, one-third of those who had never been diagnosed with PTSD also reported symptoms.

Within bereaved families, brothers and sisters are sometimes shunted aside as parents grieve.

"We know less about the effects of these events on siblings," said Cozza. "They can also feel survivors' guilt and may feel responsible for continuing some tradition within the family that the victim once did."

Parents may become overprotective with their surviving children, making it hard for the children to move on and grow up normally, he cautioned.

Most people recover from their traumatic experiences, but perhaps 10 percent to 15 percent will need some form of help at some time in the months and years to come.

"Eventually, the media lose interest, outside support begins to diminish, and the people on the scene are left to deal with their problems," said North. "Suffering remains, and the need for support continues." PN

APA Responds to Newtown Shooting

"On behalf of the leadership of the American Psychiatric Association and myself, I would like to convey our deepest sympathies to the families of the Connecticut victims touched by [Friday's] unspeakable events," said APA President Dilip Jeste, M.D., in a statement posted on APA's Web site. "APA stands ready to do whatever we can to help alleviate the sufferings caused by the tragedy and help the survivors cope with life after a trauma of this unimaginable magnitude."

And it did. Within hours of the shooting, members of APA's Committee on Psychiatric Dimensions of Disasters were in telephone and e-mail contact with the leadership of the Connecticut Psychiatric Society, providing ongoing advice and support.

In addition to Jeste's statement, APA posted a number of other items on its Web site at http://www.psychiatry.org/and pushed out links to its thousands of Twitter and Facebook followers. These items included a message from psychiatrist and AMA President Jeremy Lazarus, M.D., a CBS interview with APA President-elect Jeffrey Lieberman, M.D., and tips for parents and professionals on restoring a sense of safety after a mass shooting.

Providing such assistance and information is vital to APA's mission. "As we all know," wrote Jeste, "the impact of this tragedy will be felt in every living room and every classroom in the nation."

Psychiatrists

continued from page 1

in West Haven and a clinical assistant professor at Yale.

"You can't be completely prepared for something like this," said Stoddard. "It is such an atrocity."

Perhaps the most helpful aspect of the training in light of the later Newtown tragedy was the inclusion of a speaker from the American Red Cross, said CPS President-elect Carolyn Drazinic, M.D., Ph.D., an assistant professor of psychiatry at the University of Connecticut. The speaker explained how the Red Cross coordinates the overall response to disasters, an insight that was helpful in integrating the CPS volunteers into the general emergency response.

By Saturday afternoon, Khan had completed a needs assessment. Working through the Red Cross and state and local health agencies, the society arranged for at least two psychiatrists to be on duty along with other mental health professionals for three-hour shifts from 7 a.m. to 7 p.m. at a crisis-response center in Newtown. On Sunday, Drazinic and colleagues met with more than 300 children and adults.

Shaukat Khan, M.D.

Psychiatrists gathered at Reed Intermediate School in Newtown, Conn., to assist community members after December's shooting. From left: Frederick Stoddard, M.D., of Massachusetts General Hospital; Irvin Jennings, M.D., executive and medical director of nonprofit Family and Children's Aid; and Shaukat Khan, M.D., disaster chair of the Connecticut Psychiatric Society.

"The handoffs between professionals is critically important and were done at Newtown in a collegial and careful ways," said Stoddard, who drove from Boston to consult with the CPS.

More such help will be needed in the future

RESIDENTS' FORUM

Don't Let Borders Limit Your Perspective

BY ARSHYA VAHABZADEH, M.D., AND DAVID BUXTON, M.D..

During his inaugural speech after becoming president of APA, Dr. Dilip Jeste laid out his plan to expand the organization across international boundaries. "APA already is a big tent, but I would like to expand it even further by getting more international members, subspecialists, younger psychiatrists, and those from diverse backgrounds," he said. "APA also can contribute significantly to educational activities in various other countries, especially the developing countries where there is a serious shortage of psychiatrists."

It is no surprise that Dr. Jeste has selected this goal as a priority due to the global disease burden of mental illness, which is increasing at a dramatic rate. While the United States is the world leader in psychiatric and neuroscientific

research, it accounts for only 5 percent of the world's population. The most recent data from the World Health Organization (WHO) indicate that 76 percent to 85 percent of people with severe mental health disorders in low- and middle-income countries receive no treatment for their mental health conditions. Furthermore, more than 1 million people a year complete suicide, and depression is being projected to be the leading contributor to global disease burden by 2020.

As future leaders in psychiatry, it is essential that we residents follow Dr. Jeste's lead in establishing bidirectional opportunities in mental health care delivery, research, and education with our colleagues around the globe.

This concept has already taken hold at distinguished institutions across the country including Mount Sinai School of Medicine, Duke University, George Washington University, and Massachusetts General Hospital (MGH). As its Web site indicates, MGH has established a Global Psychiatry Research Center with a mission to "make clinical, educational, and research contributions to world mental health and to help reduce the global burden of disease by learning from our neighbors and by contributing what we know to better relieve the suffering from mental illnesses around the world."

It is clear that many more institutions are looking to collaborate with health care partners across the world.

As residents who have participated in international mental health opportunities, we feel these experiences are essential in developing a better understanding of the biopsychosocial formulation of our patients. The cultural and societal dynamics in specific geographical areas play major roles in evaluation and treatment of mental disorders. It is important to be able to delineate the role of these factors in our diagnosis to avoid labeling a common trait in an ethnic group as psychopathology.

Conversely, psychiatric illness can manifest differently depending on location, with unique factors that may predispose, precipitate, and perpetuate these disorders. For example, research in international populations may allow us to understand why schizophrenia appears to have a better prognosis in low- and moderate-income countries despite their limited investments in mental health care resources, as has been found in studies by the WHO and others. Furthermore, we may be able to explore how alternative treatments for psychiatric illness, such as mindfulness based on Japanese Zen meditation, are effective for all patients no matter their ethnic background.

We encourage residents with an interest in international aspects of psychiatry to learn more about the World Psychiatric Association (WPA), which has 135 member societies including APA, and through those societies has a total membership of more than 200,000. If a psychiatrist is a member of APA, then the WPA automatically grants that person individual membership in the WPA as well. The WPA hosts both regional and global meetings at which residents can gain unique insights and experiences in connecting with peers from across the world. Also, such experiences may allow residents to gain experience in using alternate classification systems such as the *ICD-10* and the Chinese Classification of Mental Disorders.

Mental illness will continue to be a major factor in the overall health of our patients both locally and worldwide. Even if we never practice outside of the United States or Canada, we will need to have a basic cultural proficiency to understand our ever-changing populations.

