Psychiatric Bulletin:
Late-Breaking Clinical News

Primary Care

REPORTS FROM THE APA

QUALITY OF PSYCHIATRIC TRAINING IN PRIMARY CARE RESIDENCY PROGRAMS RATES BETTER

Primary care providers are often the first and only point of contact for patients with mental illnesses. While the need for adequate preparation of this physician population is widely recognized, it is also known that there is great variability in the quality and quantity of psychiatric training in residency programs.

To evaluate the current status of mental health training during residency, researchers at the University of California conducted a survey among 1,268 US program directors. Using a 16-item questionnaire, Hoyle Leigh, MD, and colleagues asked the participants to evaluate the amount and specific areas of psychiatric education (eg, interviewing, psychopharmacology, depression), as well as the degree of satisfaction with their training programs.

Surprisingly, they found considerable differences between the family practice and all other residency programs. Of all the respondents (40%), 58% of family practice residencies rated their training optimal or extensive, compared with only 25% of internal medicine programs, 12% of obstetric programs, and 16% of pediatric programs ($P>.001$). While 55% of all programs were not satisfied with their psychiatric training ($P<.001$), primary care programs showed much more diversity in training venues, faculty, and specific topics being addressed.

Although the current status of training of nonpsychiatric residents leaves much to be desired, the results of this study indicate that enhancing the diversity and availability of teaching settings and faculty in the training programs may go a long way in improving the quality of and satisfaction with mental health education of primary care providers.

Source: Leigh H. Psychiatry training in primary care: current status and satisfaction. Presented at: APA annual meeting; May 17-22, 2003; San Francisco.

CBT MAY PROVIDE REAL IMPROVEMENT FOR SEXUALLY ABUSED CHILDREN

Can lasting benefits be achieved in the treatment of traumatized children who have been subjected to sexual abuse? While few randomized, controlled treatment trials exist, information on long-term treatment outcomes is even more obscure. With the dearth of reliable information, the results of a 1-year follow-up study, sponsored by the National Center for Child Abuse and Neglect and presented at the annual meeting of the American Psychiatric Association in San Francisco, should shed some welcome light on this critical area.

Judith A. Cohen, MD, and colleagues evaluated 81 sexually abused children aged 8-14 and randomly assigned them to trauma-focused cognitive behavior therapy or nondirective supportive therapy, which were provided individually to the child and nonoffending parent in 12 sessions. Children's long-term functioning was assessed using a variety of tools, including the Trauma Symptom Checklist for Children, the Children's Depressive Inventory, the State-Trait Anxiety Inventory for Children, the Child Sexual Behavior Inventory, and the Child Behavior Checklist.

When the children were evaluated 1 year after treatment completion, the differences between the 2 treatment groups had become more marked: Compared to the nondirective supportive therapy group, the children who received cognitive behavior therapy showed significantly greater

improvement in posttraumatic stress disorder symptoms, depression, and anxiety.

These results, while providing hopeful evidence that effective treatment of children traumatized by sexual abuse is possible, also indicate that the beneficial effects may increase even further over time.

Source: Cohen JA, Mannarino AP, Knudsen K. Treatment outcome for sexually abused children at one-year follow-up. Presented at: APA annual meeting; May 17-22, 2003; San Francisco.

MODAFINIL AS ADJUNCT TO CPAP FOR TREATMENT OF SLEEP APNEA

Because obstructive sleep apnea impedes the sufferer's normal breathing rhythm during sleep, excessive sleepiness while awake is a primary symptom of the disorder. Patients with sleep apnea often have a severely impaired quality of life. Notoriously difficult to treat, nasal continuous positive airway pressure (nCPAP), which entails wearing a breathing mask during sleep, has become the gold standard of treatment and has shown to improve quality of life.

Despite regular use of nCPAP, some patients still experience residual excessive sleepiness while awake. The wake-promoting agent modafinil has been shown to improve quality of life in patients with excessive sleepiness associated with narcolepsy. In a study funded by Cephalon, researcher Mary O'Malley, MD, conducted a randomized, double-blind, placebo-controlled, parallel-group study on the use of modafinil for sleep apnea.

Patients received modafinil, titrated to 400 mg/day over four weeks, or matching placebo as adjunct therapy to nCPAP use. Among the 157 patients enrolled, adjunct therapy with modafinil improved sleep-related function over placebo, as self-reported by patients using the Functional Outcomes of Sleep Questionnaire. The findings are encouraging given the complexity of treating sleep apnea.

