Volume 45
Number 9
May 7, 2010

Newspaper of the
American
Psychiatric
Association

PSYCHIATRIC NEWS

inside

PERIODICALS:
TIME-SENSITIVE MATERIALS

Credit: Richard Nowitz / Courtesy New Orleans Convention and Visitors Bureau

Last call for APA's 2010 annual meeting in New Orleans! The meeting runs from May 21 to May 26. Among the special presenters are actress and author Carrie Fisher and football great Terry Bradshaw. See pages 2 and 26 for registration information. Don't miss this opportunity to get the latest research and clinical updates from some of the field's most respected experts.

Oregon Governor Vetoes Bill on Psychologist Prescribing

The issue is liable to return in the Oregon legislature, but legislators may also look beyond psychologist prescribing to examine the broader issues around access to mental health care in the state.

BY MARK MORAN

Oregon Gov. Ted Kulongoski (D) vetoed a bill that would have created a panel within the Oregon Medical Board to make recommendations for psychologists in the state to prescribe medicine.

The veto of Oregon SB 1046 on April 8 was hailed by APA, the Oregon Medical Association, the Oregon Psychiatric Association, and other medical and patient-advocacy organizations after a legislative cliffhanger that involved intense last-minute lobbying by opponents and proponents of the legislation.

On March 29, Kulongoski issued a "notice of possible intent to veto" the bill, then took the next two weeks hearing arguments for and against the bill (*Psychiatric News*, April 16).

In addition to the bill's patient-safety and public-health implications, a particu-

please see ***Oregon*** *on page 28*

Managed Care Firms Sue To Stop Federal Parity Law

The dispute centers on whether MBHOs can use certain kinds of management strategies not imposed on medical-surgical services and still be in compliance with the law.

BY MARK MORAN

Some managed behavioral health care organizations (MBHOs) are suing the federal government to halt implementation of the Paul Wellstone and Pete Domenici Mental Health Parity and Addiction Equity Act of 2008.

The MBHOs—which include Magellan Health Services Inc., Beacon Health Strategies Inc., and Value Options—have filed suit as the Coalition for Parity Inc., claiming that regulatory rules issued by the federal government in February violate the original congressional intent of the parity legislation. The legislation was signed into law by President Bush in October 2008.

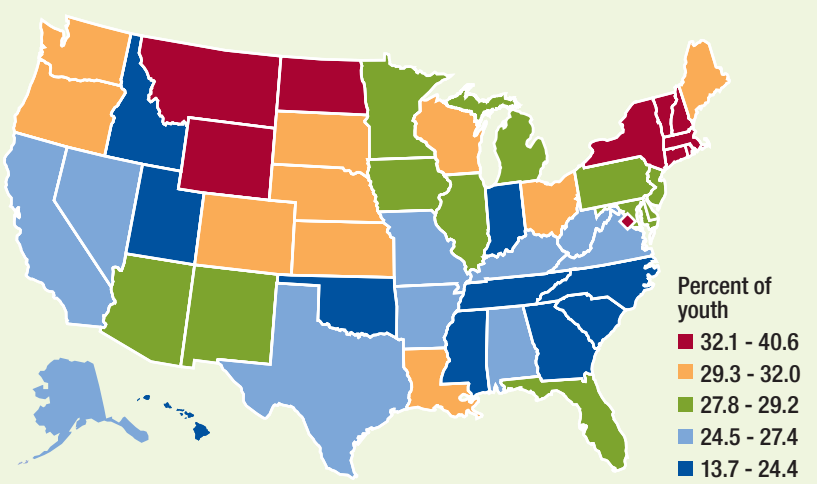
The suit was filed in the United States District Court for the District of Columbia on March 31. A motion for a restraining order filed by the group in April to delay implementation of parity regulations, currently scheduled for July 1, was denied.

At press time, Irvin "Sam" Muszynski, J.D., director of APA's Office of Healthcare Systems and Financing, said APA—along with some 15 other groups organized as the Parity Implementation Coalition—was preparing detailed responses to the suit in the form of an affidavit and legal brief in support of the government's rulemaking to implement the parity law.

please see ***MBHOs*** *on page 27*

More Than a Quarter of U.S. Youth Report Underage Drinking

According to data from the National Survey on Drug Use and Health (NSDUH) 2006 to 2008, 27.6 percent of U.S. youth aged 12 to 20 reported that they drank alcohol in the prior 30 days. Underage drinking was rarest in Utah (13.7 percent) and most common in North Dakota (40.6 percent). About 8.6 percent of the underage drinkers said they bought the alcohol themselves, which is illegal in all 50 states and the District of Columbia.



Source: Substance Abuse and Mental Health Services Administration, *The NSDUH Report*, April 1, 2010

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Call the APA Answer Center at (888) 35-PSYCH in the U.S. and Canada; in other countries: (703) 907-7300.

Genome Search Reveals Clues To Antidepressant Response

Why do some patients do well on one antidepressant but not another? Research identifies genetic variations to explain and potentially predict treatment response.

BY JUN YAN

Numerous mutations, some of which were found in unexpected places in the genome, have been linked to therapeutic response to antidepressants among patients with depression, a new genomic study reported.

Research in this area hopes to explain individual variations in patient response to different antidepressant drugs and one day help clinicians tailor the most effective treatment to each patient.

This study, published online in *AJP in Advance* on April 1, was part of the larger Genome-Based Therapeutic Drugs for Depression (GENDEP) project, a multinational collaboration by researchers in the United Kingdom, Poland, Croatia, Germany, Denmark, Italy, Belgium, Slovenia, Canada, and France.

More than 800 adult patients with a diagnosis of moderate to severe unipolar depression participated in the intervention part of the study, and 706 of the patients provided DNA samples for analysis. All participants were of white European ancestry.

Most of the participants were randomly assigned to receive either escitalopram or nortriptyline for 12 weeks on an open-label basis. A minority of patients who had contraindications to one of these antidepressants were assigned to the other drug.

The two drugs were chosen for their different mechanisms of action: Escitalopram is highly selective for inhibiting the serotonin reuptake receptor with no binding to the norepinephrine reuptake receptor, while nortriptyline is a strong inhibitor of norepinephrine reuptake with very weak binding to the serotonin reuptake receptor. Among the patients who were included in the study, 394 received escitalopram and 312 received nortriptyline.

To find genetic variations that may significantly influence patients' response to either antidepressant, the researchers tried two approaches to uncover ties between genetic variations and antidepressant response. In the first approach, they scanned the entire genome using more than half a million single nucleotide polymorphism (SNP) markers to pick up any signs of association. In the second approach, they focused on variants in 72 candidate genes and the DNA regions around these genes.

The clinical response to either antidepressant was measured by the change in Montgomery-Asberg Depression Rating Scale (MADRS) scores from baseline to the end of treatment.

In the genomewide analysis, polymorphisms in the gene encoding for uronyl 2-sulphotransferase were significantly associated with patients' response to nortriptyline. This association was the strongest in the entire study. Uronyl 2-sulphotransferase is an enzyme involved in

please see ***Antidepressant*** *on page 17*

APA's 2010 Annual Meeting: Be There!

- If you haven't registered for the annual meeting yet, there's still time! Meeting and hotel information can be accessed at <www.psych.org/MainMenu/EducationCareerDevelopment/Meetings/AnnualMeeting.aspx>. Also, on-site registration will be open at these times:

Friday, May 21	**Noon-5 p.m.**
Saturday-Tuesday, May 22-25	**7:30 a.m.-4 p.m.**
Wednesday, May 26	**7:30 a.m.-2 p.m.**

- Please note that the meeting will be held over five days instead of the usual six—**ending on Wednesday** (May 26) instead of Thursday. The full range of meeting formats (such as symposia, workshops, seminars, and master courses) **will begin on Saturday** (May 22) and run through the end of Wednesday. Plan on arriving by Friday, May 21, so you won't miss anything.

Look throughout this issue for other important annual meeting news.

APA RESOURCES

- ***Psychiatric News* Web Site:** pn.psychiatryonline.org
- **APA and the APA Answer Center:** (888) 35-PSYCH in the U.S. and Canada; in other countries: (703) 907-3700. The Answer Center is open Monday through Friday, 8:30 a.m. to 6 p.m. Eastern time. All APA departments and staff may be reached through the Answer Center. Fax: (703) 907-1085 E-Mail: apa@psych.org
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- **American Psychiatric Foundation** **Phone:** (703) 907-8512 **Web Site:** www.PsychFoundation.org
- **Mental Health Parity Watch** **Phone:** (866) 882-6227 **Web Site:** www.Mentalhealthparitywatch.org

Good Fiscal News for APA

BY ALAN F. SCHATZBERG, M.D.

As I have informed you in earlier columns, APA has faced some difficult economic challenges this past year and a half. APA's revenue comes primarily from three sources: membership dues, meetings, and publishing. In 2009, APA witnessed an approximate shortfall of $8 million in revenues, from roughly $60 million to $52 million.

Although we had budgeted for some reduction in revenues from 2008, we had not anticipated the precipitous decline that occurred during 2009. As early as March 2009, we had indicators that revenues were dropping and immediately began to take steps to reduce spending. Despite these efforts, by the end of the third quarter, the revenue shortfall pointed to an anticipated loss of $1 million for the year, and the Board of Trustees approved using reserves to cover it. There was little choice: there already had been considerable cuts in spending, and we needed to keep key operations functioning.

We have just posted the preliminary results of APA's financial status as of the end of 2009 (see our annual report at <www.psych.org/MainMenu/Newsroom/AnnualReports.aspx>). Even with the lowered revenues, the hard choices we made were effective—we finished the year with a surplus of $1.4 million.

What accounted for the striking turnaround? For one, the Institute on Psychiatric Services was more successful than in previous years. Second, a key annual expense we need to cover is the staff benefit program—and the potential amount is determined on the last day of the year. The cost of this program was offset by a very positive performance in the stock market, and our reserves earned more than expected because of the stock market performance. For another, there was a bit of an uptick in ad revenue and a decrease in paper costs for APA's major publications at year's end that were not expected. Last, our overall expenses were lower than anticipated.

Although it is a great relief to us that this was the case, the staff and the Board of Trustees have expended considerable effort to see whether we could have better anticipated the lower figure. There may be a temptation for people to jump in and say let us restore some of the items that we cut. Clearly we cannot do that without going into the red since our revenues are still way down in terms of advertising. Just take a look at the lack of pharmaceutical ads in this issue of *Psychiatric News*. APA's budgeted and actual expenses for 2010 need to be managed carefully. We will have a better sense of where we stand after the 2010 annual meeting in New Orleans. I urge all of you to attend the meeting—it has many truly superb sessions covering a wide range of scientific and clinical topics.

Reorganization Update

As you may know, APA is a 501(c)(6) not-for-profit organization and has three 501(c)(3) business affiliates—American Psychiatric Publishing Inc. (APPI), American Psychiatric Institute for Research and Education (APIRE), and American Psychiatric Foundation (APF). This structure is highly complex, expensive to run, and at times very inefficient. We must file many more tax returns and have multiple separate audits than a simpler structure would require. In addition, it is not optimal in terms of aligning revenues with expenses.

In the past year and a half, we have been working hard on a consolidation of the three affiliates and transferring the publishing business to APA. The resulting structure will be a stronger one for the Association and will allow us to meet our various missions more efficiently. The leadership and boards of all four entities have been extremely diligent and collaborative in this effort, and I hope that we can soon announce what the final structure will be and how the organization's various missions will be addressed.

Psychiatric News Update

Dr. Jim Krajeski has announced that he will be stepping down from his position as editor in chief of *Psychiatric News* at the end of the annual meeting after a dozen years of outstanding leadership. Dr. Carolyn Robinowitz will assume the editorship duties on an interim basis for up to one year. We are indebted to Jim for his superb stewardship of *Psychiatric News* and to Carolyn for spelling him on his breaks over the past year. Jim will spell Carolyn over the next year on several issues.

The means of professional communication are changing rapidly, and we have appointed a task force led by Dr. Jeff Borenstein, chair of APA's Council on Communications, to help guide us on the future role of *Psychiatric News* in APA's communication efforts. Our goal is to ensure that *Psychiatric News* is delivering the information you want in the formats (print and electronic) that are most useful to you. We anticipate asking for your feedback and recommendations as the process moves forward. ■

APA Needs Your Help

APA needs its members who have billing experience with general evaluation and management codes (99XXX series codes) to participate in a survey designed to evaluate the time, complexity, and intensity of work required to perform a procedure, relative to other procedures used for comparison. APA members interested in participating in the survey should call the Office of Healthcare Systems and Financing at (888) 357-7924, ext. 8593, or e-mail Becky Yowell at byowell@psych.org.

Psychiatry Could Benefit From Education, Workforce Changes

Psychiatrists are expected to benefit from some features of the health care reform law, such as increased payments targeted at some physicians, while other aspects of the new law may result in future payment cuts.

BY RICH DALY

Psychiatrists are likely to see benefits accruing from some of the features of the $938 billion reorganization of the nation's health care system enacted in March, including some who will qualify for expanded physician reimbursements. However, other features of the new law were opposed by APA over concerns that they would reduce reimbursements for some psychiatrists.

APA and several other physician groups endorsed the final version of the health care overhaul that passed Congress in March through two separate measures (PL111-148 and PL111-152), because it provides vastly expanded access to private and public health insurance, among other major elements. Receiving less attention during the long and contentious legislative battle, however, were the ways in which some elements of the legislation will impact psychiatrists and other physicians.

Specifically, several changes to Medicare will increase some reimbursements. The measure reestablishes—effective later in 2010—the expired national average "floor" on Medicare's geographic adjustment of physician payments, which is commonly known as the geographic practice cost index. Reestablishing this floor will result in increased reimbursements for many rural physicians. Another Medicare payment increase to adjust for rural physicians' practice expenses for much of 2010 and 2011 also is expected to benefit many physicians. Taken together, the two Medicare changes included in the health care law are expected to benefit physicians who live in or are considering relocating to rural areas in 51 localities in 42 states, Puerto Rico, and the Virgin Islands, according to an APA analysis.

Among new Medicare programs included in the law is a financial-reward initiative for Accountable Care Organizations (ACOs) that take responsibility for the costs and quality of care received by their patients over a set period of time. The measure encourages the creation of such Medicare ACOs, which can include groupings of physicians, hospitals, nurse practitioners, and physician assistants—among other health care providers—with the goal of meeting quality-of-care targets and reducing the costs of their patients' care relative to spending benchmarks. ACOs that succeed in these goals will receive a share of the Medicare savings they achieve.

The establishment of ACOs, which are a newer concept than medical homes, was supported by APA. ACOs were included in only one of the legislative versions of the health reform and so the concept maintained a low profile during the extended congressional wrangling over the complex legislation. It's also a program that APA plans to follow closely, because it is relatively new and has not been widely implemented in large health care systems.

A Medicaid initiative included in the new law would allow states to add so-called health or medical homes to their versions of the joint federal and state insurance program. These health homes will aim to improve patient health and reduce costs by assigning a single physician to coordinate all aspects of a patient's care. The program will be targeted at Medicaid enrollees with chronic conditions, including those with serious and persistent mental illness.

Training in Child MH Issues Addressed

The new law also includes several workforce-development initiatives. It establishes, for example, a loan-repayment program for clinicians who provide mental health services to children and adolescents within a federally designated Health Professional Shortage Area, Medically Underserved Area, or among a Medically Underserved Population.

In addition, the new law authorizes a series of mental health education and training grants to provide incentives for schools to develop, expand, or enhance training programs in social work, graduate psychology, professional training in child and adolescent mental health, and pre-service or in-service training for paraprofessionals in child and adolescent mental health.

"This will allow more students to go into the field," said Kristin Ptakowski, director of government affairs at the American Academy of Child and Adolescent Psychiatry, which has long urged increased federal funding for programs and training grants in this field as well as loan-forgiveness programs for professionals trained in this area of mental health care.

Potential Cuts Loom

The new law does, however, also contain features that may have a detrimental effect on psychiatrists. For instance it amends the Physician Quality Reporting Initiative (PQRI) to require all physicians participating in Medicare to report performance measures. The law will require penalties of 1.5 percent of Medicare income beginning in 2015 for physicians who fail to report "successfully."

The penalty provision was opposed by APA, which supports the general goals of the PQRI, because physicians have faced significant delays in obtaining responses from federal regulators in the existing voluntary PQRI program. Such delays in a PQRI program that penalizes physicians could result in payment cuts, but physicians would not know for up to a year that there are problems with their quality-of-care reports.

Another part of the law opposed by APA established the Independent Payment Advisory Board (IPAB) to recommend changes in Medicare's physician-payment policy. The law requires the IPAB to track spending targets preset by the government and recommend payment reductions if costs exceed targets. Congress could stop such future reductions by the IPAB, but only if legislators are able to find other cuts that would provide the same level of savings.

Some of APA's opposition to the IPAB stems from the law's exemption of hospitals and other health-related entities from its recommended cuts until 2014, which

please see ***Workforce*** *on page 28*

Law Improves Insurance Coverage For Those Needing MH Care

The new health care law is expected to benefit people with mental illness because of measures such as insurance coverage expansions and protections that should allay anxiety over possible cancellation of coverage.

BY RICH DALY

Enactment of the new health care reform law in March was celebrated by mental health advocates, who believe that many of its elements will benefit people with varying severities of psychiatric illness.

Among the signature features of the law is a ban on the use of preexisting-condition exclusions and other forms of discrimination based on health status by private health insurers. Use of such exclusions has kept some people with mental illness or their dependents from obtaining coverage in the individual insurance market.

"Doing away with [such exclusions] is important for all people, but especially for people with mental illness," APA President Alan Schatzberg, M.D., told *Psychiatric News*.

Until the ban on the use of preexisting conditions goes fully into effect in 2014, the law creates a temporary insurance program with financial assistance for people with preexisting conditions who have lacked insurance for at least six months.

Other limitations on insurers include bans on the use of lifetime or annual caps on the dollar value of benefits beginning in 2014. Some people with serious mental illness exceeded their caps due to their need for costly inpatient care or because they also suffered from expensive-to-treat coexisting nonmental illnesses. Until this provision becomes effective, the health care overhaul restricts annual limits that private insurance plans can impose to those set by the secretary of Health and Human Services.

Another insurance change will require plans to allow young adults up to age 26 to join their parents' policies if they don't have access to an insurance plan on their own. This provision will benefit young adults struck by the onset of mental illness in their early 20s.

These insurance improvements are "particularly notable given that 4 of the 10 leading causes of disability in the United States are mental disorders, and 87 percent of Americans cite lack of insurance coverage as the top reason for not seeking mental health services," Laurel Stine, director of federal relations at the Bazelon Center for Mental Health Law, told *Psychiatric News*.

High-Risk Pools Boost Access

The health care overhaul should especially benefit people with mental illness who are not in the group-insurance market.

The law requires states to set up insurance exchanges by 2014 where individuals and small businesses can shop for standardized insurance packages that include mental health care. As an interim measure until the exchanges are established, high-risk pools will be established by next month to cover adults with preexisting conditions.

The new benefits will be accompanied by new responsibilities for both individuals and employers. For example, virtually all Americans must purchase health insurance. However, both low-income and middle-income Americans will be eligible for significant subsidies.

Additionally, beginning in 2014, all employers with 50 or more workers must offer health insurance to employees; otherwise, they must pay a penalty based on the number of employees who are uninsured.

Medicaid Changes Coming

Under the health care overhaul, Medicaid will cover 16 million more beneficiaries beginning in 2014. The expansion is expected to significantly affect people with serious mental illness, who are more likely than the general population to have low incomes due to their illness. Medicaid is already the single largest payer for mental health care in the nation. Individuals and families with incomes of up to 133 percent of the federal poverty level (FPL) will be eligible for Medicaid, instead of the current system that restricts eligibility to specific low-income groups, such as pregnant women. (For 2010, the FPL is $22,050 for a family of four.)

Another Medicaid change will remove the exclusion of coverage for certain medications beginning January 1, 2014. Those drugs include smoking-cessation treatments, barbiturates, and benzodiazepines.

Psychiatric patients will benefit from a key Medicare change that will reduce the so-called doughnut hole that kicks in after beneficiaries reach a certain level of spending for their prescription medications. Beginning this year, Medicare patients whose prescription expenses fall within the doughnut hole ($2,830 to $4,550 for 2010) will receive a $250 rebate. Rebate increases over the next 10 years will lower the beneficiary co-insurance rate for this coverage gap to the standard level for other Medicare-covered medications.

More information on the patient-related mental health components of the health care reform law is posted at <www.bazelon.org/issues/healthreform/1-26AmendedSenateSummary.pdf>. ■

5:30PM
DINNER AND SIGN-IN

6:00PM
WELCOME AND OVERVIEW
Prakash Masand, MD
Activity Chairperson
Consulting Professor,
Psychiatry and Behavioral Sciences
Duke University School of Medicine
Durham, North Carolina

6:05PM
OBSTACLES AND OPPORTUNITIES IN NEW CNS DRUG DEVELOPMENT
Kenneth I. Kaitin, PhD
Director, Tufts Center for the Study of Drug Development
Professor of Medicine,
Professor of Pharmacology and Experimental Therapeutics,
Tufts University School of Medicine
Boston, Massachusetts

6:25PM
DOES PHARMACOGENETICS HAVE A ROLE IN TREATING SCHIZOPHRENIA?
Roy H. Perlis, MD, MSc
Medical Director,
Massachusetts General Hospital Bipolar Clinic and Research Program
Director of Pharmacogenomics Research
Department of Psychiatry
Associate Professor of Psychiatry,
Harvard Medical School
Boston, Massachusetts

6:45PM
SWITCHING ANTIPSYCHOTIC THERAPY: LESSONS FOR THE CLINICIAN
Prakash Masand, MD
Activity Chairperson

7:05PM
INNOVATIVE STRATEGIES TO IMPROVE ADHERENCE IN SCHIZOPHRENIA
Mehul V. Mankad, MD
Clinical Associate,
Psychiatry and Behavioral Sciences
Duke University School of Medicine
Staff Psychiatrist,
Durham Veterans Affairs Medical Center
Durham, North Carolina

7:25PM
QUESTION AND ANSWER SESSION

8:00PM
ADJOURNMENT

WHO SHOULD PARTICIPATE

This activity is designed for clinical psychiatrists and other healthcare professionals interested in the management and treatment of schizophrenia.

OVERVIEW

While the exact etiology of schizophrenia is still elusive, schizophrenia appears to reflect a convergence of pathologic processes, one or more genetic factors that alter the neurotransmitter mechanisms regulating the activity of cortical neurons, and nongenetic factors. Today, neuroscience is flourishing with discoveries and advances in all areas of brain function, particularly in the diagnostic and molecular aspects. The translation of this evidence into clinically viable treatments has been at times disappointing, hampered by multiple limitations. The discovery and development of the second-generation atypical antipsychotics has challenged the simplicity of the dopamine hypothesis and broadened understanding of the pathophysiological basis of schizophrenia. Because no one medicine or class of medications has been shown to work for all people with schizophrenia, patients and their doctors often try multiple treatment options before a successful response is achieved. Many face obstacles in achieving positive outcomes due to challenges including differential efficacy, side effects, lack of psychosocial and vocational support, and patient nonadherence. Effectively treating and managing schizophrenia remains an important area of educational need, especially as the understanding of this complex and devastating disorder continues to evolve, leading to additional therapeutic options and refinements in evidence-based medical management practices. This activity will address four distinct topics of unmet need in schizophrenia care with a focus on practical evidence-based strategies in therapy and the evidence underpinning those recommendations.

LEARNING OBJECTIVES

At the conclusion of this activity, participants should be able to

1. Describe the challenges of CNS drug development; understand the time, cost, and risk of bringing new neuropharmacologic agents to market.
2. Explain the process to translate a genetic association study into a clinically useful test.
3. Describe the clinical risks and benefits of switching antipsychotic medications and apply evidence-based strategies to adjusting therapeutic regimens.
4. Discuss strategies to increase patient adherence to clinical recommendations in the treatment of psychosis.

ACCREDITATION STATEMENT

The American Psychiatric Association (APA) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

The APA designates this educational activity for a maximum of 2 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

FACULTY DISCLOSURE STATEMENT

Participating faculty will disclose any industry affiliations, sponsorships, honoraria, monetary support, and other potentially biasing factors to the audience.

Attendees must be registered for the APA Annual Meeting to attend this symposium. Seating is limited and will be based on first-come, first-served. For more information about the meeting, please visit the APA Web site at www.psych.org or contact the APA toll free at 1.888.357.7924 (within the US or Canada) or 703.907.7300.

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Have Regulators Underestimated Cost of EHR Systems?

Proposed regulations to implement a federal program spurring physicians to adopt electronic medical records may have numerous unintended effects, say APA and other medical organizations.

BY RICH DALY

Proposed federal regulations to implement a massive federal initiative aimed at convincing physicians to adopt digital patient record systems may prove "untenable" for many small-practice and solo-practice physicians, according to comprehensive reviews of the regulations submitted to the government by APA and other physician groups.

APA joined 95 other medical groups in a March 15 letter from the AMA to federal regulators at the Centers for Medicare and Medicaid Services (CMS) regarding regulations proposed in December 2009 to govern a $19 billion federal health information technology (HIT) program.

The proposed regulations would implement a provision of the American Recovery and Reinvestment Act to provide incentives to physicians and hospitals to adopt costly HIT systems, which have at their heart digital patient record programs known as electronic health record (EHR) systems.

Among the many concerns highlighted by the AMA letter was that federal regulators have underestimated the high cost to physician practices of EHR adoption and ongoing overall HIT system maintenance. Officials at CMS estimate that EHR system adoption or upgrades of existing systems to meet federal standards will cost on average about $54,000 per physician employee in a practice, while annual maintenance will cost an average of $10,000 per physician employee.

Once the regulations are finalized, the federal program will provide "incentive payments" of up to $44,000 over five years to physicians who show "meaningful use" of qualified EHR technology (*Psychiatric News*, March 20, 2009).

But both the federal cost estimates and proposed payments could be dwarfed by the true cost to physicians of HIT systems that would comply with all of the proposed regulations.

"[P]hysicians would need to make these investments up front, and even those eligible for the maximum incentives would experience costs that could exceed the maximum incentives available," the AMA letter noted.

Many of the AMA's concerns were echoed in a letter that APA Medical Director James H. Scully Jr., M.D., sent to federal regulators on the same day that the AMA sent its letter.

Scully highlighted aspects of the proposed federal regulations likely to hurt small-group and solo practitioners, which include most psychiatrists. Specifically, Scully raised concerns that the extent and number of proposed federal regulations governing the use of qualifying EHRs would impose a serious administrative burden on smaller practices.

Additionally, APA is concerned that the proposed regulations will require all physicians who want federal EHR funds to collect patient data in 25 areas not related to mental health and record them in the EHR systems to show "meaningful use." APA urged federal regulators to allow physicians to collect a smaller number or none of these data types.

Additionally, APA urged the Department of Health and Human Services to ensure that "adequate technical support" is put in place for what will be a technologically challenging national HIT initiative. This assistance should include Web sites, toll-free telephone numbers, direct outreach to providers, and "comprehensive guidance."

Another critical concern for psychiatrists that Scully highlighted is the need for adequate patient-privacy protections. Although he praised the law's provisions and regulators' efforts to ensure robust privacy protections of sensitive information contained in EHRs, such systems will not be required to incorporate many of the strongest privacy measures until 2015. Since the EHR legislation was first debated, APA has continued to urge regulators to move the effective date of the required privacy protections to the first phase of the national EHR program implementation in 2011. Otherwise, mental health patients in particular—due to societal stigma against mental health care and people with mental illness—may not trust that their information will be well protected.

> **"There are always concerns that patients may withhold information or avoid treatment if they cannot trust that privacy of sensitive information will be protected."**

"There are always concerns that patients may withhold information or avoid treatment if they cannot trust that privacy of sensitive information will be protected," Scully wrote.

Federal regulators accepted thousands of public comments on the proposed regulations by the mid-March deadline and are expected to use them in crafting final regulations that will be issued in several months. Payments to qualifying physicians will start in 2011.

The proposed regulations are posted at <www.modernhealthcare.com/assets/pdf/CH680921230.PDF>. ■

Crumbling of Social Structures Affects Postdisaster PTSD Development

An earthquake in Peru in 2007 helps psychiatric epidemiologists better understand how the loss of one crucial element of the social structure can influence rates of PTSD.

BY AARON LEVIN

The earthquake that struck southwest Peru in 2007 left behind an all-too-familiar scene of death and devastation, along with a pattern of posttraumatic stress disorder (PTSD) that reflected both personal and social suffering.

The 8.0 magnitude quake's epicenter lay 60 km off the coast of the city of Pisco (population 53,000), where 383 of the 596 deaths were recorded. The city also lost 70 percent of its houses, and the electrical, water, and sewage systems were destroyed. One of the town's two hospitals was wrecked, and only the emergency department at the other was usable after the earthquake.

Five months later, a team of U.S. and Peruvian researchers surveyed adult residents of Pisco to estimate the rate of PTSD and identify any correlates with demographic or other factors.

One in four of the city's residents in the sample reached the threshold for PTSD, according to Javier Cairo, M.D., M.P.H., a fellow in infectious disease at the University of Texas M.D. Anderson Cancer Center in Houston, and colleagues, writing in the March *Disaster Medicine and Public Health Preparedness*.

The researchers identified 774 city blocks in Pisco and its suburbs and then randomly selected 150 for study.

They collected demographic data from residents in two randomly chosen houses in each block using the Spanish version of the PTSD Checklist and the traumatic events section of the Harvard Trauma Questionnaire. Of the 298 adults surveyed, 75 (25 percent) reached the threshold for diagnosis of PTSD.

About 68 percent of the subjects were women, and 84 percent were Catholic. Half (51 percent) lost their homes in the quake, 69 percent lost a friend or relative, and 29 percent lost their jobs.

Among the quake victims, 64 women (32 percent) and 11 men (12 percent) were diagnosed with PTSD. The overall PTSD prevalence of 25 percent in the city met a commonly accepted standard for "moderate" impact of a disaster, said the authors.

However, the categorical approach used by the authors may underestimate exposure and prevalence, said Armen Goenjian, M.D., a research professor of psychiatry at the Geffen School of Medicine at UCLA. Goenjian has studied the psychiatric aftereffects of an earthquake in Armenia and a hurricane in Nicaragua.

"PTSD is not black and white. It's a spectrum of symptoms," said Goenjian in an interview. "If you just have yes-or-no questions, you can miss a lot."

Nevertheless, after adjustment for a list of factors associated with the disaster, the researchers found five factors that significantly correlated with PTSD (see table).

Female quake survivors were five times more likely than men to have PTSD. Women in general have higher rates of PTSD after trauma, but the authors also suggested that the added burdens of providing care for others after the disaster might contribute to that fact.

Factors that may have heightened the trauma worsened the earthquake victims' risk for PTSD. For example, loss of food and water after the quake doubled the chance of PTSD, and physical injury nearly quadrupled the risk. The survey did not include the most severely injured survivors, because they were transported to Lima for treatment.

Loss of food, housing, water, and other basics disproportionately affect the poor, said Goenjian.

"Recovery is also slower for poor people," he said. "It may represent not more PTSD per se, but just more adversities. Adversities retard recovery, but they don't cause PTSD."

Nearly all the respondents (254 out of 298) lost their local church. That loss was associated with an odds ratio of 22 among those with PTSD.

"We believe that the disproportionate prevalence of PTSD seen among Catholics was most likely secondary to the destruction of the city's [three] Catholic churches during the earthquake," wrote the authors. "In addition to the churches providing a place to worship, religious congregations can provide an important resource for coping with the negative impact of a disaster."

"Religion is a powerful tool and can be a solace when people are vulnerable," agreed

please see ***PTSD*** *on page 29*

PTSD Associated With Five Factors

After adjustment, five variables proved significantly related to a diagnosis of posttraumatic stress disorder among survivors of Peru's 2007 earthquake.

Factor	Odds Ratio	P
Female sex	5.35	0.0001
Lack of food/water	2.20	0.0147
Loss of church	22.03	0.0036
Injury	3.68	0.0040
Perceived family/ friends social support	0.77	0.0478

Source: Javier Cairo, M.D., et al., *Disaster Medicine and Public Health Preparedness*, March 2010

Novel Approaches to Assessing and Treating DEPRESSION in the MEDICALLY ILL

Don't Miss This Important Educational Activity!

MONDAY, MAY 24, 2010 • 6:30PM Dinner and Sign-in • 7:00PM-9:00PM Educational Activity

HILTON NEW ORLEANS RIVERSIDE • First Level, Grand Ballroom A/B • New Orleans, Louisiana

6:30PM
Dinner and Sign-in

7:00PM
Welcome and Overview
Bradley N. Gaynes, MD, MPH
Activity Chairperson
Research Fellow of the Cecil G. Sheps Center for Health Services Research,
Professor,
Department of Psychiatry
University of North Carolina at Chapel Hill School of Medicine
Chapel Hill, North Carolina

7:05PM
Assessing Mood and Somatic Symptoms in the Medically Ill Depressed Patient
Richard C. Shelton, MD
James G. Blakemore Research Professor,
Vice Chair for Clinical Research,
Director, Mood Disorders Program
Department of Psychiatry
Professor,
Department of Pharmacology
Vanderbilt University School of Medicine
Nashville, Tennessee

7:25PM
Pathophysiology of Somatic Symptoms and Major Depressive Disorder in Medically Ill Populations
Janet M. Witte, MD, MPH
Instructor, Department of Psychiatry
Harvard Medical School
Private Practice Psychiatrist,
Boston, Massachusetts

7:45PM
Managing Depression in the Medically Ill: An Up-to-Date Evidence-Based Guide
Bradley N. Gaynes, MD, MPH
Activity Chairperson

8:05PM
Management of Treatment-Resistant Patients With Somatic Symptoms and Medical Illness
Maurizio Fava, MD
Vice Chair, Department of Psychiatry
Director, Depression Clinical and Research Program
Massachusetts General Hospital
Professor of Psychiatry,
Harvard Medical School
Boston, Massachusetts

8:25PM
Question and Answer Session

8:55PM
Closing Remarks

9:00PM
Adjournment

A Symposium Held During the APA 2010 Annual Meeting

Sponsored by the American Psychiatric Association

Supported by an educational grant from Lilly USA, LLC Lilly

WHO SHOULD PARTICIPATE
This activity is designed for clinical psychiatrists and other healthcare professionals interested in the assessment and management of major depressive disorder in medically ill patients.

OVERVIEW
Half of patients with major depressive disorder (MDD) have a coexisting medical illness. Comorbidities are associated with poorer clinical outcomes, including a slower response to treatment, a greater chance of treatment resistance, and a higher risk of relapse following successful treatment. Recent research has improved our understanding of how best to diagnose and manage depressed, medically ill patients. A key first step is the successful identification of depressive illness in the medically ill patient. Dr. Richard C. Shelton will review evidence-based strategies to identify MDD and monitor treatment response in this challenging population, with a focus on particularly relevant medical illnesses such as diabetes. Emerging evidence supports the role of cytokines and the inflammatory response in the development of depressive illness. Dr. Janet M. Witte will review the results of these and other pathophysiologic mechanisms to provide an up-to-date understanding of the biologic underpinnings of the MDD/medical illness comorbidity. Consideration of risk factors for poor outcomes can guide MDD treatment in the medically ill. Dr. Bradley N. Gaynes will review available clinical trial evidence and address how best to manage depression in this population, including considerations of both newer pharmacotherapies and nonpharmacologic treatments. Finally, given the greater risk of failure to remit in this group, strategies to address treatment-resistant depression (TRD) are crucial. Dr. Maurizio Fava will review recommendations to address patients with TRD, including findings from the STAR*D study and the use of newer pharmacotherapies.

LEARNING OBJECTIVES
At the conclusion of this activity, participants should be able to
1. Identify evidence-based strategies for diagnosing depression in medically ill populations.
2. Recognize the emerging evidence supporting the role of cytokines and the inflammatory response in the development of depressive illness.
3. Distinguish between clinical trial evidence of pharmacologic and nonpharmacologic treatment for depression in the medically ill population, including patients who are defined as treatment-resistant.

ACCREDITATION STATEMENT
The American Psychiatric Association (APA) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT
The APA designates this educational activity for a maximum of 2 *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

FACULTY DISCLOSURE STATEMENT
Participating faculty will disclose any industry affiliations, sponsorships, honoraria, monetary support, and other potentially biasing factors to the audience.

Attendees must be registered for the APA Annual Meeting to attend this symposium. Seating is limited and will be based on first-come, first-served. For more information about the meeting, please visit the APA Web site at www.psych.org or contact the APA toll free at 1.888.357.7924 (within the US or Canada) or 703.907.7300.

Physicians Urged to Join Battle Against Inhalant Use

Concerned that fewer teens preceive the dangers that come from using inhalants to get high, federal officials intensify their call to educate parents and children about the serious harm these substances pose.

BY RICH DALY

A high rate of potentially deadly inhalant use among 12-year-olds is leading federal health officials to urge clinicians to educate parents on the warning signs of inhalant use among children.

The rate of lifetime inhalant use among 12-year-olds nationally—6.9 percent—trails only the 9.8 percent rate for alcohol use among abused substances in this population from 2006 to 2008, according to the results of the National Survey on Drug Use and Health by the Substance Abuse and Mental Health Services Administration (SAMHSA). However, a University of Michigan study released in December 2009 noted some good news: past-year use among eighth graders declined from 9.5 percent in 2005 to 8.1 percent in 2009.

Serious risks from inhalant use include death, and up to 200 minors die each year from inhalant use, according to Harvey Weiss, executive director of the National Inhalant Prevention Coalition. Inhalant use has been linked to permanent damage to organs, including the heart and liver, as well as nervous system and mental health problems.

The easy accessibility of more than 1,000 products that have been used by children as inhalants makes prevention particularly challenging. And the short-term "high" these substances provide can make detection of abuse difficult. So clinicians should watch for long-term effects, such as emotional instability, cognitive impairment, persistent short-term memory loss, and loss of the sense of smell. Physicians also should educate parents to watch for such signs as chronically red or runny eyes or nose, paint or stains on the body or clothing, nausea, loss of appetite, and drooling.

Educating parents and children about the short-term and long-term dangers of inhalant abuse may be the most effective way to reduce the number of adolescents using such chemicals, said Pamela Hyde, J.D., administrator of SAMHSA, at a March press conference. Treatment is difficult once the abuse becomes a long-term behavior, she noted.

Credit: Rich Daly

Gil Kerlikowske, M.A., director of the Office of National Drug Control Policy, joined other federal officials in March to warn of indications that adolescent inhalant use could surge amid low disapproval attitudes by youth.

"Parents are not used to thinking of these products as dangerous because they weren't made to be inhaled," she said.

Physicians play an important role, too, said Weiss. "Unless physicians ask the right questions and are aware of inhalant use [as a potential problem], then it might go undetected."

Inhalant use may be a particular issue for clinicians who treat adolescents for substance use problems, because minors who abuse inhalants tend to begin abusing drugs at a younger age, according to Weiss. Thus, clinicians should watch for warning signs among all young patients, because there is no socioeconomic, ethnic, or gender profile that fits a "typical" inhalant user.

Federal health officials launched a media campaign in March to alert clinicians about adolescent inhalant abuse. They said at the March press conference that the effort aims to build on previous initiatives to raise awareness and further reduce inhalant use. They credit a recent decline in inhalant use among Texas teens to a statewide education effort there. However, some fear that recent surveys showing a drop in the perceived danger of inhalant use among teens may portend an increase in use.

"When the perceptions of risk decline, we usually see an increase in abuse," said Timothy Condon, Ph.D., deputy director of the National Institute on Drug Abuse, during the press conference.

Information on the clinician education effort through the National Inhalant Prevention Coalition is posted at <www.inhalants.org>. ■

Funding Cuts Threaten Future Of Police Intervention Programs

Programs that police departments use to help them better deal with people who have mental illness are gaining popularity, and a new report suggests factors that can make those programs successful.

BY RICH DALY

An increasing variety of police programs for responding to emergencies involving people with a serious mental illness has emerged over the last 20 years. A report prepared for the Department of Justice has now pinpointed characteristics of programs that have been successful in diffusing tense situations between police and individuals with mental illness.

Although all special response units (SPRs), as these police programs are generally called, have common features, well-functioning programs included variations in program designs that were tailored to the jurisdiction's size, demographics, mental health and law enforcement agency resources, and relevant state laws, according to the report that the Council of State Governments Justice Center prepared for the Department of Justice.

> **"We definitely have concerns about what would happen to these police programs under the president's budget."**

In addition, the cities and counties that had successful programs used approaches to forming SPRs that made collaboration between law enforcement, community members, and mental health professionals a key element of the initiatives.

Such successful programs also were designed to address specific problems that departments faced regarding their interaction with people who have a psychiatric illness, such as frequent calls for service from one individual or poor outcomes in past situations in which police were confronted with a person who was mentally ill. Others focused their resources on neighborhoods or areas to which they were frequently called or on a specific population such as homeless people with mental illness.

This first national effort to analyze how jurisdictions develop and modify effective approaches to police interaction with those who have mental illness came as a growing number of cities and counties have sought to improve the outcomes of potentially volatile situations in which police are confronted with someone who appears to be mentally ill.

The earliest of the SPR approaches is known as the Crisis Intervention Team (CIT), which was launched in Memphis in 1987 after local officers killed a mentally ill man during a confrontation. The Memphis Police Department worked with the local branch of the National Alliance on Mental Illness and local mental health professionals to teach the police more effective and nonlethal ways to manage interactions with people displaying signs of mental illness. The CIT approach was successful enough that an estimated 400 CIT programs have been launched by local and state law enforcement units nationwide.

"CITs have been extremely successful in Tennessee and elsewhere," said Laurel Stine, a lobbyist for the Bazelon Center for Mental Health Law.

In general, the CIT approach trains police officers to use response techniques that can deescalate situations involving people with mental illness. There are, however, different models of SPR programs that also are successful. One common program pairs police with mental health professionals—known as the co-responder model—who report to situations involving people suspected of being mentally ill.