One could hypothesize that the global financial crisis that began in 2008 was a sneak preview of a future in which countries are inherently tied together for common goals or misfortunes. As the anticipated global burden of psychiatric illness is enormous, and resources to deal with it are limited, we must continue to initiate bidirectional participation to share the burden. To borrow a quote from Freud, "Individual commitment to a group effort—that is what makes a team work, a company work, a society work, a civilization work." PN

Arshya Vahabzadeh, M.D., is a PGY-3 psychiatry resident at Emory University and a 2013 Laughlin Fellow. David Buxton, M.D., is a first-year fellow at the MGH/McLean Child and Adolescent Psychiatry Department.

to contain the suffering and anxiety, said Santopietro, chief medical officer at Community Health Resources in Windsor, Conn.

"I consider this to be the psychological equivalent of a nuclear blast," said Santopietro. "The immediate damage is unthinkable, and there is some rate of decay, but the fallout will continue for weeks and months and years."

The CPS will continue working with health agencies in that long-term effort.

"Concentric waves of psychological pain are rippling out from Newtown, and we want people to get excellent care," said Santopietro. Pausing between meetings and phone calls in the days just after the shooting, he reflected on the task ahead for the society's members.

"This is the work we do," he said. "We deal with human suffering and the complexity of the brain and human behavior. We deal with communities and human relationships. We help people through personal, psychological, family, and community crises. This is psychiatry." PN

Shaukat Khan, M.D.

Robyn Hoffman, A.P.R.N., of Family and Children's Aid coordinates mental health volunteers at the Reed Intermediate School after the Newtown shooting.

Board

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Two psychiatric workforce issues also garnered endorsements from the Board. In one of these the Board agreed to have APA go on record supporting the Veterans Psychiatric and Mental Health Care Enhancement Act, which would establish 50 new psychiatry residencies that are specifically oriented to addressing the mental health care needs of U.S. military veterans and would be fully funded by the federal government. On completing their residencies, trainees in these programs would have all medical-school debt forgiven once they gave at least six years of full-time service to the Veterans Health Administration.

The second workforce-related proposal that won APA Board backing called on APA to support the Native-American Psychiatric and Mental Health Care Improvement Act. This bill would establish a five-year demonstration project at "a psychiatry department at an accredited medical school or affiliated nonprofit organization with demonstrated experience in recruiting, training, and deploying physicians for work in American-Indian, Alaska-Native, and Native-Hawaiian communities." A key provision is that the act would provide funding for up to one year of "supplemental clinical and cultural competency training to not less than five psychiatric physicians and/or residents to enable them to practice successfully in Native-American population groups." PN

A summary of actions from the December 2012 Board of Trustees meeting is posted at http://www.psychiatry.org/network/board-of-trustees/governance-meeting-archives.

Aging

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(SAGE) study, Jeste and colleagues surveyed 1,006 community-dwelling adults aged 50 to 99 in San Diego County, with an oversample of people over age 80. They answered a 25-minute telephone interview followed by a comprehensive mail-in survey of physical, cognitive, and psychological domains, including positive psychological traits and self-rated successful aging, scaled from 1 (lowest) to 10 (highest).

Severity of depression was rated on the nine-item Personal Health Questionnaire. Optimism was rated according to the total score on the Life Orientation Test-Revised.

Resilience was measured with the 10-item version of the Connor-Davidson Resilience Scale. Examples of the questions include "I am able to adapt to change" and "I believe I can achieve my goals." The top third included scores of 36-40 and represented high functioning; individuals in the top third (n=338) responded with "often true" or "true nearly all of the time" on virtually all the items related to their ability to adapt and persevere in the face of hardship.

The bottom third included scores of 1–28 and represented low functioning; individuals in the bottom third (n=282) responded with "not true at all" or "rarely true" on a majority of the items.

The average self-rating of successful aging was 8.2, with older individuals in the cohort reporting higher rates of successful aging despite worsening physical and cognitive functioning. People with poor physical health but high resilience scores had self-ratings of successful aging similar to those of physically healthy people with low resilience. Likewise, people with poor physical functioning but no or minimal depression had scores for successful aging comparable to those of physically healthy people with moderate to severe depression.

"While no causality can be inferred from these cross-sectional data, it is possible to speculate that increasing resilience and reducing depression might have effects on successful aging as strong as the effects of reducing physical disability," Jeste and colleagues wrote. "This finding points to an important role for psychiatry in enhancing successful aging in older adults, even in those with physical disabilities."

Key Points

- Community-dwelling aging individuals who score high on a scale assessing resilience and who do not suffer from clinical depression also reported high rates of "successful aging" even in the face of worsening physical and/or cognitive functioning.
- Older age was associated with a higher rating of successful aging, despite worsening physical and cognitive functioning.
- "Resilience" was especially important; people with poor physical health but high resilience scores had self-ratings of successful aging similar to those of physically healthy people with low resilience.
- Depression is also critical in one's self-rating of successful aging; people with poor physical functioning but no or minimal depression had scores for successful aging comparable to those of physically healthy people with moderate to severe depression.

Jeste told *Psychiatric News* that the message for clinicians is that an optimistic approach to the care of seniors may help reduce societal ageism. "There is considerable discussion in public forums about the financial drain on society due to rising costs of health care for older adults. . . . But successfully aging older adults can be a great resource for younger generations. Perfect physical health is neither necessary nor sufficient" for successful aging, Jeste said. "There is potential for enhancing successful aging by fostering resilience and treating or preventing depression."

This study was supported, in part, by NIMH, the NIH National Center for Research Support, the John A. Hartford Foundation, and the Sam and Rose Stein Institute for Research on Aging. PN

"Association Between Older Age and More Successful Aging: Critical Role of Resilience and Depression" is posted at http://ajp.psychiatryonline.org/Article.aspx?ArticleID=1478351.<

Norway

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from their families, from their social networks, and from their communities," said Jensen. "They will spend most of their lives outside the armed forces, so it's best that they remain rooted in civilian society."

When troops return from deployment, they don't go straight back to Norway. The unit makes a stopover on the way—usually in Denmark or Sweden—for a few days to unwind and go through a tactical military debriefing.

Jensen and other clinicians also talk individually with each returning soldier.

"We get them out of the activation phase, out of the war zone," he said. "I tell them: Today you're in Sweden and tomorrow you'll be in Norway, but your hormones will still be in Afghanistan for another fortnight."

Soldiers seem to prefer biological explanations for what they are experiencing. "Cortisol" works better as an explanation than "feelings" or "anxiety," he said. "We hope that this will reduce the risk of PTSD in the future."

In addition, like the British Army and others, the Norwegians schedule their troops to remain at home for longer stretches than those for which they are deployed. Norway uses a 4-to-1 ratio; after six-months away, a soldier should remain at home for two years.

Jensen realized the value of this rule of thumb after talking with one officer who went through seven six-month tours of duty in the Balkans in seven years and developed severe posttraumatic stress disorder.

Once their military careers are over, Norwegian troops often face barriers to specialized care because Norway does not have the equivalent of a VA health system, said Jensen. Part of that problem arose with the shift from a draft to a volunteer, professional army.

"In the past, the army was seen as part of the nation, so it was assumed that the general health service should care for soldiers after they left the army," he said.

However, too few civilian clinicians understood about the stressors faced by military personnel, although there are increased training opportunities now, he said.

