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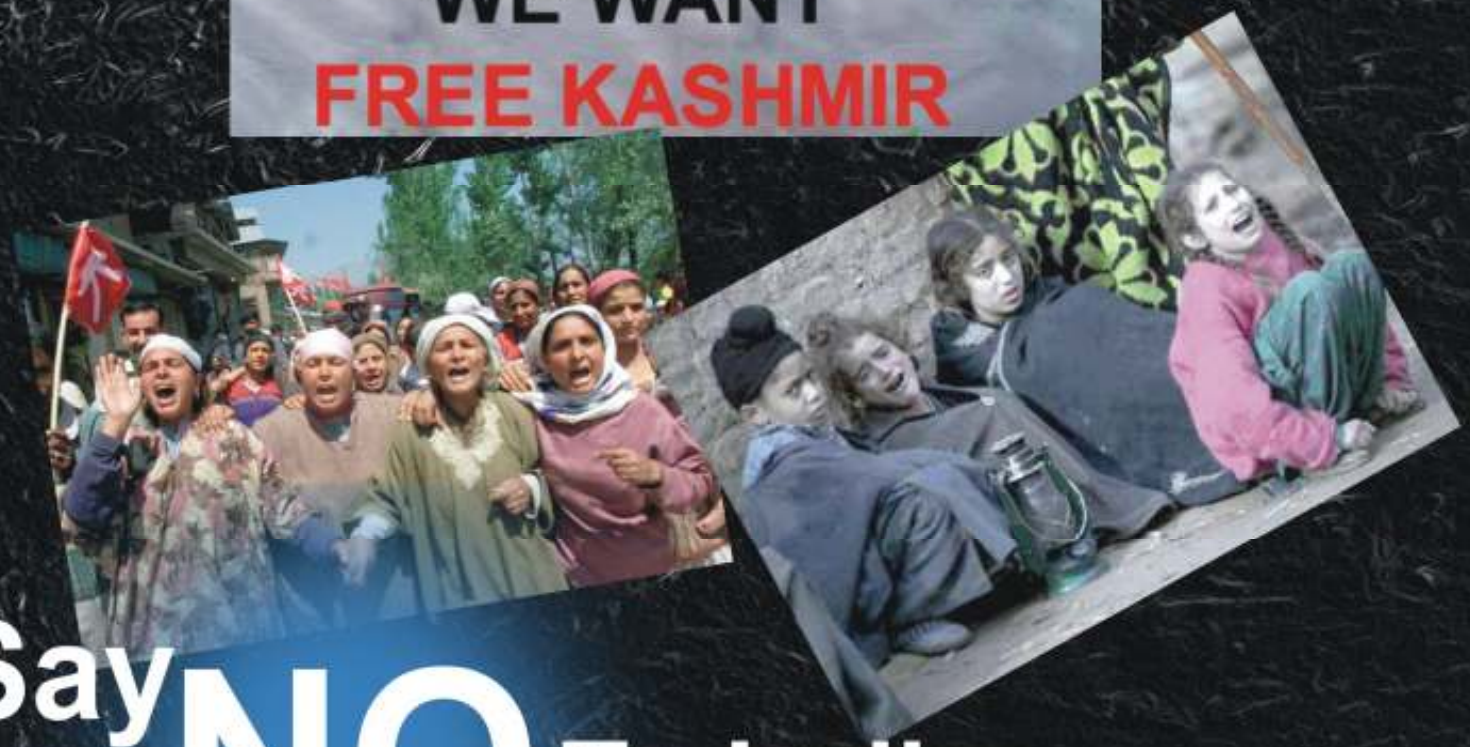

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Interventions for Perpetrators of Intimate Partner Violence

Christopher I. Eckhardt, PhD-colleagues

August 28,

Substantial progress has been made in the development of etiologic models of intimate partner violence and interventions for individuals who assault their intimate partners. These authors provide details.

Intimate partner violence (IPV) occurs at an alarmingly high rate. According to the most recent survey of US adults, almost 7 million women and 5.5 million men experience physical violence, stalking, or rape by an intimate partner each year. Psychological/emotional abuse, including threats of violence and a wide range of intimidating, denigrating, humiliating, and controlling behaviors, is also highly prevalent. Common physical health sequelae from IPV include contusions, soft tissue injuries, sprains, strains, fractures, maxillofacial injuries, and traumatic brain injuries.[2] In addition, the prevalence of PTSD; depression; and anxiety, mood, and substance use disorders is elevated in victims of IPV.