Source: O'Malley MB. Modafinil improves quality of life as adjunct treatment of obstructive sleep apnea. Presented at: APA annual meeting; May 17-22, 2003; San Francisco.

INCIDENT DEPRESSIVE EPISODES IN BLACK WOMEN VS WHITE WOMEN

African American women may be at greater risk for a first lifetime depressive episode during midlife than white women, according to a study undertaken to better understand the predisposing factors for incident depression. Researchers from the University of Pittsburgh, Pennsylvania, led by Joyce T. Bromberger, PhD, examined a cohort of 443 African American and white women between the ages of 42 to 52 years who were participants in the Study of Women's Health Across the Nation (SWAN). The Structured Clinical interview for *DSM-IV* (*SCID-IV*) was used at baseline and annually. Among the participants, 196 women had no history of major depressive episodes (MDE) or depression not otherwise specified (DNOS) at baseline and during at least 3 assessments.

During the 4-year follow-up, demographic, psychosocial, and health characteristics of women with and without MDE or DNOS were compared. Among the study subjects, diagnostic criteria for depression were met by 46 (23%) women, with rates of depressive episodes higher among African Americans than whites (30% versus 19%, *P*=.08). The baseline predictors of depressive episodes that were found to be of significance included, in addition to subsyndromal mood symptoms, poor role functioning, having at least 1 chronic stressor, personality traits such as anxiety and cynicism, and higher somatic sensitivity. While it appears that African American women may be at greater risk of developing incident depressipon during midlife, one can hope that better understanding of the potential predisposing factors will enable clinicians to more effectively monitor, prevent, and treat depression in patients at risk. MF

Source: Bromberger JT, Kravitz HM, Wei H-L, et al. Predictors of first depressive episode in black and white women in midlife. Presented at: APA annual meeting; May 17-22, 2003; San Francisco.

Psychiatry

HRT AND DEMENTIA RISK

HRT: MORE CAUSE FOR PESSIMISM

A new study has once again stirred up heated debates related to the ongoing controversy of hormone replacement therapy (HRT). The study, published on May 28th in the *Journal of the American Medical Association*, claims that not only does the administration of estrogen and progestin not protect menopausal women from the development of cognitive impairment and dementia, but it actually increases the risk of probable dementia. These results are in striking contrast to much of the earlier research that has suggested that estrogen deficiency may be one of the contributing factors to the greater risk of older women for developing Alzheimer's disease (AD), and that HRT may offer protective effects on the brain after menopause.

The Women's Health Initiative Memory Study (WHIMS), an ancillary study to the 2 larger Women's Health Initiative (WHI) trials, was designed to examine the effects of postmenopausal hormone supplementation and the incidence of dementia and mild cognitive impairment (MCI). This randomized, double-blind, placebo-controlled clinical trial recruited 4532 participants—postmenopausal women aged 65 years or older and determined to be free of probable dementia—from the WHI estrogen plus progestin trial.

Following 3 screening visits, the women were randomly assigned to take either a daily tablet containing conjugated equine estrogen (0.625 mg) and medroxyprogesterone acetate (2.5 mg), or a matching placebo. Through structured clinical assessment, the incidence of probable dementia and MCI were identified. While the researchers planned to continue the administration of HRT for 8.5 years, the trial was stopped after just 5 years, following the publication of data from the WHI study indicating that women using the estrogen/progestin combination were at increased risk for a variety of serious health problems. The estrogen-only component of the WHI, as well as of the WHIMS, continues.

Overall, 61 participants in the WHIMS were diagnosed with probable dementia: 40 (66%) in the estrogen and progestin group, and 21 (34%) in the placebo group. Therefore, the rate of women experiencing probable dementia in the hormone intervention group was more than twice that of women in the placebo group (HR; 2.5; 95% CI, 1.21-3.48; 45 vs 22 per 10, 000 person-years, P=.01). AD was the most common classification of dementia in both groups. The risk of being diagnosed with MCI was not statistically significant between the groups (HR, 1.07; 95% CI, 0.74-1.55; 63 vs 59 cases per 10,000 person-years; P=.72).

Because of the significantly increased risk of probable dementia, as well as the finding that the estrogen/progestin combination did not prevent MCI, the authors recommend that this therapy should no longer be prescribed to postmenopausal women with the expectation that it would increase their cognitive performance. However, despite the importance of these findings, clinicians are also urged to keep in mind that these results are specific to the use of the particular combination, dosage, and route of administration of conjugated equine estrogen and medroxyprogesterone acetate, and that in the broader context of things, the absolute relative risk of dementia is relatively small.