In the absence of a veterans health care system, Norway's military health service will care for veterans for 14 months after their enlistments end.

"Now, any veteran with any mental health issue can be evaluated by a military psychiatrist and get short-term therapy," he pointed out.

"If they need more treatment, we arrange it with a psychiatric outpatient clinic in the civilian health system," said Jensen. "We want to give our soldiers good care while they're serving and good follow-up for the rest of their lives." PN

From the Experts

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that show promise for impulse control and enhance cognition may also be used to treat stimulant dependence.

Doxazosin is a repurposed NE blocker used for hypertension that Newton et al. (2012) recently found blocks cocaine's positive subjective effects and the feeling "likely to use cocaine" in cocaine-dependent volunteers after a cocaine infusion. An outpatient clinical trial is presently examining this medication for decreasing cocaine use. Another repurposed medication, the angiotensin-converting enzyme inhibitor and antihypertensive perindopril blocks the cardiovascular and positive subjective effects of methamphetamine. The commonly prescribed antidepressant bupropion has also shown some efficacy in decreasing methamphetamine use in moderate users. Rivastigmine, used in the treatment of dementia, significantly decreased "likely to use methamphetamine" in dependent volunteers. Finally, the atypical stimulant modafinil, used to treat narcolepsy, blocks cocaine's positive subjective effects and has decreased cocaine use in a select subpopulation.

Psychiatric addiction research has benefited from repurposing a wide range of medications. The science behind using these medications is based on understanding from neuroimaging of damaged and reinforcing human neural circuits due to addictive stimulants. For the most part, the development of effective treatments for this pernicious disorder appears promising. PN

References are posted at http://www.psychnews.org/update/experts_2_32.html.

Experimental Drug

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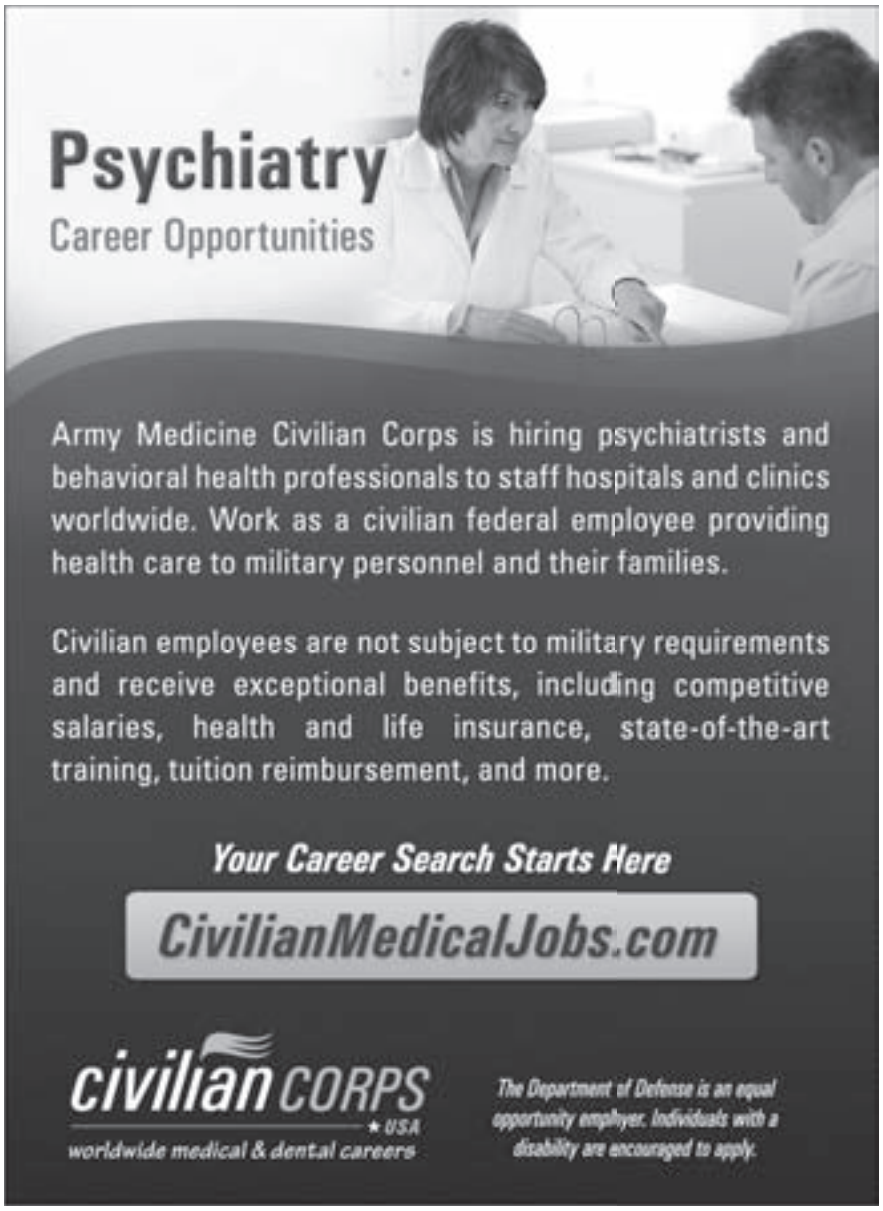
cations," B. Timothy Walsh, M.D., a professor of pediatric psychopharmacology at Columbia University and chair of the *DSM-5* Feeding and Eating Disorders Work Group, said in an interview.

The study was funded by GlaxoSmithKline as part of the Academic Discovery Performance Unit program with the University of Cambridge. "This novel initiative is a joint academia-industry collaboration pioneered here in Cambridge to optimize the early development of new therapeutic agents," Ziauddeen said. PN

"Effects of the Mu-opioid Receptor Antagonist GSK1521498 on Hedonic and Consummatory Eating Behavior: A Proof of Mechanism Study in Binge-Eating Obese Subjects," is posted at www.nature.com/mp/journal/vaop/ncurrent/full/mp2012154a.html.



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Reporting to the Psychiatrist in Chief IOL/Vice President of Behavioral Health, Hartford Hospital and in collaboration with the Director of Clinical Operations and the Director of Nursing, the Medical Director oversees day to day management of the clinical operations of the IOL and is responsible for the quality of care in all clinical services. The Medical Director also works closely with the residency directors to facilitate the integration of the training programs with the delivery of clinical care.

The successful candidate will be an outstanding clinician with demonstrated leadership ability and strong administrative, interpersonal and communication skills. He/she should demonstrate an understanding of the importance of clinical outcomes, investigation, and teaching in a patient driven service culture. Candidates will be board certified in psychiatry, and have a track record of professional accomplishment sufficient to be eligible for an appointment at the University of Connecticut School of Medicine. Outstanding research, and/or teaching credentials will enhance candidacy.

Nominations, inquires and expressions of interest should be directed to Linda Komnick or Claudia Teschky at Witt/Kieffer, claudiat@wittkieffer.com or (630)-575-6172.