Although the rates of physical IPV are roughly similar for men and women, the rates of physical injury and death are higher for women, and men are most frequently referred for treatment as perpetrators of IPV. "Common couple violence," which is typically bidirectional, non-injurious, and an outgrowth of poor conflict resolution, is distinguished from "intimate terrorism," which is often unilateral, injurious, intensely controlling, and more gender-based in nature. Nevertheless, the findings on gender similarity and mutuality of violence challenge the common assumption that IPV is solely a male-to-female problem.

Risk factors

Although there is no singular profile of the IPV perpetrator, there are several well-documented risk factors and correlates. A high percentage of court-referred IPV perpetrators have been physically abused and/or witnessed inter-adult abuse in childhood. A history of conduct disorder in adolescence and antisocial personality traits or disorder have been found to confer risk for IPV, and adolescent and young adult couples with a history of IPV are characterized by a tendency of both partners to possess similar antisocial traits (ie, assortative partnering).

PTSD is a substantial risk factor for IPV in veteran populations. A number of psychiatric disorders have been associated with men committing IPV, including depression, dysthymia, generalized anxiety, alcohol dependence, adult antisocial behavior, and nonaffective psychosis.[14] A variety of indicators of negative emotion dysregulation are also associated with IPV, including borderline personality features, disorganized and insecure patterns of attachment, and anger problems. The incidence of IPV is typically greater than 50% among both men and women who seek treatment for substance use disorders as well as for couples in marriage therapy. The incidence of head

injuries among IPV perpetrators is very high, as is that of subtle neurocognitive impairments that involve impulsivity, poor response inhibition, and deficits in executive functions.

Assessment

IPV is not commonly reported as a presenting concern, but it is readily detected through a brief structured interview or questionnaire. In addition to more extensive self-report measures, such as the Revised Conflict Tactics Scale, a number of brief IPV screening instruments have been developed and validated. Several appear to have good sensitivity for detecting IPV, including the Partner Violence Screen, the Woman Abuse Screening Tool, and the Abuse Assessment Screen. Although it is important to note that research on medical screening of IPV focuses almost exclusively on victims, clinical experience suggests that individuals seeking treatment for other problems, such as substance abuse, are often quite forthcoming about being abusive.

Intervention strategies

Psychosocial counseling for IPV perpetrators is widely available, with well over 1000 programs in the US. Most of these programs predominantly serve court-mandated populations and are focused on men who have assaulted women. Although a range of program philosophies and practices exist, programs for perpetrators of IPV, often labeled batterer intervention programs (BIPs), tend to advocate an open admissions group modality and can last from 8 to 52 weeks.

There are 2 common types of BIPs. The first assumes a gender-themed root cause of IPV, such that the patriarchal nature of societal and institutional structures reward male domination and justify any means (including physical aggression) that reinforce male power, control, and privilege. For example, the widely adopted Duluth Abuse Intervention Project model aims to prevent IPV via largely didactic psychoeducational reprogramming of (male) offenders. This model focuses on exposing patriarchal/misogynistic attitudes, encourages accountability and personal responsibility, and promotes gender-egalitarian behaviors. Although this approach has been criticized because of theoretical inconsistencies and lack of empirical support, most existing intervention programs use some variation of this model.

A second BIP model uses cognitive-behavioral therapy (CBT). This model aims to change behavior through a collaborative therapeutic relationship, exposure and disputation of distorted cognitions, and various problem-solving and mood-regulating techniques. Couples-based CBT that focuses on enhancing communication and problem-solving skills between partners remains controversial because of concerns about a heightened risk of injury to partners who remain with an abusive individual while simultaneously receiving treatment for potentially volatile relationship conflicts.

Despite the widespread adoption of BIPs, evidence for their effectiveness is limited and inconclusive. Most studies of BIP effectiveness have substantial methodological limitations, including very high rates of sample attrition, inadequate treatment standardization, little or no documentation of treatment fidelity, and systematic biases in random assignment. For men assigned to BIPs, average violence recidivism rates are about 5% lower than those for men assigned to control conditions (eg, probation monitoring), with no differences in effectiveness

between the Duluth model and therapeutic CBT programs. Couples-based approaches have not been found to be more effective, or more dangerous, than gender-specific IPV treatments. Thus, the empirical status of BIPs is decidedly uncertain, despite the enormous public health and safety concerns about IPV and the promise that such interventions have in rehabilitating offenders.

Alternative strategies

Interventions designed to enhance motivation and readiness to change have added value, beyond traditional BIP services. In recent years, the focus has been on developing and evaluating alternative interventions, including medication therapy, comprehensive mental health case management, integrated treatment for substance use problems and IPV, culturally specific interventions, trauma-informed therapies, and interventions targeting motivation to change. Whereas all of these approaches can be well justified conceptually, empirical support remains limited.