The new guidance for jurisdictions looking to add special police programs to better serve people with mental illness came as the leading federal program to encourage such approaches faced difficulty. The Fiscal 2011 budget proposed by President Obama would direct the Problem Solving Court Initiative to absorb the Mentally Ill Offender Treatment and Crime Reduction program, which provides grants to develop both police programs and local courts for crimes involving people with serious mental illness. Mental health advocates worry that the change could result in phasing out funding for the police program in favor of the the courts program.

"We definitely have concerns about what would happen to these police programs under the president's budget," said Stine.

Mental health advocates hope not only to stop the proposed consolidation but to boost the allotted annual funding for the police program from $12 million to $50 million. The increase is needed because the number of state and local governments seeking federal help to launch such programs continues to far outstrip federal resources. For instance, due primarily to a lack of funds in both Fiscal 2006 and Fiscal 2008, only 11 percent of the grant applications for assistance in planning such police programs were approved.

"Local jurisdictions are definitely interested in [these training programs]," Stine said.

"Improving Responses to People With Mental Illnesses" is posted at <www.ojp.usdoj.gov/BJA/pdf/CSG_LE_Tailoring.pdf>. ■

NIMH Head Wants Psychiatrists To Rethink Industry Ties

Thomas Insel, M.D., calls for clear lines of demarcation between science and marketing, saying it is appropriate for academic and industry investigators to collaborate on science—but not on promotion of patented drugs.

BY MARK MORAN

"I set out to try to understand whether the problems of industry influence were worse in psychiatry than in other specialties, and I came to the conclusion that we just can't determine that," Thomas Insel, M.D., director of the National Institute of Mental Health (NIMH), told *Psychiatric News*.

"But that's not the key question. Whether the problem is better or worse in psychiatry, there is a still a problem. And I think that [the public perception regarding the problem of industry influence] is more hurtful for psychiatry than it is for other specialties. While this problem may be endemic, my sense is that it probably will do more damage to psychiatry than in other areas of medicine. We have less public trust to waste."

Insel spoke with *Psychiatric News* following the publication of a commentary in the *Journal of the American Medical Association* titled "Psychiatrists' Relationships With Pharmaceutical Companies: Part of the Problem or Part of the Solution?"

In that article, Insel cited a "culture of influence" among academic researchers, practitioners, and pharmaceutical companies and warned against "a defiant embrace of the status quo, in which psychiatrists are seen as a leading source of the problem rather than as leaders in finding the solution for financial conflicts of interest."

Speaking with *Psychiatric News*, Insel expanded on those views and reiterated his belief that psychiatry as a profession needs to be "out in front" of the issue of conflict of interest. He acknowledged that he was unfamiliar with some actions APA has taken (Insel is not an APA member), including requiring speakers at APA meetings to disclose conflicts and monitoring speakers at industry-supported symposia for possible bias.

Disclosure Not Enough

Insel said, however, that he believes that disclosure of conflicts of interest alone is not enough and cited findings from cognitive science showing that disclosure may actually *increase* bias rather than work to decrease it. "There has been a presumption in the academic community and among practitioners that somehow disclosure is the way to mitigate conflict of interest," Insel said. "I think disclosure of conflicts is necessary but not sufficient."

In the *JAMA* article, Insel suggested that what is needed are clear lines of demarcation between science and marketing. "The focus on financial conflicts of interest in psychiatry is an opportunity to take the lead in setting new standards for interactions between all medical disciplines and industry," Insel wrote. "Academic leaders, professional societies, and patient-advocacy groups could turn the tables of public trust by developing a culture of transparency for psychiatry's collaborations with industry, including the clear separation of academic-clinical missions from industry marketing."

Empowering Academics to Develop Drugs

So what is the future of drug development and discovery, how should psychiatrists and industry collaborate going forward, and what is the role of NIMH?

Those questions are at the heart of a Weblog posting Insel wrote in March on the NIMH Web site titled "Who Will Develop the Next Generation of Medications for Mental Illness?" In that posting, he cited evidence that pharmaceutical companies were pulling back from research on central nervous system targets because of the costs and difficulty associated with developing new drugs in this area.

As a response, he cited some federal government initiatives, such as the Molecular Libraries Program, an effort throughout the National Institutes of Health to enable academic researchers to screen for molecules that could become lead compounds for drug development.

"For the last five or six years, we have been working on empowering academic investigators to become more involved in drug development through specific programs at NIMH," Insel told *Psychiatric News*. "This is really the key question—how is drug development going to happen in the future?

"There are three answers—the first is that NIMH can continue to do more in drug discovery and development," he said. "We have experience doing research on neglected targets—such as autism—in which pharma may have had less interest. Second, we can catalyze what happens in the pharmaceutical industry by making the kinds of discoveries that encourage pharma to stay in the game. And we can create opportunities for partnerships between academic researchers and industry. It is a gross misreading of NIMH's position to say that we are antagonistic to pharma or that we don't want academic investigators to work with industry. It's not true.

"But there is a difference between having academic and industry investigators collaborating on science and having them collaborate on marketing," Insel continued. "Pharma is a complex industry, and to the extent that we are talking about drug development, there is a lot of interest in working together. To the extent that we are talking about marketing of patented compounds, that is the job of people who work for pharma. I don't think government or academic researchers will gain a lot of trust by participating in that."

"Psychiatrists' Relationships With Pharmaceutical Companies: Part of the Problem or Part of the Solution?" is posted at <http://jama.ama-assn.org/cgi/content/full/303/12/1192?home>. "Who Will Develop the Next Generation of Medications for Mental Illness?" is posted at <www.nimh.nih.gov/about/director/index.shtml>. ■

Psychiatric Leaders Agree Changes Due In Psychiatry-Industry Relationship

Recommendations of an APA work group that focused on possible conflicts of interest in the relationship between psychiatrists and industry will come before the Assembly this month.

BY MARK MORAN

As director of the National Institute of Mental Health, Thomas Insel, M.D., commands some attention.

So a commentary by Insel in the *Journal of the American Medical Association* on what has become one of the most contentious issues in psychiatry today—psychiatrists' relationships with the pharmaceutical industry—was bound to attract attention (see article above).

In that article he cited a "culture of influence" among academic researchers, practitioners, and the pharmaceutical industry and reviewed data about conflict of interest and its effect on research and clinical practice. And he suggested that academic leaders, specialty societies, and patient-advocacy organizations could "turn the tables of public trust by developing a culture of transparency for psychiatry's collaborations with industry, including the clear separation of academic-clinical missions from industry marketing."

APA leaders who spoke with *Psychiatric News* said Insel's commentary, though tough on psychiatry, was largely accurate and will likely have an impact.

"I think it was a very fair analysis of the situation," said APA past President Paul Appelbaum, M.D. "I read him as saying that although it's hard to know whether psychiatry has more problems than other specialties with its relationships with industry, it certainly has problems. And that it is incumbent upon the specialty to get out in front of those problems. I think he is right on target."

Appelbaum chaired a work group that last year formulated stringent recommendations regarding psychiatrists' interactions with industry. They include, among others, recommendations that psychiatrists avoid participating in or attending company-supported promotional talks unless those talks are sponsored by organizations and institutions accredited by the Accreditation Council on Continuing Medical Education, avoid accepting gifts of any kind from industry, and avoid participation in consulting arrangements "in which they are unlikely to make substantive contributions."

After a contentious debate last year, the APA Assembly did not approve the recommendations. However, they were endorsed by the Assembly Executive Committee in January and will return to the Assembly for a vote this month at its meeting in New Orleans.

"The ball is in the Assembly's court," Appelbaum said. "I am hopeful that perhaps Insel's commentary will help to stimulate the field to adopt a set of recommendations. The direction in general is toward greater recognition that relationships are problematic and the need for guidelines to limit adverse consequences."

Robert Freedman, M.D., editor in chief of the *American Journal of Psychiatry*, agreed that Insel's perspective is accurate, but indicated that the pharmaceutical industry bears some of the blame for a relationship that has gone awry. "I think [Insel's] conclusion is exactly the one I would make," Freedman said. "We have important things to do with the drug industry for our patients in terms of developing new treatments. But I would say there is a responsibility on the part of industry with regard to overly aggressive sales techniques that end up denigrating the psychiatric profession. Psychiatrists' acceptance of a role in those techniques makes our whole profession look bad."

Wade Myers, M.D., chair of APA's Ethics Committee, said psychiatrists' involvement with the pharmaceutical industry

> **"I am hopeful that perhaps Insel's commentary will help to stimulate the field to adopt a set of recommendations."**

had "dashed forward faster than a sound ethical foundation could be established underfoot."

He added, "Some psychiatrists who entered this arena unwittingly strayed beyond the limits of professional morals, others reportedly did so with less naivete. The challenge we now face is to create a transparent, ethically sustainable field of collaboration, cleared of the mines of bias and financial conflicts of interest, that is respectful of our professional values."

Daniel Carlat, M.D., an Assembly representative from Massachusetts who has been vocal about conflict-of-interest issues, called Insel's commentary "courageous" and said he hoped it would have an impact on the Assembly's deliberations this month.

"I would be very surprised if it didn't have a concrete effect on decision making within APA," Carlat said. "I think the Assembly meeting in New Orleans could be a turning point." ■

Education in Substance Abuse No Longer Missing in Action

NIDA hopes that its educational campaign aimed at trainees and medical schools will make screening and treatment for substance use disorders widely available in primary care.

BY JUN YAN

Free resources have been made available to medical schools and residency programs by the National Institute on Drug Abuse (NIDA) to help faculty teach students and residents about substance abuse.

As a part of NIDA's efforts to broaden effective substance-related screening and treatment in primary care settings, several medical education curricula have been added to the agency's NIDAMed Web site at <www.drugabuse.gov/coe/coe.htm>. The curricula can be incorporated together or selectively into medical-school syllabuses and residency training.

Eight medical schools have partnered with NIDA to create the educational materials, which include lectures, case studies, faculty workshops, and videos.

The curricula are part of NIDA's broader physician outreach initiative, Gaya Dowling, Ph.D., deputy chief of the Science Policy Branch in NIDA's Office of Science Policy and Communications, told *Psychiatric News*. The initiative involves creating and disseminating information about substance use disorders to a range of audiences, from physicians and medical students to patients, to improve communication on a subject that many find difficult to discuss.

Substance Use Affects Primary Care

Most of the curricula consist of case-based teaching materials to help medical students and residents understand how diagnosing and treating substance use disorders are an integral part of primary care, Dowling emphasized. "There are so many demands on primary care physicians," she said, "it is difficult to spend time on substance use. Nevertheless, primary care physicians cannot afford to overlook the problem."

"Over 20 million Americans are in need of substance abuse treatment," Dowling pointed out. Long-term addictive behaviors such as smoking, excessive drinking, and illicit drug use can lead to symptoms and illnesses in the cardiovascular and other organ systems and affect overall health, she noted, but patients' access to treatment for substance abuse is seriously inadequate. Therefore, training medical students and early-career general practitioners is essential to begin to address this large gap between needs and available care.

"We had a lot of interest from [medical] schools on developing curricula about treating pain appropriately and adequately while managing patients at risk for abuse. . . . This is an issue that really resonates with the medical community," said Dowling.

Practicing physicians who struggle to manage patients with substance use problems will also find the resource materials useful.

Stigma not only makes patients reluctant to admit to problems but also affects physicians' attitudes, said psychiatrist and educator Barbara Schindler, M.D., in an interview with *Psychiatric News*. "The attitude of hopelessness among physicians over substance use disorders impacts their willingness to treat substance use," she said.

Even general psychiatrists often overlook signs of substance use disorders, she said, noting that in her clinical practice, female patients frequently present with dual diagnoses: a mood disorder or posttraumatic stress disorder with comorbid substance use problems, for example. "Physicians have to view patients as a whole and treat all symptoms," she emphasized.

Credit: Mariya Bibikova/istockphoto

Schindler is the William Maul Measey Chair in Medical Education, vice dean of educational and academic affairs, and a professor of psychiatry at Drexel University College of Medicine. In the teaching module produced by Drexel, Schindler gives a demonstration of initial and follow-up visits with a typical patient played by an actor.

Curriculum Tackles Key Competencies

The topics in the curricula were selected by the participating medical schools, Dowling explained. Particularly relevant to issues common to general medicine, several curricula focus on prescription-drug misuse and treating chronic pain with opioids, which are growing concerns in the primary care setting, according to Dowling. In addition, Creighton University produced a curriculum on methamphetamine abuse, and the University of North Dakota created one on substance abuse among physicians.

Although most curricula are case-based written materials designed for faculty members, the curriculum created by Drexel University contains multimedia presentations, including video demonstrations of clinical assessments, and lectures. It also includes videos of five patients in recovery from alcohol or substance use disorders being interviewed about their experience with the disease, treatment, relapse, and recovery.

"To actually hear from real people with substance use disorders is very valuable for students and residents," said Schindler. The images and words of people in recovery are important for dispelling the negative attitude that some students and physicians have toward these patients.

For this module, Drexel University staff made use of its distance-learning technologies. Drexel's medical school created a Web-based medical education tool known as Doc.com, which can be accessed at <webcampus.drexelmed.edu/doccom/user>, in collaboration with the American Academy on Communication in Healthcare. Doc.com contains dozens of multimedia teaching modules and video-based clinical assessment tests. Students can log on and interact live with a standardized patient, played by an actor or faculty member, and then be evaluated by their professor.

Doc.com has close to 10,000 registered users from 20 medical schools around the world, Dennis Novack, M.D., a professor of medicine and associate dean of medical education at Drexel, told *Psychiatric News*. Access to other modules on the Web site requires a subscription fee to offset some of the cost of maintaining and expanding the site, but the module on substance use, developed with support from NIDA, is free.

"It is the most comprehensive and compelling module to date," said Novack. "We hope it has an impact in changing the behaviors, skills, and attitudes of physicians in treating these patients."

NIDA provided approximately $60,000 to each participating school to fund curriculum development.

Drexel will begin to implement the teaching module on substance use screening and intervention in its medical school curriculum next year and examine its effectiveness on changing students' attitudes and competency in this area, said Schindler.

NIDA plans to continue its collaboration with the schools as well as the AMA to "market" these teaching curricula and develop additional content on treating addiction in general medicine, said Dowling. "We need to convey to [medical] schools the importance of the substance use issue and integrate it into the medical mindset." ■

Residents Learn What Makes The Military a Unique Culture

Psychiatry residents at the University of Maryland use their annual exploration of culture as a factor in mental health to break new ground.

BY AARON LEVIN

All human beings live within some kind of culture—a term that usually encompasses race or religion or geography. Parallel to those lie other cultures. Age cohorts are well-known subcultures and so are professions and workplaces.

"To be a psychiatrist requires cultural awareness," said Maria Trent-Watson, M.D., a PGY-3 resident in the Department of Psychiatry at the University of Maryland School of Medicine in Baltimore. Over the last 17 years, the program's cultural diversity committee has looked not only at racial and ethnic groups but at those defined by gender, sexual orientation, immigration status, and social class, as well as the special niche in U.S. society of people who have biracial or multiracial identities.

That understanding prompted residents in Trent-Watson's program to choose military culture as this year's theme for its annual Cultural Diversity Day in March.

An anthropologist might describe military culture like any other, noting values, norms, customs, traditions, languages, symbols, and clothing, said Trent-Watson in her introduction.

But there are intangibles, too, as in any culture, said the first speaker of the day, an active-duty military officer with a doctorate in social work.

"Loyalty, commitment, intimacy, cohesion with unit" describe the bonds that hold military people together, explained Lt. Col. Jeffrey Yarvis, chief of the Behavioral Health Service at Walter Reed Army Medical Center in Washington, D.C., and an assistant professor of family medicine and director of social work at the Uniformed Services University of the Health Sciences in Bethesda, Md.

Overall, this shared experience defines members of the group and separates them from nonmembers.

A culture also supports and protects its members. As an example, Yarvis ran a video clip taken in a field hospital in Iraq of an Army captain telling his soldiers that another man in their unit had died of his wounds. The officer is clearly affected emotionally by the loss, but does his best to rally his men to finish their assigned mission while saying, "I'm here for you." It's a telling display of the modern American military force, where the focus on the mission is mixed with the duty to care for each other.

In general, troops want to go back on duty, even after some traumatic action, said Yarvis. They don't want to let down their teammates. "It may harm them more if they

please see ***Military*** *on page 28*

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GEODON® (ziprasidone HCl) Capsules

GEODON is indicated for acute treatment as monotherapy of manic or mixed episodes associated with bipolar I disorder and for maintenance treatment of bipolar I disorder as an adjunct to lithium or valproate. For full symptoms and diagnostic criteria, see the *DSM-IV-TR*® (2000).

IMPORTANT SAFETY INFORMATION

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death compared to placebo. GEODON is not approved for the treatment of patients with dementia-related psychosis.

GEODON is contraindicated in patients with a known history of QT prolongation, recent acute myocardial infarction, or uncompensated heart failure, and should not be used with certain other QT-prolonging drugs. GEODON has a greater capacity to prolong the QT_c interval than several antipsychotics. In some drugs, QT prolongation has been associated with torsade de pointes, a potentially fatal arrhythmia. In many cases this would lead to the conclusion that other drugs should be tried first. Hypokalemia may increase the risk of QT prolongation and arrhythmia.

As with all antipsychotic medications, a rare and potentially fatal condition known as neuroleptic malignant syndrome (NMS) has been reported with GEODON. NMS can cause hyperpyrexia, muscle rigidity, diaphoresis, tachycardia, irregular pulse or blood pressure, cardiac dysrhythmia, and altered mental status. If signs and symptoms appear, immediate discontinuation, treatment, and monitoring are recommended.

Prescribing should be consistent with the need to minimize tardive dyskinesia (TD), a potentially irreversible dose- and duration-dependent syndrome. If signs and symptoms appear, discontinuation should be considered since TD may remit partially or completely.

Hyperglycemia-related adverse events, sometimes serious, have been reported in patients treated with atypical antipsychotics. There have been few reports of hyperglycemia or diabetes in patients treated with GEODON, and it is not known if GEODON is associated with these events. Patients treated with an atypical antipsychotic should be monitored for symptoms of hyperglycemia.

Precautions include the risk of rash, orthostatic hypotension, and seizures.

The most common adverse events associated with GEODON in bipolar mania were somnolence, extrapyramidal symptoms, dizziness, akathisia, and abnormal vision.

The most common adverse events (≥5%) associated with GEODON in the bipolar maintenance study were tremor and insomnia.

Please see brief summary of prescribing information on adjacent page.

For more information, please visit www.pfizerpro.com/GEODON

GEODON® (ziprasidone HCl) Capsules

GEODON® (ziprasidone mesylate) injection for intramuscular use

BRIEF SUMMARY: See package insert for full prescribing information.

INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS—Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen 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. GEODON (ziprasidone) is not approved for the treatment of patients with Dementia-Related Psychosis (see WARNINGS).

INDICATIONS

GEODON is indicated for the treatment of schizophrenia, as monotherapy for the acute treatment of bipolar manic or mixed episodes, and as an adjunct to lithium or valproate for the maintenance treatment of bipolar disorder. GEODON intramuscular is indicated for acute agitation in schizophrenic patients.

DOSAGE AND ADMINISTRATION

Schizophrenia GEODON Capsules should be administered at an initial daily dose of 20 mg twice daily with food. In some patients, daily dosage may subsequently be adjusted on the basis of individual clinical status up to 80 mg twice daily. Dosage adjustments, if indicated, should generally occur at intervals of not less than 2 days, as steady-state is achieved within 1 to 3 days. In order to ensure use of the lowest effective dose, patients should ordinarily be observed for improvement for several weeks before upward dosage adjustment. Efficacy in schizophrenia was demonstrated in a dose range of 20 mg to 100 mg twice daily in short-term, placebo-controlled clinical trials. There were trends toward dose response within the range of 20 mg to 80 mg twice daily, but results were not consistent. An increase to a dose greater than 80 mg twice daily is not generally recommended. The safety of doses above 100 mg twice daily has not been systematically evaluated in clinical trials. *Maintenance Treatment*—While there is no body of evidence available to answer the question of how long a patient treated with ziprasidone should remain on it, a maintenance study in patients who had been symptomatically stable and then randomized to continue ziprasidone or switch to placebo demonstrated a delay in time to relapse for patients receiving GEODON. No additional benefit was demonstrated for doses above 20 mg twice daily. Patients should be periodically reassessed to determine the need for maintenance treatment. **Bipolar I Disorder** *Acute Treatment of Manic or Mixed Episodes*—Dose Selection: Oral ziprasidone should be administered at an initial daily dose of 40 mg twice daily with food. The dose may then be increased to 60 mg or 80 mg twice daily on the second day of treatment and subsequently adjusted on the basis of tolerance and efficacy within the range 40 mg to 80 mg twice daily. In the flexible-dose clinical trials, the mean daily dose administered was approximately 120 mg. *Maintenance Treatment* (as an adjunct to lithium or valproate)—Continue treatment at the same dose on which the patient was initially stabilized, within the range of 40 mg to 80 mg twice daily with food. Patients should be periodically reassessed to determine the need for maintenance treatment. **Acute Treatment of Agitation in Schizophrenia** *Intramuscular Dosing*—The recommended dose is 10 mg to 20 mg administered as required up to a maximum dose of 40 mg per day. Doses of 10 mg may be administered every two hours; doses of 20 mg may be administered every four hours up to a maximum of 40 mg/day. Intramuscular administration of ziprasidone for more than three consecutive days has not been studied. If long-term therapy is indicated, oral ziprasidone hydrochloride capsules should replace the intramuscular administration as soon as possible. Since there is no experience regarding the safety of administering ziprasidone intramuscular to schizophrenic patients already taking oral ziprasidone, the practice of co-administration is not recommended. Ziprasidone intramuscular is intended for intramuscular use only and should not be administered intravenously. Intramuscular Preparation for Administration GEODON for Injection (ziprasidone mesylate) should only be administered by intramuscular injection and should not be administered intravenously. Single-dose vials require reconstitution prior to administration. Add 1.2 mL of Sterile Water for Injection to the vial and shake vigorously until all the drug is dissolved. Each mL of reconstituted solution contains 20 mg ziprasidone. To administer a 10 mg dose, draw up 0.5 mL of the reconstituted solution. To administer a 20 mg dose, draw up 1.0 mL of the reconstituted solution. Any unused portion should be discarded. Since no preservative or bacteriostatic agent is present in this product, aseptic technique must be used in preparation of the final solution. This medicinal product must not be mixed with other medicinal products or solvents other than Sterile Water for Injection. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. **Dosing in Special Populations** *Oral:* Dosage adjustments are generally not required on the basis of age, gender, race, or renal or hepatic impairment. GEODON is not approved for use in children or adolescents. *Intramuscular:* Ziprasidone intramuscular has not been systematically evaluated in elderly patients or in patients with hepatic or renal impairment. As the cyclodextrin excipient is cleared by renal filtration, ziprasidone intramuscular should be administered with caution to patients with impaired renal function. Dosing adjustments are not required on the basis of gender or race.

CONTRAINDICATIONS

QT Prolongation Because of ziprasidone's dose-related prolongation of the QT interval and the known association of fatal arrhythmias with QT prolongation by some other drugs, ziprasidone is contraindicated in patients with a known history of QT prolongation (including congenital long QT syndrome), with recent acute myocardial infarction, or with uncompensated heart failure (see **WARNINGS**). Pharmacokinetic/pharmacodynamic studies between ziprasidone and other drugs that prolong the QT interval have not been performed. An additive effect of ziprasidone and other drugs that prolong the QT interval cannot be excluded. Therefore, ziprasidone should not be given with dofetilide, sotalol, quinidine, other Class Ia and III anti-arrhythmics, mesoridazine, thioridazine, chlorpromazine, droperidol, pimozide, sparfloxacin, gatifloxacin, moxifloxacin, halofantrine, mefloquine, pentamidine, arsenic trioxide, levomethadyl acetate, dolasetron mesylate, probucol or tacrolimus. Ziprasidone is also contraindicated with other drugs that have demonstrated QT prolongation as one of their pharmacodynamic effects and have this effect described in the full prescribing information as a contraindication or a boxed or bolded warning [see **WARNINGS**]. Ziprasidone is contraindicated in individuals with a known hypersensitivity to the product.

WARNINGS

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. GEODON is not approved for the treatment of dementia-related psychosis (see BOXED WARNING).

QT Prolongation and Risk of Sudden Death Ziprasidone use should be avoided in combination with other drugs that are known to prolong the QT_c interval. Additionally, clinicians should be alert to the identification of other drugs that have been consistently observed to prolong the QT_c interval. Such drugs should not be prescribed with ziprasidone. Ziprasidone should also be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias (see **CONTRAINDICATIONS**).

QT Prolongation in Clinical Trials A study directly comparing the QT/QT_c prolonging effect of oral ziprasidone with several other drugs effective in the treatment of schizophrenia was conducted in patient volunteers. The mean increase in QT_c from baseline for ziprasidone ranged from approximately 9 to 14 msec greater than for four of the comparator drugs (risperidone, olanzapine, quetiapine, and haloperidol), but was approximately 14 msec less than the prolongation observed for thioridazine. In this study, the effect of ziprasidone on QT_c length was not augmented by the presence of a metabolic inhibitor (ketoconazole 200 mg twice daily). In placebo-controlled trials, oral ziprasidone increased the QT_c interval compared to placebo by approximately 10 msec at the highest recommended daily dose of 160 mg. In clinical trials the electrocardiograms of 2/2988 (0.06%) patients who received GEODON and 1/440 (0.23%) patients who received placebo revealed QT_c intervals exceeding the potentially clinically relevant threshold of 500 msec. In the ziprasidone-treated patients, neither case suggested a role of ziprasidone. **QT Prolongation and Torsade De Pointes** Some drugs that prolong the QT/QT_c interval have been associated with the occurrence of torsade de pointes and with sudden unexplained death. The relationship of QT prolongation to torsade de pointes is clearest for larger increases (20 msec and greater) but it is possible that smaller QT/QT_c prolongations may also increase risk, or increase it in susceptible individuals. Although torsade de pointes has not been observed in association with the use of ziprasidone in premarketing studies and experience is too limited to rule out an increased risk, there have been rare post-marketing reports (in the presence of multiple confounding factors) (see **ADVERSE REACTIONS**). A study evaluating the QT/QT_c prolonging effect of intramuscular ziprasidone, with intramuscular haloperidol as a control, was conducted in patient volunteers. In the trial, ECGs were obtained at the time of maximum plasma concentration following two injections of ziprasidone (20 mg then 30 mg) or haloperidol (7.5 mg then 10 mg) given four hours apart. Note that a 30 mg dose of intramuscular ziprasidone is 50% higher than the recommended therapeutic dose. The mean change in QT_c from baseline was calculated for each drug, using a sample-based correction that removes the effect of heart rate on the QT interval. The mean increase in QT_c from baseline for ziprasidone was 4.6 msec following the first injection and 12.8 msec following the second injection. The mean increase in QT_c from baseline for haloperidol was 6.0 msec following the first injection and 14.7 msec following the second injection. In this study, no patients had a QT_c interval exceeding 500 msec. As with other antipsychotic drugs and placebo, sudden unexplained deaths have been reported in patients taking ziprasidone at recommended doses. The premarketing experience for ziprasidone did not reveal an excess risk of mortality for ziprasidone compared to other antipsychotic drugs or placebo, but the extent of exposure was limited, especially for the drugs used as active controls and placebo. Nevertheless, ziprasidone's larger prolongation of QT_c length compared to several other antipsychotic drugs raises the possibility that the risk of sudden death may be greater for ziprasidone than for other available drugs for treating schizophrenia. This possibility needs to be considered in deciding among alternative drug products. Certain circumstances may increase the risk of the occurrence of torsade de pointes and/or sudden death in association with the use of drugs that prolong the QT_c interval, including (1) bradycardia; (2) hypokalemia or hypomagnesemia; (3) concomitant use of other drugs that prolong the QT_c interval; and (4) presence of congenital prolongation of the QT interval. **Electrolyte Disturbances May Increase The Risk of QT Prolongation** It is recommended that patients being considered for ziprasidone treatment who are at risk for significant electrolyte disturbances, hypokalemia in particular, have baseline serum potassium and magnesium measurements. Hypokalemia (and/or hypomagnesemia) may increase the risk of QT prolongation and arrhythmia. Hypokalemia may result from diuretic therapy, diarrhea, and other causes. Patients with low serum potassium and/or magnesium should be repleted with those electrolytes before proceeding with treatment. It is essential to periodically monitor serum electrolytes in patients for whom diuretic therapy is introduced during ziprasidone treatment. Persistently prolonged QT_c intervals may also increase the risk of further prolongation and arrhythmia, but it is not clear that routine screening ECG measures are effective in detecting such patients. Rather, ziprasidone should be avoided in patients with histories of significant cardiovascular illness, e.g., QT prolongation, recent acute myocardial infarction, uncompensated heart failure, or cardiac arrhythmia. Ziprasidone should be discontinued in patients who are found to have persistent QT_c measurements >500 msec. **Neuroleptic Malignant Syndrome (NMS)** A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with administration of antipsychotic drugs. 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. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported. **Tardive Dyskinesia** A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients undergoing treatment 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. If signs and symptoms of tardive dyskinesia appear in a patient on ziprasidone, drug discontinuation should be considered. **Hyperglycemia and Diabetes Mellitus** Hyperglycemia-related adverse events, sometimes serious, have been reported in patients treated with atypical anti-psychotics. There have been few reports of hyperglycemia or diabetes in patients treated with GEODON, and it is not known if GEODON is associated with these events. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia.

PRECAUTIONS

Leukopenia, Neutropenia, and Agranulocytosis In clinical trial and postmarketing experience, events of leukopenia/neutropenia and agranulocytosis (including fatal cases) have been reported temporally related to antipsychotic agents. 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 should discontinue GEODON 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/mm3) should discontinue GEODON and have their WBC followed until recovery. **Rash** In premarketing trials with ziprasidone, about 5% of patients developed rash and/or urticaria, with discontinuation of treatment in about one-sixth of these cases. The occurrence of rash was related to dose of ziprasidone, although the finding might also be explained by the longer exposure time in the higher dose patients. Several patients with rash had signs and symptoms of associated systemic illness, e.g., elevated WBCs. Most patients improved promptly with adjunctive treatment with antihistamines or steroids and/or upon discontinuation of ziprasidone, and all patients experiencing these reactions were reported to recover completely. Upon appearance of rash for which an alternative etiology cannot be identified, ziprasidone should be discontinued. **Orthostatic Hypotension** Ziprasidone may induce orthostatic hypotension associated with dizziness, tachycardia, and, in some patients, syncope, especially during the initial dose-titration period, probably reflecting its α_1-adrenergic antagonist properties. Syncope was reported in 0.6% of the patients treated with ziprasidone. Ziprasidone should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemic heart disease, heart failure or conduction abnormalities), cerebrovascular disease, or conditions which would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications). **Seizures** In clinical trials, seizures occurred in 0.4% of patients treated with ziprasidone. There were confounding factors that may have contributed to the occurrence of seizures in many of these cases. As with other antipsychotic drugs, ziprasidone 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. **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, and ziprasidone and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia (see **BOXED WARNING** and **Increased Mortality in Elderly Patients with Dementia-Related Psychosis in WARNINGS**). **Hyperprolactinemia** As with other drugs that antagonize dopamine D2 receptors, ziprasidone elevates prolactin levels in humans. 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. 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. **Potential for Cognitive and Motor Impairment** Somnolence was a commonly reported adverse reaction in patients treated with ziprasidone. In the 4- and 6-week placebo-controlled trials, somnolence was reported in 14% of patients on ziprasidone compared to 7% of placebo patients. Somnolence led to discontinuation in 0.3% of patients in short-term clinical trials. Since ziprasidone has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about performing activities requiring mental alertness, such as operating a motor vehicle (including automobiles) or operating hazardous machinery until they are reasonably certain that ziprasidone therapy does not affect them adversely. **Priapism** One case of priapism was reported in the premarketing database. **Body Temperature Regulation** Although not reported with ziprasidone in premarketing trials, disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. **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 ziprasidone should be written for the smallest quantity of capsules consistent with good patient management in order to reduce overdose risk. **Patients With Concomitant Illnesses** Clinical experience with ziprasidone in patients with certain concomitant systemic illnesses is limited. Ziprasidone 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 studies. Because of the risk of QT_c prolongation and orthostatic hypotension with ziprasidone, caution should be observed in cardiac patients (see **QT Prolongation and Risk of Sudden Death** in **WARNINGS** and **Orthostatic Hypotension in PRECAUTIONS**). **Information for Patients** To assure safe and effective use of GEODON, the information and instructions provided in the patient information should be discussed with patients. **Laboratory Tests** Patients being considered for ziprasidone treatment who are at risk of significant electrolyte disturbances should have baseline serum potassium and magnesium measurements. Low serum potassium and magnesium should be replaced before proceeding with treatment. Patients who are started on diuretics during Ziprasidone therapy need periodic monitoring of serum potassium and magnesium. Discontinue ziprasidone in patients who are found to have persistent QT_c measurements >500 msec (see **WARNINGS**).

DRUG INTERACTIONS

(1) Ziprasidone should not be used with any drug that prolongs the QT interval. (2) Given the primary CNS effects of ziprasidone, caution should be used when it is taken in combination with other centrally acting drugs. (3) Because of its potential for inducing hypotension, ziprasidone may enhance the effects of certain antihypertensive agents. (4) Ziprasidone may antagonize the effects of levodopa and dopamine agonists. **Effect of Other Drugs on Ziprasidone** *Carbamazepine*, 200 mg bid for 21 days, resulted in a decrease of approximately 35% in the AUC of ziprasidone. Ketoconazole, a potent inhibitor of CYP3A4, 400 mg qd for 5 days, increased the AUC and Cmax of ziprasidone by about 35-40%. *Cimetidine*, 800 mg qd for 2 days, did not affect ziprasidone pharmacokinetics. Co-administration of 30 mL of Maalox® did not affect ziprasidone pharmacokinetics. Population pharmacokinetic analysis of schizophrenic patients enrolled in controlled clinical trials has not revealed evidence of any clinically significant pharmacokinetic interactions with benztropine, propranolol, or lorazepam. **Effect of Ziprasidone on Other Drugs** *In vitro* studies revealed little potential for ziprasidone to interfere with the metabolism of drugs cleared primarily by CYP1A2, CYP2C9, CYP2C19, CYP2D6 and CYP3A4, and little potential for drug interactions with ziprasidone due to displacement. Ziprasidone 40 mg bid administered concomitantly with *lithium* 450 mg bid for 7 days did not affect the steady-state level or renal clearance of lithium. *In vivo* studies have revealed no effect of ziprasidone on the pharmacokinetics of estrogen or progesterone components. Ziprasidone 20 mg bid did not affect the pharmacokinetics of concomitantly administered *oral contraceptives*, ethinyl estradiol (0.03 mg) and levonorgestrel (0.15 mg). Consistent with *in vitro* results, a study in normal healthy volunteers showed that ziprasidone did not alter the metabolism of *dextromethorphan*, a CYP2D6 model substrate, to its major metabolite, dextrorphan. There was no statistically significant change in the urinary dextromethorphan/dextrorphan ratio.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility Lifetime carcinogenicity studies were conducted with ziprasidone in Long Evans rats and CD-1 mice. In male mice, there was no increase in incidence of tumors relative to controls. In female mice, there were dose-related increases in the incidences of pituitary gland adenoma and carcinoma, and mammary gland adenocarcinoma at all doses tested. Increases in serum prolactin were observed in a 1-month dietary study in female, but not male, mice. Ziprasidone had no effect on serum prolactin in rats in a 5-week dietary study at the doses that were used in the carcinogenicity study. The relevance for human risk of the findings of prolactin-mediated endocrine tumors in rodents is unknown (see **Hyperprolactinemia** in **PRECAUTIONS**). *Mutagenesis:* There was a reproducible mutagenic response in the Ames assay in one strain of *S. typhimurium* in the absence of metabolic activation. Positive results were obtained in both the *in vitro* mammalian cell gene mutation assay and the *in vitro* chromosomal aberration assay in human lymphocytes. *Impairment of Fertility:* Ziprasidone increase time to copulation in Sprague-Dawley rats in two fertility and early embryonic development studies at doses of 10 to 160 mg/kg/day (0.5 to 8 times the MRHD of 200 mg/day on a mg/m2 basis). Fertility rate was reduced at 160 mg/kg/day (8 times the MRHD on a mg/m2 basis). There was no effect on fertility at 40 mg/kg/day (2 times the MRHD on a mg/m2 basis). The fertility of female rats was reduced.

USE IN SPECIFIC POPULATIONS

Pregnancy *Pregnancy Category C:* There are no adequate and well-controlled studies in pregnant women. Ziprasidone should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Labor and Delivery** The effect of ziprasidone on labor and delivery in humans is unknown. **Nursing Mothers** It is not known whether ziprasidone or its metabolites are excreted in human milk. It is recommended that women receiving ziprasidone should not breastfeed. **Pediatric Use** The safety and effectiveness of ziprasidone in pediatric patients have not been established. **Geriatric Use** Of the total number of subjects in clinical studies of ziprasidone, 2.4 percent were 65 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Nevertheless, the presence of multiple factors that might increase the pharmacodynamic response to ziprasidone, or cause poorer tolerance or orthostasis, should lead to consideration of a lower starting dose, slower titration, and careful monitoring during the initial dosing period for some elderly patients.