Source: Shumaker SA, Legault C, Thal L, et al. *JAMA*. 2003;289: 2651-2662.

RESULTS FROM THE STEP-BD STUDY

ANTIDEPRESSANT-INDUCED MANIA: PREVALENCE AND RISK

Estimates of the prevalence of antidepressant-induced mania are murky; the most reliable estimates place prevalence at 20% to 40%. Also unclear are the actual characteristics and risk factors associated with the drug-induced state, as well as comorbidities that may obscure its recognition. It is thought that family history of bipolar

disorder, history of substance abuse, and multiple antidepressant trials may confer an increased risk of affective switch on antidepressants. But empiric data are scant, and clinicians are often on their own regarding this particular risk of antidepressant therapy.

A welcome step in clarifying these uncertainties is the undertaking of the Systematic Treatment Enhancement Program for bipolar disorder (STEP-BD) study. Funded by the National Institute of Mental Health, the multicenter STEP-BD is designed to evaluate the longitudinal outcome of patients with bipolar disorder.

Several early findings from STEP-BD were presented at the American Psychiatric Association annual meeting in San Francisco to help bring clearer focus to understanding the disorder. Christine J. Truman, MD, of New York Presbyterian Hospital, and colleagues found that of the first 500 patients enrolled in this naturalistic sample of bipolar patients, 177, or 37%, reported a history of antidepressant-induced mania or hypomania. No significant gender differences were identified. All subjects were then compared across several variables that may increase risk. The researchers called their work useful, but preliminary, and say future prospective analyses are needed in this sample to help identify the subgroup of bipolar patients at increased risk for a treatment-induced affective switches.

Naomi Simon, MD, of Massachusetts General Hospital and colleagues used the same cross-sectional sample of STEP-BD enrollees and found lifetime comorbid anxiety disorders to be common, occurring in over half the sample. Anxiety disorders were associated with younger age of the onset of bipolar disorder, a decreased likelihood of recovery, poorer quality of life, less time euthymic, and a greater likelihood of suicide attempts. Because of the apparent independent association of anxiety comorbidity with greater severity and impairment in bipolar patients, the authors note a need for increased clinical monitoring of these patients, particularly for suicidality. They call for studies that assess the effectiveness of treating anxiety in these patients.

Sources: Truman CJ, Baldassano CF, Goldberg JF, et al. History of antidepressant-induced mania in the STEP 500. Presented at: Annual Meeting of the American Psychiatric Association; May 17-22, 2003; San Francisco.

Simon NM, Sagduyu K, Otto MW, et al. Anxiety comorbidity in bipolar disorder: the first 500 STEP-BD participants. Presented at: Annual Meeting of the American Psychiatric Association; May 17-22, 2003; San Francisco.

HEAD TRAUMA

EFFECT OF PREVIOUS HEAD TRAUMA IN THE PRESENTATION OF PSYCHIATRIC PATIENTS

Although head trauma has long been thought to predispose a person to psychiatric symptoms, the prevalence of prior head injuries in psychiatric populations has not been systematically studied. Edward Kim, MD, of Robert Wood Johnson Medical School, and colleagues surveyed 127 patients consecutively admitted to an acute psychiatric inpatient service to assess history of head injury in this population.

The rater-administered instrument inquired about discrete head injuries and repetitive head injuries with or without altered consciousness. Eighty percent of the subjects reported a history of discrete head injury; 40% reported repeated head injuries without altered consciousness; and 28% said they had experienced repetitive injuries to the head with altered consciousness. Both types of repetitive injuries tended to start in childhood and adolescence, the authors noted, and were either short-lived (<5 years) or chronic (>15 years).

Perhaps not surprisingly, though importantly, repetitive head injuries with altered consciousness were significantly associated with increased admission scores on the psychosis subscale of the Behavior and Symptom Identification Scale. This finding led the researchers to conclude that a history of head injuries is common among psychiatric inpatients and may affect clinical presentation. MF

Source: Kim E, Gara M, Minsky S. Previous head injuries in psychiatric inpatients. Presented at: APA annual meeting; May 17-22, 2003; San Francisco.