An integrated CBT program for substance use problems and IPV produced significant short-term benefits in violence reduction during treatment; however, these differences were not maintained at a 6-month follow-up. Kraanen and colleagues evaluated the effectiveness of a CBT program that primarily targeted substance use disorders with a single session dedicated to IPV. At the 8-week follow-up, significant reductions in IPV and substance abuse were seen. The researchers concluded that a CBT program that targets substance abuse with some content regarding IPV may be a more economical solution in terms of financial and labor costs.

One study of a culturally focused program compared a group of African American men with mixed-race and same-race groups receiving a conventional BIP program. The results did not support same-race or culturally specific programs—the re-arrest rate for participants in the same-race groups was higher than for men in the conventional mixed-race groups.

A trauma-informed treatment for veterans who have perpetrated IPV was recently developed. The treatment was designed to help veterans understand the effect of military and combat experiences on intimate relationships while emphasizing strength and coping resources and the development of new relationship skills. Initial pilot findings suggest that this approach was favorably received by veterans; however, no controlled trial data have been presented.

The focus of several interventions is on motivation and readiness to change, areas of considerable challenge in working with IPV perpetrators (who are often forced by courts or partners to seek treatment). Brief motivational interviewing—a supportive and highly empathic counseling style designed to resolve ambivalence about change—has been shown to enhance positive treat-ment engagement and compliance with behavior change recommendations. Group approaches designed to help clients move through the stages of intentional behavior change have increased treatment adherence for highly resistant IPV offenders in one study and produced lower posttreatment violence relative to standard BIP services in another.

Research on medication thera-pies for IPV perpetrators is woefully limited. One randomized placebo-controlled trial examined flu-oxetine in combination with alcohol treatment and CBT for

alcohol-dependent men who were perpetrators of IPV. Medication produced significant reductions relative to placebo on measures of irritability and partner-reported IPV during this 12-week trial.

Practice recommendations supported by studies

Structured screening for IPV in mental health practice may be warranted for all cases but is particularly indicated for individuals with substance use problems, antisocial behavior, anger problems, a history of head injury, notable impulsivity, or emotion dysregulation. When possible, including a confidential interview with the relationship partner can improve screening outcomes. Screening for IPV victimization in general medical settings remains a controversial topic, in part because a large multisite study found no significant benefits regarding morbidity or mortality. Findings indicate that in more than half of the patients who screened positive for IPV, doctors never discussed the issue with them. Clearly, screening alone is not a magic bullet without subsequent intervention.

Strategies that focus on motivation and readiness to change appear to have added value in engaging IPV perpetrators into treatment and enhancing participation in behavior change interventions. Motivational interviewing uses a high level of empathic reflection and gentle guidance to evoke individuals' articulation of motivation and commitment to change.

Effective treatment for substance use problems can have a substantial benefit in reducing IPV. Integrated approaches that teach relationship skills or involve partners in dyadic relationship enhancement may have added benefit for substance-abusing populations.

Conclusion

Substantial progress has been made in the development of etiologic models of IPV and interventions for individuals who assault their intimate partners. Although clinical approaches based on long-standing models of IPV intervention have modest efficacy, there is a solid conceptual rationale for several alternative strategies for IPV perpetrators. Careful screening for IPV in mental health practice; supportive strategies to motivate behavior change; and integrated services that address IPV in the context of treatment for substance abuse, traumatic stress, neurocognitive conditions, and emotion dysregulation are amenable to integration into regular clinical practice and may have effects that match or exceed standard group interventions that take a one-size-fits-all approach to the treatment of IPV.

Disclosures:

Dr Eckhardt is Associate Professor and Director of the Purdue Institute for Relationship Research and Mr Sprunger is an advocate doctoral student in clinical psychology in the department of psychological sciences at Purdue University in West Lafayette, Ind. Dr Murphy is Professor and Chair in the department of psychology at the University of Maryland, Baltimore County. They report no conflicts of interest concerning the subject matter of this article.

Increasing Chlamydia Screening Rates in Adolescent Girls

Robin Drucker, MD reviewing Tebb KP et al. Arch Pediatr Adolesc Med 2009 Jun. By redesigning work flow during urgent care visits, physicians can increase chlamydia screening rates among sexually active teens.