ADVERSE REACTIONS

Adverse Findings Observed in Short-term, Placebo-Controlled Trials The following findings are based on the short-term placebo-controlled premarketing trials for schizophrenia (a pool of two 6-week, and two 4-week fixed-dose trials) and bipolar mania (a pool of two 3-week flexible-dose trials) in which GEODON was administered in doses ranging from 10 to 200 mg/day. **Adverse Events Associated With Discontinuation** *Schizophrenia:* Approximately 4.1% (29/702) of ziprasidone-treated patients in short-term, placebo-controlled studies discontinued treatment due to an adverse reaction, compared with about 2.2% (6/273) on placebo. The most common reaction associated with dropout was rash, including 7 dropouts for rash among ziprasidone patients (1%) compared to no placebo patients (see **PRECAUTIONS**). *Bipolar Mania:* Approximately 6.5% (18/279) of ziprasidone-treated patients in short-term, placebo-controlled studies discontinued treatment due to an adverse reaction, compared with about 3.7% (5/136) on placebo. The most common reactions associated with dropout in the ziprasidone-treated patients were akathisia, anxiety, depression, dizziness, dystonia, rash and vomiting, with 2 dropouts for each of these reactions among ziprasidone patients (1%) compared to one placebo patient each for dystonia and rash (1%) and no placebo patients for the remaining adverse events. **Adverse Events at an Incidence of ≥5% and at Least Twice the Rate of Placebo** The most commonly observed adverse events associated with GEODON in schizophrenia trials were somnolence (14%) and respiratory tract infection (8%). The most commonly observed adverse events associated with the use of GEODON in bipolar mania trials were somnolence (31%), extrapyramidal symptoms (31%), dizziness (16%), akathisia (10%), abnormal vision (6%), asthenia (6%), and vomiting (5%). The following list enumerates the treatment-emergent adverse events that occurred during acute therapy, including only those events that occurred in 2% of GEODON patients and at a greater incidence than in placebo. Schizophrenia: *Body as a Whole*—asthenia, accidental injury, chest pain. *Cardiovascular*—tachycardia. *Digestive*—nausea, constipation, dyspepsia, diarrhea, dry mouth, anorexia. *Nervous*—extrapyramidal symptoms, somnolence, akathisia, dizziness. *Respiratory*—respiratory tract infection, rhinitis, cough increased. *Skin and Appendages*—rash, fungal dermatitis. *Special Senses*—abnormal vision. Bipolar Mania: *Body as a Whole*—headache, asthenia, accidental injury. *Cardiovascular*—hypertension. *Digestive*—nausea, diarrhea, dry mouth, vomiting, increased salivation, tongue edema, dysphagia. *Musculoskeletal*—myalgia. *Nervous*—somnolence, extrapyramidal symptoms, dizziness, akathisia, anxiety, hypesthesia, speech disorder. *Respiratory*—pharyngitis, dyspnea. *Skin and Appendages*—fungal dermatitis. *Special Senses*—abnormal vision. **Dose Dependency** An analysis for dose response in the schizophrenia 4-study pool revealed an apparent relation of adverse reaction to dose for the following reactions: asthenia, postural hypotension, anorexia, dry mouth, increased salivation, arthralgia, anxiety, dizziness, dystonia, hypertonia, somnolence, tremor, rhinitis, rash, and abnormal vision. **Extrapyramidal Symptoms (EPS)** The incidence of reported EPS for ziprasidone patients in the short-term, placebo-controlled schizophrenia trials was 14% vs. 8% for placebo. Objectively collected data from those trials on the Simpson-Angus Rating Scale (for EPS) and the Barnes Akathisia Scale (for akathisia) did not generally show a difference between ziprasidone and placebo. **Dystonia** Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first few days of treatment. 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. Elevated risk of acute dystonia is observed in males and younger age groups. **Vital Sign Changes** Ziprasidone is associated with orthostatic hypotension (see **PRECAUTIONS**). **Weight Gain** In short-term schizophrenia trials, the proportions of patients meeting a weight gain criterion of ≥7% of body weight were compared, revealing a statistically significantly greater incidence of weight gain for ziprasidone (10%) compared to placebo (4%). A median weight gain of 0.5 kg was observed in ziprasidone patients compared to no median weight change in placebo patients. Weight gain was reported as an adverse event in 0.4% of both ziprasidone and placebo patients. During long-term therapy with ziprasidone, a categorization of patients at baseline on the basis of body mass index (BMI) revealed the greatest mean weight gain and highest incidence of clinically significant weight gain (>7% of body weight) in patients with low BMI (<23) compared to normal (23-27) or overweight patients (>27). There was a mean weight gain of 1.4 kg for those patients with a "low" baseline BMI, no mean change for patients with a "normal" BMI, and a 1.3 kg mean weight loss for patients who entered the program with a "high" BMI. **ECG Changes** Ziprasidone is associated with an increase in the QT_c interval (see **WARNINGS**). In the schizophrenia trials, ziprasidone was associated with a mean increase in heart rate of 1.4 beats per minute compared to a 0.2 beats per minute decrease among placebo patients. **Other Adverse Events Observed During the Premarketing Evaluation of Ziprasidone in Schizophrenia** Frequent adverse events are those occurring in at least 1/100 patients; infrequent adverse events are those occurring in 1/100 to 1/1000 patients; rare adverse events are those occurring in fewer than 1/1000 patients. *Body as a Whole*—Frequent: abdominal pain, flu syndrome, fever, accidental fall, face edema, chills, photosensitivity reaction, flank pain, hypothermia, motor vehicle accident. *Cardiovascular System*—Frequent: tachycardia, hypertension, postural hypotension. Infrequent: bradycardia, angina pectoris, atrial fibrillation. Rare: first degree AV block, bundle branch block, phlebitis, pulmonary embolus, cardiomegaly, cerebral infarct, cerebrovascular accident, deep thrombophlebitis, myocarditis, thrombophlebitis. *Digestive System*—Frequent: anorexia, vomiting. Infrequent rectal hemorrhage, dysphagia, tongue edema. Rare: gum hemorrhage, jaundice, fecal impaction, gamma glutamyl trans-peptidase increased, hematemesis, cholestatic jaundice, hepatitis, hepatomegaly, leukoplakia of mouth, fatty liver deposit, melena. *Endocrine*—Rare: hypothyroidism, hyperthyroidism, thyroiditis. *Hemic and Lymphatic System*—Infrequent: anemia, ecchymosis, leukocytosis, leukopenia, eosinophilia, lymphadenopathy. Rare: thrombocytopenia, hypochromic anemia, lymphocytosis, monocytosis, basophilia, lymphedema, polycythemia, thrombocythemia. *Metabolic and Nutritional Disorders*—Infrequent: thirst, transaminase increased, peripheral edema, hyperglycemia, creatine phosphokinase increased, alkaline phosphatase increased, hypercholesteremia, dehydration, lactic dehydrogenase increased, albuminuria, hypokalemia. Rare: BUN increased, creatinine increased, hyperlipemia, hypocholesteremia, hyperkalemia, hypochloremia, hypoglycemia, hyponatremia, hypoproteinemia, glucose tolerance decreased, gout, hyperchloremia, hyperuricemia, hypocalcemia, hypoglycemic reaction, hypomagnesemia, ketosis, respiratory alkalosis. *Musculoskeletal System*—Frequent: myalgia. Infrequent: tenosynovitis. Rare: myopathy. *Nervous System*—Frequent: agitation, extrapyramidal syndrome, tremor, dystonia, hypertonia, dyskinesia, hostility, twitching, paresthesia, confusion, vertigo, hypokinesia, hyperkinesia, abnormal gait, oculogyric crisis, hypesthesia, ataxia, amnesia, cogwheel rigidity, delirium, hypotonia, akinesia, dysarthria, withdrawal syndrome, buccoglossal syndrome, choreoathetosis, diplopia, incoordination, neuropathy. Infrequent: paralysis. Rare: myoclonus, nystagmus, torticollis, circumoral paresthesia, opisthotonos, reflexes increased, trismus. *Respiratory System*—Frequent: dyspnea Infrequent pneumonia, epistaxis. Rare: hemoptysis, laryngismus. *Skin and Appendages*—Infrequent: maculopapular rash, urticaria, alopecia, eczema, exfoliative dermatitis, contact dermatitis, vesiculobullous rash. *Special Senses*—Frequent: fungal dermatitis. Infrequent: conjunctivitis, dry eyes, tinnitus, blepharitis, cataract, photophobia. Rare: eye hemorrhage, visual field defect, keratitis, keratoconjunctivitis. *Urogenital System*—Infrequent: impotence, abnormal ejaculation, amenorrhea, hematuria, menorrhagia, female lactation, polyuria, urinary retention, metrorrhagia, male sexual dysfunction, anorgasmia, glycosuria. Rare: gynecomastia, vaginal hemorrhage, nocturia, oliguria, female sexual dysfunction, uterine hemorrhage. **Adverse Findings Observed in Trials of Intramuscular Ziprasidone** In these studies, the most commonly observed adverse reactions associated with the use of intramuscular ziprasidone (≥5%) and observed at a rate on intramuscular ziprasidone (in the higher dose groups) at least twice that of the lowest intramuscular ziprasidone group were headache (13%), nausea (12%), and somnolence (20%). **Adverse Events at an Incidence of ≥1% in Short-Term Fixed-Dose Intramuscular Trials** The following list enumerates the treatment-emergent adverse events that occurred in ≥1% of patients during acute therapy with intramuscular ziprasidone: *Body as a Whole*—headache, injection site pain, asthenia, abdominal pain, flu syndrome, back pain. *Cardiovascular*—postural hypotension, hypertension, bradycardia, vasodilation. *Digestive*—nausea, rectal hemorrhage, diarrhea, vomiting, dyspepsia, anorexia, constipation, tooth disorder, dry mouth. *Nervous*—dizziness, anxiety, insomnia, somnolence, akathisia, agitation, extrapyramidal syndrome, hypertonia, cogwheel rigidity, paresthesia, personality disorder, psychosis, speech disorder. *Respiratory*—rhinitis. *Skin and Appendages*—furunculosis, sweating. *Urogenital*—dysmenorrhea, priapism. **Other Events Observed During Post-marketing Use** Adverse reaction reports not listed above that have been received since market introduction include rare occurrences of the following—*Cardiac Disorders:* Tachycardia, torsade de pointes (in the presence of multiple confounding factors), (see **WARNINGS**); *Digestive System Disorders:* Swollen Tongue; *Reproductive System and Breast Disorders:* Galactorrhea, priapism; *Nervous System Disorders:* Facial Droop, neuroleptic malignant syndrome, serotonin syndrome (alone or in combination with serotonergic medicinal products), tardive dyskinesia; *Psychiatric Disorders:* Insomnia, mania/hypomania; *Skin and subcutaneous Tissue Disorders:* Allergic reaction (such as allergic dermatitis, angioedema, orofacial edema, urticaria), rash; *Urogenital System Disorders:* Enuresis, urinary incontinence; *Vascular Disorders:* Postural hypotension, syncope.

DRUG ABUSE AND DEPENDENCE

Controlled Substance Class Ziprasidone is not a controlled substance.

OVERDOSAGE

In premarketing trials in over 5400 patients, accidental or intentional overdosage of oral ziprasidone was documented in 10 patients. All patients survived without sequelae. In the patient taking the largest confirmed amount (3240 mg), the only symptoms reported were minimal sedation, slurring of speech, and transitory hypertension (200/95).

Lawmakers Follow DB Exec On Weight-Loss Crusade

The Mississippi Psychiatric Association's executive director launches an exercise program in her obesity-plagued state, and 105 Mississippians lose 1,401 pounds. As a side effect, program participation also may benefit mental health legislation.

BY JOAN AREHART-TREICHEL

Figuratively speaking, Angela Ladner is a heavyweight in the world of Mississippi psychiatry. She is executive director and lobbyist for the Mississippi Psychiatric Association. Her husband is a psychiatrist and currently president of the district branch, and her father-in-law is also a psychiatrist.

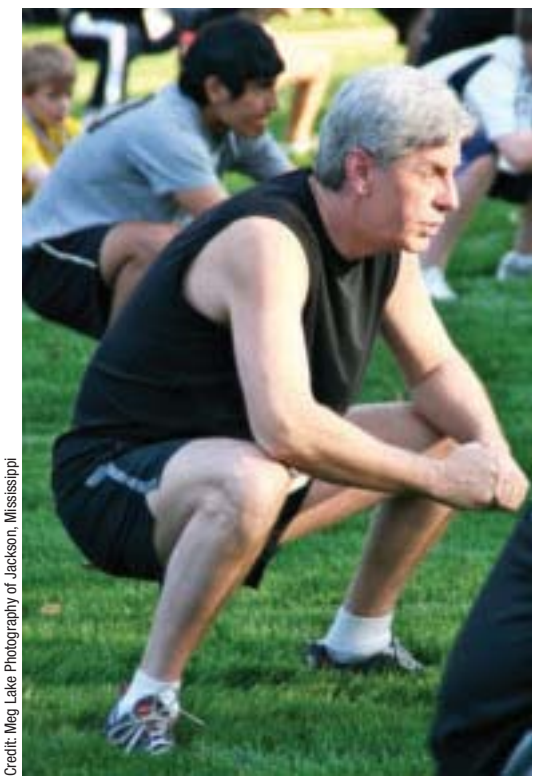
Literally speaking, Ladner was also a heavyweight four years ago. She weighed 320 pounds.

Since then she has been committed to achieving something remarkable—a physical makeover of some of Mississippi's elected officials. Moreover, the makeover has brought people of different political stripes, gender, and color together and has given mental health legislation in Mississippi a boost.

"It all started with a personal journey," Ladner explained in a recent interview. In 2006 she served on the AMA Council on Legislation as the only nonphysician member. At one point during her tenure, she thought, "How ironic that out of all the physician spouses in the United States, I who weigh 320 pounds was asked to serve on this council. If we as physicians and physicians' spouses are going to represent the medical family, shouldn't we set a good example ourselves?" The answer, of course, was yes, and in January 2007 she started her quest to lose weight.

By February 2008 she had lost 100 pounds via a strict diet modification, but she knew that if she wanted to maintain it and lose even more weight, she would have to start exercising on a regular basis. So she joined an exercise program headed by former professional football player and personal trainer Paul Lacoste.

In fall 2009 Lacoste told Ladner that he would like to initiate an exercise program for Mississippi business or government employees. Ladner suggested that he target members of the Mississippi legislature instead—"the people who make our laws and should lead by example." She also said that she would help him launch such a venture. Thus their Fit 4 Change exercise program was born.



Credit: Meg Lake Photography of Jackson, Mississippi

Left: Lt. Gov. Phil Bryant stretches using a "sumo squat" before the 5K. Top left: Rep. John Hines of Greenville runs toward the finish line at the 5K. Hines lost 78 pounds in 11 weeks. Top right: Fit 4 Change athletes react with pleasure after hearing the governor speak. Above: Coach Clark Bruce, House team member Lisa Davis, Senate team member Pat Trowles, coaches Aaron Hyatt and Ryan Jones, and civilian team members Emily Wilemon and Donna Weathers enjoy showing off their results at the capitol.

Sponsors Recruited

First they recruited sponsors for the program, notably the Mississippi Psychiatric Association, St. Dominic Hospital, Millsaps College, and the Mississippi Organ Recovery Agency—all located in Jackson, the state capital. Staff at the organ recovery group were candid about why they were willing to sponsor it: "We don't need a bunch of overweight organs."

Then Ladner recruited team captains, notably state Sen. Terry Burton, chair of the Mississippi Senate Public Health and Welfare Committee, and state Rep. Steve Holland, chair of the Mississippi House Public Health and Welfare Committee. "What better place to start than with our public health and welfare committees—the leaders who are making our health policy?" Ladner commented.

Ladner and Lacoste then called each of the other 172 members of the Mississippi legislature, as well as staff at the governor's office and some civilians, to pitch the program. During these conversations, they often mentioned that Burton and Holland would be serving as team captains for the program, and that the training, which would ordinarily cost $600 per person, would be available to them for free because the tab was being picked up by the program's sponsors. These facts, they hoped, would sweeten the offer.

Other lobbyists who heard about their efforts laughed and said, "You'll never get anybody to sign up." But they were wrong: 130 did.

Participants Commit to Workout Schedule

Each of the 130 individuals—who ranged in age from 17 to 74—received a physical exam at Saint Dominic Hospital. All were found fit enough to take part in the program. They committed themselves to working out for one hour four times a week for 11 weeks and selected one of the time slots that would work best for them.

The program got under way in January. The workouts took place on the football field and in the gym of Millsaps College and included jogging, running, speed and agility drills, resistance training, weight-lifting, and mixed martial arts.

At the start of the program and also at the end of each week, participants were weighed. The person who had lost the most weight by the end of each week received a monetary award that could be allocated to his or her school physical education program of choice. Program participants were also divided into four teams—a Senate team, a House team, a governor's-office team, and a civilian team. The team that lost the most weight at the end of each week was also recognized.

By March 5, 25 people had dropped out of the program, but 105 were still at it. As a group, they had lost 1,000 pounds. By March 31, the end of the program, their total weight loss was 1,401 pounds. "For 105 people to do that in 11 weeks, we think that's pretty good," Ladner declared.

Indeed, "it was a life-changing experience for all of us who participated," Burton testified. "I lost 26 pounds from the program. I've changed the way I eat. In fact, I think it could be life changing for the whole state if people follow our lead, doing away with our number-one ranking in obesity and other health-risk factors."

Holland agreed: "I lost 23 pounds and ran for the first time in 20 years in a 5K. It felt fantastic. . . . I feel healthy, I'm thinking healthily; you cannot imagine how young my mind now feels."

Benefits Go Forward

Other benefits have accrued from the program as well.

One is a commitment to spread the word of the program's benefits. "I'm in the process of developing a video and a package to send to every speaker, lieutenant governor, and governor in this nation to show them what we have done in Mississippi and to ask them to join us, to lead by example for their people as for what can happen when

please see ***Weight Loss*** *on page 29*

Remission Common in BPD, But Good Functioning Lags

Recovery from BPD is akin to a process of maturation—it occurs slowly, but once a level of functioning is reached, patients tend to maintain that level and fall back only in the face of major stressors.

BY MARK MORAN

A substantial majority of patients with borderline personality disorder (BPD) experience remission of symptoms, and their remission tends to be stable over time compared with other mental disorders—but only half of patients also achieve good social and vocational functioning.

Those were among the findings of a 10-year study of remission and recovery in BPD patients. The study was published online in *AJP in Advance* on April 15 and will appear in the June print edition of the *American Journal of Psychiatry*.

In the study, 290 inpatients at McLean Hospital in Belmont, Mass., who met both *DSM-III-R* and Revised Diagnostic Interview for Borderlines criteria for BPD were assessed at admission using a series of semi-structured interviews and self-report measures. The same instruments were readministered every two years for 10 years.

At the 10-year mark, 249 patients remained in the study. (Of the 41 patients who were no longer in the study, 12 had committed suicide, seven died of other causes, nine discontinued their participation, and 13 were lost to follow-up.)

Recovery was defined as not only remission of symptoms, but being able to function both socially and vocationally. Social functioning was defined as having at least one emotionally sustainable relationship with a friend, spouse, partner, or other non-blood-related individual. Vocational functioning was defined as the ability to perform full-time work competently and consistently.

Study results showed that 93 percent of the patients achieved remission of symptoms lasting at least two years, and 86 percent achieved remission lasting at least four years. However, only 50 percent achieved the full definition of recovery including social and vocational functioning (see chart).

Zanarini speculated that many patients may have temperamental problems—anger and/or extreme abandonment issues—that persist after the remission of symptoms and that hold them back socially and vocationally. "All of our manualized treatments for BPD are aimed at acute symptoms—self-mutiliation and suicidality—and those are the symptoms that remit the most quickly," she told *Psychiatric News*.

She said that a rehabilitation model of treatment incorporating training in life skills—use of public transportion, budgeting, personal care, and vocational training—is key to fully addressing the recovery needs of patients who achieve remission of BPD symptoms.

The study's other notable finding was that despite the difficulty many patients have in achieving full recovery, both remission of symptoms and full recovery, when they do occur, tend to be stable over time. Of those who achieved recovery, only 34 percent relapsed. Of those who achieved a two-year remission of symptoms, 30 percent had a symptomatic recurrence, and of those who achieved a sustained remission at four years, only 15 percent experienced a recurrence.

Zanarini and colleagues noted in their report that those rates compare favorably with remission and recurrence rates for common Axis I disorders studied longitudinally, such as major depression and dysthymic disorder. "[T]he high rate of sustained symptomatic remission and the low rate of symptomatic recurrence after sustained remission are among the most optimistic findings about borderline personality disorder reported to date," they said.

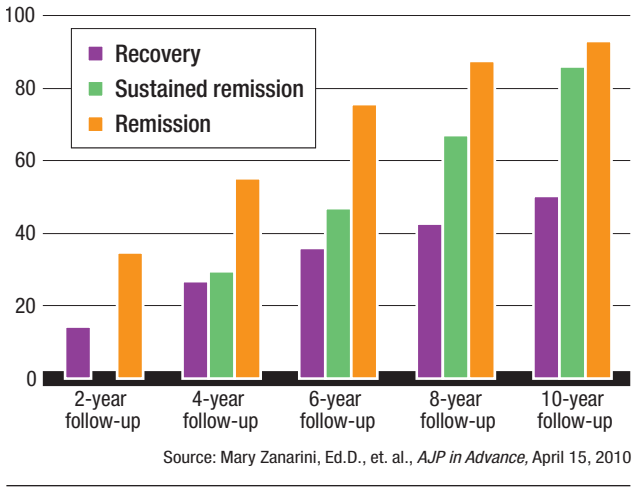
> **"As much as [people with BPD] get better symptomatically, it's clear that we need to pay attention to psychosocial and vocational functioning. Just to talk about symptoms isn't enough."**

In an interview with *Psychiatric News*, Zanarini said, "Depression and bipolar disorder tend to remit quickly but recur much more often. Recovery from BPD is more akin to the process of maturation. It occurs slowly, but once you achieve a certain level, you stay there, and it

please see ***BPD*** *on page 28*

BPD Symptoms Remit, But Full Recovery Elusive

In a study that began with 290 inpatients with borderline personality disorder at McLean Hospital, researchers measured remission and recovery rates at two-year intervals. Recovery was defined as having remission of symptoms and having good social and vocational functioning during the previous two years. There were 249 subjects at the 10-year mark.



Source: Mary Zanarini, Ed.D., et. al., *AJP in Advance,* April 15, 2010

"Symptomatically, this is a good prognosis," said Mary Zanarini, Ed.D., lead author of the study, in an interview with *Psychiatric News*. "The idea that people with BPD never get better isn't true. But as much as they get better symptomatically, it's clear that we need to pay attention to psychosocial and vocational functioning. Just to talk about symptoms isn't enough."

APA Voting Moving to Online Only

Is Your Correct E-Mail Address on File?

APA's national elections are transitioning to an all-electronic process with a fast, easy, and secure means to vote online. Online voter participation has steadily increased, reaching a rate of 50 percent in APA's last election, and shows promise of continued growth. Beginning with the 2011 election, all eligible voting members with a valid e-mail address on file will receive only an electronic ballot.

To ensure that you get your ballot, please update your contact information in Members Corner on APA's Web site at <https://myaccount.psych.org/MembershipProfileUpdate/tabid/163/Default.aspx>. E-mails sent directly from APA will include a link to personalized electronic ballots, voting instructions, and candidate information.

Voting members without a valid e-mail address on file will still be sent a paper ballot for the 2011 election. APA members with questions or comments may e-mail them to election@psych.org.

Raising GABA Levels Might Undo Cognitive Defect in Schizophrenia

Drugs that alter the neurotransmitter GABA might correct some of the cognitive problems caused by schizophrenia. Researchers have developed a model system for evaluating such candidate drugs.

BY JOAN AREHART-TREICHEL

The neurotransmitter GABA is decreased in the brains of individuals with schizophrenia, researchers reported in the March 10 *Journal of Neuroscience*.

They used a technique called magnetic resonance spectroscopy to measure the levels of GABA in the visual cortex of 13 subjects with schizophrenia and 13 demographically matched control subjects. GABA concentration in the schizophrenia subjects was 10 percent less than in the control group.

Furthermore, the researchers found a highly significant link between the GABA deficiency in the visual cortex of the schizophrenia subjects and a particular cognitive defect—a visual perception problem already known to be present in individuals with schizophrenia. The problem is called orientation-specific surround suppression, a behavioral measure of visual inhibition thought to be dependent on GABA neurotransmission.

So it looks as if a GABA deficiency may be responsible for this cognitive defect in schizophrenia and perhaps for others as well, the researchers believe.

Or as Cameron Carter, M.D., senior author and a professor of psychiatry at the University of California, Davis, put it, "This work provides tremendous support for targeting the GABA system for treatment of cognitive decline in schizophrenia."

Still another positive aspect of their study, Jong Yoon, M.D., lead investigator and an assistant professor of clinical psychiatry at the university, explained, is "that not only have we found that GABA is deficient in living [schizophrenia] subjects, but we have developed a model system with which we can evaluate GABA function and evaluate interventions targeting GABA function." In other words, the hope is that a drug that acts on GABA might be found to correct some of the cognitive deficiencies that accompany schizophrenia, since antipsychotic medications currently on the market have a modest effect at best on cognition, he said.

There are already some indications that drugs that act on GABA might be of benefit in this regard. A small pilot study headed by David Lewis, M.D., a professor of psychiatry and neuroscience at the University of Pittsburgh, and published in the December 2008 *American Journal of Psychiatry* found that subjects with schizophrenia performed better on cognitive tests after being given a particular GABA agonist than after being given a placebo. And an Israeli company reported last year that subjects with schizophrenia who received an investigational drug that acts on GABA receptors experienced a significantly greater improvement in cognition than did subjects with schizophrenia who received a placebo (*Psychiatric News*, November 20, 2009).

The study was funded by NARSAD and the National Institute of Mental Health.

An abstract of "GABA Concentration Is Reduced in Visual Cortex in Schizophrenia and Correlates With Orientation-Specific Surround Suppression" is posted at <www.jneurosci.org/cgi/content/abstract/30/10/3777>. ■

Psychoactive Drugs Rarely Prescribed For Nonpsychiatric Use

Over 90 percent of antidepressants and antipsychotics are prescribed for psychiatric diagnoses, even though some may be prescribed for off-label indications.

BY JUN YAN

A very small minority of antidepressant and antipsychotic prescriptions and about one-third of antianxiety prescriptions are written for nonpsychiatric diagnoses, according to a recent analysis of national physician survey data.

The use of psychoactive drugs has risen rapidly since the 1990s, and expenditures for this category have grown faster than the total prescription drug market. This trend has raised concerns that psychoactive drugs are being prescribed excessively and too frequently for unapproved uses. Research and debate about off-label prescribing of psychiatric drugs have focused on unapproved uses within the realm of psychiatric disorders, and very little is known about whether these drugs are used for nonpsychiatric diagnoses such as pain.

The study, by Tami Mark, Ph.D., director of analytic strategies at Thomson Reuters, examined physician-reported data in the National Disease and Therapeutic Index, a continuous survey of physicians conducted by IMS Health, a private market-research company. The survey randomly selects a representative sample of 4,000 physicians every quarter from office-based physicians in private practice within the continental United States. Each participating physician is surveyed by telephone on two consecutive days per month and asked about the diagnoses and associated treatment in every patient visit during these two days. Multiple diagnoses and prescriptions may be reported for each visit.

The study analyzed data from 2005 and included three major types of psychoactive medications: antidepressants, antianxiety drugs, and antipsychotics.

Of the antidepressants prescribed in 2005, 92.7 percent were associated with psychiatric diagnoses. About two-thirds (65.3 percent) were prescribed for mood disorders, and 16.4 percent for anxiety disorders (see chart). The nonpsychiatric diagnoses associated with antidepressant prescriptions included headaches, connective tissue diseases such as fibromyalgia, nervous-system disorders other than the psychiatric diagnoses defined in *ICD-9-CM* codes 290-314, and female disorders such as premenstrual tension.

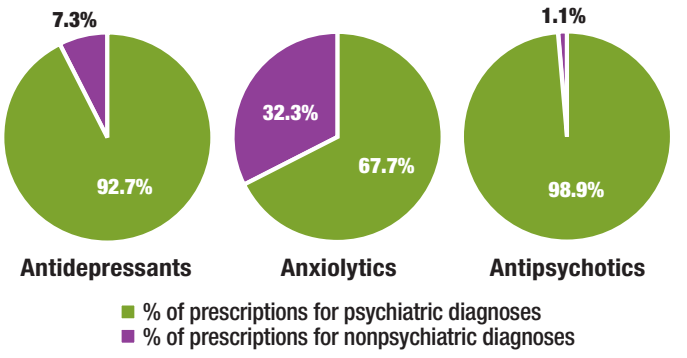
Antipsychotics were prescribed almost exclusively (98.9 percent) for psychiatric diagnoses. The most common indications were mood disorders (39.0 percent) and schizophrenia and other psychotic disorders (34.5 percent).

Certain uses of antipsychotics are controversial, and the study did not directly analyze whether these psychoactive drugs were used for unapproved psychiatric indications. The data showed that 7.4 percent of the antipsychotics were prescribed for delirium, dementia, amnestic disorders, or other cognitive disorders commonly diagnosed in the elderly. A mandatory boxed warning in all antipsychotic drug labels states that this type of use is associated with increased risk of death. About 1 in 20 (5.7 percent) antipsychotic prescriptions was written for attention-deficit/hyperactivity disorder, conduct disorder, or disruptive behavior disorders, and 2.3 percent of the antipsychotics were prescribed for other psychiatric disorders usually diagnosed in infancy, childhood, and adolescence, such as autism. This use is also controversial. However, the study did not include the age of patients in the analysis.

Although the antianxiety class was associated with the lowest proportion of psychiatric diagnoses, two-thirds (67.7 percent) of the prescriptions were written for psychiatric disorders. The diagnosis of an anxiety disorder was linked to 39.6 percent of the prescriptions, and mood disorders accounted for 18.9 percent.

Most Psychoactive Medications Prescribed for Psych Diagnoses

Data on psychotropic prescriptions written by physicians were extracted from the 2005 National Disease and Therapeutic Index, a continuous survey of office-based private-practice physicians throughout the continental United States.



Source: Tami Mark, Ph.D., *CNS Drugs*, April 2010

Among the uses not associated with a psychiatric diagnosis, preparation for medical examination or procedures was the reason for 6.0 percent of the antianxiety-drug prescriptions. In addition, allergic reactions were cited in 4.1 percent of these prescriptions. Indications related to back pain accounted for 2.5 percent of the prescriptions.

The study was sponsored by the Substance Abuse and Mental Health Services Administration and published in the April *CNS Drugs*.

An abstract of "For What Diagnoses Are Psychotropic Medications Being Prescribed? A Nationally Representative Survey of Physicians" is posted at <adisonline.com/cnsdrugs/Abstract/2010/24040/For_What_Diagnoses_Are_Psychotropic_Medications.4.aspx>. ■

Brain Region's Dopamine Levels Linked to Psychopathy Trait

Just as deficits in the amygdala and prefrontal cortex may prompt antisocial people to be fearless and lack empathy, an overly responsive nucleus accumbens may prompt them to be aggressive.

BY JOAN AREHART-TREICHEL

Ah, the "bad guy" is thinking, "I'm going to take that sucker for all he's worth."

What's going on in his brain? His brain's reward center—the nucleus accumbens—may be goading him into action, a new study suggests.

The study found a link between the personality trait of psychopathy and an overly responsive nucleus accumbens.

Joshua Buckholtz, a doctoral candidate in neuroscience at Vanderbilt University, headed the study. Results were reported online March 14 in *Nature Neuroscience*.

The personality trait of psychopathy is characterized by charm, egocentricity, manipulation of others, sensation-seeking, poor reflection, and blunted empathy. Psychopathy in turn is a robust predictor of antisocial behavior.

Moreover, alcohol, nicotine, and many other drugs of abuse are known to stimulate the nucleus accumbens, and psychopathic individuals are known to be at heightened risk for developing substance abuse problems. So Buckholtz and his colleagues suspected that there might be a link between the personality trait of psychopathy and the nucleus accumbens. They conducted a study to find out.

They recruited 24 community volunteers and used the Psychopathic Personality Inventory, a validated measurement of psychopathy, to determine how each subject scored on a subdomain of the trait called "impulsive antisociality." This subdomain in turn has been linked with antisocial behavior, aggression, impulsivity, and substance abuse both in prison and community samples.

In a first experiment, the subjects were given an amphetamine, which is known to increase levels of the neurotransmitter dopamine in the nucleus accumbens. After that, PET scans were used to measure the amount of dopamine released in the nucleus accumbens of each subject. The researchers looked to see whether there was any correlation between how high subjects had scored on impulsive antisociality and the amount of dopamine released in their nucleus accumbens.

The higher subjects had scored on impulsive antisociality, the more dopamine they released. In fact, when the highest-scoring subjects were compared with the lowest-scoring ones, the former released four times more dopamine in the nucleus accumbens than the latter did.

Credit: Gregory Samanez-Larkin and Joshua Buckholtz, Vanderbilt University

An overly responsive nucleus accumbens—illustrated in this brain image—may prompt antisocial individuals to be aggressive.

In a second experiment, the subjects played a game in which they could win a cash reward. While they were playing the game, fMRI scans were used to see how much dopamine was released in their nucleus accumbens. The higher subjects had scored on impulsive antisociality, the more dopamine they released.

So the combined results from both experiments appear to indicate that people who score high on impulsive antisociality possess an especially responsive nucleus accumbens, or reward system.

But what do these findings mean in practical terms? One possibility is that people with an especially responsive reward system might be aggressive about obtaining whatever they consider rewarding, whether it is drugs, sex, money, or something else. Indeed, rodent studies have shown that dopamine is released from the nucleus accumbens during aggressive behavior, and aggressive behavior is common among antisocial or psychopathic individuals.

Although Buckholtz and his group believe that they've taken an important first step in linking impulsive antisociality to an exaggerated dopamine response in the nucleus accumbens, they now hope to confirm their results in subjects who have been diagnosed as having antisocial personality disorder.

And if they manage to do so, then an especially responsive reward system might be considered one of the biological hallmarks of antisocial individuals, just as deficits in the prefrontal cortex and amygdala already are (*Psychiatric News*, April 5, 2002; October 16, 2009).

The study was funded by the National Institute on Drug Abuse.

An abstract of "Mesolimbic Dopamine Reward System Hypersensitivity in Individuals With Psychopathic Traits" is posted at <www.nature.com/neurojournal/vaop/ncurrent/pdf/nn.2510.pdf>. ■

Depression Screening Can't Get Much Briefer Than This

A screening tool with just two questions may help busy primary care physicians begin to identify depression in adolescent patients.

BY AARON LEVIN

Brevity may not only be the soul of wit, it may also be the key to identifying a pediatrician's patients who may be struggling with depression.

The U.S. Preventive Services Task Force last year recommended screening for depression among adolescents, but how can busy primary care clinicians shoehorn yet another screen into a typical office visit?

One way is to make the screening instrument as short as possible. Researchers have found that two inquiries, drawn from the Patient Health Questionnaire (PHQ)-9, can serve as a useful first-pass signal to decide which young people need further evaluation.

The PHQ-2 was "promising as a first step" and had "good sensitivity and specificity for detecting major depression," they wrote in the May *Pediatrics*.

"The PHQ-2 is well-suited as a first-line screening tool for depression because it is brief, easy to score, and available without cost," wrote Laura Richardson, M.D., M.P.H., an associate professor of adolescent medicine and an adjunct associate professor of psychiatry and behavioral sciences at the University of Washington; Wayne Katon, M.D., a professor of psychiatry and behavioral sciences at that university; and colleagues.

Studies like this are encouraging to many of those working at the intersection of pediatrics and psychiatry.

"The more research on primary care screens, the better," said Rachel Zuckerbrot, M.D., an assistant professor of clinical psychiatry at Columbia University. Zuckerbrot is board certified in pediatrics, child and adolescent psychiatry, and general psychiatry. She was the lead author of the American Academy of Pediatrics' 2007 guideline for identifying and assessing adolescent depression in primary care settings.

The new study carries added weight because the researchers validated the results they obtained with the PHQ-2 by comparing them with scores on the Diagnostic Interview Schedule for Children-IV (DISC-IV), considered the "gold standard" for diagnosing depression in young people, said Zuckerbrot.

She and the authors acknowledged, however, that the PHQ-2 focuses only on major depression and may miss milder forms of depression or irritability, a *DSM-IV* criterion for depression in adolescents but not in adults.

A question about suicidality on the PHQ-9 is not part of the PHQ-2, so the 20 percent of youth with suicidal ideation could be missed by the two-question screener, the researchers noted. They recommend adding a question about suicidality to the PHQ-2 to compensate.

The test of the PHQ-2 was part of the Adolescent Health Study jointly run by the University of Washington and the Group Health Research Institute in Seattle.

The researchers began by randomly selecting 4,000 adolescents aged 13 to 17 who had been seen at a Group Health site in the previous year.

Of those, 2,291 (61 percent) completed a brief 10-item mail-in survey that included the PHQ-2 questions on depressed mood and/or lack of pleasure in usual activities in the previous two weeks. Respondents indicate severity on a 0-3 scale for each question.

A score of 3 (out of 6) or higher in adults has been shown to have good specificity and sensitivity for major depression.

Most youths with a PHQ-2 score of 3 or higher and an age- and gender-matched control group completed a more extensive phone interview that included the PHQ-9, the DISC-IV, the Columbia Impairment Scale, the Screen for Child Anxiety Related Emotional Disorders, and the Brief Pediatric Symptom Checklist.

In all, 242 teens who screened positive and 202 controls, and the parents of both groups, completed the study.

The false negative rate was 26 percent, and the false positive rate was about 25 percent. However, 76 percent of the false-positive group had some other cause for concern, such as intermediate depression, externalizing symptoms, anxiety, or depression in the prior year although not in the preceding two weeks. Follow-up with those patients would presumably identify those symptoms.

Follow-up to a positive screen depends on a number of factors at the patient, provider, and system levels, said Zuckerbrot. "How comfortable is the patient in primary care versus specialty mental health care?" she said. "How comfortable is the primary care doctor in treating depression? And what are the constraints on services caused by geography, insurance, or ability to schedule an appointment with a specialist."

The study received supported from the Group Health Community Foundation Child and Adolescent Grant Program, the University of Washington Royalty Research Fund, a Seattle Children's Hospital Steering Committee Award, and an award for Richardson from the National Institute of Mental Health.

"Evaluation of the PHQ-2 as a Brief Screen for Detecting Major Depression Among Adolescents" can be accessed at <http://pediatrics.aappublications.org/content/vol125/issue5> by clicking on the study title. ■

Two Questions Give Heads Up On Teens' Depression

A two-question test for 12- to-18-year-olds is "well suited as a first-line screening tool" for identifying patients who need further evaluation for major depressive disorder. A score of 3 or more on the Patient Health Questionnaire-2 was found to have good sensitivity and specificity in primary care settings.

PHQ-2 Score	PHQ-9 Diagnosis of MDD				C-DISC Daignosis of MDD			
	Sens %	Spec %	PPV	NPV	Sens %	Spec %	PPV	NPV
1	100.0	39.5	18.1	100.0	100.0	36.4	6.6	100.0
2	100.0	62.0	26.0	100.0	89.5	56.7	8.5	99.2
3	96.2	82.3	42.0	99.4	73.7	75.2	11.8	98.5
4	71.2	94.9	64.9	96.1	52.6	88.9	17.5	97.7
5	46.2	99.7	96.0	93.3	42.1	96.0	32.0	97.4
6	19.2	100.0	100.0	90.3	15.8	98.4	30.0	96.3

Source: Laura Richardson M.D., et al., *Pediatrics,* May 2010

Brief Screening Tool Could Be Used To Assess Suicide Risk

One thing missing from the PHQ-2 screening tool for depression is a way to identify teens at risk for suicide. However, a small study conducted at three clinics indicates that some physician training and two questions for patients could raise rates of inquiry and case detection of suicidality, according to Matthew Wintersteen, Ph.D., an assistant professor in the Department of Psychiatry and Human Behavior at Thomas Jefferson University in Philadelphia. His results appear in the May *Pediatrics.*

Clinic providers were offered a 90-minute training session on the epidemiology of youth suicide, along with risk and protective factors, assessment, clinical management, and treatment. Then two items were added to the standard electronic psychosocial screen used in the clinics. One question inquired about thoughts of death without suicidal ideation: "Have you ever thought that life was not worth living?"The second directly addressed suicidal ideation: "Have you ever felt like you wanted to kill yourself?"

Patients who answered yes to either question were then automatically asked a series of six additional questions covering suicidal ideation, preparation, and attempts.

Wintersteen compared pre- and post-intervention rates of inquiry and identification.

Overall, the rate of clinicians who inquired about suicidality more than doubled, from 36.5 percent to 82.1 percent (odds ratio = 2.49), wrote Wintersteen. The rate of youth detected with suicidal ideation rose from 0.8 percent to 3.6 percent (OR = 4.33). Rates of referrals to behavioral health services paralleled the increase in detection rates.

While these increases seem large, the absolute numbers were still manageable, said Wintersteen. For instance, 13 adolescents were identified before the intervention and 51 after—"approximately one youth per week over a 12-month period"—out of a 2,000-patient caseload.

While the study suggests that primary care providers can detect young people at risk for suicidality, the provider's time and the availability of referral resources still remain obstacles to broader implementation, said Wintersteen.

An abstract of "Standardized Screening for Suicidal Adolescents in Primary Care" is posted at <http://pediatrics.aappublications.org/cgi/content/abstract/peds.2009-2458v1>.

Antidepressant

continued from page 2

neurogenesis and the migration of neurons. The observation that the gene for this enzyme is associated with response to nortriptyline appears to corroborate the neurogenesis theory of antidepressant effects, the researchers pointed out.

They also identified SNPs concentrated in two intergenic regions on chromosomes 1 and 10 as potentially associated with response to antidepressants. Intergenic regions are stretches of DNA that neither code for any genes nor regulate the expression of close-by genes. However, when DNA strands are folded, they may have a spatial or structural influence on the expression of certain genes that are linearly far away. These regions had not been associated with a clinical response to antidepressants in past research, and a possible mechanism for this connection is unknown.

In addition, variants in the gene encoding for interleukin-11 (IL-11), a cytokine, were linked to response to escitalopram.

The targeted analysis of 72 preselected candidate genes did not generate any strong association with antidepressant response. However, a potential but weak link was identified between response to escitalopram and the gene coding for interleukin-6, which is closely related to the gene for IL-11. This and the significant association with the IL-11 gene support the theory that inflammatory cytokines play a role in the therapeutic effect of antidepressants. Both cytokines are extensively expressed in the brain and have been shown to play a role in serotonin signaling.

The authors noted that because the study sample was not large enough to provide sufficient statistical power, genes with moderate effects on the clinical response were likely to be missed by the analysis.

The GENDEP project was supported primarily by a European Commission grant. GlaxoSmithKline and several U.K. organizations provided additional funding. Lundbeck, a Danish drug company, donated both study drugs.

"Genome-Wide Pharmacogenetics of Antidepressant Response in the GENDEP Project" is posted at <http://ajp.psychiatryonline.org/cgi/reprint/appi.ajp.2009.09070932v1>. ■

Depression Treatment May Overlook Severe Sleep Disorder

Psychiatrists have a key role to play in treating patients with obstructive sleep apnea, who often have comorbid depression.

BY LYNNE LAMBERG

Your depressed patient may have a potentially life-threatening sleep disorder.

A man taking prescribed antidepressant medication for eight years was referred for a sleep study only after his second driving crash. The study showed that he had obstructive sleep apnea (OSA), a disorder in which breathing stops repeatedly in sleep for 10 seconds or longer, lowering oxygen supply to the brain.

Another man's treatment-resistant depression forced him to quit work at age 45. He, too, was diagnosed later with severe OSA. Given first-line treatment for this disorder—use of continuous positive airway pressure (CPAP) to keep his airway open in sleep—the man's mood and cognition improved, along with his breathing. Restarting treatment with antidepressant medications brought further gains and enabled him to resume his career.

Mood-disorder prevalence rates in people with OSA in most studies range from about 30 percent to 50 percent, said Andrew Krystal, M.D., a professor of psychiatry and behavioral sciences and director of the insomnia and sleep research program at Duke University School of Medicine.

Psychiatrists likely have several patients with OSA in their practices, said Krystal, who co-chaired a conference in Washington, D.C., in March on sleep health and safety. The conference was sponsored by the National Sleep Foundation and the Atlanta School of Sleep Medicine.

Depression-related fatigue is hard to distinguish from excessive daytime sleepiness, the most common presenting symptom of OSA, he noted. "In our sleep-deprived society, it's easy to overlook sleepiness," he said. Asking patients "Do you ever fall asleep without meaning to?" may help clarify their complaint.

Causes Go Beyond Obesity

An estimated 18 million adults in the United States have OSA, the National Sleep Foundation reports. OSA's prevalence has soared in recent years in tandem with the nation's expanding girth, said Meir Kryger, M.D., lead editor of the book *Principles and Practice of Sleep Medicine.* He is a professor of medicine at the University of Connecticut and director of sleep medicine research and education at Gaylord Hospital in Wallingford, Conn.

Two-thirds of American adults are overweight or obese, and excess fat can narrow the airway.

Even thin people may develop OSA, however, particularly those who have a small airway, large tongue, jaw deformities, or neurological disorders that reduce neuromuscular support for the airway in sleep.

OSA symptoms to explore in sleepy patients include snoring, observed pauses in breathing in sleep, difficulty concentrating and making decisions, morning headaches and dry mouth, impotence, and hypertension, Krystal said. Patients may not report difficulty sleeping, because brief interruptions in sleep often go unremembered in the morning. OSA boosts risks of heart disease, stroke, and premature death.

Initially thought to be more common in obese, middle-aged men, OSA occurs in both sexes and at all ages, said Kryger. It may be underdiagnosed in women, he added. In a review of charts of 130 women and 130 men matched for OSA of equal severity at time of diagnosis, he and his colleagues found both sexes had reported sleepiness, snoring, and observed pauses in breathing in sleep. Twenty-one percent of the women but only 7 percent of the men, however, had been diagnosed with depression. Women also took psychiatric medications more often than men.