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Excellent Opportunities to be part of the foundation of a **NEW University of Texas System Medical School** in South Texas. The University of Texas Health Science Center at San Antonio (UTHSCSA), through its Regional Academic Health Center (RAHC) in Harlingen, Texas, is leading the effort to develop two new residency training programs in South Texas that will eventually be central components of the future medical school. Recruitment is open for several positions, including a full-time **Director of Adult Psychiatric Residency Training**, a full-time **Director of Child and Adolescent Psychiatry Fellowship Training, and four full time clinical faculty (at least one with added credentials in Child and Adolescent Psychiatry).**

Qualifications include:
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- Evidence of leadership and innovation in psychiatric residency training
- Administrative experience to develop and manage a residency program
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- Working knowledge of the principles of adult and/or child learning and educational objectives of Psychiatry

Responsibilities of the Training Directors:
- Finalization and submission of the Program Information form for ACGME approval.
- Program oversight and maintenance of ACGME accreditation standards by regular program review

Responsibilities of the Faculty:
- Devote a minimum of 50% time to supervision and training of residents
- Devote approximately 50% time to clinical care in one of the affiliated private or public hospitals, or the local Department of Veterans Affairs regional healthcare system.

The two Director positions are at the Associate Professor or Professor level and the Clinical Faculty positions can be at any rank. Both tenure and non-tenure track positions are available and individuals with research experience or current grant funding are especially encouraged to apply. **Salary and compensation are commensurate with prior experience, but will be highly competitive.**

Interested individuals should send a letter of intent and curriculum vitae:
Mail: The University of Texas Health Science Center at San Antonio
Attn: Pedro L. Delgado, MD – Chairman and Professor
Department of Psychiatry, MSC 7792
7703 Floyd Curl Drive
San Antonio TX 78229-3900
Email: delgadop@uthscsa.edu
Fax: 210-567-6941 Attn: Pedro L. Delgado, MD

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All faculty appointments are designated as security sensitive positions.

Mood and Anxiety Disorders Division Director. The Department of Psychiatry at **The University of Texas Health Science Center** at San Antonio (UTHSCSA) seeks a full-time tenure-track leader for its Mood and Anxiety Disorders Division. This full time faculty leadership position is supported in part through a named endowed professorship.

Qualifications:

- board-certified or board-eligible academic psychiatrist
- strong track record of independent research and excellent leadership and mentoring abilities.
- expertise in one or more mood/anxiety disorders, preferably including translational methods

Responsibilities:

- administration and scientific leadership of division faculty and staff
- medical direction of research clinic
- leadership in collaborative, multicenter research groups

The department has over $20 million per year in current NIH and Department of Defense research, including an NIH P30 Center grant, a world class brain imaging institute, a brain bank, outstanding programs in psychopharmacology and genomics, and strong education and clinical programs. Division investigators have developed a comprehensive electronic record system that allows secure use of de-identified clinical data for research and facilitates recruitment of patients into studies. Located in one of the most scenic parts of Texas, San Antonio is a culturally rich city with a pleasant climate, an excellent public school system and abundant recreational activities.

Interested individuals should forward their curriculum vitae to:
Mail: Pedro L. Delgado, M.D., Professor and Chairman
The University of Texas Health Science Center at San Antonio
Department of Psychiatry, Mail Code 7792
7703 Floyd Curl Drive
San Antonio TX 78229-3900
Fax: 210-567-6941 Attn: Pedro L. Delgado, MD

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The successful applicant will have completed four years of post graduate psychiatric training and be board eligible at the start of the program. Additionally, the applicant must be eligible to obtain a New Jersey license to practice medicine. The trainee will spend 70% of time at Otsuka and 30% of time at nearby Robert Wood Johnson Medical School and enjoy the benefits of living in central New Jersey, equidistant from New York City and Philadelphia.

For additional information regarding the position and its requirements, please contact **Barbara Palmeri, MD, 671 Hoes Lane, Room D325, Piscataway, NJ 08854; E-mail: palmerba@umdnj.edu; Phone: 732-235-4433**. The University of Medicine and Dentistry of New Jersey is an Affirmative Action/Equal Opportunity Employer.

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ARIZONA

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UC DAVIS SCHOOL OF MEDICINE DEPARTMENT OF PSYCHIATRY AND BEHAVIORAL SCIENCES

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For full consideration, applications must be received by January 2. 2013. However, the position will remain open until filled through March 01, 2013.**Interested candidates should email a curriculum vitae and letter of interest in response to Position #PY-02R-13 to Nicole Prine at Nicole.prine@ucdmc.ucdavis.edu.** For more information concerning these positions, please contact the search committee chair, Dr. Robert Hales at rehales@ucdavis.edu. In conformance with applicable law and University policy, the University of California, Davis, is an equal opportunity/affirmative action employer.

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No reservation required.
NEW JOB FAIR PLUS
will provide insurance info, starting a practice, etc. Reservation required. For information, call 415/334-2419; FAX 415/239-2533; or email phanny@ncps.org.

COLORADO

Horizon Health seeks a **Medical Director** and **Attending Psychiatrist** for a new 22-bed Senior Behavioral Health program at our client hospital **Exempla Lutheran Medical Center** in **Wheat Ridge, CO.** Excellent practice opportunity and income. For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com. EOE

CONNECTICUT

Adult/ Child Psychiatrist
Fairfield, CT

Group Psychiatry practice is seeking a full-time Psychiatrist. Excellent salary and benefits. Email CV to:doctorbeach52@gmail.com or fax to Attn: Melissa B. 203-255-3126.

FLORIDA

PSYCHIATRIST; FULL TIME, FL LICENSE REQUIRED; Aventura, FL; private practice located equidistant between Miami and Ft. Lauderdale; children/adolescent/adult/geriatric pts; email CV to aventuraoffices@bellsouth.net or FAX to Dusty: 305-935-1717.

GEORGIA

Geriatric Psychiatrist

WellStar Medical Group is seeking Board Certified Psychiatrist with Geriatric Fellowship training for full-time position. Will provide services in Gero Psych Unit at WellStar Cobb Hospital, located in Austell, northwest of Atlanta, GA. Competitive salary with comprehensive benefit package.

To apply please do online application www.wellstarcareers.org or contact 770-792-7539 for additional information.

DBHDD

The State of Georgia Department of Behavioral Health and Developmental Disabilities is currently recruiting for board-certified and board eligible psychiatrists to work at any of our six hospitals located throughout Georgia. We have current openings for full-time, part-time and hourly Psychiatrists. Positions are available on both acute and chronic forensic and adult mental health units. All psychiatrists will lead a multi-disciplinary team of professionals providing quality care to both voluntary and involuntary patients. Our state facilities provide academic affiliations and promote academic collaborations, along with an excellent benefits package and competitive salary.

Come join our incredible behavioral health team!!