Chlamydia trachomatis infections are the most common reportable sexually transmitted infections (STIs) in the U.S. Annual screening of sexually active adolescents and young adults is recommended, but only about 20% of 18- to 19-year-olds report any STI testing. One obstacle to screening is that most adolescents use urgent care or same-day appointments for medical care rather than scheduled preventive health visits. Investigators evaluated the effectiveness of an intervention to increase chlamydia screening rates in sexually active adolescent girls during acute care visits at a large HMO in California.

Five pediatric clinics were randomly assigned to the intervention, and five clinics served as controls. Each clinic in the intervention group formed a team to develop a system to identify sexually active teens, obtain urine specimens, transport specimens, communicate results confidentially, and arrange follow-up treatment. During the 3-month baseline period, the intervention and control clinics screened statistically similar proportions of adolescent girls for chlamydia (23%–29%) and reported similar sexual activity rates, chlamydia infection rates, number and gender of providers, and ages of adolescent patients. During the subsequent 15 months, a significantly greater proportion of girls were screened for chlamydia in the intervention group than in the control group (likelihood ratio, 18.7). The proportion of girls screened for chlamydia increased from baseline by almost 16% in the intervention group and decreased by 2% in the control group. During the last 3 months of the study, 42% of sexually active teens were screened in the intervention group versus 30% in the control group.

Conduct Disorders: New Pathway, New Treatment

Barbara Geller, MD reviewing Cecil CAM et al. Mol Psychiatry 2014 Sep 9. Raine A et al. J Child Psychol Psychiatry 2014 Aug 22.

Treatment with omega-3 supplementation improves internalizing and externalizing behaviors in the usually treatment-resistant childhood conduct disorders.

The grim prognosis of childhood conduct disorders (CD) warrants efforts to understand their etiologies and treatments (NEJM JW Psychiatry Oct 15 2012). Two studies provide insights.

Oxytocin affects empathy and sociality, which are deficient in individuals with callous-unemotional traits (CUT). To study genetic and environmental pathways in CD and CUT, Cecil and colleagues genotyped 84 children with conduct problems for oxytocin receptor gene (*OXTR*) methylation at birth and at ages 7 and 9 years. At age 13, participants were assessed for CUT and internalizing problems. In those with low internalizing problems, higher *OXTR* methylation (which decreases oxytocin expression) at birth was associated with higher CUT at age 13 and higher prenatal maternal psychopathology, antisocial behaviors, and substance abuse. In those with higher internalizing behaviors, CUT was associated with postnatal intrafamilial risks (e.g., domestic violence).

Raine and colleagues conducted a double-blind, placebo-controlled, 6-month study of daily omega-3 fatty acid supplementation (including docosahexaenoic acid 300 mg and eicosapentaenoic acid 200 mg) in 200 children with CD (age range, 8–16). Supplementation improved externalizing and internalizing behaviors at 6 months and at 12-month follow-up on caregiver ratings and improved aggression at 6 months on child reports. Notably, parents' ratings of their own antisocial behaviors improved in the supplementation group.

FDA: Risk for Venous Thromboembolism with All Testosterone Products

By Kristin J. Kelley
Edited by Susan Sadoughi, MD, and Jaye Elizabeth Hefner, MD

The FDA is requiring an expanded label change to all approved testosterone products to warn of the increased risk for venous thromboembolism. Labels currently address the risk for clots associated with polycythemia caused by testosterone treatment.

The action follows reports of blood clots in testosterone users unrelated to polycythemia. The agency says the warning is not related to an ongoing investigation announced in January about possible cardiovascular risks associated with testosterone treatment.

Smoking Bans Are Associated with Mortality Benefits Among the Incarcerated

Paul S. Mueller, MD, MPH, FACP reviewing Binswanger IA et al. BMJ 2014 Aug 5.
Smoking-related deaths fell by 9% in prisons that implemented smoking bans.

The U.S. Supreme Court has indicated that exposing nonsmoking prisoners to secondhand smoke can be construed as "cruel and unusual punishment" (*Helling v. McKinney,* 509 U.S. 25 [1993]). In response, many states have enacted prison tobacco control policies, including bans on smoking. To determine whether such bans are associated with reductions in smoking-related mortality, investigators examined data on smoking prevalence, deaths, and tobacco control policies in all state prisons in the U.S. between 2001 and 2011. Of the more than 1.2 million people incarcerated in state prisons in 2004, 76% were current or former smokers; 56% smoked daily before their arrest.

During the study period, the age-adjusted rate of smoking-attributable deaths was 360 per 100,000, and the number of age-adjusted years of potential life lost was 5149 per 100,000 — figures considerably higher than those of the U.S. population (248 and 3501 per 100,000, respectively). In 2001, 25 states had prison smoking bans; by 2011, 48 states had implemented such bans. Adjusted for multiple variables, any smoking ban was associated with a significant reduction in smoking-related deaths (incidence rate ratio, 0.9).