Antidepressants Can Aggravate OSA

Antidepressants may, however, add to OSA symptom burden.

Some antidepressants complicate recognition of OSA by exacerbating sleepiness, Krystal said. Some worsen OSA by prompting weight gain.

A nonamphetamine wakefulness-promoting medication, armodafinil, may reduce sleepiness in patients with comorbid OSA and depression, Krystal and colleagues reported in the January *Journal of Clinical Psychiatry.* This trial was the first to assess armodafinil in patients receiving treatment for both disorders, Krystal said.

The 249 participants used CPAP and stable monotherapy with a serotonergic antidepressant throughout the 12-week, randomized, double-blind, parallel-group study, conducted at 60 outpatient sites from September 2007 to March 2009. The researchers assessed outcomes using standard depression and sleepiness scales, as well as overnight and daytime sleep studies. The armodafinil group improved more than the placebo group. Few participants developed worsening depression; none dropped out.

"Some symptoms of depression overlap with those of OSA. . . . You don't want to miss either diagnosis."

Motor-vehicle crashes are another risk in people with OSA.

"OSA is one of the few clinical entities of any sort associated with increased crashes and injuries in the transportation environment," Mitchell Garber, M.D., M.P.H., a medical officer with the National Transportation Safety Board, said at the sleep conference. OSA has been implicated in performance errors by plane and ship pilots and drivers of trains, trucks, and automobiles.

Most states limit the right of individuals with medical conditions to drive, but only six states mention sleep disorders

please see ***Sleep*** *on page 28*

Consider Special Needs of Elderly In Planning Disaster Response

It is difficult to anticipate precisely the devastation caused by disasters, but planning and preparation can minimize harm and ensure a speedy recovery to normal life in elderly individuals.

BY JUN YAN

Despite frequent physical frailty and lack of resources, older adults are often more mentally resilient in coping with disasters than younger people are.

At a symposium at the American Association for Geriatric Psychiatry (AAGP) annual meeting in March in Savannah, Ga., geriatric psychiatrists offered advice on how mental health professionals can help older people prepare for and respond to disasters so that the disaster's adverse impact on those with age-related vulnerabilities will be minimized.

Whether natural or manmade, disasters occur almost every day somewhere in the world. They overwhelm communities and disrupt normal lives. Elderly individuals' unique vulnerabilities expose them to additional harm beyond that of other adults, Maria Llorente, M.D., said at the symposium. For example, older people generally have more physical impairments, including visual and hearing deficits. When electricity is cut off or streets are filled with debris after a flood or earthquake, older people with poor eyesight are more likely to get injured. In addition, many retirees live on fixed incomes and have limited financial means. They may not be able to stock up on canned foods and emergency supplies before a storm hits.

Llorente is a professor of psychiatry at the University of Miami School of Medicine and chief of psychiatry at the Miami Veterans Affairs Healthcare System.

Nonetheless, "our seniors are extremely resilient," Llorente said. Studies have shown that elderly individuals are no more likely than those of other ages to suffer from posttraumatic stress disorder after a disaster; in some cases they demonstrate better psychological recovery. As many older adults have had prior experience in coping with disasters or adversities, they may be more prepared than younger people and better able to offer advice and guidance to people around them, she pointed out.

As communities and mental health professionals devise disaster-preparedness plans, they should not neglect or underestimate the special needs of the elderly, Llorente and other speakers emphasized.

After Hurricane Katrina hit in 2005, "there was one viable hospital in the city of New Orleans and one viable hospital in the suburbs," said Kenneth Sakauye, M.D., a professor of psychiatry and director of geriatric psychiatry at the University of Tennessee Health Science Center in Memphis. Like much of the rest of the health care infrastructure, psychiatric services were devastated in New Orleans.

And it is the elderly who are particularly likely to be affected by the loss of the health care infrastructure, Llorente noted, as many have chronic illnesses that need continued medical attention. At emergency departments around Houston after Katrina, the most common problems seen in New Orleans evacuees were, as expected, scrapes, cuts, and other physical injuries, while the second most common problem was getting prescription refills, she said. For most of these patients, their medical records had been lost or destroyed in the storm. "This presented enormous problems" for local emergency departments, she said.

Therefore, Llorente recommended that clinicians should help elderly patients who have chronic illnesses prepare a record of their diagnoses and ongoing prescriptions to keep safely with other important documents, thus minimizing postdisaster disruption to treatment access and crucial medical information.

Despite the resilience of many elderly individuals, they are also susceptible to increased stress and reactivity to stress during and after a disaster. Llorente pointed to research data documenting a spike in heart-attack and stroke rates immediately following a disaster, especially in elderly people who already had underlying cardiovascular disease.

Frontline responders should be trained to anticipate and meet the specific needs of older adults, according to Llorente. In Florida, for example, some shelters are set up for people with special needs, such as people who need dialysis or continual medical attention. Clinicians can devise contingency plans if the primary plan falls short and screen older patients for disaster preparedness and special needs long before a disaster hits, she suggested.

To help older adults and their family members and caregivers, AAGP's Disaster Preparedness Task Force has developed a brochure, "Older Adults and Disaster: Preparedness and Response."

The AAGP brochure is posted at <www.gmhfonline.org/gmhf/consumer/disaster.html> or available from the Geriatric Mental Health Foundation at (301) 654-7850. ■

Treat your patients with the demonstrated efficacy of LEXAPRO[1-5]

In adolescents aged 12 to 17 with Major Depressive Disorder (MDD)[1]

In adults with MDD and Generalized Anxiety Disorder (GAD)[1]

Lexapro escitalopram oxalate®

WARNING: 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 Lexapro 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. Lexapro is not approved for use in pediatric patients less than 12 years of age.

Please see additional Important Safety Information on following pages.

There is no generic available for LEXAPRO

- Significantly improved MDD symptoms in adolescents[2]

Lexapro (escitalopram oxalate) is indicated for the acute and maintenance treatment of major depressive disorder (MDD) in adults and adolescents aged 12-17 years. Lexapro is also indicated for the acute treatment of generalized anxiety disorder (GAD) in adults.

*LEXAPRO is indicated as an integral part of a total treatment program for MDD. Drug treatment may not be indicated for all adolescents with this syndrome.

IMPORTANT SAFETY INFORMATION (continued)

Contraindications

- Lexapro is contraindicated in patients taking monoamine oxidase inhibitors (MAOIs). There have been reports of serious, sometimes fatal, reactions with some cases resembling neuroleptic malignant syndrome (NMS) and serotonin syndrome. Features may include hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. These reactions have also been reported in patients who have recently discontinued SSRI treatment and have been started on an MAOI. Serotonin syndrome was reported for two patients who were concomitantly receiving linezolid, an antibiotic which has MAOI activity. Lexapro should not be used in combination with an MAOI or within 14 days of discontinuing an MAOI. MAOIs should not be initiated within 14 days of discontinuing Lexapro.
- Lexapro is contraindicated in patients taking pimozide or with hypersensitivity to escitalopram or citalopram.

Warnings and Precautions

- All patients treated with antidepressants should be monitored appropriately and observed closely for clinical worsening, suicidality and unusual changes in behavior, especially within the first few months of treatment or when changing the dose. Consideration should be given to changing the therapeutic regimen, including discontinuing medication, in patients whose depression is persistently worse, 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 treated with antidepressants should be alerted about the need to monitor patients daily for the emergence of agitation, irritability, unusual changes in behavior, or the emergence of suicidality, and report such symptoms immediately. Prescriptions for Lexapro should be written for the smallest quantity of tablets, consistent with good patient management, in order to reduce the risk of overdose.

- Significantly higher rates of response and remission vs placebo in MDD and GAD in adults[4,5]

- A major depressive episode may be the initial presentation of bipolar disorder. In patients at risk for bipolar disorder, treating such an episode with an antidepressant alone may increase the likelihood of precipitating a mixed/manic episode. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine if they are at risk for bipolar disorder. Lexapro should be used cautiously in patients with a history of mania or seizure disorder. Lexapro is not approved for use in treating bipolar depression.
- The concomitant use of Lexapro with other SSRIs, SNRIs, triptans, tryptophan, antipsychotics or other dopamine antagonists is not recommended due to potential development of life-threatening serotonin syndrome or neuroleptic malignant syndrome (NMS)-like reactions. Reactions have been reported with SNRIs and SSRIs alone, including Lexapro, but particularly with drugs that impair metabolism of serotonin (including MAOIs). Management of these events should include immediate discontinuation of Lexapro and the concomitant agent and continued monitoring.
- Patients should be monitored for adverse reactions when discontinuing treatment with Lexapro. During marketing of Lexapro and other SSRIs and SNRIs, there have been spontaneous reports of adverse events occurring upon discontinuation, including dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias), anxiety, confusion, headache, lethargy, emotional lability, insomnia and hypomania. A gradual dose reduction rather than abrupt cessation is recommended whenever possible.
- SSRIs and SNRIs have been associated with clinically significant hyponatremia. Elderly patients and patients taking diuretics or who are otherwise volume-depleted appear to be at a greater risk. Discontinuation of Lexapro should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted.

Please see Boxed Warning on first page and additional Important Safety Information on next page.

Lexapro®
escitalopram oxalate

Visit the LEXAPRO website at www.lexapro.com

LEXAPRO: Proven efficacy in MDD in adolescents aged 12 to 17, and in MDD and GAD in adults[1-5]

Warnings and Precautions (continued)

- SSRIs (including Lexapro) and SNRIs may increase the risk of bleeding. Patients should be cautioned that concomitant use of aspirin, NSAIDs, warfarin or other anticoagulants may add to the risk.
- Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro does not affect their ability to engage in such activities.
- Lexapro should be used with caution in patients with severe renal impairment or with diseases or conditions that alter metabolism or hemodynamic responses. In subjects with hepatic impairment, clearance of racemic citalopram was decreased and plasma concentrations were increased. The recommended dose of Lexapro in hepatically impaired patients is 10 mg/day.
- For pregnant or nursing mothers, Lexapro should be used only if the potential benefit justifies the potential risk to the fetus or child.

Adverse Reactions

- In clinical trials of MDD, the most common adverse reactions in adults treated with Lexapro (approximately 5% or greater and at least twice the incidence of placebo) were nausea (15% vs 7%), insomnia (9% vs 4%), ejaculation disorder (9% vs <1%), fatigue (5% vs 2%), somnolence (6% vs 2%), and increased sweating (5% vs 2%). In pediatric patients, the overall profile of adverse reactions was similar to that seen in adults; however, the following additional adverse reactions were reported at an incidence of at least 2% for Lexapro and greater than placebo: back pain, urinary tract infection, vomiting, and nasal congestion.
- In clinical trials of GAD, the most common adverse reactions in adults treated with Lexapro (approximately 5% or greater and at least twice the incidence of placebo) were nausea (18% vs 8%), ejaculation disorder (14% vs 2%), insomnia (12% vs 6%), fatigue (8% vs 2%), decreased libido (7% vs 2%) and anorgasmia (6% vs <1%).

Please see accompanying brief summary of Prescribing Information for LEXAPRO, including Boxed Warning.

References: 1. LEXAPRO [package insert]. St. Louis, Mo: Forest Pharmaceuticals, Inc.; 2009. **2.** Emslie GJ, Ventura D, Korotzer A, Tourkodimitris S. Escitalopram in the treatment of adolescent depression: a randomized placebo-controlled multisite trial. *J Am Acad Child Adolesc Psychiatry*. 2009;48:721-729. **3.** Burke WJ, Gergel I, Bose A. Fixed-dose trial of the single isomer SSRI escitalopram in depressed outpatients. *J Clin Psychiatry*. 2002;63:331-336. **4.** Davidson JRT, Bose A, Korotzer A, Zheng H. Escitalopram in the treatment of generalized anxiety disorder: double-blind, placebo controlled, flexible dose study. *Depress Anxiety*. 2004;19:234-240. **5.** Wade A, Lemming OM, Hedegaard KB. Escitalopram 10 mg/day is effective and well tolerated in a placebo-controlled study in depression in primary care. *Int Clin Psychopharmacol*. 2002;17:95-102.

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Lexapro® escitalopram oxalate

LEXAPRO® (escitalopram oxalate) TABLETS/ORAL SOLUTION **Rx Only**

Brief Summary: For complete details, please see full Prescribing Information for Lexapro.

WARNINGS: 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 Lexapro 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. Lexapro is not approved for use in pediatric patients less than 12 years of age. *[See Warnings and Precautions: Clinical Worsening and Suicide Risk, Patient Counseling Information: Information for Patients, and Used in Specific Populations: Pediatric Use].*

INDICATIONS AND USAGE: Major Depressive Disorder-Lexapro (escitalopram) is indicated for the acute and maintenance treatment of major depressive disorder in adults and in adolescents 12 to 17 years of age [*see Clinical Studies*]. A major depressive episode (DSM-IV) implies a prominent and relatively persistent (nearly every day for at least 2 weeks) depressed or dysphoric mood that usually interferes with daily functioning, and includes at least five of the following nine symptoms: depressed mood, loss of interest 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. **Generalized Anxiety Disorder**-Lexapro is indicated for the acute treatment of Generalized Anxiety Disorder (GAD) in adults [*see Clinical Studies*]. Generalized Anxiety Disorder (DSM-IV) is characterized by excessive anxiety and worry (apprehensive expectation) that is persistent for at least 6 months and which the person finds difficult to control. It must be associated with at least 3 of the following symptoms: restlessness or feeling keyed up or on edge, being easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension, and sleep disturbance.

CONTRAINDICATIONS: Monoamine oxidase inhibitors (MAOIs)-Concomitant use in patients taking monoamine oxidase inhibitors (MAOIs) is contraindicated [*see Warnings and Precautions*]. **Pimozide**-Concomitant use in patients taking pimozide is contraindicated [*see Drug Interactions*]. **Hypersensitivity to escitalopram or citalopram**-Lexapro is contraindicated in patients with a hypersensitivity to escitalopram or citalopram or any of the inactive ingredients in Lexapro.

WARNINGS AND PRECAUTIONS: Clinical Worsening and Suicide Risk-Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The pooled analyses of placebo-controlled 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 4400 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 1000 patients treated) are provided in Table 1.

TABLE 1

Age Range	Drug-Placebo Difference in Number of Cases of Suicidality per 1000 Patients Treated
	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. The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms [*see Dosage and Administration*]. Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers [*see also Patient Counseling Information*]. Prescriptions for Lexapro should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. **Screening Patients for Bipolar Disorder**-A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled 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. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that Lexapro is not approved for use in treating bipolar depression. **Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like Reactions**-The development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported with SNRIs and SSRIs alone, including Lexapro treatment, but particularly with concomitant use of serotonergic drugs (including triptans) with drugs which impair metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Serotonin syndrome, in its most severe form can resemble neuroleptic malignant syndrome, which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms. The concomitant use of Lexapro with MAOIs intended to treat depression is contraindicated. If concomitant treatment of Lexapro with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. The concomitant use of Lexapro with serotonin precursors (such as tryptophan) is not recommended. Treatment with Lexapro and any concomitant serotonergic or antidopaminergic agents, including antipsychotics, should be discontinued immediately if the above events occur and supportive symptomatic treatment should be initiated. **Discontinuation of Treatment with Lexapro**-During marketing of Lexapro and other SSRIs and SNRIs (serotonin and norepinephrine reuptake inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, and hypomania. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment with Lexapro. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate [*see Dosage and Administration*]. **Seizures**-Although anticonvulsant effects of racemic citalopram have been observed in animal studies, Lexapro has not been systematically evaluated in patients with a seizure disorder. These patients were excluded from clinical studies during the product's premarketing testing. In clinical trials of Lexapro, cases of convulsion have been reported in association with Lexapro treatment. Like other drugs effective in the treatment of major depressive disorder, Lexapro should be introduced with care in patients with a history of seizure disorder. **Activation of Mania/Hypomania**-In placebo-controlled trials of Lexapro in major depressive disorder, activation of mania/hypomania was reported in one (0.1%) of 715 patients treated with Lexapro and in none of the 592 patients treated with placebo. One additional case of hypomania has been reported in association with Lexapro treatment. Activation of mania/hypomania has also been reported in a small proportion of patients with major affective disorders treated with racemic citalopram and other marketed drugs effective in the treatment of major depressive disorder. As with all drugs effective in the treatment of major depressive disorder, Lexapro should be used cautiously in patients with a history of mania. **Hyponatremia**-Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including Lexapro. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH), and was reversible when Lexapro was discontinued. Cases with serum sodium lower than 110 mmol/L have been reported. Elderly patients may be at greater risk of developing hyponatremia with SSRIs and SNRIs. Also, patients taking diuretics or who are otherwise volume depleted may be at greater risk [*see Geriatric Use*]. Discontinuation of Lexapro should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted. Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death. **Abnormal Bleeding**-SSRIs and SNRIs, including Lexapro, may increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs, warfarin, and other anticoagulants may add to the risk. Case reports and epidemiological studies (case-control and cohort design) have demonstrated an association between use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal bleeding. Bleeding events related to SSRIs and SNRIs use have ranged from ecchymoses, hematomas, epistaxis, and petechiae to life-threatening hemorrhages. Patients should be cautioned about the risk of bleeding associated with the concomitant use of Lexapro and NSAIDs, aspirin, or other drugs that affect coagulation. **Interference with Cognitive and Motor Performance**-In a study in normal volunteers, Lexapro 10 mg/day did not produce impairment of intellectual function or psychomotor performance. Because any psychoactive drug may impair judgment, thinking, or motor skills, however, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that Lexapro therapy does not affect their ability to engage in such activities. **Use in Patients with Concomitant Illness**-Clinical experience with Lexapro in patients with certain concomitant systemic illnesses is limited. Caution is advisable in using Lexapro in patients with diseases or conditions that produce altered metabolism or hemodynamic responses. Lexapro has not been systematically evaluated in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were generally excluded from clinical studies during the product's premarketing testing. In subjects with hepatic impairment, clearance of racemic citalopram was decreased and plasma concentrations were increased. The recommended dose of Lexapro in hepatically impaired patients is 10 mg/day [*see Dosage and Administration*]. Because escitalopram is extensively metabolized, excretion of unchanged drug in urine is a minor route of elimination. Until adequate numbers of patients with severe renal impairment have been evaluated during chronic treatment with Lexapro, however, it should be used with caution in such patients [*see Dosage and Administration*]. **Potential for Interaction with Monoamine Oxidase Inhibitors**-In patients receiving serotonin reuptake inhibitor drugs in combination with a monoamine oxidase inhibitor (MAOI), there have been reports of serious, sometimes

fatal, reactions including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. These reactions have also been reported in patients who have recently discontinued SSRI treatment and have been started on an MAOI. Some cases presented with features resembling neuroleptic malignant syndrome. Furthermore, limited animal data on the effects of combined use of SSRIs and MAOIs suggest that these drugs may act synergistically to elevate blood pressure and evoke behavioral excitation. Therefore, it is recommended that Lexapro should not be used in combination with an MAOI, or within 14 days of discontinuing treatment with an MAOI. Similarly, at least 14 days should be allowed after stopping Lexapro before starting an MAOI. Serotonin syndrome has been reported in two patients who were concomitantly receiving linezolid, an antibiotic which is a reversible non-selective MAOI.

ADVERSE REACTIONS: Clinical Trials Experience-Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice. **Clinical Trial Data Sources; Pediatrics (6 -17 years)**-Adverse events were collected in 576 pediatric patients (286 Lexapro, 290 placebo) with major depressive disorder in double-blind placebo-controlled studies. Safety and effectiveness of Lexapro in pediatric patients less than 12 years of age has not been established. **Adults**-Adverse events information for Lexapro was collected from 715 patients with major depressive disorder who were exposed to escitalopram and from 592 patients who were exposed to placebo in double-blind, placebo-controlled trials. An additional 284 patients with major depressive disorder were newly exposed to escitalopram in open-label trials. The adverse event information for Lexapro in patients with GAD was collected from 429 patients exposed to escitalopram and from 427 patients exposed to placebo in double-blind, placebo-controlled trials. Adverse events during exposure were obtained primarily by general inquiry and recorded by clinical investigators using terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of events into a smaller number of standardized event categories. In the tables and tabulations that follow, standard World Health Organization (WHO) terminology has been used to classify reported adverse events. The stated frequencies of adverse reactions represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed. An event was considered treatment-emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation. **Adverse Events Associated with Discontinuation of Treatment; Major Depressive Disorder; Pediatrics (6 -17 years)**-Adverse events were associated with discontinuation of 3.5% of 286 patients receiving Lexapro and 1% of 290 patients receiving placebo. The most common adverse event (incidence at least 1% for Lexapro and greater than placebo) associated with discontinuation was insomnia (1% Lexapro, 0% placebo). **Adults**-Among the 715 depressed patients who received Lexapro in placebo-controlled trials, 6% discontinued treatment due to an adverse event, as compared to 2% of 592 patients receiving placebo. In two fixed-dose studies, the rate of discontinuation for adverse events in patients receiving 10 mg/day Lexapro was not significantly different from the rate of discontinuation for adverse events in patients receiving placebo. The rate of discontinuation for adverse events in patients assigned to a fixed dose of 20 mg/day Lexapro was 10%, which was significantly different from the rate of discontinuation for adverse events in patients receiving 10 mg/day Lexapro (4%) and placebo (3%). Adverse events that were associated with the discontinuation of at least 1% of patients treated with Lexapro, and for which the rate was at least twice that of placebo, were nausea (2%) and ejaculation disorder (2% of male patients). **Generalized Anxiety Disorder; Adults**-Among the 429 GAD patients who received Lexapro 10-20 mg/day in placebo-controlled trials, 8% discontinued treatment due to an adverse event, as compared to 4% of 427 patients receiving placebo. Adverse events that were associated with the discontinuation of at least 1% of patients treated with Lexapro, and for which the rate was at least twice the placebo rate, were nausea (2%), insomnia (1%), and fatigue (1%). **Incidence of Adverse Reactions in Placebo-Controlled Clinical Trials; Major Depressive Disorder; Pediatrics (6 -17 years)**-The overall profile of adverse reactions in pediatric patients was generally similar to that seen in adult studies, as shown in Table 2. However, the following adverse reactions (excluding those which appear in Table 2 and those for which the coded terms were uninformative or misleading) were reported at an incidence of at least 2% for Lexapro and greater than placebo: back pain, urinary tract infection, vomiting, and nasal congestion. **Adults**-The most commonly observed adverse reactions in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were insomnia, ejaculation disorder (primarily ejaculatory delay), nausea, sweating increased, fatigue, and somnolence. Table 2 enumerates the incidence, rounded to the nearest percent, of treatment-emergent adverse events that occurred among 715 depressed patients who received Lexapro at doses ranging from 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients.

TABLE 2
Treatment-Emergent Adverse Reactions Observed with a Frequency of ≥ 2% and Greater Than Placebo for Major Depressive Disorder

Adverse Reaction	Lexapro (N=715)	Placebo (N=592)
Autonomic Nervous System Disorders		
Dry Mouth	6%	5%
Sweating Increased	5%	2%
Central & Peripheral Nervous System Disorders		
Dizziness	5%	3%
Gastrointestinal Disorders		
Nausea	15%	7%
Diarrhea	8%	5%
Constipation	3%	1%
Indigestion	3%	1%
Abdominal Pain	2%	1%
General		
Influenza-like Symptoms	5%	4%
Fatigue	5%	2%
Psychiatric Disorders		
Insomnia	9%	4%
Somnolence	6%	2%
Appetite Decreased	3%	1%
Libido Decreased	3%	1%
Respiratory System Disorders		
Rhinitis	5%	4%
Sinusitis	3%	2%
Urogenital		
Ejaculation Disorder[1,2]	9%	<1%
Impotence[2]	3%	<1%
Anorgasmia[3]	2%	<1%

[1]Primarily ejaculatory delay.
[2]Denominator used was for males only (N=225 Lexapro; N=188 placebo).
[3]Denominator used was for females only (N=490 Lexapro; N=404 placebo).

Generalized Anxiety Disorder; Adults-The most commonly observed adverse reactions in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were nausea, ejaculation disorder (primarily ejaculatory delay), insomnia, fatigue, decreased libido, and anorgasmia. Table 3 enumerates the incidence, rounded to the nearest percent of treatment-emergent adverse events that occurred among 429 GAD patients who received Lexapro 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients.

TABLE 3
Treatment-Emergent Adverse Reactions Observed with a Frequency of ≥ 2% and Greater Than Placebo for Generalized Anxiety Disorder

Adverse Reactions	Lexapro (N=429)	Placebo (N=427)
Autonomic Nervous System Disorders		
Dry Mouth	9%	5%
Sweating Increased	4%	1%
Central & Peripheral Nervous System Disorders		
Headache	24%	17%
Paresthesia	2%	1%
Gastrointestinal Disorders		
Nausea	18%	8%
Diarrhea	8%	6%
Constipation	5%	4%
Indigestion	3%	2%
Vomiting	3%	1%
Abdominal Pain	2%	1%
Flatulence	2%	1%
Toothache	2%	0%
General		
Fatigue	8%	2%
Influenza-like Symptoms	5%	4%
Musculoskeletal System Disorder		
Neck/Shoulder Pain	3%	1%
Psychiatric Disorders		
Somnolence	13%	7%
Insomnia	12%	6%
Libido Decreased	7%	2%
Dreaming Abnormal	3%	2%
Appetite Decreased	3%	1%
Lethargy	3%	1%
Respiratory System Disorders		
Yawning	2%	1%
Urogenital		
Ejaculation Disorder[1,2]	14%	2%
Anorgasmia[3]	6%	<1%
Menstrual Disorder	2%	1%

[1]Primarily ejaculatory delay.
[2]Denominator used was for males only (N=182 Lexapro; N=195 placebo).
[3]Denominator used was for females only (N=247 Lexapro; N=232 placebo).

Dose Dependency of Adverse Reactions-The potential dose dependency of common adverse reactions (defined as an incidence rate of ≥5% in either the 10 mg or 20 mg Lexapro groups) was examined on the basis of the combined incidence of adverse events in two fixed-dose trials. The overall incidence rates of adverse events in 10 mg Lexapro-treated patients (66%) was similar to that of the placebo-treated patients (61%), while the incidence rate in 20 mg/day Lexapro-treated patients was greater (86%). Table 4 shows common adverse reactions that occurred in the 20 mg/day Lexapro group with an incidence that was approximately twice that of the 10 mg/day Lexapro group and approximately twice that of the placebo group.

TABLE 4
Incidence of Common Adverse Reactions in Patients with Major Depressive Disorder

Adverse Reaction	Placebo (N=311)	10 mg/day Lexapro (N=310)	20 mg/day Lexapro (N=125)
Insomnia	4%	7%	14%
Diarrhea	5%	6%	14%
Dry Mouth	3%	4%	9%
Somnolence	1%	4%	9%
Dizziness	2%	4%	7%
Sweating Increased	<1%	3%	8%
Constipation	1%	3%	6%
Fatigue	2%	2%	6%
Indigestion	1%	2%	6%

Male and Female Sexual Dysfunction with SSRIs-Although changes in sexual desire, sexual performance, and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that SSRIs can cause such untoward sexual experiences. Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance cited in product labeling are likely to underestimate their actual incidence.

TABLE 5
Incidence of Sexual Side Effects in Placebo-Controlled Clinical Trials

Adverse Event	Lexapro	Placebo
	In Males Only	
	(N=407)	(N=383)
Ejaculation Disorder (primarily ejaculatory delay)	12%	1%
Libido Decreased	6%	2%
Impotence	2%	<1%
	In Females Only	
	(N=737)	(N=636)
Libido Decreased	3%	1%
Anorgasmia	3%	<1%

There are no adequately designed studies examining sexual dysfunction with escitalopram treatment. Priapism has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects. **Vital Sign Changes**-Lexapro and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, and diastolic blood pressure) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses did not reveal any clinically important changes in vital signs associated with Lexapro treatment. In addition, a comparison of supine and standing vital sign measures in subjects receiving Lexapro indicated that Lexapro treatment is not associated with orthostatic changes. **Weight Changes**-Patients treated with Lexapro in controlled trials did not differ from placebo-treated patients with regard to clinically important change in body weight. **Laboratory Changes**-Lexapro and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables, and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Lexapro treatment. **ECG Changes**-Electrocardiograms from Lexapro (N=625), racemic citalopram (N=351), and placebo (N=527) groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed (1) a decrease in heart rate of 2.2 bpm for Lexapro and 2.7 bpm for racemic citalopram, compared to an increase of 0.3 bpm for placebo and (2) an increase in QTc interval of 3.9 msec for Lexapro and 3.7 msec for racemic citalopram, compared to 0.5 msec for placebo. Neither Lexapro nor racemic citalopram were associated with the development of clinically significant ECG abnormalities. **Other Reactions Observed During the Premarketing Evaluation of Lexapro**-Following is a list of treatment-emergent adverse events, as defined in the introduction to the ADVERSE REACTIONS section, reported by the 1428 patients treated with Lexapro for periods of up to one year in double-blind or open-label clinical trials during its premarketing evaluation. The listing does not include those events already listed in Tables 2 & 3, those events for which a drug cause was remote and at a rate less than 1% or lower than placebo, those events which were so general as to be uninformative, and those events reported only once which did not have a substantial probability of being acutely life threatening. Events are categorized by body system. Events of major clinical importance are described in the Warnings and Precautions section. Cardiovascular - hypertension, palpitation. Central and Peripheral Nervous System Disorders - light-headed feeling, migraine. Gastrointestinal Disorders - abdominal cramp, heartburn, gastroenteritis. General - allergy, chest pain, fever, hot flushes, pain in limb. Metabolic and Nutritional Disorders - increased weight. Musculoskeletal System Disorders - arthralgia, myalgia jaw stiffness. Psychiatric Disorders - appetite increased, concentration impaired, irritability. Reproductive Disorders/Female - menstrual cramps, menstrual disorder. Respiratory System Disorders - bronchitis, coughing, nasal congestion, sinus congestion, sinus headache. Skin and Appendages Disorders - rash. Special Senses - vision blurred, tinnitus. Urinary System Disorders - urinary frequency, urinary tract infection. **Post-Marketing Experience; Adverse Reactions Reported Subsequent to the Marketing of Escitalopram**-The following additional adverse reactions have been identified from spontaneous reports of escitalopram received worldwide. These adverse reactions have been chosen for inclusion because of a combination of seriousness, frequency of reporting, or potential causal connection to escitalopram and have not been listed elsewhere in labeling. However, because these adverse reactions were 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. These events include: Blood and Lymphatic System Disorders: anemia, agranulocytis, aplastic anemia, hemolytic anemia, idiopathic thrombocytopenia purpura, leukopenia, thrombocytopenia. Cardiac Disorders: atrial fibrillation, bradycardia, cardiac failure, myocardial infarction, tachycardia, torsade de pointes, ventricular arrhythmia, ventricular tachycardia. Ear and Labyrinth Disorders: vertigo Endocrine Disorders: diabetes mellitus, hyperprolactinemia, SIADH. Eye Disorders: diplopia, glaucoma, mydriasis, visual disturbance. Gastrointestinal Disorders: dysphagia, gastrointestinal hemorrhage, gastroesophageal reflux, pancreatitis, rectal hemorrhage. General Disorders and Administration Site Conditions: abnormal gait, asthenia, edema, fall, feeling abnormal, malaise. Hepatobiliary Disorders: fulminant hepatitis, hepatic failure, hepatic necrosis, hepatitis. Immune System Disorders: allergic reaction, anaphylaxis. Investigations: bilirubin increased, decreased weight, electrocardiogram QT prolongation, hepatic enzymes increased, hypercholesterolemia, INR increased, prothrombin decreased. Metabolism and Nutrition Disorders: hyperglycemia, hypoglycemia, hypokalemia, hyponatremia. Musculoskeletal and Connective Tissue Disorders: muscle cramp, muscle stiffness, muscle weakness, rhabdomyolysis. Nervous System Disorders: akathisia, amnesia, ataxia, choreoathetosis, cerebrovascular accident, dysarthria, dyskinesia, dystonia, extrapyramidal disorders, grand mal seizures (or convulsions), hypoaesthesia, myoclonus, nystagmus, Parkinsonism, restless legs, seizures, syncope, tardive dyskinesia, tremor. Pregnancy, Puerperium and Perinatal Conditions: spontaneous abortion. Psychiatric Disorders: acute psychosis, aggression, agitation, anger, anxiety, apathy, completed suicide, confusion, depersonalization, depression aggravated, delirium, delusion, disorientation, feeling unreal, hallucinations (visual and auditory), mood swings, nervousness, nightmare, panic reaction, paranoia, restlessness, self-harm or thoughts of self-harm, suicide attempt, suicidal ideation, suicidal tendency. Renal and Urinary Disorders: acute renal failure, dysuria, urinary retention. Reproductive System and Breast Disorders: menorrhagia, priapism. Respiratory, Thoracic and Mediastinal Disorders: dyspnea, epistaxis, pulmonary embolism, pulmonary hypertension of the newborn. Skin and Subcutaneous Tissue Disorders: alopecia, angioedema, dermatitis, ecchymosis, erythema multiforme, photosensitivity reaction, Stevens Johnson Syndrome, toxic epidermal necrolysis, urticaria. Vascular Disorders: deep vein thrombosis, flushing, hypertensive crisis, hypotension, orthostatic hypotension, phlebitis, thrombosis.

DRUG INTERACTIONS: Serotonergic Drugs-Based on the mechanism of action of SNRIs and SSRIs including Lexapro, and the potential for serotonin syndrome, caution is advised when Lexapro is coadministered with other drugs that may affect the serotonergic neurotransmitter systems, such as triptans, linezolid (an antibiotic which is a reversible non-selective MAOI), lithium, tramadol, or St. John's Wort [*see Warnings and Precautions*]. The concomitant use of Lexapro with other SSRIs, SNRIs or tryptophan is not recommended. **Triptans**-There have been rare postmarketing reports of serotonin syndrome with use of an SSRI and a triptan. If concomitant treatment of Lexapro with a triptan is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases [*see Warnings and Precautions*]. **CNS Drugs**- Given the primary CNS effects of escitalopram, caution should be used when it is taken in combination with other centrally acting drugs. **Alcohol**-Although Lexapro did not potentiate the cognitive and motor effects of alcohol in a clinical trial, as with other psychotropic medications, the use of alcohol by patients taking Lexapro is not recommended. **Monoamine Oxidase Inhibitors (MAOIs)**-[*see Contraindications and Warnings and Precautions*]. **Drugs That Interfere With Hemostasis (NSAIDs, Aspirin, Warfarin, etc.)**-Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of the case-control and cohort design that have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding have also shown that concurrent use of an NSAID or aspirin may potentiate the risk of bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs and SNRIs are coadministered with warfarin. Patients receiving warfarin therapy should be carefully monitored when Lexapro is initiated or discontinued. **Cimetidine**-In subjects who had received 21 days of 40 mg/day racemic citalopram, combined administration of 400 mg/day cimetidine for 8 days resulted in an increase in citalopram AUC and C_{max} of 43% and 39%, respectively. The clinical significance of these findings is unknown. **Digoxin**-In subjects who had received 21 days of 40 mg/day racemic citalopram, combined administration of citalopram and digoxin (single dose of 1 mg) did not significantly affect the pharmacokinetics of either citalopram or digoxin. **Lithium**-Coadministration of racemic citalopram (40 mg/day for 10 days) and lithium (30 mmol/day for 5 days) had no significant effect on the pharmacokinetics of citalopram or lithium. Nevertheless, plasma lithium levels should be monitored with appropriate adjustment to the lithium dose in accordance with standard clinical practice. Because lithium may enhance the serotonergic effects of escitalopram, caution should be exercised when Lexapro and lithium are coadministered. **Pimozide and Celexa**-In a controlled study, a single dose of pimozide 2 mg co-administered with racemic citalopram 40 mg given once daily for 11 days was associated with a mean increase in QTc values of approximately 10 msec compared to pimozide given alone. Racemic citalopram did not alter the mean AUC or C_{max} of pimozide. The mechanism of this pharmacodynamic interaction is not known. **Sumatriptan**-There have been rare postmarketing reports describing patients with weakness, hyperreflexia, and incoordination following the use of an SSRI and sumatriptan. If concomitant treatment with sumatriptan and an SSRI (e.g., fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, escitalopram) is clinically warranted, appropriate observation of the patient is advised. **Theophylline**-Combined administration of racemic citalopram (40 mg/day for 21 days) and the CYP1A2 substrate theophylline (single dose of 300 mg) did not affect the pharmacokinetics of theophylline. The effect of theophylline on the pharmacokinetics of citalopram was not evaluated. **Warfarin**-Administration of 40 mg/day racemic citalopram for 21 days did not affect the pharmacokinetics of warfarin, a CYP3A4 substrate. Prothrombin time was increased by 5%, the clinical significance of which is unknown. **Carbamazepine**-Combined administration of racemic citalopram (40 mg/day for 14 days) and carbamazepine (titrated to 400 mg/day for 35 days) did not significantly affect the pharmacokinetics of carbamazepine, a CYP3A4 substrate. Although trough citalopram plasma levels were unaffected, given the enzyme-inducing properties of carbamazepine, the possibility that carbamazepine might increase the clearance of escitalopram should be considered if the two drugs are coadministered. **Triazolam**-Combined administration of racemic citalopram (titrated to 40 mg/day for 28 days) and the CYP3A4 substrate triazolam (single dose of 0.25 mg) did not significantly affect the pharmacokinetics of either citalopram or triazolam. **Ketoconazole**-Combined administration of racemic citalopram (40 mg) and ketoconazole (200 mg), a potent CYP3A4 inhibitor, decreased the C_{max} and AUC of ketoconazole by 21% and 10%, respectively, and did not significantly affect the pharmacokinetics of citalopram. **Ritonavir**-Combined administration of a single dose of ritonavir (600 mg), both a CYP3A4 substrate and a potent inhibitor of CYP3A4, and escitalopram (20 mg) did not affect the pharmacokinetics of either ritonavir or escitalopram. **CYP3A4 and -2C19 Inhibitors**-*In vitro* studies indicated that CYP3A4 and -2C19 are the primary enzymes involved in the metabolism of escitalopram. However, coadministration of escitalopram (20 mg) and ritonavir (600 mg), a potent inhibitor of CYP3A4, did not significantly affect the pharmacokinetics of escitalopram. Because escitalopram is metabolized by multiple enzyme systems, inhibition of a single enzyme may not appreciably decrease escitalopram clearance. **Drugs Metabolized by Cytochrome P4502D6**-*In vitro* studies did not reveal an inhibitory effect of escitalopram on CYP2D6. In addition, steady state levels of racemic citalopram were not significantly different in poor metabolizers and extensive CYP2D6 metabolizers after multiple-dose administration of citalopram, suggesting that coadministration, with escitalopram, of a drug that inhibits CYP2D6, is unlikely to have clinically significant effects on escitalopram metabolism. However, there are limited *in vivo* data suggesting a modest CYP2D6 inhibitory effect for escitalopram, i.e., coadministration of escitalopram (20 mg/day for 21 days) with the tricyclic antidepressant desipramine (single dose of 50 mg), a substrate for CYP2D6, resulted in a 40% increase in C_{max} and a 100% increase in AUC of desipramine. The clinical significance of this finding is unknown. Nevertheless, caution is indicated in the coadministration of escitalopram and drugs metabolized by CYP2D6. **Metoprolol**-Administration of 20 mg/day Lexapro for 21 days in healthy volunteers resulted in a 50% increase in C_{max} and 82% increase in AUC of the beta-adrenergic blocker metoprolol (given in a single dose of 100 mg). Increased metoprolol plasma levels have been associated with decreased cardioselectivity. Coadministration of Lexapro and metoprolol had no clinically significant effects on blood pressure or heart rate. **Electroconvulsive Therapy (ECT)**-There are no clinical studies of the combined use of ECT and escitalopram.