Please forward your CV to the following email address: ncnathaniel@dhr.state.ga.us

PSYCHIATRIST

New Horizons Community Service Board in Columbus, Georgia is seeking an Adult Psychiatrist for its Outpatient/Court Services programs. This growing community offers a pleasing climate and is situated within a short distance to Atlanta and the Gulf Coast. The qualified applicant will possess or be eligible for a valid physician's license from the state of Georgia, have completed a three-year residency in an accredited facility and be board eligible or board certified. Excellent salary with a comprehensive benefits package. Interested parties should send their curriculum vitae to:

Shannon Robertson
srobertson@newhorizonscsb.org
706/317-5001
706/317-5004 (Fax)

HAWAII

Psychiatrists

This is your opportunity to live and work in Hawaii! The Adult Mental Health Division of the State of Hawaii Department of Health is recruiting psychiatrists. We have openings for outpatient psychiatrists to work at Community Mental Health Centers in Hilo, Maui, and Honolulu, and for inpatient psychiatry at the Hawaii State Hospital in Kaneohe, on Oahu.

Employment with the State of Hawaii offers competitive salaries and benefits. Benefits include 21 days of vacation per year, 21 days of sick leave per year, 13 paid state holidays, liability insurance, medical/vision/dental insurance, and a generous pension plan.

For more information visit our website at http://amhd.org/about/employment.asp. Inquiries about the outpatient positions, contact Mr. Wayne Law at 808-832-5770. For the Hawaii State Hospital, contact Dr. Jim Westphal at 808-236-8473.

ILLINOIS

NEW POSITION DUE TO EXPANSION.
Attending Psychiatrist

Excellent career opportunity for psychiatrist with skills and interest in addictions, eating disorders, PTSD, and mood disorders utilizing a recovery model. Nationally known treatment center in Chicagoland area serving women has an opening for a full-time attending psychiatrist. Excellent salary, full benefits, and malpractice insurance is paid. Send CV to Holly Dorna, President, PsychPros, Inc., at Holly@psychpros.com or call 513-333-4770 for more information.

North Shore practice of Child Psychiatrists, Psychologists and Social Workers is seeking a part time adult/adolescent psychiatrist. Built in patient base from recently relocating psychiatrist. Very busy practice with numerous referral bases. No in-patient responsibilities. Applicant must be Board Eligible. Flexible hours and great work environment. Potential for full time exists. Please fax resume to Michael Greenbaum, M.D. at 847-680-3832 or e mail to blindquist@counselingconnections.net. Please see website for more information www.counselingconnections.net.

FORENSIC CLINICAL SERVICES
CIRCUIT COURT OF COOK COUNTY

Full-time position available for a Board Certified Psychiatrist with the Cook County Circuit Court in Chicago, Illinois. Perform evaluations of adult offenders in a large, urban, court setting. Forensic training preferred. **Contact: Peter Lourgos, M.D., Assistant Director, Forensic Clinical Services; 773.674.6078 or Fax your CV to 773.674.5113.**

INDIANA

Join a well-trained group of Psychiatrists and professional support staff at **The Samaritan Center,** a comprehensive behavioral health center with a 22-bed dedicated adult inpatient unit at Good Samaritan Hospital, a JCAHO accredited Regional Referral Center located in Vincennes, IN. Opportunity for Chief Inpatient or Outpatient Psychiatrist. The Samaritan Center has been in operation since 1971 and is committed to providing quality behavioral health assistance to individuals who are facing difficulties and challenges. Services include, but are not limited to: diagnostic evaluations, individual, family, and group therapy, substance abuse services, medicine evaluation and management, psychological testing, and 24 hour emergency services. Historic river community in southwestern Indiana. 220,000 base salary, $25,000 in call pay, excellent benefit, paid malpractice and relocation package. Contact Todd Dillon at 800-883-7345; tdillon@cejkasearch.com; or visit www.cejkasearch.com. ID#147601PY

LOUISIANA

Tulane University School of Medicine

is recruiting a full-time faculty member to serve as Professor and Chair in the Department of Psychiatry and Behavioral Sciences. The Department of Psychiatry and Behavioral Sciences is well established and currently has 59 full-time faculty. The residency programs are fully accredited as are the fellowship programs in child and adolescent psychiatry and forensic psychiatry, and the clinical psychology internship program.

Faculty and trainees work in a diverse of outpatient settings plus several major institutions - Tulane University Hospital and Clinic, Southeast Louisiana Veterans Health Care System in New Orleans, and the ELMHS Feliciana Forensic Hospital. The Department includes the special Tulane Institute of Infant and Early Childhood Mental Health, the Tulane Institute of Forensic Neuropsychiatry, and the new Tulane Center for Autism and Related Disorders.

Candidates for the position must be Board Certified in Psychiatry and must have a strong proven commitment to medical student and resident education, have a strong track record of research development as well as personal research accomplishments, and must be able to develop innovative approaches to expand the departmental and institutional clinical enterprise. Administrative experience and familiarity with managing a clinical operation are also strongly sought skills. Applicants should qualify for the rank of Professor on the tenure track.

An attractive recruitment package is available which includes research and recently renovated office space, several faculty positions and development funding.

Applications will be considered until a suitable qualified candidate is found. Interested and qualified candidates should send a letter of interest, and update CV, and a list of references to Tanya Haase, preferable

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electronically to **thaase@tulane.edu or to Tanya Haase, Tulane University School of Medicine, 1430 Tulane Avenue, #8001, New Orleans, LA 70112.**

Tulane is strongly committed to policies of non-discrimination and affirmative action in student admissions and in employment. Women and minority candidates are urged to apply.

MARYLAND

POSITION AVAILABLE — PSYCHIATRIST, F/T or P/T. Private CMHC on beautiful Eastern Shore of Maryland in Dorchester County. NO ON CALL. Strong professional clinical and support staff. Great work environment. Contact Medical Director, Donna Beitel, MD, PO Box 1103, Cambridge, MD 21613-1103 or marshyfam @DMV.com.

FORENSIC PSYCHIATRIST

Springfield Hospital Center in Sykesville, MD is accepting applications for a Forensic Psychiatrist. Eligible candidates must have board certification including added qualifications in forensic psychiatry (or equivalent). Duties include pretrial evaluations of competency to stand trial and criminal responsibility, competency restoration, risk assessment, and training of residents and students. Please forward a CV and inquiry to Erik Roskes, MD, Director, Forensic Services, Springfield Hospital Center, by fax (410.970.7105) or email (erik.roskes@maryland.gov).

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 **Jonathan Book, M.D., Clinical Director, SHC, 6655 Sykesville Road, Sykesville, MD 21784. For questions, call (410)970-7006 or e-mail JBook@dhmh.state.md.us.** EOE

MASSACHUSETTS

CAMBRIDGE HEALTH ALLIANCE: Inpatient Child/Adolescent Psychiatry Position

Cambridge Health Alliance, Division of Child and Adolescent Psychiatry, Harvard Medical School. Full time inpatient staff psychiatry position available at our Cambridge campus. Work in a dynamic setting with multidisciplinary teams using a nationally recognized program for restraint reduction. Opportunities to teach child psychiatry fellows, general psychiatry residents, medical students, and other trainees. Academic appointment, as determined by the criteria of Harvard Medical School, is anticipated.