Smoking Cessation Intervention Is Effective with Post–Hospital Discharge Follow-Up

Thomas L. Schwenk, MD reviewing Rigotti NA et al. JAMA 2014 Aug 20.
Success was due in part to free medication and to innovative use of interactive voice-response telephone calls.

Smoking cessation interventions in hospitalized patients can be particularly effective, because the consequences of smoking often are more apparent to patients who are admitted for smoking-related issues. But evidence suggests such interventions are effective only with longer-term outpatient follow-up, which can be expensive. In addition, smoking-cessation medications often are not covered by insurance.

Boston investigators randomized 432 hospitalized adult smokers to a postdischarge treatment program or to usual care (access to a telephone quit line and discharge recommendation for a smoking-cessation medication). Patients were excluded if they were admitted to an obstetrical or psychiatric unit or had substance abuse problems, cognitive impairment, or language difficulties. Intervention patients received five interactive voice response telephone calls during the subsequent 3 months, during which they received encouragement, quit advice, medication refills, and problem-solving approaches; they also could request a call-back from a trained counselor. Free smoking-cessation medication, chosen by the patient and an inpatient counselor, was provided for the entire 3 months.

Smoking cessation at 6 months postdischarge, measured by saliva cotinine analysis, was 26% in the intervention group and 15% in the control group — a significant difference. Nine patients would need to be treated for one to benefit.

Smoking Cessation Interventions After Hospitalization for Acute MI

Arun Mohan, MD, MBA, Daniel D. Dressler, MD, MSc, SFHM, FACP reviewing Ladapo JA et al. Arch Intern Med 2011 Jan 10.
Intensive smoking cessation interventions lower healthcare costs after myocardial infarction.

Physicians routinely counsel patients against smoking after hospitalization for acute myocardial infarction (MI). However, as many as 70% of patients who smoked previously continue to smoke after hospital discharge.

In this study, researchers constructed a model to estimate health and economic outcomes for more than 300,000 hypothetical smokers hospitalized with MI. Usual care (consisting of standard counseling and printed materials) was compared with usual care plus follow-up (consisting of a behavioral counseling session before discharge, a DVD, and follow-up telephone calls for 3 months after discharge). They estimated that annual mortality would be 5.7% for patients who continued to smoke and 3.4% for those who stopped.

Total medical expenses during 10 years were nearly identical for the usual-care and follow-up groups. When productivity losses and nonmedical expenditures were included, however, a US$894 million net economic benefit to society would accrue by adding follow-up. The incremental cost-effectiveness ratio was $5050 per quality-adjusted life-year (QALY).

Risk for Invasive Anal Cancer in HIV-Infected Patients According to Baseline Anal Histology

Keith Henry, MD reviewing Cachay E et al. HIV Med 2014 Sep 6.

HIV-infected patients with baseline high-grade intraepithelial lesions had a 1.65% 5-year probability of invasive anal cancer.

HIV-infected individuals are at increased risk for human papilloma virus–related cervical and anal cancers. Although the benefit of cervical pap smears and treatment for cervical abnormalities is established, uncertainty remains about the risk for anal cancer and the potential benefit of screening with anal pap tests and treating precancerous anal lesions.

In a retrospective, single-clinic study, 2804 HIV-infected patients who were receiving care between 2001 and 2012 and met the eligibility criteria (≥2 anal cytology results without diagnosis of invasive anal carcinoma [IAC] or ≥1 result with subsequent IAC diagnosis) were followed for a median of 4 years. Eighty-nine percent of the participants were male, 78% were men who have sex with men, 38% were nonwhite, and 30% were smokers. At baseline, the median age was 40, and the median CD4 count was 384 cells/mm^3; 47% had viral loads <400 copies/mL on antiretroviral therapy (ART), and 11% had high-grade squamous intraepithelial lesion (HSIL) anal cytology.

Patients with baseline HSILs had an estimated 1.65% 5-year probability of progressing to IAC, with an estimated annual progression risk of 1 in 263. Patients with HSILs were referred for high-resolution anoscopy (HRA); after 2007, such patients were offered infrared photocoagulation (IRC) ablation. ART, viral load, smoking status, and IRC use were not associated with IAC incidence.