USE IN SPECIFIC POPULATIONS: Pregnancy; Pregnancy Category C-In a rat embryo/fetal development study, oral administration of escitalopram (56, 112, or 150 mg/kg/day) to pregnant animals during the period of organogenesis resulted in decreased fetal body weight and associated delays in ossification at the two higher doses (approximately ≥ 56 times the maximum recommended human dose [MRHD] of 20 mg/day on a body surface area [mg/m^2] basis). Maternal toxicity (clinical signs and decreased body weight gain and food consumption), mild at 56 mg/kg/day, was present at all dose levels. The developmental no-effect dose of 56 mg/kg/day is approximately 28 times the MRHD on a mg/m^2 basis. No teratogenicity was observed at any of the doses tested (as high as 75 times the MRHD on a mg/m^2 basis). When female rats were treated with escitalopram (6, 12, 24, or 48 mg/kg/day) during pregnancy and through weaning, slightly increased offspring mortality and growth retardation were noted at 48 mg/kg/day which is approximately 24 times the MRHD on a mg/m^2 basis. Slight maternal toxicity (clinical signs and decreased body weight gain and food consumption) was seen at this dose. Slightly increased offspring mortality was also seen at 24 mg/kg/day. The no-effect dose was 12 mg/kg/day which is approximately 6 times the MRHD on a mg/m^2 basis. In animal reproduction studies, racemic citalopram has been shown to have adverse effects on embryo/fetal and postnatal development, including teratogenic effects, when administered at doses greater than human therapeutic doses. In two rat embryo/fetal development studies, oral administration of racemic citalopram (32, 56, or 112 mg/kg/day) to pregnant animals during the period of organogenesis resulted in decreased embryo/fetal growth and survival and an increased incidence of fetal abnormalities (including cardiovascular and skeletal defects) at the high dose. This dose was also associated with maternal toxicity (clinical signs, decreased body weight gain). The developmental no-effect dose was 56 mg/kg/day. In a rabbit study, no adverse effects on embryo/fetal development were observed at doses of racemic citalopram of up to 16 mg/kg/day. Thus, teratogenic effects of racemic citalopram were observed at a maternally toxic dose in the rat and were not observed in the rabbit. When female rats were treated with racemic citalopram (4.8, 12.8, or 32 mg/kg/day) from late gestation through weaning, increased offspring mortality during the first 4 days after birth and persistent offspring growth retardation were observed at the highest dose. The no-effect dose was 12.8 mg/kg/day. Similar effects on offspring mortality and growth were seen when dams were treated throughout gestation and early lactation at doses ≥ 24 mg/kg/day. A no-effect dose was not determined in that study. There are no adequate and well-controlled studies in pregnant women; therefore, escitalopram should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Pregnancy-Nonteratogenic Effects-Neonates exposed to Lexapro and other SSRIs or SNRIs, late in the third trimester, have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome [*see Warnings and Precautions*]. Infants exposed to SSRIs in late pregnancy may have an increased risk for persistent pulmonary hypertension of the newborn (PPHN). PPHN occurs in 1-2 per 1000 live births in the general population and is associated with substantial neonatal morbidity and mortality. In a retrospective, case-control study of 377 women whose infants were born with PPHN and 836 women whose infants were born healthy, the risk for developing PPHN was approximately six-fold higher for infants exposed to SSRIs after the 20th week of gestation compared to infants who had not been exposed to antidepressants during pregnancy. There is currently no corroborative evidence regarding the risk for PPHN following exposure to SSRIs in pregnancy; this is the first study that has investigated the potential risk. The study did not include enough cases with exposure to individual SSRIs to determine if all SSRIs posed similar levels of PPHN risk. When treating a pregnant woman with Lexapro during the third trimester, the physician should carefully consider both the potential risks and benefits of treatment [*see Dosage and Administration*]. Physicians should note that in a prospective longitudinal study of 201 women with a history of major depression who were euthymic at the beginning of pregnancy, women who discontinued antidepressant medication during pregnancy were more likely to experience a relapse of major depression than women who continued antidepressant medication. **Labor and Delivery**-The effect of Lexapro on labor and delivery in humans is unknown. **Nursing Mothers**-Escitalopram is excreted in human breast milk. Limited data from women taking 10-20 mg escitalopram showed that exclusively breast-fed infants receive approximately 3.9% of the maternal weight-adjusted dose of escitalopram and 1.7% of the maternal weight-adjusted dose of desmethylcitalopram. There were two reports of infants experiencing excessive somnolence, decreased feeding, and weight loss in association with breastfeeding from a racemic citalopram-treated mother; in one case, the infant was reported to recover completely upon discontinuation of racemic citalopram by its mother and, in the second case, no follow-up information was available. Caution should be exercised and breastfeeding infants should be observed for adverse reactions when Lexapro is administered to a nursing woman. **Pediatric Use**-Safety and effectiveness of Lexapro has not been established in pediatric patients (less than 12 years of age) with Major Depressive Disorder. Safety and effectiveness of Lexapro has been established in adolescents (12 to 17 years of age) for the treatment of major depressive disorder [*see Clinical Studies*]. Although maintenance efficacy in adolescent patients with Major Depressive Disorder has not been systematically evaluated, maintenance efficacy can be extrapolated from adult data along with comparisons of escitalopram pharmacokinetic parameters in adults and adolescent patients. Safety and effectiveness of Lexapro has not been established in pediatric patients less than 18 years of age with Generalized Anxiety Disorder. **Geriatric Use**-Approximately 6% of the 1144 patients receiving escitalopram in controlled trials of Lexapro in major depressive disorder and GAD were 60 years of age or older; elderly patients in these trials received daily doses of Lexapro between 10 and 20 mg. The number of elderly patients in these trials was insufficient to adequately assess for possible differential efficacy and safety measures on the basis of age. Nevertheless, greater sensitivity of some elderly individuals to effects of Lexapro cannot be ruled out. SSRIs and SNRIs, including Lexapro, have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event [*see Hyponatremia*]. In two pharmacokinetic studies, escitalopram half-life was increased by approximately 50% in elderly subjects as compared to young subjects and C_{max} was unchanged [*see Clinical Pharmacology*]. 10 mg/day is the recommended dose for elderly patients [*see Dosage and Administration*]. Of 4422 patients in clinical studies of racemic citalopram, 1357 were 60 and over, 1034 were 65 and over, and 457 were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but again, greater sensitivity of some elderly individuals cannot be ruled out.

DRUG ABUSE AND DEPENDENCE: Abuse and Dependence; Physical and Psychological Dependence-Animal studies suggest that the abuse liability of racemic citalopram is low. Lexapro has not been systematically studied in humans for its potential for abuse, tolerance, or physical dependence. The premarketing clinical experience with Lexapro did not reveal any drug-seeking behavior. However, these observations were not systematic and it is not possible to predict on the basis of this limited experience the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed. Consequently, physicians should carefully evaluate Lexapro patients for history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse (e.g., development of tolerance, incrementations of dose, drug-seeking behavior).

OVERDOSAGE: Human Experience-In clinical trials of escitalopram, there were reports of escitalopram overdose, including overdoses of up to 600 mg, with no associated fatalities. During the postmarketing evaluation of escitalopram, Lexapro overdoses involving overdoses of over 1000 mg have been reported. As with other SSRIs, a fatal outcome in a patient who has taken an overdose of escitalopram has been rarely reported. Symptoms most often accompanying escitalopram overdose, alone or in combination with other drugs and/or alcohol, included convulsions, coma, dizziness, hypotension, insomnia, nausea, vomiting, sinus tachycardia, somnolence, and ECG changes (including QT prolongation and very rare cases of torsade de pointes). Acute renal failure has been very rarely reported accompanying overdose. **Management of Overdose**-Establish and maintain an airway to ensure adequate ventilation and oxygenation. Gastric evacuation by lavage and use of activated charcoal should be considered. Careful observation and cardiac and vital sign monitoring are recommended, along with general symptomatic and supportive care. Due to the large volume of distribution of escitalopram, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. There are no specific antidotes for Lexapro. 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.

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Disorders Other Than Depression Pose Highest Dropout Risk

A new national survey of people who had attended college found some surprising patterns connecting mental disorders with the odds of completing school.

BY AARON LEVIN

The association between having a psychiatric diagnosis and failing to graduate from college might seem obvious, but an analysis of national survey data indicates a pattern of diagnoses that departs from the common wisdom.

Depression is generally seen as a widespread problem on college campuses, for example, but the new study found that people with bipolar I disorder, antisocial personality disorder, and three types of substance use disorders were all less likely to graduate from college than those with depression.

The study provided fresh evidence that "psychiatric factors play a significant role in college academic performance," wrote Justin Hunt, M.D., M.S., Daniel Eisenberg, Ph.D., and Amy Kilbourne, Ph.D., M.P.H., in the April *Psychiatric Services*. "[T]he benefits of prevention, detection, and treatment may therefore include higher graduation rates."

Prior research by others found that mental disorders in young people were associated with shortened school careers at every level from primary school to college, with the greatest problem coming at the high-school level.

"It's very expensive when a kid drops out of school," said Jerald Kay, M.D., professor and chair of psychiatry at the Boonshoft School of Medicine at Wright State University in Dayton, Ohio.

On a practical level, the college loses the revenue that accompanies a student, said Kay, a former chair of APA's Corresponding Committee on Mental Health on College and University Campuses. Society at large loses the added productivity contributed by a college graduate compared with someone who never earned a college degree. Most important, the former student loses out on the personal benefits of having a college degree, he noted.

"You can't be lulled into a sense of complacency by thinking that [not having a college degree] does not have a dramatic effect on a young person's life," said Kay in an interview.

Hunt and colleagues analyzed data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). The survey was conducted in 2001-2002 by the National Institute on Alcohol Abuse and Alcoholism and included 15,800 adults over age 21 who had entered college but had never graduated.

Questions on the NESARC covered lifetime diagnoses of six psychiatric disorders (mania/bipolar I disorder, major depression, panic disorder with agoraphobia, social anxiety disorder, generalized anxiety disorder, and antisocial personality disorder) and four substance use disorders (alcohol, marijuana, amphetamine, and cocaine abuse or dependence).

"These diagnoses were selected because they represent some of the most common diagnoses among adolescents and young adults, and their symptoms have plausible effects on academic success," said the researchers.

The study did not ask about other diagnoses common to young people such as attention-deficit/hyperactivity disorder, obsessive-compulsive disorder, and psychotic disorders.

Major depression, generalized anxiety, and social anxiety presented some initial associations with failure to graduate, but were not significant after sociodemographic factors influencing college completion (such as racial or ethnic background and geographic region) were accounted for.

In contrast, bipolar I disorder, antisocial personality disorder, and marijuana, amphetamine, and cocaine use disorders were all "significantly and positively associated with failure to graduate from college," they said.

Hunt and colleagues speculated on why bipolar I disorder might show a strong positive association with dropping out of college, while no such association was found with other serious conditions including major depression, generalized anxiety, or panic disorder with agoraphobia.

The general stress of college study, combined with drinking, poor sleep patterns, and the emotional ups and downs of interpersonal relationships might contribute to the development of bipolar disorder, they suggested.

One surprise to the researchers was the slightly negative and statistically insignificant association of alcohol use disorder with college completion. A previous study of mental disorders and educational attainment did find a significant role for alcohol abuse in limiting college careers.

Hunt and colleagues' finding that alcohol abuse did not contribute to college failure is also at odds with the experience of college health officials in the United States, said Kay. Heavy drinking is associated with a host of educational and personal problems, like missing classes, poorer schoolwork, increased unprotected sex, and trouble involving police.

"It's important not to underestimate the importance of alcohol use," Kay emphasized.

Why use of cocaine, marijuana, or amphetamines but not alcohol might contribute to poor college outcomes posed another question.

"In the college population, it may be difficult to sort out recreational drinking from true problem drinking with *DSM-IV* diagnostic criteria alone," the researchers said.

Disorders that did not show an association might have affected college students less because they created fewer problems for the students, said the authors. Perhaps the students with those conditions may simply be more resilient, or maybe some traits—such as anxiety—may actually push some students to work harder, they said.

Improved awareness and treatment may be having an effect, too, said Kay. "I think we've made a dent in the problem, and it may point to success in treating depression and anxiety on campus."

"Consequences of Receipt of a Psychiatric Diagnosis for Completion of College" is posted at <http://psychservices.psychiatryonline.org/cgi/content/full/61/4/399>. ■

Cynical Hostility Personality Trait Strongly Predicts Depressed Mood

A long-term study finds that people who score high for cynical hostility are five times more likely to have depressed mood almost two decades after an initial evaluation.

BY JOAN AREHART-TREICHEL

"A cynic is a man who, when he smells flowers, looks around for a coffin," the American satirist H.L. Mencken once wrote.

Whether true or not, it looks as if cynics have a predilection toward depression, a large prospective study conducted by European investigators has found.

The lead investigator was Hermann Nabi, Ph.D., an epidemiologist and research fellow at INSERM (the French National Institute of Health and Medical Research). Results were published in the March *Psychological Medicine*.

The study included 3,399 London civil servants aged 35 to 55. Subjects were evaluated for the personality trait of cynical hostility, which is characterized by cynicism, distrust, resentment, and suspicion.

A reliable, validated instrument called the Cook-Medley Hostility Scale was used for this analysis. Subjects were also evaluated for common mental disorders with the General Health Questionnaire; for health-related behaviors such as exercise, smoking, and alcohol consumption; for stressful life events; and for existence of social supports. Also, they were asked whether they were taking antidepressants. Several times during the following 19 years, they were again evaluated for stressful life events and social support.

Nineteen years later, that is, when they were between the ages of 54 and 74, subjects were evaluated for depressive mood as determined by the Center for Epidemiologic Studies Depression Scale. Nabi and his colleagues then looked to see whether there was a statistically significant link between possessing the personality trait of cynical hostility and having a depressed mood 19 years later.

There was. In fact, it was a dose-response one, with persons scoring in the highest quartile of cynical hostility being five times more likely to have a depressed mood 19 years later than persons scoring in the lowest quartile.

Moreover, these findings were attenuated only a little when some possibly confounding variables were considered, including sociodemographic factors, health-related behaviors at baseline, depression at baseline, use of antidepressants at baseline, and stressful life events and emotional support both at baseline and several times during the next 19 years.

Cynical hostility is "a long-term vulnerability factor for depressive mood," Nabi and his team concluded.

But why might this be? "The personality characteristic of cynical hostility is associated with increased interpersonal conflicts, lower social support, and more stressful life events," Nabi told *Psychiatric News*. "All these factors have been found to be associated with an increased likelihood of being depressed."

Their findings also have clinical implications, Nabi believes. "Since cynical hostility is a strong predictor of depressed mood over the long term, it could explain why some individuals are persistently depressed or resistant to depression treatment."

The study was funded by the European Science Foundation, United Kingdom Medical Research Council, Academy of Finland, British Heart Foundation, U.S. National Institutes of Health, U.S. Agency for Health Care Policy and Research, and the John D. and Catherine T. MacArthur Foundation.

An abstract of "Hostility and Depressive Mood: Results From the Whitehall II Prospective Cohort Study" can be accessed at <http://journals.cambridge.org/action/displayJournal?jid=PSM> by clicking on the March 2010 issue and then the article title. ■

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References: 1. Reisberg B, Doody R, Stöffler A, Schmitt F, Ferris S, Möbius HJ, for the Memantine Study Group. Memantine in moderate-to-severe Alzheimer's disease. *N Engl J Med.* 2003;348:1333-1341. **2.** Tariot PN, Farlow MR, Grossberg GT, Graham SM, McDonald S, Gergel I, for the Memantine Study Group. Memantine treatment in patients with moderate to severe Alzheimer disease already receiving donepezil: a randomized controlled trial. *JAMA.* 2004;291:317-324. **3.** Cummings JL, Schneider E, Tariot PN, Graham SM, for the Memantine MEM-MD-02 Study Group. Behavioral effects of memantine in Alzheimer disease patients receiving donepezil treatment. *Neurology.* 2006;67:57-63. **4.** Data on file. Forest Laboratories, Inc. **5.** NAMENDA® (memantine HCl) Prescribing Information. Forest Pharmaceuticals, Inc., St Louis, Mo. **6.** Wimo A, Winblad B, Stöffler A, Wirth Y, Möbius HJ. Resource utilisation and cost analysis of memantine in patients with moderate to severe Alzheimer's disease. *Pharmacoeconomics.* 2003;21:327-340. **7.** Winblad B, Poritis N. Memantine in severe dementia: results of the ³M-BEST Study (Benefit and efficacy in severely demented patients during treatment with memantine). *Int J Geriatr Psychiatry.* 1999;14:135-146.

Forest Pharmaceuticals, Inc.

For more details, please visit **www.namenda.com**.

Please see brief summary of Prescribing Information on the adjacent page.

62-1014307R R2 03/09

Namenda
memantine HCl ®

Tablets/Oral Solution
Rx Only

Brief Summary of Prescribing Information.

For complete details, please see full Prescribing Information for Namenda.

INDICATIONS AND USAGE
Namenda (memantine hydrochloride) is indicated for the treatment of moderate to severe dementia of the Alzheimer's type.

CONTRAINDICATIONS
Namenda (memantine hydrochloride) is contraindicated in patients with known hypersensitivity to memantine hydrochloride or to any excipients used in the formulation.

PRECAUTIONS
Information for Patients and Caregivers: Caregivers should be instructed in the recommended administration (twice per day for doses above 5 mg) and dose escalation (minimum interval of one week between dose increases).

Neurological Conditions
Seizures: Namenda has not been systematically evaluated in patients with a seizure disorder. In clinical trials of Namenda, seizures occurred in 0.2% of patients treated with Namenda and 0.5% of patients treated with placebo.

Genitourinary Conditions
Conditions that raise urine pH may decrease the urinary elimination of memantine resulting in increased plasma levels of memantine.

Special Populations
Hepatic Impairment
Namenda undergoes partial hepatic metabolism, with about 48% of administered dose excreted in urine as unchanged drug or as the sum of parent drug and the N-glucuronide conjugate (74%). No dosage adjustment is needed in patients with mild or moderate hepatic impairment. Namenda should be administered with caution to patients with severe hepatic impairment.

Renal Impairment
No dosage adjustment is needed in patients with mild or moderate renal impairment. A dosage reduction is recommended in patients with severe renal impairment (see CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION in Full Prescribing Information).

Drug-Drug Interactions
N-methyl-D-aspartate (NMDA) antagonists: The combined use of Namenda with other NMDA antagonists (amantadine, ketamine, and dextromethorphan) has not been systematically evaluated and such use should be approached with caution.

Effects of Namenda on substrates of microsomal enzymes: In vitro studies conducted with marker substrates of CYP450 enzymes (CYP1A2, -2A6, -2C9, -2D6, -2E1, -3A4) showed minimal inhibition of these enzymes by memantine. In addition, *in vitro* studies indicate that at concentrations exceeding those associated with efficacy, memantine does not induce the cytochrome P450 isoenzymes CYP1A2, CYP2C9, CYP2E1, and CYP3A4/5. No pharmacokinetic interactions with drugs metabolized by these enzymes are expected.

Effects of inhibitors and/or substrates of microsomal enzymes on Namenda: Memantine is predominantly renally eliminated, and drugs that are substrates and/or inhibitors of the CYP450 system are not expected to alter the metabolism of memantine.

Acetylcholinesterase (AChE) inhibitors: Coadministration of Namenda with the AChE inhibitor donepezil HCl did not affect the pharmacokinetics of either compound. In a 24-week controlled clinical study in patients with moderate to severe Alzheimer's disease, the adverse event profile observed with a combination of memantine and donepezil was similar to that of donepezil alone.

Drugs eliminated via renal mechanisms: Because memantine is eliminated in part by tubular secretion, coadministration of drugs that use the same renal cationic system including hydrochlorothiazide (HCTZ), triamterene (TA), metformin, cimetidine, ranitidine, quinidine, and nicotine, could potentially result in altered plasma levels of both agents. However, coadministration of Namenda and HCTZ/TA did not affect the bioavailability of either memantine or TA, and the bioavailability of HCTZ decreased by 20%. In addition, coadministration of memantine with the antihyperglycemic drug Glucovance® (glyburide and metformin HCl) did not affect the pharmacokinetics of memantine, metformin, and glyburide. Furthermore, memantine did not modify the serum glucose lowering effect of Glucovance®.

Drugs that make the urine alkaline: The clearance of memantine was reduced by about 80% under alkaline urine conditions at pH 8. Therefore, alterations of urine pH towards the alkaline condition may lead to an accumulation of the drug with a possible increase in adverse effects. Urine pH is altered by diet, drugs (e.g. carbonic anhydrase inhibitors, sodium bicarbonate), and clinical state of the patient (e.g. renal tubular acidosis or severe infections of the urinary tract). Hence, memantine should be used with caution under these conditions.

Carcinogenesis, Mutagenesis and Impairment of Fertility
There was no evidence of carcinogenicity in a 113-week oral study in mice at doses up to 40 mg/kg/day (10 times the maximum recommended human dose [MRHD] on a mg/m² basis). There was also no evidence of carcinogenicity in rats orally dosed at up to 40 mg/kg/day for 71 weeks followed by 20 mg/kg/day (20 and 10 times the MRHD on a mg/m² basis, respectively) through 128 weeks.

Memantine produced no evidence of genotoxic potential when evaluated in the *in vitro S. typhimurium* or *E. coli* reverse mutation assay, an *in vitro* chromosomal aberration test in human lymphocytes, an *in vivo* cytogenetics assay for chromosome damage in rats, and the *in vivo* mouse micronucleus assay. The results were equivocal in an *in vitro* gene mutation assay using Chinese hamster V79 cells.

No impairment of fertility or reproductive performance was seen in rats administered up to 18 mg/kg/day (9 times the MRHD on a mg/m² basis) orally from 14 days prior to mating through gestation and lactation in females, or for 60 days prior to mating in males.

Pregnancy
Pregnancy Category B: Memantine given orally to pregnant rats and pregnant rabbits during the period of organogenesis was not teratogenic up to the highest doses tested (18 mg/kg/day in rats and 30 mg/kg/day in rabbits, which are 9 and 30 times, respectively, the maximum recommended human dose [MRHD] on a mg/m² basis).

Slight maternal toxicity, decreased pup weights and an increased incidence of non-ossified cervical vertebrae were seen at an oral dose of 18 mg/kg/day in a study in which rats were given oral memantine beginning pre-mating and continuing through the postpartum period. Slight maternal toxicity and decreased pup weights were also seen at this dose in a study in which rats were treated from day 15 of gestation through the post-partum period. The no-effect dose for these effects was 6 mg/kg, which is 3 times the MRHD on a mg/m² basis.

There are no adequate and well-controlled studies of memantine in pregnant women. Memantine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
It is not known whether memantine is excreted in human breast milk. Because many drugs are excreted in human milk, caution should be exercised when memantine is administered to a nursing mother.

Pediatric Use
There are no adequate and well-controlled trials documenting the safety and efficacy of memantine in any illness occurring in children.

ADVERSE REACTIONS
The experience described in this section derives from studies in patients with Alzheimer's disease and vascular dementia.

Adverse Events Leading to Discontinuation: In placebo-controlled trials in which dementia patients received doses of Namenda up to 20 mg/day, the likelihood of discontinuation because of an adverse event was the same in the Namenda group as in the placebo group. No individual adverse event was associated with the discontinuation of treatment in 1% or more of Namenda-treated patients and at a rate greater than placebo.

Adverse Events Reported in Controlled Trials: The reported adverse events in Namenda (memantine hydrochloride) trials reflect experience gained under closely monitored conditions in a highly selected patient population. In actual practice or in other clinical trials, these frequency estimates may not apply, as the conditions of use, reporting behavior and the types of patients treated may differ. Table 1 lists treatment-emergent signs and symptoms that were reported in at least 2% of patients in placebo-controlled dementia trials and for which the rate of occurrence was greater for patients treated with Namenda than for those treated with placebo. No adverse event occurred at a frequency of at least 5% and twice the placebo rate.

Table 1: Adverse Events Reported in Controlled Clinical Trials in at Least 2% of Patients Receiving Namenda and at a Higher Frequency than Placebo-treated Patients

Body System Adverse Event	Placebo (N = 922) %	Namenda (N = 940) %
Body as a Whole		
Fatigue	1	2
Pain	1	3
Cardiovascular System		
Hypertension	2	4
Central and Peripheral Nervous System		
Dizziness	5	7
Headache	3	6
Gastrointestinal System		
Constipation	3	5
Vomiting	2	3
Musculoskeletal System		
Back pain	2	3
Psychiatric Disorders		
Confusion	5	6
Somnolence	2	3
Hallucination	2	3
Respiratory System		
Coughing	3	4
Dyspnea	1	2

Other adverse events occurring with an incidence of at least 2% in Namenda-treated patients but at a greater or equal rate on placebo were agitation, fall, inflicted injury, urinary incontinence, diarrhea, bronchitis, insomnia, urinary tract infection, influenza-like symptoms, abnormal gait, depression, upper respiratory tract infection, anxiety, peripheral edema, nausea, anorexia, and arthralgia.

The overall profile of adverse events and the incidence rates for individual adverse events in the subpopulation of patients with moderate to severe Alzheimer's disease were not different from the profile and incidence rates described above for the overall dementia population.

Vital Sign Changes: Namenda and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, diastolic blood pressure and weight) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. There were no clinically important changes in vital signs in patients treated with Namenda. A comparison of supine and standing vital sign measures for Namenda and placebo in elderly normal subjects indicated that Namenda treatment is not associated with orthostatic changes.

Laboratory Changes: Namenda and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Namenda treatment.

ECG Changes: Namenda and placebo groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in ECG parameters associated with Namenda treatment.

Other Adverse Events Observed During Clinical Trials
Namenda has been administered to approximately 1350 patients with dementia, of whom more than 1200 received the maximum recommended dose of 20 mg/day. Patients received Namenda treatment for periods of up to 884 days, with 862 patients receiving at least 24 weeks of treatment and 387 patients receiving 48 weeks or more of treatment.

Treatment emergent signs and symptoms that occurred during 8 controlled clinical trials and 4 open-label trials were recorded as adverse events by the clinical investigators using terminology of their own choosing. To provide an overall estimate of the proportion of individuals having similar types of events, the events were grouped into a smaller number of standardized categories using WHO terminology, and event frequencies were calculated across all studies.

All adverse events occurring in at least two patients are included, except for those already listed in Table 1, WHO terms too general to be informative, minor symptoms or events unlikely to be drug-caused, e.g., because they are common in the study population. Events are classified by body system and listed using the following definitions: frequent adverse events - those occurring in at least 1/100 patients; infrequent adverse events - those occurring in 1/100 to 1/1000 patients. These adverse events are not necessarily related to Namenda treatment and in most cases were observed at a similar frequency in placebo-treated patients in the controlled studies.

Body as a Whole: *Frequent:* syncope. *Infrequent:* hypothermia, allergic reaction.

Cardiovascular System: *Frequent:* cardiac failure. *Infrequent:* angina pectoris, bradycardia, myocardial infarction, thrombophlebitis, atrial fibrillation, hypotension, cardiac arrest, postural hypotension, pulmonary embolism, pulmonary edema.

Central and Peripheral Nervous System: *Frequent:* transient ischemic attack, cerebrovascular accident, vertigo, ataxia, hypokinesia. *Infrequent:* paresthesia, convulsions, extrapyramidal disorder, hypertonia, tremor, aphasia, hypoesthesia, abnormal coordination, hemiplegia, hyperkinesia, involuntary muscle contractions, stupor, cerebral hemorrhage, neuralgia, ptosis, neuropathy.

Gastrointestinal System: *Infrequent:* gastroenteritis, diverticulitis, gastrointestinal hemorrhage, melena, esophageal ulceration.

Hemic and Lymphatic Disorders: *Frequent:* anemia. *Infrequent:* leukopenia.

Metabolic and Nutritional Disorders: *Frequent:* increased alkaline phosphatase, decreased weight. *Infrequent:* dehydration, hyponatremia, aggravated diabetes mellitus.

Psychiatric Disorders: *Frequent:* aggressive reaction. *Infrequent:* delusion, personality disorder, emotional lability, nervousness, sleep disorder, libido increased, psychosis, amnesia, apathy, paranoic reaction, thinking abnormal, crying abnormal, appetite increased, paronia, delirium, depersonalization, necrosis, suicide attempt.

Respiratory System: *Frequent:* pneumonia. *Infrequent:* apnea, asthma, hemoptysis.

Skin and Appendages: *Frequent:* rash. *Infrequent:* skin ulceration, pruritus, cellulitis, eczema, dermatitis, erythematous rash, alopecia, urticaria.

Special Senses: *Frequent:* cataract, conjunctivitis. *Infrequent:* macula lutea degeneration, decreased visual acuity, decreased hearing, tinnitus, blepharitis, blurred vision, corneal opacity, glaucoma, conjunctival hemorrhage, eye pain, retinal hemorrhage, xerophthalmia, diplopia, abnormal lacrimation, myopia, retina detachment.

Urinary System: *Frequent:* frequent micturition. *Infrequent:* dysuria, hematuria, urinary retention.

Events Reported Subsequent to the Marketing of Namenda, both US and Ex-US
Although no causal relationship to memantine treatment has been found, the following adverse events have been reported to be temporally associated with memantine treatment and are not described elsewhere in labeling: aspiration pneumonia, asthenia, atrioventricular block, bone fracture, carpal tunnel syndrome, cerebral infarction, chest pain, cholelithiasis, claudication, colitis, deep venous thrombosis, depressed level of consciousness (including loss of consciousness and rare reports of coma), dyskinesia, dysphagia, encephalopathy, gastritis, gastroesophageal reflux, grand mal convulsions, intracranial hemorrhage, hepatitis (including increased ALT and AST and hepatic failure), hyperglycemia, hyperlipidemia, hypoglycemia, ileus, increased INR, impotence, lethargy, malaise, myoclonus, neuroleptic malignant syndrome, acute pancreatitis, Parkinsonism, acute renal failure (including increased creatinine and renal insufficiency), prolonged QT interval, restlessness, sepsis, Stevens-Johnson syndrome, suicidal ideation, sudden death, supraventricular tachycardia, tachycardia, tardive dyskinesia, thrombocytopenia, and hallucinations (both visual and auditory).

ANIMAL TOXICOLOGY
Memantine induced neuronal lesions (vacuolation and necrosis) in the multipolar and pyramidal cells in cortical layers III and IV of the posterior cingulate and retrosplenial neocortices in rats similar to those which are known to occur in rodents administered other NMDA receptor antagonists. Lesions were seen after a single dose of memantine, in a study in which rats were given daily oral doses of memantine for 14 days, the no-effect dose for neuronal necrosis was 6 times the maximum recommended human dose on a mg/m² basis. The potential for induction of central neuronal vacuolation and necrosis by NMDA receptor antagonists in humans is unknown.

DRUG ABUSE AND DEPENDENCE
Controlled Substance Class: Memantine HCl is not a controlled substance.

Physical and Psychological Dependence: Memantine HCl is a low to moderate affinity uncompetitive NMDA antagonist that did not produce any evidence of drug-seeking behavior or withdrawal symptoms upon discontinuation in 2,504 patients who participated in clinical trials at therapeutic doses. Post marketing data, outside the U.S., retrospectively collected, has provided no evidence of drug abuse or dependence.

OVERDOSAGE
Signs and symptoms associated with memantine overdosage in clinical trials and from worldwide marketing experience include agitation, confusion, ECG changes, loss of consciousness, psychosis, restlessness, slowed movement, somnolence, stupor, unsteady gait, visual hallucinations, vertigo, vomiting, and weakness. The largest known ingestion of memantine worldwide was 2.0 grams in a patient who took memantine in conjunction with unspecified antidiabetic medications. The patient experienced coma, diplopia, and agitation, but subsequently recovered.

Because strategies for the management of overdose are continually evolving, it is advisable to contact a poison control center to determine the latest recommendations for the management of an overdose of any drug. As in any cases of overdose, general supportive measures should be utilized, and treatment should be symptomatic. Elimination of memantine can be enhanced by acidification of urine.

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Rev. 04/07

COMPILED BY JUN YAN

Regulatory Briefs

• The Food and Drug Administration (FDA) Division of Drug Marketing, Advertising, and Communications (DDMAC) sent a warning letter to Takeda Pharmaceuticals concerning "false and misleading" promotional materials for the sleep medicine ***ramelteon***. The January 28 letter stated that a sell sheet for the drug made unsubstantiated claims for its superiority, omitted and minimized risks, and made a misleading claim. The sell sheet, a promotional brochure, claims that ramelteon has no abuse potential and implies that the drug has no toxicity compared with other sleep medications, which the FDA considers unsubstantiated and misleading.

The FDA warning letter to Takeda is posted at <www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM205265.pdf>.

• Eisai Medical Research Inc. was issued a warning letter on February 3 from the FDA's DDMAC for misleading TV advertisements for ***donepezil***. The advertisements, according to the FDA, overstated the drug's efficacy by depicting dramatic changes in simulated patients' behaviors before and after taking the Alzheimer's drug and implying that patients' functioning and cognition can return to normal with the medication. Such claims are unsubstantiated by clinical-trial results and are thus considered misleading. The company was asked to cease distributing the advertisement.

The FDA warning letter to Eisai is posted at <www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM201238.pdf>.

• During a March 15 meeting, experts on the FDA's Neurological Devices Advisory Committee were divided over whether Medtronic's ***deep brain stimulation device*** should be approved for treating severe epilepsy. The device was previously approved for treating Parkinson's disease and for compassionate use in patients with severe obsessive-compulsive disorder. In a randomized, double-blind clinical trial conducted with patients refractory to multiple antiepileptic drugs, the deep brain stimulation failed to show significant efficacy over sham stimulation in which the device was implanted but not turned on. The panel voted 7-5 to approve the device, which leaves the FDA with no clear recommendation for the device's approval or rejection.

• The FDA granted fast-track review status to a treatment intended for autism, according to an announcement by Curemark LLC in February. The treatment, known as ***CM-AT***, is an undisclosed proprietary formulation of enzymes developed by the company and is being tested in phase 3 clinical trials.

• The ***Physician Payments Sunshine Act of 2009*** was signed into law on March 23 as a part of the sweeping health care reform legislation. It requires all U.S. manufacturers of drugs, devices, biologics, and medical supplies to report payments to physicians and teaching hospitals that exceed $100 annually to the Department of Health and Human Services (HHS). Effective January 1, 2012, all manufacturers are required to begin recording the physician's name, address, and national provider identifier; the amount of payments; and the purpose of the payment. These data will be transferred to HHS annually, and HHS will then post the data on a public Web site.

Certain categories are exempt from this reporting requirement, including educational materials given to benefit patients, rebates and discounts, and dividend or investment interest paid through a publicly traded stock or mutual fund. However, physician ownership or investment interest in manufacturers and group-purchasing organizations is required to be disclosed. Physicians who are employees of a company are also exempt. Companies can delay reporting the names of physicians who are paid to conduct clinical trials on developing new drugs or products for four years or until the product is approved for marketing, whichever comes first.

The text of this law is posted at <www.prescriptionproject.org/tools/sunshine_docs/files/Sunshine_Leg_Language.pdf>.

Industry Briefs

• A long-acting formulation of ***buprenorphine*** is being tested in a randomized, controlled, phase 3 clinical trial, its developer, Titan Pharmaceuticals, announced on March 30. This formulation, known as Probuphine, is a subcutaneous injection that purportedly delivers a continuous, therapeutic level of buprenorphine for six months with one administration. In this phase 3 trial, two groups of patients are being given the long-acting buprenorphine product or placebo in a double-blind manner and followed for 24 weeks. In addition, a second comparison group will receive Suboxone sublingual tablets in an open-label fashion for the same duration.

• The FDA approved low-dose formulations of the tricyclic antidepressant ***doxepin,*** at 3 mg and 6 mg, for treatment of transient or chronic insomnia due to sleep-maintenance difficulty, according to a March 18 announcement by Somaxon Pharmaceuticals. The effect of doxepin on sleep maintenance is believed to be derived from its antagonism of the histamine-H_1 receptor. Unlike other insomnia medications, doxepin is not a controlled substance.

• A drug candidate in late-stage clinical development for treating Alzheimer's disease failed two phase 3 trials, Pfizer and Medivation Inc. announced March 3. In the randomized, double-blind, placebo-controlled clinical trials, ***dimebon*** (also known as ***latrepirdine***) did not meet the primary or secondary endpoints in nearly 600 patients with mild to moderate Alzheimer's after six months of treatment. Outcome endpoints included cognitive function, measured by the Alzheimer's Assessment Scale–cognition subscale (ADAS-cog); global functioning, based on the Clinician's Interview-Based Impression of Change Plus Caregiver Input (CIBIC-plus); and activities of daily living, measured by the Alzheimer's Cooperative Study Activities of Daily Living Scale (ADCS-ADL). Dimebon was tested in two dosages, 5 mg or 20 mg three times daily, but neither dosage showed significant difference from placebo.

These results are a major disappointment for the two companies that are co-developing the drug, which showed some promise in phase 2 trials. Four other phase 3 clinical trials are still ongoing.

• Several phase 3 clinical trials will be conducted to test the efficacy and tolerability of two antidepressant candidate drugs being jointly developed by Lundbeck and Takeda, the two companies announced on March 3. Of the two investigational drugs, ***Lu AA21004*** is an antagonist of the serotonin 5-HT_3, 5-HT_7, and $5HT_{1B}$ receptors and an agonist of the 5-HT_{1A} receptor. It also inhibits serotonin reuptake. ***Lu AA24530*** inhibits the reuptake of multiple monoamines and inhibits the $5HT_3$ and 5-HT_{2C} receptors.

Lu AA21004 is currently in phase 3 development for treating moderate to severe depression, and data have shown "encouraging results," according to the companies' announcement. Lu AA24530 has passed phase 2 development and been deemed favorable for phase 3 trials, which are scheduled to begin this year.

• In January and March, Allon Therapeutics released promising results from clinical trials of its investigational drug ***davunetide,*** which is being studied for treatment of schizophrenia, amnestic mild cognitive impairment, and frontotemporal dementia. A phase 2a trial suggested that treatment with davunetide was associated with significantly increased levels of N-acetyl aspartate in the dorsolateral prefrontal cortex, a biomarker whose level is decreased in patients with schizophrenia and patients with brain injuries and dementia. A phase 1 trial validated the tolerability and pharmacokinetics of an intranasal formulation of the drug.

Davunetide, a molecule derived from an endogenous protein called activity-dependent neuroprotective protein, may improve cognitive function in a range of neurodegenerative diseases. The drug has already received orphan-drug designation from both the FDA and European regulatory authority for treatment of progressive supranuclear palsy, a neurodegenerative brain disease.

• AstraZeneca, the maker of quetiapine, will discontinue its research programs in schizophrenia, bipolar disorder, and depression as part of its corporate restructuring, according to a March 2 report by Reuters. Other diseases, including acid-reflux disease and thrombosis, will also be cut from its research portfolio as the company plans to eliminate 1,800 global research staff. ■

Allied Groups to Meet at Annual Meeting

The Indo-American Psychiatric Association and the American Academy of Psychoanalysis and Dynamic Psychiatry are among the organizations that will be meeting in conjunction with APA's 2010 annual meeting in New Orleans later this month.

• The 31st annual meeting and banquet of the Indo-American Psychiatric Association will be held on Sunday, May 23, at the Loews Hotel Conference Center at 300 Poydras Street.

The scientific portion of the meeting, which begins at 1:30 p.m., will feature lectures by Nutan Vaidya, M.D., a professor and chair of the Department of Psychiatry and Behavioral Sciences at the Rosalind Franklin University of Medicine and Science, Chicago Medical School; Razia Kosi, L.C.S.W.-C., a cultural proficiency specialist in the Howard County Public Schools in Maryland.; Anand Kumar, M.D., a professor and chair of the Department of Psychiatry at the University of Illinois at Chicago; and Neha Navsari, Ph.D., a therapist and researcher in the Early Emotional Development Program at Washington University School of Medicine.

The business meeting and banquet will be held from 6:30 p.m. to 11 p.m. The evening begins with a reception at 6:30 p.m., with the president's address and awards ceremony at 8 p.m. Dinner and dancing will follow.

Registration is required; the cost of the banquet is $30. More information is available from Rudra Prakash, M.D., at (615) 364-7406 or rudraprakash@comcast.net.

• "Trauma, Resiliency and Psychodynamic Psychiatry" is the theme of the 54th annual meeting of the American Academy of Psychoanalysis and Dynamic Psychiatry. The meeting will be held May 20 to 22 at the Astor Crowne Plaza at 739 Canal Street.

The American Academy of Psychoanalysis and Dynamic Psychiatry works closely with APA, translating the applicability of the concepts of psychoanalysis and psychodynamics into the fields of neurobiology, psychopharmacology, cross-cultural psychiatry, creativity and the arts, and related disciplines. Under the leadership of Eugenio Rothe, M.D., and co-chairs David Lopez, M.D., and Juan Raul Condemarin, M.D., this meeting draws upon regional, national, and international speakers to pursue this goal.

The meeting will feature presentations by Glen Gabbard, M.D., Richard Friedman, M.D., Howard Osofsky, M.D., Charles Zeanah, M.D., Marty Drell, M.D., Clarice Kestenbaum, M.D., Sheila Hafter-Gray, M.D., and Richard Chessick, M.D.

More information about the meeting is posted at <http://aapdp.org/index.php/meetings/meeting_details/54th_annual_meeting_-_new_orleans_la/>. ■

Cajun Country Journey Reveals Region's Unique Culture, History

One need not travel far from New Orleans to find the mangrove trees, Spanish moss, and languid bayous that distinguish the area and remain protected through Jean Lafitte National Historical Park and Preserve.

BY EVE BENDER

Credit: National Park Service

Visitors walking along the marsh trail, which rises above the swamps, are treated to spectacular views of the marsh wildlife in the Barataria Preserve.

The man for whom Jean Lafitte National Historical Park and Preserve was named when it was established in 1978 is as mysterious as the murky and vast swamplands that characterize one of its six sites, the Barataria Preserve.

Known by some as the "Gentleman Pirate of New Orleans" and others as the "Terror of the Gulf," Lafitte preferred to be known as a privateer and not a pirate—he never plundered an American ship—yet he organized a crew of fisherman to smuggle goods into the Mississippi Delta region, including linens, furniture, spices, and trinkets, during the early 1800s.

At the time, the delta was abundant in wildlife. To this day, much of the area's natural beauty and cultural traditions have been preserved through the national park's six sites.

The **Barataria Preserve** is located in Marrero, about a half hour south of New Orleans, and borders the Bayou des Families. The preserve protects 20,000 acres of bayous, swamps, marshes, and dense forests of cypress and mangrove trees. Natural inhabitants of the preserve include alligators, armadillos, and more than 300 species of birds. Visitors can explore the preserve on land by traversing the preserve's many trails and boardwalks or the waterways via canoes and kayaks.

The preserve's visitor center features exhibits about Louisiana's wetlands and the humans and animals who have inhabited the area for centuries, and there are ranger-guided walks daily at 10 a.m. and 2 p.m.

Just six miles down river from New Orleans in Chalmette is the **Chalmette Battlefield and National Cemetery**, site of the 1815 Battle of New Orleans. The cemetery is the final resting place for more than 15,000 troops who fought in the Civil War, the Spanish-American War, World Wars I and II, and the Vietnam War.

On the grounds of the battlefield stands the Chalmette Monument, which pays tribute to General Andrew Jackson and the men under his command in the Battle of New Orleans.

The historic Malus-Beauregard House, built in the 1830s and named for its first and last owners, also stands on the battlefield grounds. The mansion is a stately example of French architecture and served as the country home for a number of wealthy families in the 19th century.

At the **French Quarter Visitor Center**, located on Decatur Street in the heart of the French Quarter, visitors can learn about the history of the city. Each day, park rangers offer a free walking tour through the French Quarter at 9:30 a.m. The rangers distribute 25 free tickets beginning at 9 a.m., and tours last about an hour.