Qualifications: BE/BC, demonstrated commitment to public sector populations, strong clinical skills, strong leadership and management skills, team oriented, problem solver. Bilingual and/or bicultural abilities are desirable. Interest and experience with dual diagnosis and/or substance use disorders preferred. Competitive compensation, excellent benefit package. Cambridge Health Alliance is an Equal Employment Opportunity employer, and women and minority candidates are strongly encouraged to apply.

CV & letter to Joel Goldstein, MD, Chief of Child/Adolescent Psychiatry, 1493 Cambridge Street, Cambridge, MA 02139. Fax 617-665-1204. Email: JoGoldstein@challiance.org (email preferred).

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.

On-Call Psychiatrists / Northampton, MA- Cooley Dickinson Hospital is seeking BC/BE adult psychiatrists to join its on-call coverage pool for a 20-bed adult inpatient psychiatric unit. Call coverage consists of nightly telephone back-up from 5p-8a, and in-house rounding responsibilities on weekend days. Compensation $2,500-3,000 per week. Schedule is flexible depending on interest and availability. If interested, please contact Josh Maybar at 413-582-2720 or josh_maybar@cooley-dickinson.org.

Berkshire Health Systems

Massachusetts. Consult-Liaison Psychiatrist Needed. 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 a consultation-liaison 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 alentine@bhs1.org.

DEPARTMENT OF PSYCHIATRY MASSACHUSETTS GENERAL HOSPITAL HARVARD MEDICAL SCHOOL ATTENDING POSITION

The MGH Department of Psychiatry is recruiting for an Inpatient Attending on our 24 bed Medical Psychiatry Unit. Additional opportunities may exist in other areas, including Emergency Psychiatry, Addiction Medicine, Geriatric Psychiatry and Urgent Care. Rated among the leading psychiatry departments by US News and World Report, the Department is comprised of a staff of approximately 600 faculty committed to excellence in clinical care, teaching, research and community service. Candidates should be: a) board certified/board eligible in Psychiatry with expertise in the care of patients with psychiatric disorders complicated by co-morbid medical illness; b) dedicated to excellence in the teaching of psychiatry residents, medical students and other trainees, to scholarship in psychiatry, and to quality improvement; and c) qualified for an academic appointment at Harvard Medical School at the rank of Instructor or above. Fellowship training in consult-liaison, emergency or geriatric psychiatry or addictions medicine as well as previous attending experience are highly desirable. Interested individuals should apply to Jonathan E. Alpert MD PhD, Associate Chief/Clinical Director (jalpert@partners.org). The Massachusetts General Hospital is an affirmative action/equal opportunity employer. Minorities and women are strongly urged to apply.

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

The Department of Psychiatry at UMass Memorial Health Care is actively seeking an Attending Physician for its affiliated program at Marlborough Hospital. The position primarily involves the provision of inpatient psychiatric care, leading an interdisciplinary treatment team and participating in medical student education on the service. The unit at Marlborough involves 0.8 FTE, although full 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. The physician will 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.

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

St. Joseph, MO – Close to Kansas City – Wonderful city to live and work, great schools, and so close to the metro area—one of the Midwest's best kept secrets! 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; Call 1:5. Offering attractive student loan repayment plan if needed. Come join our incredible behavioral health team on this growing psych service. This is a "must see" opportunity! Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

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NEW HAMPSHIRE

PSYCHIATRIST
Portsmouth, NH

Beautiful Seacoast area with four seasons, 55 minutes from Boston. Expanding private, non-profit community mental health center seeks a Child and Adolescent Psychiatrist to join a staff of ten psychiatrists, for outpatient care. Vibrant collegial atmosphere with competitive salary.

Interested candidates should send cover letter and C.V. to W.M. Hanna, M.D., Medical Director.

Seacoast Mental Health Center, Inc.
1145 Sagamore Avenue
Portsmouth, NH 03801
Fax: 603-433-5093

Department of Psychiatry
Faculty Position

The Geisel School of Medicine at Dartmouth, Department of Psychiatry, is seeking an adult or child psychiatrist to serve as Medical Director for the behavioral health services at Cheshire Medical Center/Dartmouth-Hitchcock Clinic in Keene, NH. The successful applicant will provide direct clinical service and oversee state-of-the-art inpatient and outpatient services. The faculty member will lead an experienced interdisciplinary team with the ongoing goal of offering exceedingly high-value care for the region's population. Full-time preferred but part-time will be considered.

Candidates should be board certified or eligible in Psychiatry and be interested in functioning as a leader. Academic rank and salary will be commensurate with experience. Curriculum vitae and three letters of reference, addressed to Dr. William C. Torrey, Vice Chair for Clinical Services, should be e-mailed to psychiatry.jobs@dartmouth.edu. Please reference Search Number PS1012D.

The Geisel School of Medicine at Dartmouth College is an Equal Opportunity/Affirmative Action employer strongly committed to achieving excellence through cultural diversity. The College actively encourages applications and nominations from women, minorities, veterans and persons with disabilities.

NEW JERSEY

Pharmaceutical Leader Seeks Physician Talent

Dynamic pharmaceutical company in Central New Jersey is recruiting talented physicians to accelerate our growth. We provide a challenging and rewarding experience for physicians intent on advancing human health.

Ideal candidates will have at least 5 years of post-residency clinical experience and Board Certification in one of these areas:

- Cardiology
- Nephrology
- Psychiatry
- Oncology

This is a unique opportunity to make a personal impact on the future of medicine.

An equal opportunity employer.

Candidates are invited to contact us at MDPharmaTalent@gmail.com

Physician recruitment will be maintained in the strictest confidence.

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.

Adult and/or Child Psychiatrist

P/T – 15-20 hours per week (evenings and weekends) in an outpatient mental health facility in Brooklyn. Competitive compensation. Submit CV by fax or email only: 718-837-5676 or email to admin@nccny.com.

Rockland Psychiatric Center, Orangeburg, NY
Psychiatrists

Rockland Psychiatric Center, the largest NY State psychiatric hospital, is affiliated with New York University and located 18 miles north of Manhattan in the scenic lower Hudson Valley. We are looking for Psychiatrists for our outpatient and inpatient units, serving seriously mentally ill adults. RPC offers regular hours, optional on-call for extra pay, excellent benefits, including NYS retirement system. Weekly Grand Rounds, large medical staff, collegial atmosphere. With 400 inpatient beds and an extensive regional outpatient network, there are many opportunities for movement and advancement once on staff.

Send CV to Mary Barber, MD, Clinical Director, mary.barber@omh.ny.gov.

Manhattan Psychiatric Center is seeking a Board Certified Psychiatrist to assume the duties of ward psychiatrist on the sex offender unit. This is a ward dedicated to the treatment of Article 10 sex offenders, with a manualized comprehensive program utilizing the latest in cognitive and relapse prevention strategies to engage this population.