Draw-a-Child Test at Age 4 Years Correlates with Intelligence at Age 14 Years

Martin T. Stein, MD reviewing Arden R et al. Psychol Sci 2014 Aug 20.
Data confirm its value as a screening tool at school-readiness visits and beyond.
A child's performance in drawing a picture of his or her family — a part of well-child visits in many pediatric practices — reflects cognitive, motor, perceptual, attentional, and motivational capacities.
To determine whether childhood drawing is predictive of later intelligence, investigators conducted a cohort study including 7752 pairs of twins representative of the U.K. population in socioeconomic status, ethnicity, and parental occupation. At age 4 years, each twin was separately administered the Draw-a-Child Test by a parent, who asked the child to do the following: "Draw a picture of a (girl/boy [same gender as child]). Do the best that you can. Make sure that you draw all of (him/her)." Scoring of each drawing was based on the Goodenough Draw-a-Person Test. Standardized intelligence tests were administered at ages 4 and 14 years.
Figure-drawing scores at age 4 years correlated significantly with verbal and nonverbal intelligence at ages 4 and 14 years. When drawing and intelligence scores in monozygotic and dizygotic twins were analyzed, 99% of the phenotypic correlation between drawing at age 4 and intelligence at age 14 was mediated genetically.

In Utero Antidepressant Exposure and Risks for Autism and ADHD

Deborah Cowley, MD reviewing Clements CC et al. Mol Psychiatry 2014 Aug 26.
Maternal depression, not antidepressant use, raises risk for autism spectrum disorder in offspring, but risk for ADHD seems to stem from both factors.

Studies in rodents have linked prenatal serotonergic drug exposure to autism-like behaviors, but investigations in humans of the possible risk for autism spectrum disorder (ASD) after in utero antidepressant exposure have yielded conflicting results. Now, researchers have examined electronic data from a large healthcare system to assess risk for ASD and another neurodevelopmental disorder, attention-deficit/hyperactivity disorder (ADHD), after prenatal antidepressant exposure. Analyses controlled for maternal psychopathology. In all, 1377 children with ASD and 2243 with ADHD were matched 1:3 with unaffected children (age range, 2–19 years).

Maternal history of major depression was associated with increased risk for ASD and ADHD in offspring. Antidepressant use before or during pregnancy was associated with elevated risks for both ASD and ADHD; however, in analyses adjusted for maternal major depression, ASD risk was no longer significantly elevated but ADHD risk remained significantly elevated. Furthermore, ASD risk was not higher with use of more-serotonergic antidepressants. Risks for ASD and ADHD were lower when measures of maternal illness severity (e.g., comorbid diagnoses, number of mental health visits) were incorporated.

Integrated Mental Health and Medical Care Improves Treatment of Depression in Cancer Patients

Bruce Soloway, MD reviewing Sharpe M et al. Lancet 2014 Aug 28.
Depression severity fell substantially in 62% of patients who received collaborative care, compared with 17% of those who received usual care.

Many patients with chronic diseases also suffer from depression, which can lower quality of life, complicate medical management, and increase healthcare costs. Because primary care services often treat patients with depression inadequately and are coordinated only poorly with mental health services, programs that integrate mental health and primary care have attracted attention. Researchers in Scotland randomized 500 cancer patients (life expectancies, ≥12 months) who screened positive for major depression to receive usual care from their primary care physicians (PCPs) or to participate in a program called Depression Care for People with Cancer (DCPC). Patients enrolled in DCPC had as many as 10 sessions with trained oncology nurse case managers (at a cancer center or primary care clinic or, if necessary, by telephone) during the first 4 months, then 8 months of follow-up via an automated telephone system and additional face-to-face sessions as needed. Psychiatrists supervised nurses' care of all patients and advised PCPs on antidepressant medications. Most study participants were women with breast cancer or gynecological cancers.

After 24 weeks, depression severity (measured on the 20-item Symptom Checklist Depression Scale) decreased by ≥50% in 62% of DCPC patients and in 17% of usual-care patients. Patients in DCPC also had significantly better outcomes on a range of secondary measures, including anxiety; pain; fatigue; quality of life; and physical, social, and role functioning. Mean additional cost per patient of the DCPC intervention was about US$1000.

Psychotherapy for Disordered Thinking in Schizophrenia

Steven Dubovsky, MD reviewing Moritz S et al. JAMA Psychiatry 2014 Oct.
Not only does metacognitive training yield immediate benefits, but others emerge only after time.

Psychotherapeutic approaches to patients with schizophrenia are receiving renewed attention, but how long do the improvements endure? Researchers in Germany randomized 150 patients with schizophrenia spectrum diagnoses (mean age, 35) who were taking antipsychotics to one of two 16-session therapies. Metacognitive training (MCT) is a manual-based group treatment addressing attributional style, jumping to conclusions, flexible beliefs, theory of mind/social cognition, avoiding overconfidence in false memories, and mood/self-esteem. The control treatment, COGPACK, is an individualized, computer-based program, conducted in a group setting, to improve memory. Assessors were blinded as to treatment group.