OB/GYN

SCIENTIFIC AND CLINICAL REPORTS

EFFECTIVENESS OF SERTRALINE IN POSTPARTUM DEPRESSION

Women who have experienced bouts of major depression before childbirth are at high-risk for additional episodes after childbirth—a finding reinforced in very recent, sound studies. One small, double-blind, randomized trial, led by Katherine L. Wisner, MD, of the University of Pittsburgh, examined the use of sertraline in preventing recurrent depression during the postpartum period.

The study, funded by the National Institute of Mental Health, recruited pregnant women with a previous history of at least 1 episode of major depression. Women received either sertraline or placebo as immediate postpartum treatment. They were assessed over 20 consecutive weeks using the Hamilton Rating Scale for Depression and the Structured Clinical Interview for *DSM-IV* to gauge recurrence of major depression.

Of the 12 women who took sertraline preventively, 1 had a recurrent episode, while 4 of the 8 women who took placebo had a recurrence. Although the sample size was small, the researchers concluded that this significant difference in the rate of recurrence appeared attributable to sertraline taken to prevent postpartum major depressive episodes. This study should pave the way for other, larger studies on the use of sertraline during the postpartum period. The researchers presented their findings in abstract at the American Psychiatric Association's annual meeting in San Francisco.

Source: Wisner, KL, Peindl KS, Perel JM. Sertraline prevents postpartum depression. Presented at: APA annual meeting; May 17-22, 2003; San Francisco.

SEARCHING FOR THE LINK BETWEEN DEPRESSION AND HEART DISEASE IN WOMEN

Depression is a known risk factor for heart disease, though the exact mechanisms remain unclear. Could depression lead to hypercoagulability of the blood, thereby raising a woman's risk of heart disease? That question was addressed in a large study undertaken by Ruby Castilla-Puentes, MD, of the University of Pittsburgh and colleagues.

Researchers measured levels of fibrinogen, factor VIIc, plasminogen activator inhibitor antigen-1, and tissue plasminogen activator antigen in 3,167 women enrolled in the Study of Women's Health Across the Nation (SWAN). The women were between the ages of 42 and 52, and their depression status was determined at the time of testing using the Center for Epidemiological Studies-Depression Scale (CES-D).

Among all women, the prevalence of depression (represented by a CES-D score ≥16) was 24.3%. Depression was associated with higher levels of all coagulation factors, and levels of fibrinogen and factor VIIc were high even after controlling for variables such as smoking, ethnicity, and use of medications, including psychotropics.

These findings are consistent, the authors report, with the hypothesis that a balance between hemostatic and fibrinolytic activity may contribute to the complex relation of depression with cardiovascular disease. This is an important contribution for doctors who treat women with depression. These providers should be aware of the increased risk of hypercoagulability in midlife women with depression, regardless of current psychotropic medication use.

Source: Castilla-Puentes R, Yangang Z, Bromberger JT. Depressed women have elevated coagulation factors in midlife. Presented at: APA annual meeting; May 17-22, 2003; San Francisco.

MORE ON HRT

HRT WITH ANDROGENS SHOWN EFFECTIVE IN POSTMENOPAUSAL DEPRESSION

The use of steroid hormones for the treatment of postmenopausal depression needs to be carefully analyzed, particularly in light of ever-evolving findings on the wide-ranging effects of hormone replacement therapy (HRT).

With this in mind, Rodrigo Dias, MD, of the University of San Paulo in Brazil, and colleagues presented their findings on the use of HRT with and without androgens on 32 menopausal depressive women.

The women (mean age 53.6 years) were treated with venlafaxine and randomly assigned to 1 of 4 treatment groups, 3 of which included some form of HRT treatment and a fourth that consisted of no treatment. The design was double-blind, and the women were followed for 24 weeks. Outcomes were measured by the Montgomery-Asberg Depression Rating Scale (MADRS).

Although no statistical difference in outcome among the groups was observed at study's end, HRT with androgen helped to better reduce the MADRS score during treatment. This reduction, the authors note, was not related to venlafaxine doses. These preliminary results suggest better patient outcome with HRT plus androgens, though because of the size of the study, further research is warranted. MF

Source: Dias R, Kerr-Correa F, Trinca LA, et al. HRT with androgens as a strategy to treat postmenopausal depression. Presented at: APA annual meeting; May 17-22, 2003; San Francisco.

FDA WATCH

Wyeth hopes to have a lower dose formulation of its hormone replacement therapy (HRT) medication **Prempro** on the market this summer. The new formulation has been in development for more than 4 years. It gained FDA approval this spring.