People who want to strike out on their own can stop by the visitor's center and pick up a map of a self-guided walking tour and a guide of historic homes and museums in the French Quarter.

Three of the park's six sites are dedicated to educating the public about Cajun culture and history.

The **Acadian Cultural Center** features educational ranger programs, films, exhibits, storytelling, dance, and food to inform visitors about the traditions of the Acadians, or Cajuns, who have inhabited the prairies, bayous, and marshes of Southern Louisiana for centuries. The center is located in Lafayette, about 25 minutes south of New Orleans by car. Each day at 2:45 p.m., rangers give free talks on the history and culture of the area.

Saturdays are a good day to visit the **Prairie Acadian Cultural Center** in Eunice. On exhibit are old photographs and artifacts of Cajun people over the years. On Saturdays at 3 p.m., the center offers free Cajun music and dancing as a zydeco band performs. There are also free cooking demonstrations each Saturday at 4 p.m. in which rangers and volunteers share their recipes for seafood gumbo and etoufee, for instance.

The public can also learn more about Cajun history and culture at the **Wetlands Acadian Cultural Center** in Thibodaux, located about 45 minutes west of New Orleans. Exhibits showcase Cajun furniture and clothing. Mondays at 5:30 p.m., there is a free delta-music jam at which visitors can sit in on blues, zydeco, country, gospel, jazz, and Cajun performances.

Information about the six sites of the Jean Lafitte National Park and Preserve, including hours of operation and phone numbers, is posted at <www.nps.gov/jela/index.htm>. Admission to all sites is free. ■

Interested in College MH?

APA members who are working or interested in college mental health are invited to attend the meeting of APA's College Mental Health Caucus on Tuesday, May 25, from 9 a.m. to 11 a.m. in the Burgundy Room on the first floor of the Hilton New Orleans Riverside hotel.

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REGISTER NOW FOR THE MEETING!

There are two easy ways to register in advance for APA's 2010 annual meeting and courses. Forms to register by mail or fax can be accessed at APA's Web site at <www.psych.org/MainMenu/EducationCareerDevelopment/Meetings/AnnualMeeting.aspx> under "Meeting Registration." Faxed and mailed forms are assessed a $10 administrative fee.

FAX REGISTRATION FORM

Fax your completed registration form with credit card information to (703) 907-1097.

MAIL REGISTRATION FORM

Mail your completed registration form and payment by credit card or check made payable to APA to APA Annual Meeting, Department 235, Washington, D.C. 20055-0235.

During the meeting, you can register on site at the Morial Convention Center. For registration dates and times, see page 2.

APA Lifers to Host Special Events at Meeting

The APA Lifers will hold a series of events during APA's 2010 annual meeting in New Orleans. The group's mission is to support APA and its members who have achieved life member, life fellow, and distinguished life fellow status.

These members work with APA in furthering its work to benefit patients and advancing the future of psychiatric research and services. In doing so, the Lifers engage in related charitable, educational, and social endeavors in psychiatry and bring into closer fellowship the members who have reached life status within APA.

Here is the schedule of the Lifers' events:

Sunday, May 23
9 a.m.-10:30 a.m.
Workshop: From Narrative and Theory to Evidence-Based Support for Psychiatrists Working Under Extreme Stress, led by Sheila Hafter Gray, M.D., APA Lifers president
Room 237, Morial Convention Center

Tuesday, May 25
7:30 a.m.-9 a.m.
Lifers Business Meeting/Educational Forum
Bell Chase Room, Third Floor, Hilton New Orleans Riverside hotel

7 p.m.-9 p.m.
Lifers reception and presentation of the Harold E. Berson, M.D., Lifers Award to Edward Hanin, M.D.
Marlbourough Room B, Second Floor, Hilton New Orleans Riverside hotel ■

Doping and Athletics

Given the big stakes in scholastic and professional athletics, it's not surprising that athletes succumb to the temptation or pressure to take performance-enhancing drugs. And sometimes athletes need to take substances that are banned for medical reasons. These are just some of the issues and problems that will be discussed in the symposium "Doping and the Athlete" at APA's 2010 annual meeting.

The symposium, which will be held Saturday, May 22, at 1 p.m., will be led by Antonia Baum, M.D. Topics include the history of doping in athletics and the anti-doping movement, a guide to the therapeutic-use exemption for psychiatrists treating athletes with medications on the banned-substance list and how to make the case to get such an exemption, the role of the U.S. Anti-Doping Agency in the therapeutic-exemption process, doping-control efforts in collegiate athletics from the NCAA perspective, and the ethics of doping in athletics. Questions will be taken from the audience at the end of the session. ■

MBHOs

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The government will issue its brief this month, and a decision is expected before the July 1 effective date of the parity regulations, Muszynski told *Psychiatric News.*

In response to a "request for information" issued last summer by the Department of Health and Human Services, APA argued for a stringent interpretation of the parity bill—one that views parity as "not just about equality of coverage, but equality of access to care and equality in how providers are treated relative to other providers," as Muszynski told *Psychiatric News* at the time *(Psychiatric News*, June 19, 2009).

The government's final interim rule, issued on February 2, was largely in line with APA's interpretation, and it is essentially that interpretation that is at the heart of the dispute: can MBHOs impose certain kinds of management strategies not imposed on medical-surgical services and still comply with the parity law?

The MBHOs state in their suit that they can—indeed, that those strategies are essential to providing coverage that is comparable to medical-surgical services. But APA and other groups in the Coalition for Parity Implementation are urging the court to uphold the government's rule and to proceed with the July 1 implementation of parity.

"APA has had a long-term commitment to parity, and it took many years and many battles to make sure it happened," said Robert Cabaj, M.D., chair of APA's Council on Advocacy and Government Relations. "I believe it would be to the detriment of patients if there were further delays in implementing parity."

Management Should Be Comparable

The suit revolves around substantive issues regarding the management of mental health benefits under parity and one procedural complaint about the process the government used in issuing its final interim rule (see box; a report on the rule appeared in the March 5 *Psychiatric News).*

The substantive issues relate to two items spelled out in the government's interim final rule—one that requires a single deductible for both mental health and other medical conditions and one that prohibits "nonquantitative" treatment limitations.

Nonquantitative treatment limitations (NQTLs) are distinct from quantitative treatment limitations that can be measured numerically—such as annual and lifetime dollar limits and limits on office visits per year—and refer to a range of practices that MBHOs have used to manage behavioral health care costs.

These include medical management standards, prescription drug formulary design, standards for provider admission to networks, fail-first policies or step-therapy protocols, and conditioning benefits on completion of a course of treatment.

Such practices are prohibited under the government's interpretation if they are not applied comparably to medical-surgical services.

"It's clear enough what the law is referring to when it speaks of quantitative treatment limits," Muszynski said. "The debate centers around what Congress meant about 'other similar' limitations. Our legal analysis of what was intended by 'other similar treatment limitations' included such things as medication management, step therapy, or other practices that were not equivalent to the medical-surgical side.

"The regulations don't say—and we are not saying—that they can't manage the benefit," he continued. "But we say you can't manage the benefit in a way that is not comparable to medical-surgical services."

In its suit, the MBHOs insist that the nonquantitative treatment limitations are essential to managing behavioral health care costs and maintaining equality of coverage.

"For example, precertification [and] preauthorization for outpatient care are critical tools to ensure that plan members are receiving the behavioral health care services they need from the most appropriate level of provider and in the most appropriate setting," the MBHOs state in their suit. "[T]he nonquantitative treatment limitation requirements could result in these tools being stripped away merely because there is oftentimes no need for preauthorization in the medical-surgical context."

The second contention by MBHOs concerns the government's rule requiring one deductible for both "physical and mental health" conditions. APA, in its comments to the government last summer, argued for the single deductible.

In the interim final rule, the government conceded that the statutory language around whether plans should have a single or two separate deductibles is not clear and could support either interpretation, and that cost implications for MBHOs of a unified deductible were unclear. But the interim final rule states that the government chose to require the single deductible "because this position is more consistent with the policy goals that led to the enactment" of the parity bill.

APA Medical Director James H. Scully Jr., M.D., argues that no plan imposes two separate deductibles for, say, diabetes and cancer care. "Why should there be separate deductibles for psychiatric care and other medical care?" he remarked to *Psychiatric News.* "In the interest of the patient, general medical and psychiatric care should be better integrated."

But the MBHOs claim in their suit that the unified deductible will result in cost increases and serve as a barrier to care for lower-income individuals. "[T]he single deductible inevitably will be higher than the stand-alone behavioral health deductible, which in many group health plans is lower than the medical deductible."

MBHOs Face New Challenges

Colleen Barry, Ph.D., a health policy researcher at Yale University who has studied the effects of parity, said that the government's rule presents an unprecedented challenge to the behavioral carveout industry—and with regard to the rules around NQTLs, one that was not expected.

"It's fair to say that the plans and employers were not expecting this broad an interpretation of the law," Barry told *Psychiatric News.* "The carveouts are facing a substantial burden given that the requirements are far reaching and that the carveouts are not well set up to mirror how plan management occurs on the medical-surgical side. It's clearly not without cost for the industry to comply with these regulations. It's also important to keep in mind that this is the first real regulation that the carveout industry has had to contend with other than HIPAA."

She noted as well that in studies showing that parity did not add significantly to overall costs for health plans under the Federal Employees Health Benefits Program, the health plans were allowed broad leeway in managing mental health benefits.

With regard to the unified deductible, Barry suggested that the government's ruling was somewhat less surprising than the ruling on NQTLs. She noted that since mental health comprises just 2 percent to 5 percent of total health plan costs, establishing a separate deductible could result in a disproportionately high cost burden on individuals seeking care for mental health conditions.

Are MBHOs overreacting or do the new rules truly threaten their business?

"I don't think the regulations threaten the survival of the industry, but I do think it will take some work for them to figure out how to comply," Barry said. "The industry hasn't had to contend with this type of regulation before, and so this is a big change. It could also put some pressure on employers to not carve out and to provide an integrated benefit." ■

MBHOs Claim Government Bypassed Right to Comment

Managed behavioral health care organizations, in their suit against the government's interpretation of the new parity law, are alleging that the government bypassed due process by issuing an interim final rule implementing the law.

The plaintiffs claim the government missed its own deadline of October 1, 2009, for issuing a "proposed rule for comment" and instead issued the interim final rule in February with the expectation that employers and health plans would be in compliance by July 1. The plaintiffs also claim they were denied the chance to comment on substantive issues that were included as regulations in the interim final rule (see article beginning on page 1).

"The absence of a true and complete notice and comment period resulted in confusing, flawed, and untested requirements," the plaintiffs state in their suit.

Irvin "Sam" Muszynski, J.D., director of APA's Office of Healthcare Systems and Financing, said that the Department of Health and Human Services did issue a "request for information" (RFI) in April 2009 to which APA and many other groups—including the managed behavioral health care industry—provided voluminous documentation.

Muszynski emphasized, for instance, that Magellan Health Services submitted comments to the wDepartment of Health and Human Services at the time of the RFI that address all of the issues the MBHOs are now citing as grievances in the interim final rule, including treatment limitations and the single deductible.

He called their complaint specious and said, "There is no new information they could have provided to the government that they didn't already provide in the request for information."

Pamela Greenberg, M.P.P., executive director of the Association for Behavioral Health and Wellness—which represents behavioral health care organizations but is not a party to the suit—said there was nothing in the RFI about nonquantitative treatment limits (NQTLs).

"Therefore, comments submitted did not reflect concerns/implications on this topic," she told *Psychiatric News.* "As a result the regulators did not have a full sense for the impact the NQTLs would have."

But a 14-page response from Magellan Health Services to the government's RFI reveals that the company did specifically address the issue of treatment limitations, arguing that nonquantiative treatment limits were not "similar" to the limits proscribed by the parity law, and that therefore the law does not apply to them.

"The regulations should clarify that the term 'other similar limits on the scope or duration of treatment' includes only those elements of a plan design which limit the treatment in terms of time, frequency, or duration," Magellan stated. "We do not believe it was the intent of the legislation to include, nor does the actual language support inclusion of, nonnumerical or nonquantifiable limits. . . . "

The interim final rule and Magellan's comments are posted at <www.regulations.gov/search/Regs/home.html#documentDetail?R=09000064809c321d>.

Register to Receive Drug Alerts Online

APA has worked with the FDA, AMA, state medical societies, and liability carriers to bring a new service—the Health Care Notification Network (HCNN)—to APA members. The HCNN, which is a private network for physicians and health care professionals, provides secure online delivery of news about drug and medical-device recalls and patient-safety alerts, replacing the current paper process that is both slow and prone to error.

These are among other HCNN features:

- The HCNN is free to physicians and their staff members.
- A copy of alerts can be sent automatically to practice administrators and added to their physician account.
- Privacy is protected by the not-for-profit board that governs the HCNN.
- The HCNN does no advertising or selling.
- Recipients can opt out at any time.

Alerts sent through the HCNN are paid for by manufacturers who use the network for alert delivery.

APA members may enroll online at <www.hcnn.net/registration/apa/registration.aspx>. Additional information is available at <www.hcnn.net> or (866) 925-5155.

Oregon

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lar concern of the governor's was the lack of public hearings on legislation that had been crafted during a short, special legislative session in February.

"I am concerned that SB 1046 as written creates serious policy and regulatory conflicts," Kulongoski wrote in a letter to Oregon Secretary of State Kate Brown alerting her to the veto. "Furthermore, I believe that a policy change of this significance requires more safeguards, further study, and greater public input than was provided during the February special session. . . . I have a serious concern as to whether the Special Session in February provided opportunity for citizens and interested stakeholders to be adequately involved in the development of these proposed major policy changes.

"The public give-and-take is critical to crafting and amending legislation by allowing all interested parties to be involved in the development of public policy."

John McCulley, executive director of the Oregon Psychiatric Association (OPA), said the governor had acted with courage in the face of enormous pressure from advocates for the bill.

Those advocates had touted the bill as a solution to problems with access to mental health care in the state. "On average there are less than four psychiatrists per 100,000 residents in rural parts of our country," Oregon Sen. Monnes Anderson commented in remarks made on behalf of the bill in the legislature. "That means the majority of mental health patients are getting treated by nonpsychiatric physicians. We do not have enough psychiatrists, which has left it to primary care providers to do diagnosis and prescribing for mental health patients."

In the letter announcing the veto, Kulongoski urged legislators to initiate in the next legislative session "a pilot program that would generate data on which to inform and guide solutions that give greater access to broader mental and physical health care."

McCulley told *Psychiatric News* that the issue was very likely to surface again. He noted, for instance, that should a special legislative session be required this year to address the state's fiscal constraints, legislators could override the governor's veto with a two-thirds majority in both the House and the Senate.

McCulley said that OPA was "reasonably confident" that the veto would not be overriden in the event of a special legislative session—20 of the Oregon Senate's 30 members would need to vote for an override, and 11 had voted against the bill originally. Forty of the State House of Representative's 60 members would also need to approve an override.

If approved, Oregon SB 1046 would have established within the Oregon Medical Board the seven-member Committee on Prescribing Psychologists charged with making recommendations to the board on "educational requirements, clinical training requirements, standards, examinations, and continuing education for prescribing psychologists." The committee would also have been charged with making recommendations to the board regarding the formulary for psychologist prescribing and annual formulary revisions.

A number of organizations—APA, the AMA, the Oregon Medical Association, and the Oregon Council of Child and Adolescent Psychiatry, among others—had weighed in against the bill. APA Medical Director James H. Scully Jr., M.D., in a letter to Kulongoski, said the bill "puts patients' lives at risk by creating a dangerous, substandard level of care."

McCulley said a new version of psychologist prescribing—possibly involving a physician-assistant model in which physicians would have supervisory authority over prescribing psychologists—is liable to return in the next legislative session.

"Another possibility is to step back and take an overall look at access-to-service issues in the state," he told *Psychiatric News*. "There is a need for more therapy services throughout the state, so it's an issue that's bigger than psychologist prescribing. So legislators may choose to look more broadly at what we could do to improve access to care."

In the meantime, McCulley expressed gratitude to APA and other district branches for their support, as well as that of the AMA and other organizations. He also cited the support of individual pharmacists, nurse practitioners, and psychologists who opposed the prescribing bill.

"There was strong support for a veto from a broad spectrum of the health care and consumer communities" McCulley said. "From an organizational standpoint, it was gratifying to see the number of different people and organizations that supported us." ■

education & training

Military

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don't complete their mission. So if they say they don't want to go back, it's a red flag."

Mental health services in the field can be provided at different levels by psychiatrists, psychologists, social workers, chaplains, and trained enlisted personnel.

Sometimes "care" is much less formal, said Yarvis. After-action debriefings by unit leaders serve partly to gather information and partly to vent the emotions generated by a firefight or patrol. "That's when you bring in the social worker or the chaplain, if needed," he said.

In nonmilitary settings, practitioners should establish if their patients have a military connection, said Yarvis. Either they or a member of their family may be in the Armed Forces and may be facing the stresses of military life or trying to cope with its effects.

"Family members include parents, spouses, siblings, grandparents," he said. "Any of them may be affected by the experience of their soldier."

The more inclusive phrase "service member" might even be a better choice than soldier or even veteran, said another speaker, Harold Kudler, M.D., mental health coordinator for the Veterans Integrated Service Network, Number 6, and an associate clinical professor of psychiatry at Duke University. Also, therapists should ask women patients about combat duty, since many have experienced it in Iraq or Afghanistan, he said.

U.S. Army veteran Lorie Morris, Psy.D., now a psychologist at the Baltimore VA, added that therapists should ask patients which military branch they served in, as well as whether their unit had good leadership and support. "Start by asking, 'What was it like where you were stationed?' "

Yarvis has one advantage over civilian and many military therapists: he is a former Armored Corps officer who later earned degrees in social work. In Iraq, he was embedded and went out on patrol with the soldiers.

"You have to be with them to build trust," he said. "I'm a soldier first, an officer second, and a social worker third."

For civilian practitioners, trust building may have to come secondhand, but can be learned just as with any other cultural competency.

To be able to discuss and understand patients' military experiences, a clinician with no military background must find a way to bridge the cultural gap and make patients feel safe to talk about what are often traumatic, even horrific, incidents, he said.

Asking if a soldier has killed someone is probably the worst possible opening, said Yarvis.

"Maybe the best way is to ask what your expectations were before you went in," he said. "What was your job? Were you adequately trained for what you found during deployment?

"Get beyond the 'what-if?' stuff surrounding a specific incident," he told listeners. "And as with any case where you need help, request supervision from people who have more experience with this population."

The strains on troops and their families of the last eight years of fighting have been well documented. So has the need for mental health services for many of those who have returned from combat. That need could be filled by civilian mental health practitioners—provided they have a sufficient understanding of military culture. ■

government news

Workforce

continued from page 4

would leave any needed spending reductions to come from payments to physicians and other health professionals. This situation is expected to complicate the issue of pending physician reimbursment cuts under a Medicare payment structure that was established long before the new law and left unaddressed by health care reform.

Citing its excessive costs, Democratic leaders in Congress dropped from the final health care legislation a fix to the Medicare physician payment system, which is slated to steeply cut physician reimbursements.

However, APA President Alan Schatzberg, M.D., described the unaddressed Medicare payment formula and the 21 percent cut it is threatening to impose as one of the major outstanding issues in federal health policy for physicians.

(At press time, Congress voted to delay the implementation of the cut until June 1, and later that day President Obama signed into law legislation that contained that postponement.)

More information on the new law's impact on psychiatrists is posted at <http://archive.constantcontact.com/fs091/1101795608829/archive/1103249925487.html>. ■

clinical & research news

BPD

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takes some enormous stressor to push you back."

Joel Paris, M.D., an expert in BPD, reviewed the study for *Psychiatric News*. He said that it confirms and extends findings from the Collaborative Longitudinal Personality Disorders Study and the McLean Study of Adult Development. This study found that while symptomatic improvement is sufficient for many patients to stop meeting criteria for the disorder—such as no longer cutting themselves or overdosing—functional improvement is much slower.

"The study suggests that while BPD is by no means incurable, many patients continue to function at a low level for years," Paris said. "So what are the clinical implications? On the one hand, when we thought that BPD was a life sentence, we avoided treating patients who can in fact be helped. And some people do make a full recovery, going on to live normal lives. On the other hand, other cases are more chronic. If we become too optimistic, we may mislead our patients into expecting the impossible and not provide the supportive and rehabilitative services they need."

"Time to Attainment of Recovery From Borderline Personality Disorder and Stability of Recovery: A 10-Year Prospective Follow-Up Study" is posted at <http://ajp.psychiatryonline.org/pap.dtl>. ■

Sleep

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and only three name OSA, according to Allan Pack, M.B.Ch.B., Ph.D., a professor of medicine and chief of sleep medicine at the University of Pennsylvania School of Medicine.

Most states call for physicians to voluntarily report patients with medical conditions that may affect driving performance. While it is difficult to define who actually is at risk, Pack said, physicians need to warn patients who may be at risk and tell those who have had fall-asleep crashes to stop driving until assessed and effectively treated. CPAP therapy reduces OSA patients' crash risk.

People with OSA for whom CPAP has been prescribed need to use the device four or more hours per night to gain significant clinical benefits. Education, support, and counseling improve CPAP adherence.

"People with OSA need follow-up. This isn't unique in OSA. It's true of any chronic illness," Gregory Belenky, M.D., a research professor of psychiatry and director of sleep and performance research at Washington State University, told *Psychiatric News*.

"Psychiatrists are attuned to encouraging patients to stick with treatment," he noted. "They are used to working with patients' families, using behavioral interventions as well as medications, and adjusting therapy as necessary to improve outcomes," all essential in treating people with OSA, Belenky said. Consultation-liaison psychiatry, he predicted, will expand its role in sleep medicine. ■

ECT Devices

I realize that the article "ECT Device Reclassification Raises Access Concerns" in the January 1 issue relates to the device rather than to ECT itself. However, it is interesting to note that after paying a premium of twice my base malpractice insurance coverage for many years because I administer ECT, my malpractice insurance company abolished this extra premium entirely here in Massachusetts. Its actuaries apparently determined that ECT is no more dangerous than psychotherapy. I see this as stronger evidence for ECT as a treatment option than any clinical trial could provide, in light of the well-known suspicious attitude of all insurance companies.

CLIVE DALBY, M.D.
Methuen, Mass.

Suicide Rates in Military

In his letter in the February 5 issue, Dr. Wayne Weisner gave invaluable comments on military psychiatry from the time of the Korean War. But the issue, I fear, is not that simple. Suicide rates in the military began to rise well before the commencement of the wars in Afghanistan and Iraq.

I was chief of psychiatry at the hospital at Fort Benning, Ga., from 1995 to 1998. During the first year, there were seven suicides among active-duty personnel. With strong command interest and intense suicide-awareness training, that number was reduced in the following two years. Nevertheless, the consensus among commanders and medical staff throughout the Army was that if such training slacked off, the suicide rate would rise again. Our assessment then was that most of the suicides were, sadly, more closely associated with cluster B character traits than with anything else. A few were murder-suicides. The increasing trend was, in turn, felt to be a reflection of evolving character traits in the general population.

In any event, a military draft is not likely to resolve the issue of repeated deployments. True, draftees might be serving only for a single combat tour. Yet the backbone of the Army consists of professional officers and noncommissioned officers, who would still be required, during protracted wars, to return again and again to the combat zones.

JAMES SPINELLI, M.D.
Columbia, S.C.

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PTSD

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Goenjian. "The connection of the loss of churches to PTSD is an important finding and needs to be included in future studies."

Finally, people with better family and social supports were less likely to have PTSD, as expected. Other research suggests that levels of perceived social support predict the presence of PTSD between 6 and 12 months after a disaster, but the reverse occurs 18 to 24 months later: PTSD symptoms predict social support, wrote the authors.

They concluded that further research into the effects of the loss of social networks, including those centered on churches, on the psychiatric outcomes of disasters would be useful.

"The authors' findings highlight the need to better understand the range of behavioral health challenges occurring in the aftermath of unanticipated, catastrophic natural disasters," said an accompanying editorial in *Disaster Medicine and Public Health Preparedness* by Carol Fullerton, Ph.D., a research professor in the Department of Psychiatry at the Uniformed Services University of the Health Sciences in Bethesda, Md., and colleagues.

An abstract of "The Prevalence of Posttraumatic Stress Disorder Among Adult Earthquake Survivors in Peru" is posted at <www.dmphp.org/cgi/content/short/4/1/39>. ■

Weight Loss

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one commits about an hour a day to health and well-being," Holland said.

"Because program participants were literally in the trenches working out together, and some of this was really difficult stuff, a sense of camaraderie developed among them," Ladner reported. "It crossed party lines, it crossed male and female boundaries, it crossed black and white boundaries. People who would never have had a conversation in the capitol were now walking down the hallways high-fiving each other."

"And the other thing that is amazing is that once the program started, the number of bills that were introduced into the legislature concerning mental health tripled," she noted. "Also, every piece of legislation that other mental health advocates and I have worked on is alive and well and has not been modified at all. These developments are due at least in part, I think, to the relationships that I built with legislators during the Fit 4 Change program."

Ladner's husband, Mark Ladner, M.D., concurred: "The Fit 4 Change program has given Angela the ability to form new legislative contacts and enhance existing relationships which have helped promote mental health legislation. Angela, in brief, is one of those people who can make things happen, and the Fit 4 Change program is a great example." ■

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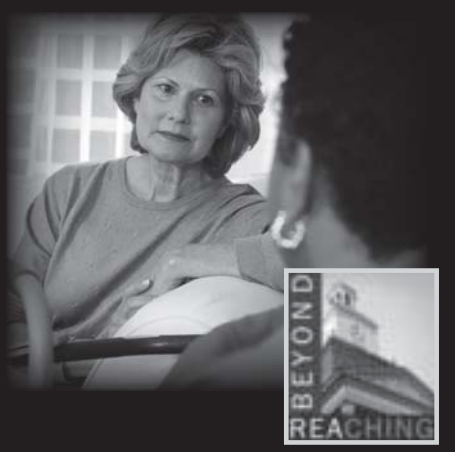

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For consideration, please send your C.V. and letter of interest to Sally Fangman at: **Aurora Behavioral Health Systems, 6015 W. Peoria Avenue, Glendale, AZ 85302, or call 623-344-4403.**

UNIVERSITY OF ARIZONA

The University of Arizona **Department of Psychiatry** is recruiting adult psychiatrists to join a progressive and growing academic department located in the beautiful Southwest. These two new positions, in addition to recent hires, will support residency expansion and major new facilities opening in early 2011. Both positions below are located at the University Physicians Healthcare Hospital, which is a federally recognized underserved area. Candidates must have current credentials to practice medicine in the United States and be Board-certified or -eligible in Psychiatry.

Assistant/Associate Professor, Clinical Psychiatry (NTE) - Emergency Room/Consultation Liaison Psychiatrist
The successful candidate will assist in caring for patients that present at the University Physicians Healthcare Hospital Emergency Room needing psychiatric care. The position involves working Saturday and Sunday in the Emergency Room and three other days of their choosing during the week. The candidate will also manage crisis evaluations and work with behavioral health workers, residents, and emergency room staff. There are opportunities to perform consultation liaison work, as well as outpatient psychiatry. Other duties may include participation in committees and department services as directed by the Department Head and other clinical duties as assigned.

Assistant/Associate Professor, Clinical Psychiatry (NTE) - Inpatient & Outpatient Psychiatrist

The successful candidate will provide inpatient and outpatient psychiatric services at the University Physicians Healthcare Hospital. The inpatient unit currently has 72 beds, and outpatient work will be performed in the new residency outpatient clinic. Incumbent will also be responsible for direct supervision of psychiatry residents, interns and other trainees. Other duties may include participation in committees and department services as directed by the Department Head and other clinical duties as assigned.

For additional information and/or to apply visit www.uacareertrack.com and reference specific title from above. If you have questions, please contact:

Ashley Lott, Human Resources
Department of Psychiatry
1501 N. Campbell Avenue, P.O. Box 245002
Tucson, AZ 85724-5002
(520) 626-3819 or aelott@email.arizona.edu.

Review of applications is ongoing until positions are filled. The University of Arizona is an EEO/AA Employer M/W/D/V

ARKANSAS

FAYETTEVILLE- General or Child Psychiatrists. Staff position. Inpatient & partial programs. Fulltime or part-time with highly competitive salary, benefits & bonus. **Student loan assistance.** Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

CALIFORNIA

Psychiatrist

Butte County Behavioral Health Department invites applications for the position of Psychiatrist. This position, under general direction, provides clinical assessments and treatment services to alleviate suffering in clients with behavioral health disorders. The monthly equivalent salary range for this position is $11,803-$15,817, and includes a comprehensive benefits package featuring retirement, health insurance, leave time, life insurance, and more.

Please submit a Butte County regular help application to: Butte County Human Resources, 3-A County Center Drive, Oroville, CA 95965, Recruitment# 104125045.

The application can be obtained and submitted to the Human Resources Department website at www.buttecounty.net/personnel. Applications may also be mailed to the above address. For additional information, please feel free to call (530) 538-6950 or (530) 538-7651. **The filing period is 04/20-05/21/2010. Applications must be received by 11:59 p.m. on the closing date. Butte County is an Equal Opportunity Employer.**

Adventist Health
Central Valley Network

PRIVATE PRACTICE OPPORTUNITY-
CENTRAL CALIFORNIA

Adventist Health Hospitals seek full time general psychiatrist for private practice. Offer includes practice establishment assistance, two year income guarantee, sign on bonus, five weeks paid time off, stipend for CME, and relocation reimbursement. Only California licensed BC/BE need apply.
- **Email CV to Physician Services: larkinme@ah.org or Tel: (559) 585-5275.**

Immediate need for **BE/BC Psychiatrists** for multiple CA locations. **$160-$185 an hour.** $320k-$370k yr for 40 hr week. Wknds available. 8-12 hr days. On call $42 an hr.

Bay Area Doctors, Inc.
Tel:(707)694-6890/(707)226-2426/
(707)694-3805.
Fax:(415)814-5764/email CV to
bayareadoctors@gmail.com.

Full Time contract psychiatrists needed at Napa & Coalinga State Hospitals, CA. No weekends or calls. Pays $180/hr+ malpractice. Call 661-274-9674. Fax CV to 800-758-7013. E-mail hahacorp@gmail.com. Work with recruiters.

Mental Health
CARE AND TREATMENT WITH RESPECT AND DIGNITY
PATTON STATE HOSPITAL
PATTON CA

CALIFORNIA
BC/BE STAFF PSYCHIATRIST

Patton State Hospital is recruiting board certified/eligible psychiatrists. Patton is a Joint Commission accredited, 1500 bed, adult forensic psychiatric hospital, with an extremely interesting and challenging patient population. The hospital is nestled below Arrowhead and the San Bernardino Mountains, 65 miles east of Los Angeles; an hour's drive to beaches, Palm Springs, or mountain lakes and skiing. Salary with Board Certification starts at **$18,622 and goes to $21,311 monthly.** Salary for Board Eligible starts at **$18,146 and goes to $20,711 monthly.** In addition, Patton offers excellent benefits (health, dental, and vision; license renewal; malpractice insurance; tax-deferred compensation; paid annual leave and 12 holidays (plus one personal holiday), as well as seven days per fiscal year of Continuing Medical Education leave). Voluntary on call duty is compensated on an hourly basis over and above base salary. We provide civil service security and retirement plans (including safety retirement). For confidential consideration, send CV to George Christison, M.D., (A) Medical Director, 3102 East Highland Avenue, Patton, California 92369, (909) 425-7326 or Fax (909) 425-6635.

San Diego County needs Psychiatrists. Salary extremely competitive for San Diego - up to 170K plus 10% Boards and extra 5% second Boards. CV to Marshall Lewis, MD, Clinical Dir, County Behavioral Health Div, Marshall.Lewis@sdcounty.ca.gov. Must apply at www.sdcounty.ca.gov/hr.

FACULTY POSITIONS - UCSD

The Department of Psychiatry at the University of California, San Diego is currently recruiting for contracted positions at the Assistant or Associate Clinical Professor level. We are seeking **board certified or board eligible psychiatrists** with a California medical license to practice in our community outpatient clinics. Preference will be given to candidates with a strong track record in clinical care, teaching experience and an interest or experience in clinical research. The positions offer flexible scheduling, along with potential teaching and research opportunities. Contract positions may become permanent faculty appointments. The appointment level will be determined by the candidate's qualifications and the salary is based on University of California staff psychiatrist pay scales.

Applicants should send their curriculum vitae and other supporting documents to: Attn: Dr. Lohr and Dr. Soliman, Search Committee K, UCSD Department of Psychiatry, 9500 Gilman Drive, La Jolla, CA 92093-0603. ***The University of California, San Diego, is an equal opportunity employer.***

Psychiatrist

Butte County Behavioral Health Department invites applications for the position of Contracted Psychiatrist. This position, under general direction, provides clinical assessments and treatment services to promote recovery in clients with behavioral health disorders. Compensation is $125.00 an hour.

Please submit a curriculum vitae or resume to: Butte County Behavioral Health Department, attn: Scott Kennelly, LCSW, 109 Parmac Rd., Ste. 2, Chico, CA 95926. Resumes may also be faxed to 530/895-6549 or e-mailed to skennelly@buttecounty.net For additional information, please feel free to call Scott Kennelly at (530) 879-3839 or (530) 891-2859 .

Contracts are on an annual basis, and positions are to be filled ***immediately***.

Medical Director

Butte County Behavioral Health Department invites applications for the position of Medical Director. This position, under administrative direction, plans, organizes, and manages the medical services component of the Butte County Department of Behavioral Health. The salary range for this position is $211,584 -$259,000 annually, and includes a comprehensive benefits package featuring retirement, health insurance, leave time, life insurance, and more.

Please submit a Butte County regular help application to: Butte County Human Resources, 3-A County Center Drive, Oroville, CA 95965, Recruitment# 104116044.

The application can be obtained and submitted to the Human Resources Department website at www.buttecounty.net/personnel. Applications may also be mailed to the above address. For additional information, please feel free to call (530) 538-6950 or (530) 538-7651. **The filing date for this position is April 20, 2010 through May 21, 2010. All applications must be received by 11:59 pm on the closing date, May 21, 2010. Butte County is an Equal Opportunity Employer.**

COLORADO

BOULDER: General or Child Psychiatrist. Fulltime position for inpatient and partial programs. Salary, benefits & incentive plan. Contact: Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

Horizon Health, the nation's leader in psychiatric contract management seeks an **Attending Psychiatrist** for a **10-bed Gero-psych** unit approximately one hour from the Denver airport. The opportunity includes the development of a community based outpatient practice. The hospital is fully accredited by JCAHO, and has a Level III Trauma Center, a 24-hour Emergency Room and many other services.Contact: Mark Blakeney, Horizon Health, 972-420-7473, fax CV: 972-420-8233, or email mark.blakeney@horizonhealth.com. EOE.

Experienced Psychiatrist Wanted To Care for Our Nation's Finest at Evans Army Community Hospital - *Fort Carson*

Humana Military is seeking a Psychiatrist to provide part-time services to military personnel and their dependents in the Adult Behavioral Health Department of Evans Army Community Hospital in Colorado Springs. Provider will work approximately 20 hours per week. Requirements include board certification by the American Board of Psychiatry and Neurology, current, unrestricted licensure to practice as a Psychiatrist in any U.S. State, current DEA registration and a minimum of 6 months practice experience within the past year. U.S. citizenship and current BCLS certification are also required prior to start. Competitive remuneration package available including paid time off and sign-on bonus.

For confidential consideration please send your CV to: cfitzpatrick@humana.com or fax to (954)785-6508, or you may call Mrs. Fitzpatrick toll-free at 1-888-241-1475.

CONNECTICUT

Psychiatrist/Child Psychiatrist to work in Stamford, CT in a private practice, part time, seeing quality patients of all age groups and better than average rate of pay ($120+). Fax resume to 203-930-3655 or email at childpsychny@aol.com.

INPATIENT ADULT PSYCHIATRIST-*CENTRAL CT*

FT/PT opportunity for BC/BE adult psychiatrist in 16-bed inpatient service with a community hospital offering a comprehensive mental health continuum. Enjoy working with an established team bringing a multidisciplinary approach to patient care. Crisis Center located in emergency department. This position offers a competitive salary and benefits and adaptable hours for the right individual. Call 1:5.

The practice is located in a family-oriented city located approximately two hours from NYC and Boston and 20 minutes to the capitol city of Hartford. Enjoy the charm of four seasons with a choice of attractive communities with Connecticut's best rated schools, shopping, award-winning restaurants, and regional theatre and easy access to skiing and the coast.

For more information about this opportunity, please contact Carolyn Doughtie of Physician Recruitment at 800.892.3846 or fax/email your CV to 860.585.3133. EOE

Email address: cdoughti@bristolhospital.org.

DELAWARE

DOVER: General or Child Psychiatrist. Inpatient/partial programs for adolescents & adults. Highly competitive salary, benefits & incentive plans. Contact Joy Lankswert In-house recruiter @ 866-227-5415; OR email joy.lankswert@uhsinc.com.

FLORIDA

Located along South Florida's beautiful east coast just minutes from the Atlantic Ocean, a CARF accredited community mental health center is seeking ***Full-Time Psychiatrists*** to provide comprehensive psychiatric care to children and adults. Children's inpatient crisis and addictions facility and adult inpatient and outpatient opportunities are available. A competitive salary with a signing bonus and benefits, complemented by very attractive housing opportunities are just a few of the advantages of working and living on the Treasure Coast. Seeking applications directly from candidates. ***Apply online at www.nhtcinc.org (No recruitment firms please!) EOE/ADA/DFWP***

FAMILY PRESERVATION SERVICES OF FLORIDA, INC. -*FORT MYERS*

CHILD/ADOLESCENT AND ADULT PSYCHIATRIST-PART TIME
CHILD/ADOLESCENT AND ADULT PSYCHIATRIC NURSE PRACTITIONER-PART TIME

FPSFL is seeking candidate to become part of highly professional, creative and energetic team focused on community based behavioral healthcare to children and adults. Provide pediatric and adult psychiatric evaluations, medication management and treatment planning consultation with treatment team members.

Psychiatric candidate must be board certified or board eligible in child and adolescent psychiatry. Psychiatric ARNP must have board certified psychiatric ARNP in the state of Florida.

Please email resume to: jprado@fpscorp.com or fax resume to 772-464-0087.

DAYTONA - MELBOURNE - ORLANDO - MIAMI - FORT LAUDERDALE - PALM BEACH - OCALA - GAINESVILLE - FORT MYERS - SARASOTA - PENSECOLA - JACKSONVILLE - Psychiatrists needed for rapidly expanding Nursing Home Service. Great support. No call. Average Salary 210K + benefits. Part-time available. Some travel required. Must have FL Medicare & FL Medicaid individual provider #s. No Restrictions (H1B Candidates Considered). Call our administrator, Christy, at 866-936-5250.

GEORGIA

ATLANTA: Medical Director & Staff Positions - Inpatient & partial programs.**Staff Position** - at premier Addiction Treatment Program **(Talbott Recovery Campus)** - prefer addiction interest/experience. Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

PSYCHIATRISTS NEEDED

Psychiatrist positions available for Adult Outpatient Clinic located in Dalton, GA. Seeking Board Certified/Eligible candidates with telemed experience. Full-time Position offers state employment benefits, competitive salary, and generous leave time.

Please submit cover letter with CV to Highland Rivers CSB, Attn: Human Resources, 1401 Applewood Street, Suite 4, Dalton, GA 30720 or Fax to 706-270-5129. EOE

THOMASVILLE: JC accredited state hospital with modern facilities, congenial staff, and up-to-date programs desires **BE/BC PSYCHIATRIST** to join medical staff of board-certified psychiatrists and generalists. No primary care duties; back-up call by phone. Adult and forensic programs. Excellent salary and benefits. Send CV or contact Joseph B. LeRoy, M.D., Clinical Director, Southwestern State Hospital, POB 1378, Thomasville, GA 31799. 229.227.2990; Fax 229.225.4052; email jbleroy@dhr.state.ga.us.

FLOYD℠
Behavioral Health Center

Floyd Behavioral Health is searching for a hospital-based psychiatrist and an office-based psychiatrist to join our team! Floyd Behavioral Health is a 53-bed adult behavioral health center with psychiatry, chemical dependency and geriatric programs, and all patients are admitted on a voluntary basis. The hospital-based psychiatrist will be joining a successful, experienced psychiatrist already practicing at the facility. The office-based psychiatrist will be establishing an outpatient practice in an adjacent building with another experienced psychiatrist and have privileges at Floyd Behavioral Health Center. Floyd Behavioral Health is a part of the Floyd health care system that has won numerous national and regional awards and employs more than 2,300 individuals.

Nestled in the foothills of northwest Georgia, Rome is a unique small city that has been recognized as the "Number One Small City in the Southeast." An hour from Atlanta and Chattanooga, Tenn., Rome boasts a flourishing health care community with more than 250 practicing physicians. The area enjoys a mild climate and offers quality educational and cultural opportunities. Floyd offers a competitive salary with great benefits, bonus opportunities and relocation assistance.

To learn more about Floyd, visit www.floyd.org. For confidential consideration, please e-mail Brandi Littlejohn (blittlejohn@floyd.org) or call 706.509.3963.

ILLINOIS

Division of Mental Health
Illinois Department of Human Services.

We are currently interested in the recruitment of a medical director for a Division of Mental Health Hospital in the Chicago area. The ideal candidate will have a strong clinical background in hospital psychiatry and a proven track record in psychiatric education. The medical director provides clinical supervision for the clinical disciplines and works as part of the hospital management team to maintain quality, safety and accreditation. This administrative position is full time and requires board certification.

Contact Dennis Beedle, MD Deputy Clinical Director for Clinical Inpatient Services at 312-814-8762 or email: dennis.beedle@illinois.gov for further details.

The Illinois Division of Mental Health is an equal opportunity employer.