The ward psychiatrist is the leader of a team of dedicated professionals and in this capacity will work in a multi disciplinary collaborative approach to attend to the complex needs of these patients.

Manhattan Psychiatric Center is an affiliate of NYU and there are opportunities for teaching of residents, medical students, as well as research. Forensic training is desirable, given the complexities of treatment and assessment of this population.

Please FAX CV to:
Samuel J. Langer, MD
Chief of Psychiatry
646-672-6386
or email to samuel.langer@omh.ny.gov.

NEW YORK STATE

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.

PSYCHIATRIST OPENINGS at CENTRAL NEW YORK PSYCHIATRIC CENTER

A State-operated, Forensic Facility, the first Office of Mental Health Facility to be recognized by the national accrediting body, The Joint Commission, as a Top Performer. Our Facility is seeking full time Psychiatrists for our Inpatient Facility in Marcy, NY, and for our Correction-based programs in various locations throughout the state. These positions are in proximity to Glens Falls, Middletown, Syracuse, Rochester, Batavia, and Utica as well as in the Bronx and Westchester County. Competitive salary range is $168,421 for NY State License to $181,790 for Board Certification plus additional compensation for some programs. NY State provides a generous and comprehensive benefits package including an outstanding Pension Plan and for NY State Regents Loan Forgiveness. Opportunities may exist for additional compensation.

Dr. Jonathan Kaplan
Clinical Director for
Outpatient Services
(Code 312)
Call at: 845-483-3443
Fax: 845-483-3455
Email: Jonathan.Kaplan@omh.ny.gov

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
- Voluntary low stress on call at regular pay rate
- 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; 5 ½ hr drive to Boston & DC; less than 1hr to Finger Lakes Wine Country; Watkins Glen International Racetrack.

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

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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 program. Fringe 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.

- 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)
- 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 13669-229 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.

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NORTH CAROLINA

Great Opportunity in Private Practice

Carolina Partners in Mental HealthCare, PLLC is seeking psychiatrists for new practices in Burlington, NC and Asheville, NC. Carolina Partners is a private multi-disciplinary mental health group practice with thirteen treatment sites in North Carolina. You get full partnership from day one with no buy-in. Good income, great flexibility. Full time preferred but will consider part time as well. Visit us on the web at carolinapartners.com. Send CV and letter of interest to ymonroemd@gmail.com; fax 919-354-0864; mail to 1502 W. Hwy 54, Suite 103, Durham, NC 27707, Attn: Medical Director.

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

Did you know

APA's advocacy resources include: the Legislative Action Center, where you can get updates on key issues and legislation, plus listings of elected officials and other election news; the APA political action committee; the department of Government Relations; and the APA Congressional Action Network. www.psychiatry.org/advocacy-newsroom

Fargo Veterans Health Care System,
Fargo, North Dakota

Come be a member of a team providing compassionate health care to veterans. We are an employer of choice who is a center of excellence in patient care, education and research. The Department of Veterans Affairs provides Quality through Caring.

The federal government offers a full range of benefits to include the FERS retirement plan, Thrift Savings Plan, group health insurance, long term care insurance, life insurance, and flexible spending programs.

Full time Staff Psychiatrist(two full-time positions open, Fargo, ND and Bismarck, ND). Board Certified or Board Eligible in the field of Psychiatric Medicine with an active, unrestrictive licensure to practice medicine is required from any state or territory of the United States.

The position will cover both inpatient and outpatient depending on the needs of the Mental Health Service Line. There is a rotating call schedule critical to patient care in multiple settings. Physician must be able to cross-cover all Mental Health services. Responsible clinically for evaluation and treatment of inpatient and outpatient and Community Based Outpatient Clinic's through Telemedicine, some travel may be required.

Please see www.usajobs.gov for more information and submit your CV following the directions in the announcement.

An Equal Opportunity Employer (The VHA is not permitted to hire non-US citizens when there are qualified US citizens available, for this reason CVs must clearly identify citizenship or immigration status.)

Contact:
Richard K. Pope
Fargo VAHCS
701-239-3700 ext 2353
Richard.pope@va.gov

OHIO

SOUTHERN OH – OUTPATIENT POSITION with some on-call duties for the geropsych unit. Salaried position with production & performance bonuses; medical school loan repayment plan up to $200k. Portsmouth is close to Ashland, KY, an hour from Huntington, WV; it is 80 miles from Columbus and 110 miles from Cincinnati. The hospital was named 10th in the Top 100 Best Places to Work by Modern Healthcare and 36th on Fortune's top 100 Best Companies to Work For. Join our top notch team at this beautiful, impressive hospital and enjoy working every day with a great group of people. H1/J1s welcome. Please **call Terry B. Good, Horizon Health, at 1-804-684-5661,** Fax #:804-684-5663; Email: terry.good@horizonhealth.com.

Link to
Annual Meeting Microsite:
http://annualmeeting.psychiatry.org/

OREGON

BC/BE Psychiatrists
Oregon State Hospital (OSH)
Salem, Oregon

Oregon State Hospital is looking for BC/BE psychiatrists. We have it all! A brand new hospital that incorporates modern architecture, treatment spaces, and technologies. Salary is very competitive and includes psychiatric differential, board certification pay, and opportunities for additional on-call work. OSH offers opportunities in our general adult, geriatric, and forensic programs. A generous and comprehensive benefit and PERS retirement package is included as well as opportunities to have an academic appointment with the Oregon Health Sciences University. Phone: (503) 945-2887; email: lila.m.lokey@state.or.us; fax: (503) 945-9910; www.oregon.gov/DHS/mentalhealth/ osh.

The State of Oregon is an Equal Opportunity Employer.

PORTLAND, OREGON VAMC
CLINICAL CHIEF OF PSYCHIATRY

The Portland, Oregon Veterans Affairs Medical Center (PVAMC) and the closely affiliated Oregon Health & Science University (OHSU) are seeking a Chief of Psychiatry at the PVAMC. This is a quaternary care referral center for the Pacific Northwest, with a high volume of complex patients. The successful candidate must be board certified in psychiatry, with leadership skills, strong clinical skills, and administrative experience in a matrix organization. He/she will have a strong commitment to academic medicine, to resident and student education, to faculty development, and to supporting clinical or health services research. Responsibilities include oversight of patient care, research, and education programs, and supervision of professional and technical staff. Academic appointment will be commensurate with experience and credentials. U.S. citizenship required. Applicants are subject to drug testing. Relocation and recruitment incentives may be authorized. For consideration, please email a CV and cover letter to Ruth Whitham, MD, Chief of Neurology; Ph. 503-273-5172; email ruth.whitham@va.gov. The Portland VA Medical Center is an equal opportunity/affirmative action employer.