Overall, 86% of patients stayed in the study for 6 months, and 61% stayed for 3 years of planned follow-up. Positive symptoms, especially delusions, decreased significantly more with MCT than with COGPACK at 6 months' follow-up, and this difference was maintained at 3 years. In addition, self-esteem and quality of life were significantly more improved in the MCT group at 3 years although not earlier. Attention improved more in the COGPACK group. Jumping to conclusions improved in both groups.

Risk for First Heart Attack Linked to Recent Antipsychotic Use for Schizophrenia

Joel Yager, MD reviewing Wu S-I et al. Acta Psychiatr Scand 2014 Oct 14.
The finding was particularly strong in men and in those with no known cardiovascular risk factors.

Antipsychotic medications have been associated with worsening of several cardiovascular risk factors, including obesity, hyperlipidemia, and insulin resistance. These investigators studied links between these medications and first acute myocardial infarction (AMI) in a large Taiwanese national database in 1996–2007; the study included 591 AMI patients with schizophrenia and 243 with bipolar disorder.

In this case–crossover study, investigators compared antipsychotic use in the 60 days immediately before initial AMI and the 60 days preceding that period. After adjustment for general healthcare contacts and prescriptions of antidepressants and/or mood stabilizers, recent antipsychotic use was associated with increased AMI risk in patients with schizophrenia (odds ratio, 1.87) but not in those with bipolar disorder. Risk was particularly higher for men (OR, 3.52), patients aged ≤60 (OR, 2.36), and those taking only typical antipsychotics (OR, 1.93). Paradoxically, risk was also higher in patients without cardiovascular risk factors (hypertension, diabetes, hyperlipidemia, angina, ischemic heart disease, atherosclerosis, or stroke; OR, 8.86) and in those on lower summed doses of antipsychotic medications in the previous year (OR, 2.26). Injectable antipsychotics were not associated with higher risk.

Antipsychotic Drugs and Cardiac Arrest in Outpatients

Steven Dubovsky, MD reviewing Weeke P et al. Clin Pharmacol Ther 2014 Jun 24.
The class of typical antipsychotics is associated with out-of-hospital cardiac arrest.

To address concerns about adverse effects of antipsychotic drugs (e.g., NEJM JW Psychiatry Sep 29 2008), these researchers correlated 10 years of Danish registry data on all out-of-hospital cardiac arrests (OHCAs), all prescriptions, and inpatient and outpatient treatment.

In 28,947 people with OHCA, 2205 were taking at least one antipsychotic drug (median age, 66). The risk for OHCA was significantly increased with any antipsychotic (odds ratio, 1.53). Typical antipsychotics as a class were associated with an increased OHCA risk (OR, 1.66), but atypical antipsychotics were not. In analyses of 11 individual medications, greater OHCA risk was associated with the atypical quetiapine (OR, 3.64) and the neuroleptics haloperidol (OR, 2.43) and levomepromazine, a low-potency phenothiazine not available in the U.S. (OR, 2.05). The results were not explained by typical risk factors, substance abuse, hospitalization 2 months before OHCA, or above-median doses. Only 47% of OHCA patients taking an antipsychotic drug appeared to have a psychiatric illness. Numbers were too small to assess the effect of dosage or treatment duration, and the risk

of other, less frequently prescribed antipsychotics was not explored. No data were available on whether OHCA was caused by torsades de pointes.

How Risky Are Psychiatric Medications?

Steven Dubovsky, MD reviewing Hampton LM et al. JAMA Psychiatry 2014 Jul 9.
Prescribers should be mindful of the risks for adverse reactions with psychiatric drugs, especially antipsychotics, lithium, and zolpidem.
About 12% of the U.S. population takes prescription psychiatric medications, but the comparative risks for nonintentional adverse drug reactions (ADRs) for each drug class have been little studied. To learn more, researchers examined 3 years of electronic records of adult visits to emergency departments (EDs) at 63 hospitals.
Of 89,094 ED visits for psychiatric ADRs (about 10% of all ADR visits to EDs), almost 20% resulted in hospitalization. The highest rate of ED visits relative to the number of outpatient presumed prescriptions was found for antipsychotics (especially, typical antipsychotics), primarily for severe extrapyramidal effects, and lithium, with the most common problems being "abnormal drug level," altered mental status, and movement disorder. In an examination of individual drugs, zolpidem led to more ED visits than any other psychiatric medication, especially in older patients. The analyses did not include anticonvulsants.