Inpatient Psychiatry Medical Director

The Department of Psychiatry and Behavioral Sciences at Northwestern University, Feinberg School of Medicine is recruiting a Psychiatrist for a full-time position as an Assistant or Associate Professor on the clinician track who will serve as lead Medical Director for the Inpatient unit of the Stone Institute of Psychiatry at Northwestern Memorial Hospital. We are in the process of constructing a new unit, which will be in operational in 2011, and the candidate will have the opportunity to help shape the state-of-art treatment program in this exceptional new facility. Additional responsibilities include inpatient clinical care, leadership of a 36 bed inpatient unit, and psychiatry resident and medical student teaching. Experience with, and enthusiasm for, leadership of a multidisciplinary team is required. Must be ABPN board-eligible or certified and Illinois licensure preferred or eligible. Salary and start date are negotiable. Position open until filled. **Applicants should respond by mailing or emailing a CV and letter of interest by June 1, 2010** to Cathy Frank, MD, Vice-Chair, Department of Psychiatry and Behavioral Sciences, 446 E. Ontario, Suite 7-203, Chicago, IL. 60611, or by email to Paulette Zolicoffer, p-zolicoffer@northwestern.edu. Northwestern University is an affirmative action/equal opportunity employer. Women and minorities are encouraged to apply. Hiring is contingent upon eligibility to work in the United States.

IOWA

The University of Iowa Roy J. and Lucille A. Carver College of Medicine, Department of Psychiatry is currently recruiting **Associate(s), Assistant Professor(s), Associate Professor(s), or Professor(s)** for Clinical (Non-Tenure) and Tenure Track positions in Adult and Child Psychiatry.These positions may also have a joint appointment with the Iowa City Veterans Affairs (VA) Medical Center within the Mental Health Service Line. Opportunities exist in general outpatient and inpatient settings in both Child and Adult.

Requirements: Physicians who hold MD or DO degrees and have completed a psychiatry residency. Applicants must be board eligible or board certified and have a commitment to patient care, teaching, and research. Tenure track positions require post-residency fellowship or comparable experience in research.

The Department of Psychiatry at the University of Iowa Hospitals and Clinics has a wide range of clinical programs as well as residency and research programs. Iowa City provides the unique combination of a safe, small, and attractive college town with the opportunity to take advantage of abundant local and world-class cultural events. The school system is ranked among the best in the nation.

To apply for the positions, visit our website at http://jobs.uiowa.edu, requisition #57641. The University of Iowa is an Affirmative Action/Equal Opportunity Employer. Women and minorities are strongly encouraged to apply.

KENTUCKY

Retiring child psychiatrist seeks replacement starting in August 2010 or before in Danville, KY. Large community mental health center, excellent day hours, voluntary on-call, good

array or child mental health services and an expert collegial team. Danville, Kentucky is a wonderful community and is a top rated small college town in the Bluegrass. Christine Cunha, M.D. 859-239-9232 or e-mail cdcunha@bluegrass.org.

MAINE

We are currently recruiting for outpatient psychiatrists to work with children and/or adults. BC/BE preferred. We have full-time and part-time opportunities. Positions involve direct patient care at one or more of our community mental health centers located in Kittery, Springvale, Biddeford, and Westbrook. Our physicians work with a multi-disciplinary team providing outpatient services to a variety of programs.

Counseling Services, Inc. is a comprehensive and integrated community mental health center serving adults and children with serious mental health and substance abuse issues. Our programs are comprised of Community Support Teams, including Psychiatric Services, Assertive Community Treatment (ACT), Community Integration (CI), Outpatient Therapy, Crisis Response Services, and Complementary Therapies.

We offer a comprehensive salary and benefits package. If you are interested in exploring opportunities with us, please contact the Human Resources Department at 207-294-7096. A resume and cover letter may be sent to:

Counseling Services, Inc., P.O. Box 1010, Saco, Maine 04072 or human.resources@csimaine.com. We invite you to visit us online at www.counselingservices.org. We are an equal opportunity employer.

Adult inpatient psychiatrist. Mid Coast Hospital is an independent, non-profit community hospital located in beautiful coastal Maine one of Maine's most desirable regions. We are searching for an inpatient psychiatrist for our 12-bed unit. Our team uses a multi-disciplinary approach to treat both voluntary and involuntary patients. This is a full-time position for a BC/BE psychiatrist. Must have or be willing to obtain certification for ECT and a waiver for suboxone management. Share on-call responsibilities with eight other physicians. 40-hour week. Generous benefits, excellent work environment. Please send letter of introduction with CV to: mmackellar@midcoasthealth.com.

BE/BC Adult and Child Psychiatrists
Acadia Hospital, the nation's first Psychiatric Magnet Hospital, is a 74 bed community-based, full service psychiatric hospital located in Bangor, Maine. We are currently recruiting for BE/BC adult and child psychiatrists to cover our inpatient and outpatient units. We offer acute psychiatric care for adults and children, as well as substance abuse programs, and have recently opened a 10 bed psychiatric observation unit. Acadia Hospital is a teaching site for Tufts and University of New England medical schools. Positions are tailored to specialty interest. Acadia Hospital offers a competitive salary, full benefits, moving expenses and a loan repayment program. The area offers an international airport, symphony, and the University of Maine flagship campus. Four season outdoor activities include boating, hiking, biking, skiing and golfing. The area includes excellent school systems, affordable housing and a safe living environment. Bangor is located less than one hour from Acadia National Park and two hours New England's largest ski resorts. Acadia accepts and supports candidates working toward/on a J-1 Visa Process. Contact: Nancy Barrows at nbarrows@emh.org or apply on line at www.acadiahospital.org - careers.

MAINE COAST-OUTPATIENT PSYCHIATRY

Penobscot Bay Medical Center seeks a full-time BC/BE adult psychiatrist to join our hospital-employed and community-based professionals. Participate in a multi-disciplinary team approach to serve a diverse client base. Experience & training in addiction medicine preferred, but not required. Generous salary and benefit package including medical school loan repayment program. Mid-Coast Maine offers spectacular natural beauty, incredible outdoor recreation, rich cultural opportunities and great schools all in a safe environment. Contact John Bragg at (207) 596 8214 or e-mail CV to jbragg@penbayhealthcare.org.

MARYLAND

Inpatient, Special Unit for Deaf Patients. Springfield Hospital Center is seeking a BC/BE **general psychiatrist** for the state of Maryland's special inpatient psychiatric unit for deaf patients. ASL interpreters are available 24/7. Salary is negotiable, within MHA guidelines. For other descriptive information, please see our accompanying ad for a general psychiatrist. 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

PT Psychiatrist needed in well established psychiatric practice in Gaithersburg, MD, 10-20 hours per week to treat adolescents and adults. Schedule flexible, BC only, experience in meds management a must. Mail CV to GMPS, 9055 Shady Grove Ct., Gaithersburg, MD 20877 or fax to 301/948-4333.

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

BOSTON - Central & Suburb locations - Lowell, Brookline, Pembroke, Attleboro. Medical Director & Staff Positions. Inpatient & Partial. Salary, benefits & incentive plans. **NO CALL**. Contact Joy Lankswert, In-house recruiter @ 866-227-5415; OR email joy.lankswert@uhsinc.com.

Practice Opportunity: Boston's western suburbs. Well established practice is looking for psychiatrist or other mental health professional to step into busy outpatient practice. Current practitioner leaving for personal reasons. Flexible hours. Turn-key operation and growth opportunities. Contact: Anthony Jackson, M.D., Natick, MA Tel: 508 647-0222 ext 122.

Community Psychiatrists

Psychiatry positions benefit eligible, available immediately. Jobs entail performance of Psychopharmacologic Evaluations and ongoing medication management. Psychiatrist will participate in multi-disciplinary treatment teams at full-service, public sector Outpatient clinics located throughout the Greater Boston, MA area. Additional duties include leadership role at multi-disciplinary staff meetings, consultation to the Substance Abuse Team and/or other Agency Teams, may include supervision of a prescribing Clinical Nurse Specialist, and supervision of a PGYIII Resident on Community Rotation possible, which would provide eligibility for an MGH/Harvard appointment.

- Full or part time Adult positions.
- Full or part time Child position.
- 20 hour position as Consultant to Outreach teams.
- 12% pay increase for bilingual capacity in Spanish.

Pay commensurate with credentials and experience and includes sign on bonus. NSMHA offers a comprehensive benefits package including competitive salaries, medical / dental insurance and generous paid time off - Benefits available at 20 hours.

Interested candidates should send cover letter and C.V. to North Suffolk Mental Health Association, Attn: Recruiter, 301 Broadway, Chelsea, MA 02150; Fax 617-889-4635, Email gethired@northsuffolk.org. **We are an equal opportunity employer.**

High Point Treatment Center is seeking a 40 hr week psychiatrist to allocate 20 hrs managing 8-beds Inpatient Psychiatric Unit and 20 hrs allocated to outpatient services located in Plymouth, MA. Salary ranging from $170,000 - $190,000. No weekends, paid holidays and leave time. Health benefits available. If willing to work an additional 1 hr per day salary range would be $200,000 - $215,000.

We are also seeking an Outpatient psychiatrist (up to 32 hours/wk) located in New Bedford, MA. Salary ranging from $180,000 - $200,000.

If interested in either opening, please contact Jim Horvath at 508-503-2455 or email to jim.horvath@hptc.org.

Inpatient Attending Psychiatrist

Position available at Cambridge Health Alliance Department of Psychiatry, Harvard Medical School. We are seeking a psychiatrist to join a collegial team and become an active member of a rich clinical department. This opportunity is a full-time inpatient psychiatrist position with clinical responsibility for a training team on an active community service. Clinical care is provided through a multidisciplinary team approach with psychiatrist leadership.

The Department of Psychiatry at Cambridge Health Alliance is an appointing department at Harvard Medical School. Our public health commitment to improving the health of our communities, coupled with a strong academic tradition, make this an ideal opportunity for candidates interested in caring for underserved populations in a rich clinical environment. We have strong adult and child residency training programs which provide opportunities for teaching. 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, team oriented, problem solver. Interest and/or experience with dual diagnosis patients a plus. Cambridge Health Alliance is an Equal Employment Opportunity employer, and women and minority candidates are strongly encouraged to apply. CV & letter to Susan Lewis, Department of Psychiatry, 1493 Cambridge Street, Cambridge, MA; Fax: 617-665-1204. **Email preferred: *SLewis@challiance.org*.**

Full-time position available with The Department of Psychiatry at Cape Cod Hospital. Seeking a **Board-Certified Psychiatrist** to combine the responsibilities of Medical Directorship with a half-time inpatient service of approximately seven patients. Among Directorship duties are leading a department of eight part-to-full-time physicians and five part-to-full-time APRNs, and collaborating with top-level administration on strategic planning measures (further details available upon request). Excellent salary, superb benefits package, plus large, collegial active staff of over 400 doctors; wonderful career-building opportunity. Five years experience preferred. Please contact Mary Fisher for additional information at mfisher@capecodhealth.org, telephone: 508-862-5845, fax: 508-862-7387.

MARLBOROUGH, MASSACHUSETTS - UMass Department of Psychiatry is seeking candidates for a full time psychiatrist at its affiliated general hospital in Marlborough, Massachusetts. The position is two-thirds time inpatient coverage on a 22 bed acute care unit and one-third treatment and clinical care supervision on the unit's superb partial hospital program. Our Department of Psychiatry has a large clinical faculty with clinical, teaching and academic opportunities at a wide variety of inpatient and outpatient programs. We have faculty development programs, commitment to our care, training and research missions, and a great living and learning environment in Central Massachusetts. If you want to know more about job opportunities or the department in general, please email psychiatryrecruitment@umassmemorial.org or fax to 508-856-5990. AA/EOE.

Child and/or Adult Psychiatrist to join, busy, large, established private psychiatric group practice. Work consists of outpatient psychiatric treatment, both psychotherapy and psychopharmacology, and some hospital consultations. A lot of flexibility in terms of job and schedule. Please send C.V. to Paul Menitoff, M.D. Greater Lowell Psychiatric Associates, LLC 9 Acton Road Suite 25 Chelmsford, MA 01824.

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, Dept. of Psychiatry, 1493 Cambridge Street, Cambridge, MA 02139. Fax 617-665-1204. Email: JoGoldstein@challiance.org** (email preferred).

MICHIGAN

Medical Director - An Easy Income of $220k to $240k (Or More) - No long workdays necessary to make a great income. Seeking Psychiatrist for clinical and part-time administrative responsibilities on Psychiatric Services in a hospital in Saginaw, MI. Adult and C/A psychiatric services. Salary w/benefits is also an option. Very close to Bay City on Lake Huron and Flint. Only an hour and a half to Detroit and Ann Arbor. Please call **Terry B. Good at 1-804-684-5661**, Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

Opportunity for attending psychiatrist in the U.P. of Michigan. Mostly outpatient work with some inpatient responsibility on 20-bed, adult psychiatric unit. Excellent salary and benefits. For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

MINNESOTA

Duluth Clinic
An affiliate of SMDC Health System

Psychiatry Opportunities in Beautiful Duluth, MN

SMDC Health System, a member of Essentia Health, serves a regional population of 460,000 in Northeastern Minnesota, Northwestern Wisconsin and Michigan's Upper Peninsula. The integrated health system includes five hospitals, as well as the Duluth Clinic, a nationally recognized 450+ physician multispecialty group providing care at 17 locations. Located along Lake Superior's rugged hillside, Duluth's spectacular scenery, abundant recreational opportunities and vibrant arts community earned it inclusions on best small cities lists from Outside and Money magazines. Two hours from Minneapolis/St. Paul metro area. EOE/AA

CHILD/ADOLESCENT AND ADULT PSYCHIATRISTS

Join a group of 4 adult and 1 child/adolescent psychiatrists as part of a Behavioral Health Care Team to also include doctoral level psychologists, advanced practice nurses, nurse clinicians and psychotherapists.

- Full range of psychiatric problems and diagnoses
- Opportunity to evaluate and treat chemically dependent adolescent patients
- 37-bed adult and 16-bed child/adolescent unit
- 3 partial hospital programs for adults, children and adolescents
- 24/7 referral center for triage and assessment services
- Consultation/liaison service available
- Competitive benefit package and salary with first-year guarantee
- J1-waiver opportunity

Search/Apply online AT

www.duluthclinic.org/career
Sandra Kramer, Physician Recruiter
800-342-1388; 218-786-1035;
Fax: 218-722-9952
skramer@smdc.org

Duluth Clinic.
An Affiliate of SMDC Health System
The soul and science of healing.

MISSISSIPPI

North Central Mississippi, just one hour south of **Memphis, TN.** Attending Psychiatrist position available for 15-bed Adult and 22-bed Geriatric inpatient units, in addition to a 23-bed Chemical Dependency Program. Excellent salary and benefits. For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

MISSOURI

KANSAS CITY: Medical Director &Staff Physician. Inpatient & Partial programs. Salary, benefits & incentive plan. Contact: Joy Lankswert In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

Outstanding Psychiatric Practice Opportunity! Nationally acclaimed, JCAHO **eating disorder center** seeks qualified **Psychiatrist** with **ED interest/experience**. Ideal Location! Contact Steve Weiner, Pres., F-O-R-T-U-N-E at fpccareers@aol.com or (573) 424-6624.

Weekend Call Opportunity - Seeking a Psychiatrist to cover one, preferably two weekends per month of on-call for 10-bed inpatient geropsychiatric unit at the general hospital in Bolivar, MO - close to Springfield. Please **call Terry B. Good, Horizon Health, at 1-804-684-5661**, Fax #: 804-684-5663; email: terry.good@horizonhealth.com.

MONTANA

Horizon Health invites you to consider an exciting new **Medical Director** opportunity for two NEW distinct **Adult** and **Geriatric** Inpatient Psychiatric Units, comprised of 26 total beds in Helena, MT. Nestled beneath the foothills of the Montana Rockies, **Helena**, the Capital of Montana, is alive with history and culture. This charming and beautiful Victorian city of 70,000 people provides a diverse attraction with many street festivals, theater, museums, symphonies, fairs and rodeos. There is truly something for everyone here! Excellent practice opportunity with great income ($200K+) and unparalleled quality of life! For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

NEW JERSEY

PSYCHIATRISTS
Earn up to $200K plus benefits

Get inside the criminal mind and make a difference. University Correctional HealthCare (UCHC), a branch of the University and Medicine and Dentistry of New Jersey (UMDNJ), currently has regular (full-time and part-time) and per diem openings for psychiatrists throughout the state. We are dedicated to providing excellent mental health and rehabilitative services to our patients.

As a psychiatrist, you will have the unique opportunity to work with interesting patients and stimulating colleagues within the New Jersey Department of Corrections' prisons. We offer a comprehensive benefits package and a salary of up to $200,000 depending upon location, board certification, and experience. You will work with a multidisciplinary team and a state-of-the-art medical record. With minimal call, flexible hours, no managed care, no insurance forms, and an emphasis upon treatment rather than paperwork, isn't it time you discovered the difference you can make with University Correctional HealthCare.

Please apply via our website at www.umdnj.edu/hrweb or e-mail our Director of Psychiatry, Rusty Reeves, M.D., at reevesdo@umdnj.edu. UMDNJ is an affirmative action/equal employment opportunity M/F/H/V and is a member of the University Health System of New Jersey.

Westampton - East of Philadelphia. General or Addiction Psychiatrist for Adult Dual Diagnoses Unit. Salary & Benefits. Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

CHILD & ADOLESCENT PSYCHIATRIST
WESTFIELD, CEDAR KNOLLS, RIDGEWOOD & PRINCETON

Excellent opportunity for Child/Adolescent Psychiatrist to join our Center in one of our four locations. We are a successful private fee for service comprehensive child, adolescent and adult therapy Center with locations in Westfield, Princeton, Cedar Knolls and Ridgewood, New Jersey. Candidate will be part of a multi-disciplinary team and will provide psychiatric evaluation, medication management and, if desired, psychotherapy. He/She will also clinically oversee treatment at the Center. Salary and benefit package is generous and includes medical/dental insurance, retirement plan, professional liability coverage and substantial continuing education and vacation. Supportive collegial atmosphere. Candidate must be board certified or board eligible in child/adolescent psychiatry. E-mail cv to abbazn@aol.com.

NEW YORK CITY & AREA

PSYCHIATRISTS
Best in Brooklyn!

Lutheran HealthCare, located in the Southwest section of Brooklyn, offers a continuum of community-orientedbehavioral health services within its Department of Psychiatry.

FT O/P ADULT/GERIATRIC
- Office-based, "Memory Clinic," Assisted Living, Adult Home.
- Salary with benefits.
- Bonus capability.

FT I/P ADULT
- Addictions emphasis.
- Ample cross-coverage.
- Salary with benefits.
- Bonus capability.

PER DIEM/MOONLIGHTING
- Dedicated shifts.
- Variety in night/weekend activity.
- Paid malpractice.
- Competitive hourly rates.
- Additional pay per encounter.

Please email: tirvin@lmcmc.com, fax 718-630-8594, or send your CV to: Tracey Irvin, Dept. ofPsychiatry, Lutheran Medical Center, Suite 2-45, 150 55th St., Brooklyn, NY11220. EOE/AA M/F/D/V. ***www.LutheranHealthCare.***

Westchester Suburbs of NYC. Medical Director- Child/Adol Facility. New opening! Admin duties & 30 d LOS easy inpt care, little m'gd care. Daytime-no call, wkends or ev's. Easy NYC commute. Also, 1 pos for C/A Unit Chief. AdolMD@gmail.com or 917-710-2456.

NYC/BROOKLYN HEIGHTS

Part time psychiatrist. Opportunity exists for qualified MD to engage in busy office based practice in Brownstone Brooklyn. Please fax your CV to 718-237-4434 or email to bpa.pc@hotmail.com.

Psychiatrists
JBFCS is seeking PT Adult & Adolescent Psychiatrists. Openings include 5 boroughs & Westchester. **Requirements**: NYS license, DEA Certification req. Exp with this population & Fellowship in Child & Adolescent Psychiatry pref. Email resumes to: HRRecruit2@jbfcs.org. Mention Psychiatrist and location preference in the email subject line.

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

NEW YORK STATE

Adult Residential Psychiatrist

A private residential treatment facility in Brewster, NY, seeks a P/T board certified/board eligible NY State Licensed Psychiatrist for a **52 bed** adult facility. Applicant must be able to work effectively as part of a clinical team and be comfortable with using computerized records system. ***Send applications and CV's to:*** 2505 Carmel Avenue Suite 210 Brewster, NY 10509 Attn: Danielle Quinn or fax to 845-279-7678 Attn: Danielle Quinn.

ClearView Center Inc. is looking for a part time (4-5hrs/week) Psychiatrist with an interest working in Community Psychiatry. Flexible hours, evenings possible, no call, no weekends. Responsibilities include: providing initial psychiatric evaluations, and medication reviews. Qualifications: Current license to practice medicine in NYS, with Board certification or Board eligible in Psychiatry. Send resumes to Human Resources: 500 Central Ave., Albany, NY 12206. P(518)435-9931; F(518)435-9937. E- hr1@clearviewcenter.com. **www.clearviewcenter.com.**

ELMIRA PSYCHIATRIC CENTER
Adult and Adolescent Psychiatrists

Board Certified - $172,269 - $176,903
Licensed Physician - $141,751
Limited Permit - $107, 318 - $115,905

- All positions M-F 8-4:30 with no managed care insurance demands
- Optional participation in a low stress on-call program with potential to earn up to an extra $74,000/year
- 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

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

IN-PATIENT PSYCHIATRISTS

The Mid-Hudson Forensic Psychiatric Center is a forensic facility operated by the NYS Office of Mental Health and is accredited by both CMS and Joint Commission. Located in the beautiful lower Hudson Valley area, the facility provides an excellent opportunity to work with dynamic multi disciplinary treatment teams to provide high quality care to patients mostly referred from the court system. Competitive salary with paid on call services and excellent benefit package. We have Forensic Fellowship Program affiliated with Colombia University, which gives an opportunity to participate in several educational programs. Currently we are recruiting Board Certified/Board Eligible New York State Licensed Psychiatrists. We are providing an opportunity to have an alternate work schedule to accommodate outside employment. Affirmative Action/Equal Opportunity Employer.

Contact: Gowramma Shivashankar, M.D., Clinical Director
MHFPC Box 158, Route 17M
New Hampton, NY 10958
Phone: (845) 374-8743/8796
Email: MHMDGSS@omh.state.ny.us
Fax# - (845) 374-8860.

EXCELLENT ADULT PSYCHIATRY OPPORTUNITY

Samaritan Medical Center, a not-for-profit regional referral center in northern New York, is seeking a BC/BE Psychiatrist for hospital based employment to join our excellent dedicated staff. Physician will provide adult psychiatric care in our 32 bed inpatient mental health unit. Physician will also serve as consultation liaison and participate in rotational emergency call. **Top salary, signing bonus, excellent benefits, malpractice coverage, relocation assistance, immigration assistance, etc.** Enjoy the natural beauty of northern New York 1,000 Islands Region, with the added benefit of living in a safe community with a low cost of living. **For more information contact Anne Marie Walldroff at 315-785-4632, or respond online to awalldroff@shsny.com. Visit our website: www.samaritanhealth.com.**

NORTH CAROLINA

Private Practice Opportunity: Established & busy mental health outpatient practice in Durham, NC seeks Psychiatrist, Board Certified. Managed care knowledge a plus. Send CV to: pamelatrent@gmail.com. Phone: 919-479-1600.

VERY ATTRACTIVE POSITION RIGHT NEAR RALEIGH - Adult inpatient and outpatient work in Rocky Mount - only 45 minutes from Raleigh. Offering very attractive package: salary with benefits and bonus plan. Contact **Terry B. Good at 1-804-684-5661**, Fax #: 804-684-5663; terry.good@horizonhealth.com.

Adult Staff Psychiatrist
Emergency Room Psychiatrist
Charlotte, NC

Carolinas HealthCare System has unique opportunities for Adult Staff Psychiatrists at its Behavioral Health Center. The center is part of a 874- bed regional teaching facility nestled in the heart of Charlotte. Join an outstanding team of psychiatrists in a very collegial working environment.
Adult Staff Position - Inpatient and outpatient.
Emergency Room Psychiatry Position - Work in the facility's in-house emergency department. Rotating shifts.
Excellent benefits package which includes:
- **Two weeks CME**
- **Paid vacation**
- **Short and long-term disability**
- **401K, 457B and pension plan**

Opportunity for extra income by seeing private patients or by taking shifts in the ER
Interested applicants should email their CV to Elaine Haskell at: elaine.haskell@carolinashealthcare.org **or call 800-847-5084 for more information.**

EOE/AA

OHIO

PSYCHIATRIST-FT
NO ON-CALL

Excellent opportunity to join nationally recognized not-for-profit provider of behavioral health and rehab programs that improve the lives of individuals, families and businesses in NE Ohio.
- Outpatient working environment.
- Job resp: psychiatric evaluations, treatment and adult medical mgmt.
- Regular schedule, M-F.
- No on-call. No holidays.
- Competitive Salary and Benefits.

Must be BE/BC - MD/DO with OH license. Send resume to CPS-PSYNW, 5982 Rhodes Rd, Kent, OH 44240 or apply online at www.coleman-professional.com. E.O.E.

OKLAHOMA

OKLAHOMA CITY: General Psychiatrist. Fulltime position for inpatient & partial programs. Competitive salary, benefits & bonus plan. Contact Joy Lankswert In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

PENNSYLVANIA

PHILADELPHIA and suburbs- Child Psychiatrists for Inpatient, RTC and or Partial Program.**CLARION (Western PA).** Child Psychiatrist for inpatient & partial programs. **SHIPPENBURG:** General Psychiatrist with interest in Dual Diagnoses. Fulltime positions. Salary & benefits. **Student loan assistance at Clarion**. Contact Joy Lankswert @ 866-227-5415; OR email joy.lankswert@uhsinc.com.

PHYSICIAN ADVISOR
Highmark Inc., Pennsylvania's largest health insurer based on membership, is seeking a Board Certified Psychiatrist to provide clinical support to the Behavioral Health Utilization and Case Management teams. This part time position could be based in Pittsburgh, Camp Hill, Erie, Johnstown, Altoona or Allentown PA. Candidate must have an unrestricted medical license in PA, credentialed in the KHPW or Highmark Blue Shield network and have five years of clinical experience. Submit your resume to: www.highmark.com and click on the careers link under the About Highmark section, use reference # 57947. Highmark, an equal opportunity employer, strives to capitalize on the strengths of individual differences and the advantages of an inclusive workplace. Qualified applicants will receive consideration for employment without regard to race, color, ethnicity, sex, marital status, religion, creed, national origin, disability, veteran's status, sexual orientation or any other category protected by applicable federal, state or local laws.

Horizon Health, in partnership with **Lower Bucks Hospital** in **Bristol, PA**, has an exciting opportunity for an **Associate Medical Director** for a **24-bed** Adult Inpatient Psychiatric Program. Excellent practice opportunity and income potential for local physician. Call coverage shared - 1:3 weekends, or less, and 1-2 nights per week. For more information contact: Mark Blakeney, Voice: 972-420-7473, Fax: 972-420-8233; email: mark.blakeney@horizonhealth.com EOE.

Adult and Geropsychiatric Units -Eastern PA- Seeking a Psychiatrist for inpatient work in an impressive med/surg hospital. Offering salary/benefits, relo pkg, and bonus plan. Close to Harrisburg; easy drive to Philadelphia and Baltimore. Please call **Terry B. Good at 1-804-684-5661**, Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

Stroudsburg, PA. Full Time outpatient Adult/Child Psychiatrist.ISL Psychiatric Services is looking to recruit additional psychiatrists to join our excellent group of 20 psychiatrists and other mental health workers. Starting salary of 170K and an excellent benefit package. Fax CV to (570) 424 6271, or call (570) 424 6187.

Psychiatrists:

Currently 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 and addictions psychiatrists.

There are also practice options in a traditional psychotherapy model. Psychiatric Hospitalist positions are available for weekday and weekend rounding and Crisis. Excellent salaries, no on-call nor rounding responsibilities ever and exceptional benefits package offered. Send CV to Kevin Caputo, M.D., Vice President and Chairman, Department of Psychiatry, Crozer-Keystone Health System, One Medical Center Blvd., Upland, PA 19013 or contact the department manager, Kathy Waring at 610-619-7413.

SOUTH CAROLINA

Locum Tenens Psychiatrist - Interim psychiatrist needed on 8-bed geropsychiatric unit in northeast SC-2 hours from 5 great cities: Raleigh, Charlotte, Myrtle Beach, Columbia, and Wilmington. Round 5 days per week, or split with someone: one rounding two days and one rounding three days. No weekend rounding necessary. Call **Terry B. Good, Horizon Health, 1-804-684-5661**, Fax #: 804-684-5663; email: terry.good@horizonhealth.com.

BC/BE Psychiatric Position near *SC Coast!*

McLeod Health is seeking a Full-Time BC/BE Adult Psychiatrist for our Behavioral Health Psychiatric Center located in a beautiful rural setting in Darlington, SC, just minutes away for the main flagship hospital, McLeod Regional Medical Center, a 453 bed, tertiary care, and teaching facility in Florence, SC. We have an extensive support staff for the hospital and ED consults and a twenty-four hour Access Center. Our state-of-the-art 23 bed crisis intervention in-patient facility was built and designed specifically for the needs of the psychiatric patient. We also provide out-patient therapy for patients in a private practice setting. We offer a competitive salary, comprehensive benefits and retirement package, paid professional liability insurance, CME allowance, relocation assistance, and sign on bonus. We are just over 1 hour to Myrtle Beach, SC and 2 hours from Charleston, SC.

If you are interested in joining this nationally recognized hospital, please contact Angela Stukes at 843-777-7046 or by email at astukes@mcleodhealth.org.

Go to mcleodphysicianrecruiting.org for more details regarding this position.

Income Potential $280k to $350+
Medical Director - Geropsych Unit
Very lucrative position (salaried with benefits or practice opportunity for those who prefer independence) in northeast SC-a place with a great quality of life and lots of opportunity. An easy drive to Florence, SC and Fayetteville, NC; 2 hours from Columbia, Myrtle Beach, Charlotte and Raleigh. Please **call Terry B. Good at 1-804-684-5661**, Fax #: 804-684-5663; Email: terry.good@horizonhealth.com.

GREAT PLACE TO LIVE, WONDERFUL PRIVATE PRACTICE OPPORTUNITY
Charleston, SC. Child or General Psychiatrist to join a very busy outpatient practice with unlimited growth potential and great referral sources. Share expenses, assume existing patients. CL opportunities near by. Contact 843-412-3152.

TENNESSEE

ASHLAND - just north of Nashville: Medical Director for Child/ Adolescent Residential Treatment Center. **MEMPHIS: General & Child Psychiatrist** for inpatient & partial services. **Salaried employment w/ benefits**. Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com

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Board-certified/eligible psychiatrists needed for a large Psychiatry Service at Mountain Home VAMC in Johnson City, Tennessee. Inpatient/outpatient psychiatrist on a 24 bed teaching unit staffed by two psychiatrists, 1 NP, 1 PA, and residents rotating from ETSU College of Medicine. Must be board certified in psychiatry or board eligible if within 2 years of residency completion. Join staff of 30 prescribers, including 18 psychiatrists at ETSU-affiliated residency training program with medical students, adult and med-psych residencies. Clinical appointment potential and some teaching expected. Research a plus. On-call (full time positions only) is backup to residents and shared amongst staff psychiatrists.

NO STATE INCOME TAX, LOW COST OF LIVING, BEAUTIFUL MOUNTAINOUS REGION, LOTS OF PARKS, GOLF COURSES, LAKES, NATIONAL FOREST.

Inquiries: Tana Johnson, (423) 926-1171, ext. 7184, or Tana.Johnson@va.gov and George.Brown@va.gov. Applications and/or CVs to: James H. Quillen VA Medical Center P.O. Box 4000 (05), Mountain Home, TN 37684 or Fax: (423) 979-3443 or Email: mtnhomehrmservice@va.gov
Equal Opportunity Employer

TEXAS

Interested in loving where you live and work? Then consider Lufkin.

Lufkin State Supported Living Center is looking for a psychiatrist. We are located in beautiful deep east Texas near two national forests, boasting of great lakes, parks and one of the best golf courses in Texas. According to the Chamber of Commerce - Lufkin is the #1 Micropolitan community in Texas and has many dining and shopping opportunities. The Center is a developmental facility for people with mental retardation and physical disabilities as well as persons with dual diagnosis which includes mental illness. A typical work schedule is Monday - Friday 8 a.m. to 5 p.m. The work environment is casual and the medical problems are challenging. We have a strong support system and offer excellent benefits (competitive salary, retirement, health/dental insurance, paid vacation and sick days, life insurance, longevity pay, up to 15 paid holidays per year, and more). Employee housing is available on the grounds with all bills paid and a modest rent.

For more information, call 936-853-8350, or e-mail: gale.wasson@dads.state.tx.us

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San Antonio, Dallas, Houston, Ft Worth and Austin

Immediate openings for full or part-time physicians to provide direct geriatric patient care, supervision of NP's, PA's, Additional geriatric training available.
- Flexible hours PT - $75-$125/hr
- FT - $200,000 + Bonus
- Benefits, CME leave, 3weeks vacation, and insurance.

www.seniorpsychiatry.com. mcampos@seniorpsychiatry.com. Call John Croley 713-850-0049 for more information.

AMARILLO - Hospitalist - Salaried Employment & benefits offered. Adult general psych and dual programs. Contact: Courtney Williams, In-house recruiter @ 866-227-5415 or email courtney.williams@uhsinc.com.

McALLEN: Private Practice Opportunity. Inpatient & Outpatient. Contact: Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

Psychiatrists Wanted
To Care for Our Nation's Finest;
Fort Hood, Texas
UTILIZE ANY CURRENT STATE LICENSE!

Humana Military Healthcare Services is seeking Psychiatrists to provide full time outpatient services to military personnel at Fort Hood in Killeen, TX. Provider will work full-time days, Monday - Friday, 7:30am to 4:30pm. Minimal telephonic on-call services of 1-2 weekdays and one weekend day every other month. Requirements include board certification or board eligibility by the American Board of Psychiatry and Neurology, current unrestricted licensure to practice as a Psychiatrist in any U.S. State, and current DEA registration. Candidates must have been continuously employed in the practice of Psychiatry or in training for the past 2 years. U.S. citizenship and current BCLS certification are also required prior to start. Competitive remuneration package paid as an Independent Contractor of $225,000 plus $15,000 sign on bonus, 20 days paid time off, 10 paid holidays, and $4250 relocation reimbursement.

For consideration please send your CV to: msechen@humana.com or fax to (772) 299-0550, or call toll-free at 1-877-202-9069.

Psychiatrist

The Department of Psychiatry and Behavioral Sciences of the University of Texas Medical School at Houston has extraordinary opportunities for psychiatrists seeking to develop a career in inpatient psychiatry. Under new leadership, the Department is expanding clinical and research areas and is seeking general psychiatrists, child and adolescent psychiatrists and geriatric psychiatrists to join a growing academic department dedicated to excellence in training, education, and research. The University of Texas Harris County Psychiatric Hospital is a state of the art 250 -bed facility serving patients in all age groups and affiliated with department of Psychiatry at University of Texas Medical School at Houston. The Medical School is part of the University of Texas Health Science Center at Houston, located in the Texas Medical Center - the largest medical center in the world. Houston is 4th largest metropolitan city offering the charm of southwestern hospitality and a low cost of living.

Individuals applying for these positions must be Board Certified in general psychiatry, child & adolescent psychiatry and geriatric psychiatry or have completed an accredited training in these specialty and subspecialty areas in the United States. Additionally, they must be licensed or be eligible for licensing in the State of Texas. Experience or interest in research and/or education is preferred. Recent graduates from accredited residency program are also encouraged to apply. Depending upon the applicant's qualifications and credentials, faculty appointment at the level of Assistant Professor, Associate Professor or Professor will be offered. Salary levels are very competitive and also carry excellent fringe benefit packages. For more information about these unique academically-driven positions or to apply for them, please write to Jair C. Soares, M.D., Professor and Chair, and include a copy of your curriculum vitae and a letter of interest to 1941 East Road, Houston, Texas 77054, e-mail: Jair.C.Soares@uth.tmc.edu phone 713-486-2507; fax 713-486-2553. The University of Texas Health Science Center at Houston is an EO/AA employer. M/F/D/V.

WEST TEXAS San Angelo: Child or General Psychiatrist. Salaried Employment or Private Practice. **Student loan assistance in San Angelo.**
DALLAS: Independent contractor practice position for coverage of inpatient services. Also weeknight and weekend call coverage options. Contact: Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

Salaried Opportunities for Adult Psychiatrists - San Antonio, TX

Vericare (www.vericare.com) is the leader in providing mental health services to residents of long term care. We have immediate, salaried positions for Adult or Geriatric Psychiatrists in San Antonio. We offer flexible scheduling, 100% paid malpractice, administrative support, no on call/weekend requirement and a complete benefits package. Board Certified preferred. **Call Sanel Lekic at 800-257-8715 x1166 or email your resume/inquiry to slekic@vericare.com.**

PSYCHIATRISTS: Mental Health Mental Retardation Authority of Harris County (MHMRA) in Houston, Texas is one of the largest mental health centers in the United States. Demands have created the need for additional **BC/BE Psychiatrists** throughout the Agency.

Harris County Jail
Second shift 2:00 PM to 10:00 PM.
Perform psychiatric evaluations
& medication management.
Some on call at 24/7 facility.

Texas licensure is required for all positions.

MHMRA offers competitive salary plus a generous benefit package. Houston offers excellent quality of life, lower than average cost of living, no state sales tax and exciting cultural, entertainment, sporting and tourists venues.

Contact Charlotte Simmons at (713) 970-7397, or submit your C.V. to charlotte.simmons@mhmraharris.org or fax: 713-970-3386 or go on-line at www.mhmraharris.org to complete application.

The Texas Department of Aging and Disability Services is looking for psychiatrists to fill vacancies at our state supported living centers in **El Paso, Mexia, Abilene, Brenham,Lufkin, San Angelo, San Antonio,Corpus Christi**, and **Austin**.

We offer a competitive salary, health/dental insurance, paid vacations,up to 15 paid holidays per year, an excellent retirement program, and the opportunity to make a difference.

For additional information, visit **www.careersatdads.com** or contact Judy Garner at **512-438-3268** or **judy.garner@dads.state.tx.us**.

Come to Texas - you're gonna love it!

UTAH

PSYCHIATRIST

Ski Park City and Snowbird, attend Sundance film festival, and work in nearby Provo! On-Call is optional. **Utah State Hospital** seeks psychiatrists for adult inpatient unit. JCAHO/MEDICAID/CMS accredited. Electronic chart and pharmacy. New buildings on a 300-acre campus at the base of the mountains. Collegial environment. Salary negotiable, with full benefits.

Send CV to: Richard Spencer, MD, Clinical Director, PO Box 270, Provo, UT 84603, (801) 344-4201, rspencer@utah.gov. EOE.

VIRGINIA

Ready made $330,000+ opportunity in ***Williamsburg,VA***. Private multidisciplinary outpatient psych practice seeks F/PT psychiatrist to partner with 8 therapists and 2 PT psychiatrists Current FT M.D. is retiring. FamilyLivingInstitute.com, or call Carl 757-229-7927.

Central Virginia Community Services one of Central VA's largest community mental health center's is currently seeking two **FT Child Psychiatrist (#79FT) or (#335FT)**, to provide direct services to children and adolescents. These positions will be responsible for providing psychiatric evaluations, consultations and medication management services to children and adolescent consumers in an outpatient clinic setting, serving Lynchburg and the surrounding counties. Excellent clinical, documentation and communication skills are needed. Experience working with children and adolescents is required. BC/BE.

Please forward CV to Kathy Stone at Kathy.stone@cvcsb.org.

Central Virginia Community Services offers a competitive salary with an excellent benefit package that includes medical, dental, and vision insurance; participation in the Virginia Retirement System; participation in additional annuity plans; with a generous leave policy and educational benefits. These positions also offer reasonable work hours with a Monday - Friday schedule, in a congenial work atmosphere. Lynchburg, VA is a historic and attractive city with many amenities available throughout the city and surrounding counties. Located in the beautiful foothills of the Blue Ridge Mountains, Lynchburg has something to offer everyone!

PSYCHIATRIST
Sign-On Bonus!

Catawba Hospital is accepting applications from **BE/BC Psychiatrists** interested in joining an outstanding medical staff in a 110-bed, Joint Commission accredited, psychiatric hospital. Academic affiliation exists with the local Residency Program and Medical Schools. Teaching medical staff have academic faculty appointed. Experience with serving adult and/or geriatric patients with severe mental illness is desired. Applicants must be licensed or eligible for licensure in Virginia. **NO CALL REQUIRED!**

Located just minutes from the metropolitan community of Roanoke, Virginia, the cultural hub for Southwest Virginia. The area provides excellent recreational, educational, and cultural opportunities in the Blue Ridge Mountains:

- One of the ten best places to raise a family in the United States *(Parenting magazine)*;
- Ranked among the least stressful locations in the United States *(Zero Population Growth, Inc.)*;
- Excellent School Systems within the Roanoke Valley and Blacksburg areas.
- 7th healthiest place to live *(Kiplinger's Personal Finance Magazine)*;
- One of the nation's top 20 cities for quality of life *(recent University of Kentucky study)*.
- Fantastic outdoor opportunities: Appalachian Trail within five minutes of hospital; Blue Ridge Parkway nearby; outstanding mountain biking & hiking just ten minutes away in Carvin's Cove Nature Preserve(2nd largest city park in the United States).

Salary up to $175,000/year based on experience and expertise.

In addition, the generous state employee benefits package brings your total compensation to the equivalent of $246,000/year.

- Malpractice covered by the Commonwealth of VA.
- Possibility of on grounds housing in a relaxed rural setting.
- Financial assistance with moving expenses.

No J-1 positions available. Position will remain open until filled.