The FDA seal comes just months following new recommendations by the agency that menopausal women take the lowest dose of HRT for the shortest duration possible to meet treatment goals. These recommendations were based on findings from the Women's Health Initiative, showing less risk of serious side effects with the lower doses.

The new formulation of Prempro is similar in tolerability and efficacy to the most frequently prescribed higher dose. It contains 28% less estrogen and 40% less progestin.

Prempro is approved for women with a uterus for the treatment of moderate-to-severe symptoms of menopause, such as hot flashes and night sweats, and for vulvar and vaginal atrophy.

Two new drugs were approved for the treatment of social anxiety disorder earlier this year. **Effexor XR**, initially approved in 1997 for depression and generalized anxiety disorder, and **Zoloft** will carry the new FDA indication.

Effexor is taken once a day; it is the only serotonin-norephinephrine reuptake inhibitor approved by the FDA for use in depression and anxiety disorders. It is thought to increase levels of 2 brain chemicals believed to be lacking in people with depression and anxiety disorders.

Likewise, Zoloft is the first selective serotonin reuptake inhibitor to gain FDA approval for the long-term treatment of social anxiety disorder (it was also approved for acute treatment). The medication is also indicated for depression, post-traumatic stress disorder, panic disorder, adult and pediatric obsessive-compulsive disorder, and premenstrual dysphoric disorder. MF

Commentary

INDUSTRY

GSK, CONSUMER GROUPS IN TUG-OF-WAR OVER INTERNET SALES FROM CANADA

In January, GlaxoSmithKline elected to stop supplying its medicines to Canadian wholesalers and pharmacies that export drugs to Americans, usually via the Internet. The move was met cynically by consumer advocates who saw it as a way for GSK to stem any potential loss of profits from the American market.

GSK countered that it has the public's best interest in mind, particularly with regard to patient safety. The company is concerned about Americans accessing unregulated Canadian drugs.

In an interview with *Med Ad News*, GSK spokesman Nancy Pekarek tried to dispel the notion that loss of profits was behind the company's decision to pull its drugs from Canadian shelves. Cross-border sales, she said, amount to "less than 1% of a day's sales in the United States." Rather, Pekarek said in the interview, a lack of controls on drug storage by Internet pharmacies, which are the main distributors of drugs back across the US border, created a potentially unsafe situation for consumers.

GSK's position is unlikely to sway advocacy groups like the Minnesota Senior Federation, a large grassroots organization for seniors. If anything, these groups may be more aggressive in an effort to keep other big pharmaceutical companies from following GSK's lead. Yet, in April, AstraZeneca announced it too would limit sales of its products to Canadian pharmacies and wholesalers.

According to the advocacy groups, the lure of buying drugs from Canadian distributors is consumer savings. According to a survey by the Minnesota advocacy group, GSK products are 50% less expensive on average through Canada.

In addition to the potential safety risk, Pekarek said GSK is concerned that US consumers may be depleting supplies of some drugs ticketed for Canadian patients. That position came under equal fire from consumer advocates, who claim that pharmaceutical companies can increase supply to meet demand within a matter of months.

So where does this leave the industry? Right where it always is: serving as the rope in a tug-of-war between pharmaceutical companies and consumer advocacy groups. For the time being, it does not look as if either side has any plans for giving any ground.

Source: *Med Ad News*. 2003;22(5):1,60-61.

WASHINGTON

LATE SEN. PAUL WELLSTONE TO BE HONORED

As one of the standard-bearers for mental health advocacy, Paul Wellstone helped bring mental health to the forefront of the nation's public health agenda. The National Mental Health Association (NMHA) will honor the late US senator with its Into the Light award in June.

Wellstone was influential in raising awareness of the importance of treatment for mental illness. His efforts toward ending health insurance discrimination against people with mental illness led to a majority of members of Congress supporting the Sen. Paul Wellstone Mental Health Equitable Treatment Act of 2003.

Unfortunately, Wellstone did not live to see his efforts coming to fruition. Wellstone died in a plane crash last October.

NMHA president Michael Faenza called Wellstone "one of the most articulate, passionate voices ever to speak on behalf of people with mental illness."

The Into the Light award recognizes those who have demonstrated devotion to improving care, treatment, and services for people with mental disorders. Past honorees include former US Surgeon General David Satcher, MD, Elizabeth Dole, Tipper Gore, and former First Lady Rosalynn Carter. MF