PENNSYLVANIA

One Hour to PHILADELPHIA - Two Hours from WASHINGTON, DC– Pretty Area – so close to several amazing metro areas. Inpatient position; adult and geriatric; attractive salary w/benefits plus bonus, or independent contractor arrangement if in practice already. Plans under way to open outpatient and other services. Grow with this program; join a great team! Please **call Terry B. Good at 1-804-684-5661,** Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

We have exciting full and part-time positions in a rapidly expanding department. Opportunities include responsibilities in and outside our five-hospital health system. There are immediate openings for **Child/Adolescent, Adult, Geriatric and Addictions psychiatrists**. We also seek psychiatric leadership to run our Pain Management and ECT services.

Psychiatric Hospitalist positions are also available. Excellent salaries and exceptional benefits 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.

RHODE ISLAND

Rhode Island Hospital
and The Miriam Hospital
Affiliated Hospitals of the
Warren Alpert Medical School
of Brown University
Positions in Psychiatry

We are recruiting for a number of full-time clinical positions which are part of an academic medical center program, with opportunities for Brown University Clinical Faculty appointments. There are possibilities for research participation for applicants with the appropriate background.

Outpatient Psychiatrist(s)to work with general psychiatry populations and to interface with primary care.

Inpatient Psychiatrist(s)to join our multidisciplinary treatment team providing care for 46 inpatients beds located in a general medical teaching hospital.

Emergency Psychiatrist(s): As the largest emergency psychiatry facility in the region, we are seeking to augment psychiatrist staffing with scheduled weekend coverage that includes some inpatient psychiatry coverage. The position(s) will be part of a team which includes psychiatry residents, nurses, and social workers.

Applicants must be Board Certified in Psychiatry or Board eligible (within three years of training completion). Salary and benefits are competitive and commensurate with level of training and experience.**To learn more, visit www.lifespan.org.** Please send CV's along with a letter of interest to Richard J. Goldberg, M.D., Psychiatrist-in-Chief, APC-9, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02903 and/or email: rjgoldberg@lifespan.org.

CLASSIFIEDS

SOUTH CAROLINA

Medical Director Position — 8-bed inpatient Geropsychiatric Unit; salaried with benefits or practice opportunity for those who prefer independent contract. Weekend call is one in four. Rounding on weekends is not necessary unless there is an admission on Friday or Saturday. Located in northeast SC, this small town is an 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

SCHOOL OF MEDICINE
VANDERBILT UNIVERSITY

INPATIENT PSYCHIATRIST
Vanderbilt University School of Medicine, Department of Psychiatry

The Department of Psychiatry is recruiting psychiatrists to provide inpatient services at the Vanderbilt Psychiatric Hospital located on the campus of Vanderbilt University Medical Center. The hospital offers specialized inpatient programs for children & adolescents and for adults with mood, psychotic, and substance abuse disorders. Successful BE/BC candidates will receive a faculty appointment with rank and salary commensurate to experience.

Applicants should email or send a letter of interest with an updated CV to Harsh K. Trivedi, MD, Executive Medical Director and Chief of Staff, Vanderbilt Psychiatric Hospital, 1601 23rd Avenue South, Nashville, TN 37212. Interested and eligible candidates may obtain further information by contacting Dr. Trivedi at 615-327-7024 or harsh.k.trivedi@vanderbilt.edu.

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

WEST VIRGINIA

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.

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.

WISCONSIN

Mayo Clinic Health System in Eau Claire, Wisconsin is seeking a BC/BE Psychiatrist. Outpatient unit is attached to 20 bed inpatient unit. You may expect a busy practice in a financially stable organization, committed to both high quality patient care and patient satisfaction.

- Common PACS and EMR across Mayo Clinic Health System
- Primarily outpatient practice
- Inpatient unit covered by daytime Psychiatric Hospitalists Monday through Friday
- Full benefits including a generous incentive and salary guarantee
- Call of 1:7

Mayo Clinic Health System is a family of clinics and hospitals serving over 70 communities in Iowa, Wisconsin and Minnesota. Eau Claire, home to the 11,800 students at the University of Wisconsin-Eau Claire, has a metro area of 99,000. The community offers excellent schools, abundant four season recreational opportunities, low crime and affordable housing. Eau Claire, the retail hub for West Central Wisconsin, is located 90 minutes from Minneapolis/St. Paul where you will find specialty shopping, professional sports teams and a multitude of fine arts offerings, among other metropolitan amenities.**For additional information, contact Cyndi Edwards, 800-573-2580 or e-mail edwards.cyndi@mayo.edu.**EOE

Fellowships

THE GEORGE WASHINGTON UNIVERSITY
WASHINGTON, DC

Entering its 35th year, this ACGME-accredited fellowship on Psychosomatic Medicine is currently accepting applications for **three PGY-5 positions to start July 1, 2013**. Under the guidance of Dr. Thomas Wise and Dr. Catherine Crone, the fellowship offers consultation-liaison training in a wide variety of medical specialties in both inpatient and outpatient settings. This includes: oncology, ob/gyn, HIV, trauma, organ transplantation, pulmonary medicine, and cardiology. Didactic seminars address clinical, biological, cognitive behavioral and psychodynamic approaches the understanding and treating the medically ill. Opportunities in teaching, research, and outpatient psychotherapy are readily available. Training is tailored to fellow's area of interest and career goals. The fellowship is based at Inova Fairfax Hospital, an 833-bed tertiary care teaching facility located in the heart of the DC Metro area.

Interested individuals should contact:
Catherine Crone, M.D.
PM Fellowship Program Director
George Washington University
Medical Center
c/o Inova Fairfax Hospital
3300 Gallows Road Falls Church, VA 22042
Phone: 703-776-3380
E-mail: cathy.crone@inova.org

RESEARCH TRAINING FELLOWSHIPS IN CLINICAL PSYCHIATRY AND PSYCHOLOGY

Stanford University Department of Psychiatry and Behavioral Sciences anticipates openings for post-doctoral fellows to begin 7/2013 and 9/2013 of the 2013-14 academic year. NIMH-funded training fellowships are designed for those who plan to pursue careers in clinical research with a specialization in adult disorders including mood, anxiety, eating disorders, insomnia, or related areas. These are one- to three-year positions contingent upon funding. Fellows will participate in research projects with faculty mentors and are also expected to develop their own investigations. Candidates should have a clearly identified area of interest and demonstrated capability in scholarly research. Stipends for NIMH training fellowships are approximately $50,000 plus benefits, depending on previous training. These positions are open to MDs and PhDs. Candidates must contact faculty in their area of interest before applying (http://psychiatry.stanford.edu). **REQUIREMENTS:** MD applicants must have completed an approved psychiatry residency program. PhD applicants must have completed: 1) an APA-accredited graduate program; 2) an APA-accredited internship; and 3) all requirements for their PhD prior to beginning their appointment. Applicants must be US citizens. **TO APPLY:** For detailed application information, please go to: http://psychiatry.stanford.edu/education/T32-research-fellowships/. Minorities and those with disabilities or disadvantaged backgrounds are strongly encouraged to apply.**Application deadline is 1/4/2013.**

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