For telephonic/e-mail inquiries contact:
Gary Hiler, Human Resource Manager
(540) 375-4368
gary.hiler@dbhds.virginia.gov

Submit CV to:

Human Resource Office
CATAWBA HOSPITAL
P.O. Box 200
Catawba, VA 24070-0200
TDD(540)375-4385. FAX(540)375-4359
EOE M/F/H/V

Inpatient and Outpatient Psychiatrists

Norfolk Community Services Board, a community-based behavioral healthcare organization located in Norfolk, Virginia, is seeking a full-time inpatientpsychiatrist. Opportunities for medical student/resident teaching and research. Academic appointment at Eastern Virginia Medical School is available. We are also recruiting FT/PT psychiatrists for positions within our continuum of outpatient services, including our Adult Outpatient Clinic, Adult Intake,Addiction Medicine clinics, and Emergency/Crisis Stabilization services. Excellent benefits package; paid malpractice insurance. Salary is commensurate with experience. Applicants must possess or be eligible to obtain an unrestricted Virginia medical license. BC/BE. On-line application at www.norfolkcsb.org or contact Norfolk Community Services Board, 225 West Olney Road, Norfolk, Virginia23510, (757) 823-1693. EOE M/F/D/V. Background check required.

WASHINGTON

Summit Research Network (Seattle) LLC is seeking a licensed, board certified Psychiatrist to work with adult and pediatric/adolescent populations in clinical research trials. Must be comfortable working in a team environment as a Sub Investigator and Principal Investigator in primarily psychiatric pharmaceutical research at our site in Seattle, WA.This position is part time with the potential to increase to full time. Summit offers competitive salary based on experience/credentials with an excellent benefit package. Please send inquiries and CV to: Shannon Kinzebach, Summit Research Network, 901 Boren Ave Ste 1800; Seattle, WA 98104 or via email: shannonk@summitnetwork.com.

WEST VIRGINIA

Child and Adolescent Psychiatrist
(J-1 slot available)

Westbrook Health Services, a Comprehensive Community based, not for profit behavioral health center located in the Mid-Ohio Valley is recruiting a Child and Adolescent Psychiatrist.

Metro area of 150,000. A great place to raise a family. Good schools, including colleges and universities. Very low crime rate. Practice where you are wanted and appreciated. **For details, call or send your CV to:**

Dr. Amelia McPeak, Medical Director
Westbrook Health Services
2121 Seventh StreetParkersburg, WV 26101
Phone: 304-485-1721 ext 273
Fax 304-422-0908
E-mail: amcpeak@westbrookhealth.com

Assistant/Associate Professor
J-1 Slot Available

The Department of Psychiatry and Behavioral Medicine, of the Joan C. Edwards School of Medicine at Marshall University, is recruiting for a psychiatrist with flexible responsibilities, depending on the training and interest of the applicant. Position is open until filled.

Marshall is a Medical School with a class size of 73, located in Huntington, West Virginia. The metro area has a population of approximately 300,000 with two general hospitals, a private psychiatric hospital, a VA hospital and a State hospital facility.

On the banks of the Ohio River, Huntington has a temperate four-season climate, low cost of living, excellent park system, and a major Museum of Art. Many outdoor recreational activities are available. Marshall University is a doctorate level university of approximately 13,000 students and active sporting and cultural events.

Applicant should be BC/BE in Psychiatry and have an interest in teaching. Clinical responsibilities are primarily in the University outpatient clinic, but can include inpatient services and C/L if desired. Research experience is not necessary, but is desirable.

The University offers an excellent benefits package and competitive salary, and is an Equal Opportunity employer.

CONTACT:
Samuel Januszkiewicz, M.D.
Chairman, Department of Psychiatry and Behavioral Medicine
Joan C. Edwards School of Medicine at Marshall University
1600 Medical Center Dr. Suite B500
Huntington, WV 25701
304-691-1550
januszki@marshall.edu

PSYCHIATRIST-West Virginia University School of Medicine, The Department of Behavioral Medicine and Psychiatry, has ongoing opportunities and faculty positions for full-time, part-time or per diem **BE/BC Adult and Child Psychiatrists** in various locations throughout the state of West Virginia, including its primary clinical, educational and research location in Morgantown, WV, as well as William R. Sharpe Jr. Hospital, a 150-bed, JCAHO-accredited, state psychiatric hospital in Weston, WV.Responsibilities include patient care and teaching, with opportunities for research. Positions will remain open until filled. **Contact Susan Clayton at sclayton@hsc.wvu.edu. WVU is an AA/EO employer.**

WISCONSIN

The University of Wisconsin Department of Psychiatry is a financially strong academic Psychiatry department undergoing an aggressive faculty growth plan. We are seeking BC/BE Child and Adolescent Psychiatrists and BC/BE Adult Psychiatrists to join in the expansion of innovative clinical programming and services. We have opportunities for both inpatient consult and outpatient practice settings and provide compensation equivalent to that found in private practice settings, paired with the stimulation of an academic environment. Participation in teaching activities is expected and rewarded. For more information, please e-mail a letter of interest and CV to:

Jeff Charlson
Department Administrator
jtcharls@wisc.edu

IN-PATIENT PSYCHIATRY OPPORTUNITY

Marshfield Clinic-Marshfield Center is seeking a **BE/BC Psychiatrist** to assume the role of a full time Medical Director for the 13 bed voluntary in-patient psychiatric unit for a tertiary medical center. This individual will assist with covering consultation service in rotation with other psychiatrists. This practice provides care to a full gamut of high acuity psychiatric patients including mood disorders, psychological disorders, and cognitive disorders. With over 775 physicians practicing at 50+ locations throughout Wisconsin, it's the leader in providing high quality health care to the region. Marshfield Clinic offers a very competitive compensation and benefit package.

Contact Beth Albee at: albee.beth@marshfieldclinic.org, 715-221-9775, Marshfield, WI. **www.marshfieldclinic.org.**

WYOMING

CASPER & CHEYENNE: Psychiatrist for inpatient & outpatient services. Highly competitive salary, benefits, & bonus plan. Student loan assistance negotiable. Contact Joy Lankswert, In-house recruiter @ 866-227-5415 or email joy.lankswert@uhsinc.com.

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Fellowships

FORENSIC PSYCHIATRY FELLOWSHIP

This ACGME-accredited one-year fellowship has Forensic Psychiatry Fellowship positions available at the PGY-V level or above, starting July 1, 2010. The program offers training in forensics at the University of California, San Diego, and at the Atascadero State Mental Hospital. For more information and to apply, please contact Lynn Maskel, M.D., M.A., Forensic Fellowship Director at: Department of Psychiatry, University of California, San Diego; 9500 Gilman Drive, La Jolla, California 92093-0603, (858) 534-3684, or c/o kstuart@ucsd.edu.

Rural Public Psychiatry Fellowship

The Department of Psychiatry and Behavioral Medicine at **The University of Alabama in Tuscaloosa** is seeking candidates for its newly established Rural Public Psychiatry Fellowship. The program is open to physicians who have recently completed an accredited Psychiatry residency program. The Fellowship is a 1-year, non-accredited program that will provide exposure to various Public Psychiatry settings with a unique focus on rural West Alabama. Fellow will spend approximately 40% of effort at a University-affiliated rural community mental health center and will alternate time at various other sites including VA, juvenile, geriatric, and developmental centers. The Fellowship offers diverse opportunities and dedicated time for independent research, as well as telepsychiatry consultations and extensive training in mental health administration and management. The program also features structured reading, academic seminars, and provides ample opportunity for teaching and supervision of medical students and Family Medicine residents. In addition, the Fellow will receive support for attendance at a professional meeting/conference. The Fellowship begins July 2010. Salary is $70,000, plus full benefits. Candidates must be eligible for licensing in Alabama and DEA certification. The College of Community Health Sciences is located on the main campus of The University of Alabama, a comprehensive research institution that offers a wide variety of opportunities for faculty and their families. Located in Tuscaloosa, Alabama, a community of approximately 150,000, there are many exceptional cultural and recreational opportunities.

For more information, contact Marisa Giggie, M.D., Fellowship Program Chair, at (205) 348-1325. Email magiggie@ccbs.ua.edu. Equal Opportunity, Affirmative Action Employer.

FELLOWSHIPS
and
CHIEF RESIDENCIES
in
PSYCHOSOMATIC MEDICINE
AT YALE UNIVERSITY

This ACGME-accredited one-year fellowship has Psychosomatic Medicine Fellowship positions available at the PGY-V level or above, starting July 1, 2009, as well as PGY-IV chief resident positions (PGY-IV training would not qualify for subspecialty certification). The program offers training in consultation-liaison psychiatry at Yale New Haven Hospital and at the VA Connecticut Healthcare System. Contact Paul Desan, MD, PhD, Yale New Haven Hospital, 20 York St CB2039, New Haven, CT 06504, paul.desan@yale.edu, (203) 785-2618.

PSYCHOSOMATIC MEDICINE FELLOWSHIPS
2010-2011
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Established C/L Group in tertiary care hospital, ACGME accredited. 45 minutes from NYC. Opportunity to work in Burn, High-Risk OB, HIV, Transplant as well as General Med/Surg. Research opportunities. Psychiatry residency & NYS limited permit or license required. Competitive salary and benefits. Contact: Yvette Smolin, MD, Training Director, BHC Room N301, Valhalla, NY 10595 (914) 493-8424 smoliny@wcmc.com

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Forensic Psychiatry Fellowship

ACGME-accredited fellowship program (PGY-5) sponsored by the SUNY Upstate Medical University in Syracuse, NY. One position is available beginning July 1, 2010. This is a one-year program with training at multiple clinical sites in the Medical University and at Central New York Psychiatric Center; the JCAHO accredited forensic psychiatric hospital of the New York State prison system. There is a substantial component at the Syracuse University College of Law. Dedicated research support is available. Fellows receive intensive supervision by the director, and participate in the director's private forensic consultation clinic. Fellows also collaborate with various law enforcement personnel to assist with threat assessments and workplace violence cases. Candidates must be eligible for licensing or limited permit in New York State.

For information, please contact James L. Knoll, M.D., IV, Director Forensic Psychiatry Fellowship Program, SUNY-Upstate Medical University, Department of Psychiatry, 750 E. Adams Street, Syracuse, NY 13210, (315) 464-3104, fax (315) 464-3141, email address Knollj@upstate.edu.

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Pristiq® desvenlafaxine Extended-Release Tablets

BRIEF SUMMARY. See package insert for full Prescribing Information. For further product information and current package insert, please visit www.wyeth.com or call our medical communications department toll-free at 1-800-934-5556.

WARNING: 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 Pristiq 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. Pristiq is not approved for use in pediatric patients [*see Warnings and Precautions (5.1), Use in Specific Populations (8.4), and Patient Counseling Information (17.1 in the full prescribing information)*].

INDICATIONS AND USAGE: Pristiq, a selective serotonin and norepinephrine reuptake inhibitor (SNRI), is indicated for the treatment of major depressive disorder (MDD).

CONTRAINDICATIONS: Hypersensitivity-Hypersensitivity to desvenlafaxine succinate, venlafaxine hydrochloride or to any excipients in the Pristiq formulation. **Monoamine Oxidase Inhibitors-**Pristiq must not be used concomitantly in patients taking monoamine oxidase inhibitors (MAOIs) or in patients who have taken MAOIs within the preceding 14 days due to the risk of serious, sometimes fatal, drug interactions with SNRI or SSRI treatment or with other serotonergic drugs. Based on the half-life of desvenlafaxine, at least 7 days should be allowed after stopping Pristiq before starting an MAOI [*see Dosage and Administration (2.5) in the full prescribing information*].

WARNINGS AND PRECAUTIONS: Clinical Worsening and Suicide Risk-Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled studies of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older. The pooled analyses of placebo-controlled studies in children and adolescents with MDD, obsessive-compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term studies of 9 antidepressant drugs in over 4,400 patients. The pooled analyses of placebo-controlled studies in adults with MDD or other psychiatric disorders included a total of 295 short-term studies (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1000 patients treated) are provided in Table 1 of the full prescribing information. No suicides occurred in any of the pediatric studies. There were suicides in the adult studies, but the number was not sufficient to reach any conclusion about drug effect on suicide. It is unknown whether the suicidality risk extends to longer-term use, ie, beyond several months. However, there is substantial evidence from placebo-controlled maintenance studies in adults with depression that the use of antidepressants can delay the recurrence of depression. **All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.** The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms [*see Warnings and Precautions (5.9) and Dosage and Administration (2.3) in the full prescribing information for a description of the risks of discontinuation of Pristiq*]. Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for Pristiq should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. Screening patients for bipolar disorder- A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled studies) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that Pristiq is not approved for use in treating bipolar depression. **Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like Reactions-** The development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported with SNRIs and SSRIs alone, including Pristiq treatment, but particularly with concomitant use of serotonergic drugs (including triptans), with drugs that impair metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. Serotonin syndrome symptoms may include mental status changes (eg, agitation, hallucinations, coma), autonomic instability (eg, tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (eg, hyperreflexia, incoordination) and/or gastrointestinal symptoms (eg, nausea, vomiting, diarrhea). Serotonin syndrome in its most severe form can resemble neuroleptic malignant syndrome, which includes hyperthermia, muscle rigidity, autonomic instability with possible rapid fluctuation of vital signs, and mental status changes. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms. The concomitant use of Pristiq with MAOIs intended to treat depression is contraindicated [*see Contraindications (4.2)*]. If concomitant treatment of Pristiq with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. The concomitant use of Pristiq with serotonin precursors (such as tryptophan) is not recommended. Treatment with Pristiq and any concomitant serotonergic or antidopaminergic agents, including antipsychotics, should be discontinued immediately if the above events occur, and supportive symptomatic treatment should be initiated. **Elevated Blood Pressure-** Patients receiving Pristiq should have regular monitoring of blood pressure since dose-dependent increases were observed in clinical studies. Pre-existing hypertension should be controlled before initiating treatment with Pristiq. Caution should be exercised in treating patients with pre-existing hypertension or other underlying conditions that might be compromised by increases in blood pressure. Cases of elevated blood pressure requiring immediate treatment have been reported with Pristiq. Sustained hypertension- Sustained blood pressure increases could have adverse consequences. For patients who experience a sustained increase in blood pressure while receiving Pristiq, either dose reduction or discontinuation should be considered [*see Adverse Reactions (6.1)*]. Treatment with Pristiq in controlled studies was associated with sustained hypertension, defined as treatment-emergent supine diastolic blood pressure (SDBP) ≥90 mm Hg and ≥10 mm Hg above baseline for 3 consecutive on-therapy visits. In clinical studies, regarding the proportion of patients with sustained hypertension, the following rates were observed: placebo (0.5%), Pristiq 50 mg (1.3%), Pristiq 100 mg (0.7%), Pristiq 200 mg (1.1%), and Pristiq 400 mg (2.3%). Analyses of patients in Pristiq controlled studies who met criteria for sustained hypertension revealed a dose-dependent increase in the proportion of patients who developed sustained hypertension. **Abnormal Bleeding-**SSRIs and SNRIs can increase the risk of bleeding events. Concomitant use of aspirin, other drugs that affect platelet function, nonsteroidal anti-inflammatory drugs, warfarin, and other anticoagulants can add to this risk. Bleeding events related to SSRIs and SNRIs have ranged from ecchymosis, hematoma, epistaxis, and petechiae to life-threatening hemorrhages. Patients should be cautioned about the risk of bleeding associated with the concomitant use of Pristiq and NSAIDs, aspirin, or other drugs that affect coagulation or bleeding. **Narrow-angle Glaucoma-**Mydriasis has been reported in association with Pristiq; therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma (angle-closure glaucoma) should be monitored. **Activation of Mania/Hypomania-**During all MDD and VMS (vasomotor symptoms) phase 2 and phase 3 studies, mania was reported for approximately 0.1% of patients treated with Pristiq. Activation of mania/hypomania has also been reported in a small proportion of patients with major affective disorder who were treated with other marketed antidepressants. As with all antidepressants, Pristiq should be used cautiously in patients with a history or family history of mania or hypomania. **Cardiovascular/Cerebrovascular Disease-**Caution is advised in administering Pristiq to patients with cardiovascular, cerebrovascular, or lipid metabolism disorders [*see Adverse Reactions (6.1)*]. Increases in blood pressure and heart rate were observed in clinical studies with Pristiq. Pristiq has not been evaluated systematically in patients with a recent history of myocardial infarction, unstable heart disease, uncontrolled hypertension, or cerebrovascular disease. Patients with these diagnoses, except for cerebrovascular disease, were excluded from clinical studies. **Serum Cholesterol and Triglyceride Elevation-**Dose-related elevations in fasting serum total cholesterol, LDL (low-density lipoprotein) cholesterol, and triglycerides were observed in the controlled studies. Measurement of serum lipids should be considered during treatment with Pristiq [*see Adverse Reactions (6.1)*]. **Discontinuation of Treatment with Pristiq-** Discontinuation symptoms have been systematically and prospectively evaluated in patients treated with Pristiq during clinical studies in major depressive disorder. Abrupt discontinuation or dose reduction has been associated with the appearance of new symptoms that include dizziness, nausea, headache, irritability, insomnia, diarrhea, anxiety, fatigue, abnormal dreams, and hyperhidrosis. In general, discontinuation events occurred more frequently with longer duration of therapy. During marketing of SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors) and SSRIs (Selective Serotonin Reuptake Inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (eg, paresthesia, such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment with Pristiq. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate [*see Dosage and Administration (2.4) and Adverse Reactions (6.1) in full prescribing information*]. **Renal Impairment-**In patients with moderate or severe renal impairment or end-stage renal disease (ESRD) the clearance of Pristiq was decreased, thus prolonging the elimination half-life of the drug. As a result, there were potentially clinically significant increases in exposures to Pristiq [*see Clinical Pharmacology (12.6) in full prescribing information*]. Dosage adjustment (50 mg every other day) is necessary in patients with severe renal impairment or ESRD. The doses should not be escalated in patients with moderate or severe renal impairment or ESRD [*see Dosage and Administration (2.2) in full prescribing information*]. **Seizure-** Cases of seizure have been reported in premarketing clinical studies with Pristiq. Pristiq should be prescribed with caution in patients with a seizure disorder. **Hyponatremia-** Hyponatremia can occur as a result of treatment with SSRIs and SNRIs, including Pristiq. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Elderly patients can be at greater risk of developing hyponatremia with SSRIs and SNRIs. Also, patients taking diuretics or who are otherwise volume depleted can be at greater risk [*see Use in Specific Populations (8.5) and Clinical Pharmacology (12.6) in full prescribing information*]. Discontinuation of Pristiq should be considered in patients with symptomatic hyponatremia and appropriate medical intervention should be instituted. **Coadministration of Drugs Containing Desvenlafaxine and Venlafaxine-** Desvenlafaxine is the major active metabolite of venlafaxine. Products containing desvenlafaxine and products containing venlafaxine should not be used concomitantly with Pristiq. **Interstitial Lung Disease and Eosinophilic Pneumonia-** Interstitial lung disease and eosinophilic pneumonia associated with venlafaxine (the parent drug of Pristiq) therapy have been rarely reported. The possibility of these adverse events should be considered in patients treated with Pristiq who present with progressive dyspnea, cough, or chest discomfort. Such patients should undergo a prompt medical evaluation, and discontinuation of Pristiq should be considered.

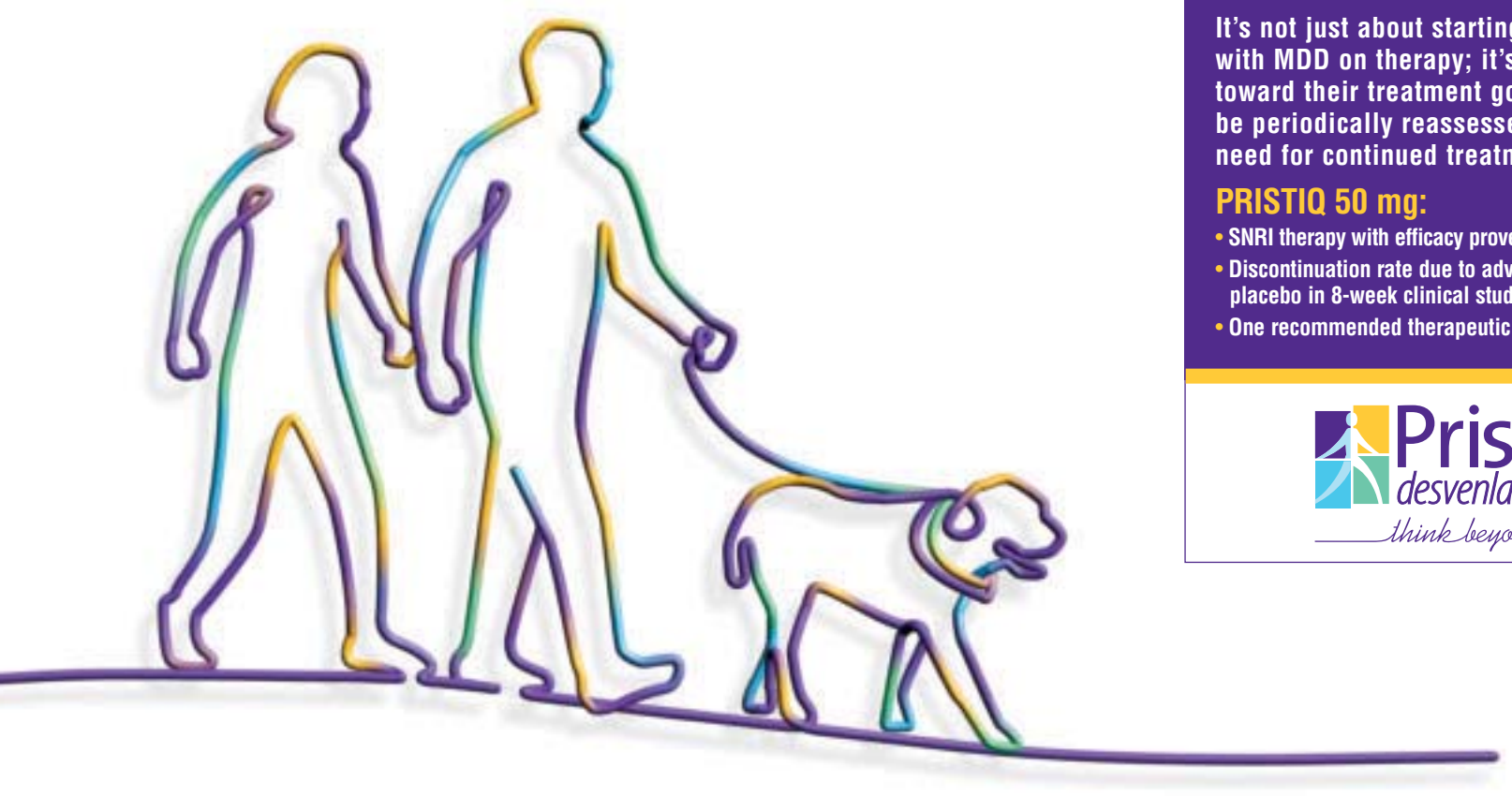
ADVERSE REACTIONS: Clinical Studies Experience: The most commonly observed adverse reactions in Pristiq-treated MDD patients in short-term fixed-dose studies (incidence ≥5% and at least twice the rate of placebo in the 50- or 100-mg dose groups) were nausea, dizziness, insomnia, hyperhidrosis, constipation, somnolence, decreased appetite, anxiety, and specific male sexual function disorders. Adverse reactions reported as reasons for discontinuation of treatment- The most common adverse reactions leading to discontinuation in at least 2% of the Pristiq-treated patients in the short-term studies, up to 8 weeks, were nausea (4%); dizziness, headache and vomiting (2% each); in the long-term study, up to 9 months, the most common was vomiting (2%). Common adverse reactions in placebo-controlled MDD studies- Table 3 in full PI shows the incidence of common adverse reactions that occurred in ≥2% of Pristiq-treated MDD patients at any dose in the 8-week, placebo-controlled, fixed-dose, premarketing clinical studies. In general, the adverse reactions were most frequent in the first week of treatment. Cardiac disorders: Palpitations, Tachycardia, Blood pressure increased; Gastrointestinal disorders: Nausea, Dry mouth, Diarrhea, Constipation, Vomiting; General disorders and administration site conditions: Fatigue, Chills, Feeling jittery, Asthenia; Metabolism and nutrition disorders: Decreased appetite, weight decreased; Nervous system disorders: Dizziness, Somnolence, Headache, Tremor, Paraesthesia, Disturbance in attention; Psychiatric Disorders: Insomnia, Anxiety, Nervousness, Irritability, Abnormal dreams; Renal and urinary disorders: Urinary hesitation; Respiratory, thoracic, and mediastinal disorders: Yawning; Skin and subcutaneous tissue disorders: Hyperhidrosis, Rash; Special Senses: Vision blurred; Mydriasis, Tinnitus, Dysgeusia; Vascular Disorders: Hot flush. Sexual function adverse reactions-Table 4 shows the incidence of sexual function adverse reactions that occurred in ≥2% of Pristiq-treated MDD patients in any fixed-dose group (8-week, placebo-controlled, fixed and flexible-dose, premarketing clinical studies). Men Only: Anorgasmia, Libido decreased, Orgasm abnormal, Ejaculation delayed, Erectile dysfunction, Ejaculation disorder, Ejaculation failure, Sexual dysfunction; Women Only: Anorgasmia; Other adverse reactions observed in premarketing clinical studies: Other infrequent adverse reactions occurring at an incidence of <2% in MDD patients treated with Pristiq were: *Immune system disorders* – Hypersensitivity. *Investigations* – Weight increased, liver function test abnormal, blood prolactin increased. *Nervous system disorders* – Convulsion, syncope, extrapyramidal disorder. *Musculoskeletal and connective tissue disorders* – Musculoskeletal stiffness. *Psychiatric disorders* – Depersonalization, hypomania. *Respiratory, thoracic and mediastinal disorders* – Epistaxis. *Vascular disorders* – Orthostatic hypotension. In clinical studies, there were uncommon reports of ischemic cardiac adverse events, including myocardial ischemia, myocardial infarction, and coronary occlusion requiring revascularization; these patients had multiple underlying cardiac risk factors. More patients experienced these events during Pristiq treatment as compared to placebo [*see Warnings and Precautions (5.7)*]. Discontinuation events-Adverse events reported in association with abrupt discontinuation, dose reduction or tapering of treatment in MDD clinical studies at a rate of ≥5% include dizziness, nausea, headache, irritability, insomnia, diarrhea, anxiety, abnormal dreams, fatigue, and hyperhidrosis. In general, discontinuation events occurred more frequently with longer duration of therapy [*see Dosage and Administration (2.4) and Warnings and Precautions (5.9) in full prescribing information*]. Laboratory, ECG and vital sign changes observed in MDD clinical studies-The following changes were observed in placebo-controlled, short-term, premarketing MDD studies with Pristiq. *Lipids*-Elevations in fasting serum total cholesterol, LDL (low-density lipoprotein) cholesterol, and triglycerides occurred in the controlled studies. Some of these abnormalities were considered potentially clinically significant [*see Warnings and Precautions (5.8)*]. *Proteinuria*-Proteinuria, greater than or equal to trace, was observed in the fixed-dose controlled studies (see Table 6 in full prescribing information). This proteinuria was not associated with increases in BUN or creatinine and was generally transient. *ECG changes*-Electrocardiograms were obtained from 1,492 Pristiq-treated patients with major depressive disorder and 984 placebo-treated patients in clinical studies lasting up to 8 weeks. No clinically relevant differences were observed between Pristiq-treated and placebo-treated patients for QT, QTc, PR, and QRS intervals. In a thorough QTc study with prospectively determined criteria, desvenlafaxine did not cause QT prolongation. No difference was observed between placebo and desvenlafaxine treatments for the QRS interval. *Vital sign changes*-Table 7 summarizes the changes that were observed in placebo-controlled, short-term, premarketing studies with Pristiq in patients with MDD (doses 50 to 400 mg). Relative to placebo, Pristiq was associated with mean increase of up to 2.1 mm Hg in systolic blood pressure, 2.3 mm Hg in diastolic blood pressure, and 4.1 bpm with supine pulse. At the final on-therapy assessment in the 6-month, double-blind, placebo-controlled phase of a long-term study in patients who had responded to Pristiq during the initial 12-week, open-label phase, there was no statistical difference in mean weight gain between Pristiq- and placebo-treated patients. *Orthostatic hypotension*- In the short-term, placebo-controlled clinical studies with doses of 50-400 mg, systolic orthostatic hypotension (decrease ≥30 mm Hg from supine to standing position) occurred more frequently in patients ≥65 years of age receiving Pristiq (8.0%, 7/87) versus placebo (2.5%, 1/40), compared to patients <65 years of age receiving Pristiq (0.9%, 18/1,937) versus placebo (0.7%, 8/1,218). **Adverse Reactions Identified During Post-Approval Use-** The following adverse reaction has been identified during post-approval use of Pristiq. Because post-approval reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: *Skin and subcutaneous tissue disorders* – Angioedema. **DRUG INTERACTIONS: Central Nervous System (CNS)-Active Agents-**The risk of using Pristiq in combination with other CNS-active drugs has not been systematically evaluated. Consequently, caution is advised when Pristiq is taken in combination with other CNS-active drugs [*see Warnings and Precautions (5.13)*]. **Monoamine Oxidase Inhibitors (MAOIs)-** Adverse reactions, some of which were serious, have been reported in patients who have recently been discontinued from a monoamine oxidase inhibitor (MAOI) and started on antidepressants with pharmacological properties similar to Pristiq (SNRIs or SSRIs), or who have recently had SNRI or SSRI therapy discontinued prior to initiation of an MAOI [*see Contraindications (4.2)*]. **Serotonergic Drugs-** Based on the mechanism of action of Pristiq and the potential for serotonin syndrome, caution is advised when Pristiq is coadministered with other drugs that may affect the serotonergic neurotransmitter systems [*see Warnings and Precautions (5.2)*]. **Drugs that Interfere with Hemostasis (eg, NSAIDs, Aspirin, and Warfarin)-** Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of case-control and cohort design have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. These studies have also shown that concurrent use of an NSAID or aspirin may potentiate this risk of bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs and SNRIs are coadministered with warfarin. Patients receiving warfarin therapy should be carefully monitored when Pristiq is initiated or discontinued. **Ethanol-** A clinical study has shown that desvenlafaxine does not increase the impairment of mental and motor skills caused by ethanol. However, as with all CNS-active drugs, patients should be advised to avoid alcohol consumption while taking Pristiq. **Potential for Other Drugs to Affect Desvenlafaxine-**Inhibitors of CYP3A4 (ketoconazole)- CYP3A4 is a minor pathway for the metabolism of Pristiq. Concomitant use of Pristiq with potent inhibitors of CYP3A4 may result in higher concentrations of Pristiq. Inhibitors of other CYP enzymes- Based on *in vitro* data, drugs that inhibit CYP isozymes 1A1, 1A2, 2A6, 2D6, 2C8, 2C9, 2C19, and 2E1 are not expected to have significant impact on the pharmacokinetic profile of Pristiq. **Potential for Desvenlafaxine to Affect Other Drugs-** Drugs metabolized by CYP2D6 (desipramine)- *In vitro* studies showed minimal inhibitory effect of desvenlafaxine on CYP2D6. Clinical studies have shown that desvenlafaxine does not have a clinically relevant effect on CYP2D6 metabolism at the dose of 100 mg daily. Concomitant use of desvenlafaxine with a drug metabolized by CYP2D6 can result in higher concentrations of that drug. Drugs metabolized by CYP3A4 (midazolam)- *In vitro*, desvenlafaxine does not inhibit or induce the CYP3A4 isozyme. Concomitant use of Pristiq with a drug metabolized by CYP3A4 can result in lower exposures to that drug. Drugs metabolized by CYP1A2, 2A6, 2C8, 2C9 and 2C19- *In vitro*, desvenlafaxine does not inhibit CYP1A2, 2A6, 2C8, 2C9, and 2C19 isozymes and would not be expected to affect the pharmacokinetics of drugs that are metabolized by these CYP isozymes. **P-glycoprotein Transporter-** *In vitro*, desvenlafaxine is not a substrate or an inhibitor for the P-glycoprotein transporter. The pharmacokinetics of Pristiq are unlikely to be affected by drugs that inhibit the P-glycoprotein transporter, and desvenlafaxine is not likely to affect the pharmacokinetics of drugs that are substrates of the P-glycoprotein transporter. **Electroconvulsive Therapy-** There are no clinical data establishing the risks and/or benefits of electroconvulsive therapy combined with Pristiq treatment. **USE IN SPECIFIC POPULATIONS: Pregnancy-** Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. Teratogenic effects– Pregnancy Category C- There are no adequate and well-controlled studies of Pristiq in pregnant women. Therefore, Pristiq should be used during pregnancy only if the potential benefits justify the potential risks. Non-teratogenic effects- Neonates exposed to SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors), or SSRIs (Selective Serotonin Reuptake Inhibitors), late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome [*see Warnings and Precautions (5.2)*]. When treating a pregnant woman with Pristiq during the third trimester, the physician should carefully consider the potential risks and benefits of treatment [*see Dosage and Administration (2.2)*]. **Labor and Delivery-** The effect of Pristiq on labor and delivery in humans is unknown. Pristiq should be used during labor and delivery only if the potential benefits justify the potential risks. **Nursing Mothers-** Desvenlafaxine (O-desmethylvenlafaxine) is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Pristiq, a decision should be made whether or not to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Only administer Pristiq to breastfeeding women if the expected benefits outweigh any possible risk. **Pediatric Use-** Safety and effectiveness in the pediatric population have not been established [*see Box Warning and Warnings and Precautions (5.1)*]. Anyone considering the use of Pristiq in a child or adolescent must balance the potential risks with the clinical need. **Geriatric Use-** Of the 3,292 patients in clinical studies with Pristiq, 5% were 65 years of age or older. No overall differences in safety or efficacy were observed between these patients and younger patients; however, in the short-term, placebo-controlled studies, there was a higher incidence of systolic orthostatic hypotension in patients ≥65 years of age compared to patients <65 years of age treated with Pristiq [*see Adverse Reactions (6)*]. For elderly patients, possible reduced renal clearance of desvenlafaxine should be considered when determining dose [*see Dosage and Administration (2.2) and Clinical Pharmacology (12.6)*]. If Pristiq is poorly tolerated, every other day dosing can be considered. SSRIs and SNRIs, including Pristiq, have been associated with cases of clinically significant hyponatremia in elderly patients, who may be at greater risk for this adverse event [*see Warnings and Precautions (5.12)*]. Greater sensitivity of some older individuals cannot be ruled out. **Renal Impairment-** In subjects with renal impairment the clearance of Pristiq was decreased. In subjects with severe renal impairment (24-hr CrCl < 30 mL/min) and end-stage renal disease, elimination half-lives were significantly prolonged, increasing exposures to Pristiq; therefore, dosage adjustment is recommended in these patients [*see Dosage and Administration (2.2) and Clinical Pharmacology (12.6) in the full prescribing information*]. **Hepatic Impairment-** The mean $t_{1/2}$ changed from approximately 10 hours in healthy subjects and subjects with mild hepatic impairment to 13 and 14 hours in moderate and severe hepatic impairment, respectively. The recommended dose in patients with hepatic impairment is 50 mg/day. Dose escalation above 100 mg/day is not recommended [*see Clinical Pharmacology (12.6)*].

OVERDOSAGE: Human Experience with Overdosage- There is limited clinical experience with desvenlafaxine succinate overdosage in humans. In premarketing clinical studies, no cases of fatal acute overdose of desvenlafaxine were reported. The adverse reactions reported within 5 days of an overdose >600 mg that were possibly related to Pristiq included headache, vomiting, agitation, dizziness, nausea, constipation, diarrhea, dry mouth, paresthesia, and tachycardia. Desvenlafaxine (Pristiq) is the major active metabolite of venlafaxine. Overdose experience reported with venlafaxine (the parent drug of Pristiq) is presented below; the identical information can be found in the *Overdosage* section of the venlafaxine package insert. In postmarketing experience, overdose with venlafaxine (the parent drug of Pristiq) has occurred predominantly in combination with alcohol and/or other drugs. The most commonly reported events in overdosage include tachycardia, changes in level of consciousness (ranging from somnolence to coma), mydriasis, seizures, and vomiting. Electrocardiogram changes (eg, prolongation of QT interval, bundle branch block, QRS prolongation), sinus and ventricular tachycardia, bradycardia, hypotension, rhabdomyolysis, vertigo, liver necrosis, serotonin syndrome, and death have been reported. Published retrospective studies report that venlafaxine overdosage may be associated with an increased risk of fatal outcomes compared to that observed with SSRI antidepressant products, but lower than that for tricyclic antidepressants. Epidemiological studies have shown that venlafaxine-treated patients have a higher pre-existing burden of suicide risk factors than SSRI-treated patients. The extent to which the finding of an increased risk of fatal outcomes can be attributed to the toxicity of venlafaxine in overdosage, as opposed to some characteristic(s) of venlafaxine-treated patients, is not clear. Prescriptions for Pristiq should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. **Management of Overdosage-** Treatment should consist of those general measures employed in the management of overdosage with any SSRI/SNRI. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also 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. Induction of emesis is not recommended. Because of the moderate volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidotes for desvenlafaxine are known. In managing an overdose, 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®).

This brief summary is based on Pristiq Prescribing Information W10529C009, revised September 2009.

FOR MAJOR DEPRESSIVE DISORDER

Help your patients



on a path forward with proven SNRI therapy

It's not just about starting your adult patients with MDD on therapy; it's about helping them toward their treatment goals. Patients should be periodically reassessed to determine the need for continued treatment.[1]

PRISTIQ 50 mg:

- **SNRI therapy with efficacy proven in 8-week clinical studies**
- **Discontinuation rate due to adverse events comparable to placebo in 8-week clinical studies**
- **One recommended therapeutic dose from the start[1]**

Pristiq® desvenlafaxine 50 mg

think beyond start™

Important Treatment Considerations for PRISTIQ

PRISTIQ is indicated for the treatment of major depressive disorder in adults.

WARNING: 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 PRISTIQ 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. PRISTIQ is not approved for use in pediatric patients.

Contraindications

- PRISTIQ is contraindicated in patients with a known hypersensitivity to PRISTIQ or venlafaxine.
- PRISTIQ must not be used concomitantly with an MAOI or within 14 days of stopping an MAOI. Allow 7 days after stopping PRISTIQ before starting an MAOI.

Warnings and Precautions

- **All patients treated with antidepressants should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the first few months of treatment and when changing the dose.** Consider changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse or includes symptoms of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia, hypomania, mania, or suicidality that are severe, abrupt in onset, or were not part of the patient's presenting symptoms. **Families and caregivers of patients being treated with antidepressants should be alerted about the need to monitor patients.**
- Development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome-like reactions have been reported with SNRIs and SSRIs alone, including PRISTIQ treatment, but particularly with concomitant use of serotonergic drugs, including triptans, with drugs that impair the metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists. If concomitant use with a triptan is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. Concomitant use of PRISTIQ with serotonin precursors is not recommended.
- Patients receiving PRISTIQ should have regular monitoring of blood pressure since increases in blood pressure were observed in clinical studies. Pre-existing hypertension should be controlled before starting PRISTIQ. Caution should be exercised in treating patients with pre-existing hypertension or other underlying conditions that might be compromised by increases in blood pressure. Cases of elevated blood pressure requiring immediate treatment have been reported. For patients who experience a sustained increase in blood pressure, either dose reduction or discontinuation should be considered.
- SSRIs and SNRIs, including PRISTIQ, may increase the risk of bleeding events. Concomitant use of aspirin, NSAIDs, warfarin, and other anticoagulants may add to this risk.
- Mydriasis has been reported in association with PRISTIQ; therefore, patients with raised intraocular pressure or those at risk of acute narrow-angle glaucoma (angle-closure glaucoma) should be monitored.
- PRISTIQ is not approved for use in bipolar depression. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine the risk of bipolar disorder.
- As with all antidepressants, PRISTIQ should be used cautiously in patients with a history or family history of mania or hypomania, or with a history of seizure disorder.
- Caution is advised in administering PRISTIQ to patients with cardiovascular, cerebrovascular, or lipid metabolism disorders. Increases in blood pressure and small increases in heart rate were observed in clinical studies with PRISTIQ. PRISTIQ has not been evaluated systematically in patients with a recent history of myocardial infarction, unstable heart disease, uncontrolled hypertension, or cerebrovascular disease.
- Dose-related elevations in fasting serum total cholesterol, LDL (low density lipoprotein) cholesterol, and triglycerides were observed in clinical studies. Measurement of serum lipids should be considered during PRISTIQ treatment.
- On discontinuation, adverse events, some of which may be serious, have been reported with PRISTIQ and other SSRIs and SNRIs. Abrupt discontinuation of PRISTIQ has been associated with the appearance of new symptoms. Patients should be monitored for symptoms when discontinuing treatment. A gradual reduction in dose rather than abrupt cessation is recommended whenever possible.
- The recommended dose in patients with severe renal impairment or end-stage renal disease (ESRD) is 50 mg every other day. The dose should not be escalated in patients with moderate or severe renal impairment or ESRD.
- Products containing desvenlafaxine and products containing venlafaxine should not be used concomitantly with PRISTIQ.
- Hyponatremia may occur as a result of treatment with SSRIs and SNRIs, including PRISTIQ. Discontinuation of PRISTIQ should be considered in patients with symptomatic hyponatremia.
- Interstitial lung disease and eosinophilic pneumonia associated with venlafaxine (the parent drug of PRISTIQ) therapy have been rarely reported.

Adverse Reactions

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

Reference: 1. Pristiq® (desvenlafaxine) Prescribing Information, Wyeth Pharmaceuticals Inc.

Please see brief summary of Prescribing Information on adjacent page.

For more information on PRISTIQ, please visit **www.PristiqHCP.com**.

Pristiq®
EXTENDED-RELEASE TABLETS

Pfizer