Atypical Antipsychotic Drugs Are Associated with Acute Kidney Injury in Older Adults

This novel finding and other adverse effects were noted in a population-based study.
Some case reports have suggested that older adults who are treated with atypical antipsychotic drugs (i.e., risperidone, quetiapine, and olanzapine) might be at elevated risk for acute kidney injury (AKI). To investigate this risk and other adverse outcomes, researchers used population-based data from Ontario, Canada, to study almost 98,000 adults 65 and older (mean age, 81; 24% in long-term care facilities; 54% with diagnoses of dementia) who received new outpatient prescriptions for oral atypical antipsychotic drugs between 2003 and 2012; data on an equal number of age-, sex-, and health-matched patients who did not receive such prescriptions also were examined.
Risk for hospitalization for AKI within 90 days was higher among prescription recipients than among nonrecipients (1.02% vs. 0.62%; relative risk, 1.73). Receipt of atypical antipsychotic drugs also was associated with roughly doubled 90-day risks for acute

urinary retention, hypotension, and all-cause mortality. In subgroup analyses, neither drug type nor dose affected the association between atypical antipsychotic drug use and hospitalization for AKI.

Simple Home Safety Improvements Are Cost-Effective for Preventing Fall-Related Injuries

Bruce Soloway, MD reviewing Keall MD et al. Lancet 2014 Sep 23. Robinovitch SN et al. Lancet 2014 Sep 23.

Low-cost modifications were associated with 26% fewer injuries annually from falls.

Falls at home are a major cause of morbidity and mortality, particularly in elders, but few studies have demonstrated that modifying the home environment can make it safer. In this study, 842 households (1848 occupants) in one region of New Zealand were randomized to undergo home modifications (e.g., outdoor and indoor hand rails, improved outside lighting, carpet edges fixed to the floor, bathroom grab rails, non-slip bathmats, and slip-resistant outdoor surfaces and steps) either immediately (treated homes) or 3 years later (controls). All homes were constructed before 1980 and had at least one occupant who was receiving a state subsidy. The age range of occupants was broad; about 40% were older than 60. Data on home injuries were collected from a national personal injury insurer.

After median follow-up of 3 years, and with adjustment for age, sex, ethnicity, and injury history, occupants of treated homes, compared with controls, had 26% fewer fall-related injuries and 39% fewer injuries specifically related to home modification for each year exposed to the modification package. Researchers found no differences between groups in injuries unrelated to falls. On average, cost of the modification package per home was about US$450, and cost per injury prevented was US$660.

Dietary Supplements Blamed for Sharp Rise in Drug-Related Liver Injuries

By Amy Orciari Herman

Dietary supplements, including many marketed for muscle-building and weight loss, account for a spike in drug-related liver injuries over the past decade, according to a front-page story in Sunday's *New York Times*. Many patients ultimately recover, but some end up requiring transplants or dying from liver failure.

Supplements accounted for nearly 20 percent of drug-related liver injuries that led to hospitalization in 2010-2012, the *Times* reports, up from 7 percent in 2004. The data, from the NIH's National Liver Network, showed that many of the products were bodybuilding supplements that contained steroids not listed on the label. Use of green tea extract was also frequently reported. The extract contains catechins, which are said to increase metabolism; in high doses, they can cause liver toxicity.

Of over 50,000 supplements sold in the U.S., less than 1% have been examined well enough to determine their adverse effect profile, one expert told the *Times*.

Notes from the Field: Reports of Expired Live Attenuated Influenza Vaccine Being Administered — United States, 2007–2014

Weekly
September 5, 2014
Penina Haber, MPH, Christopher P. Schembri, MPH[1], Paige Lewis, MSPH, Beth Hibbs, MPH, Tom Shimabukuro, MD (Author affiliations at end of text)

Annual influenza vaccination is recommended for all persons aged ≥6 months (*1*). Two vaccine types are approved in the United States, injectable inactivated influenza vaccine (IIV) and live attenuated influenza vaccine (LAIV), which is administered intranasally (*1*). Influenza vaccine typicaly becomes widely available beginning in late summer or early fall. IIV has a standard expiration date of June 30 for any given influenza season (July 1 through June 30 of the following year). In contrast, after release for distribution, LAIV generally has an 18-week shelf life (Christopher Ambrose, MedImmune, personal communication, 2014). Because of its relatively short shelf life, LAIV might be more likely than IIV to be administered after its expiration date. To assess that hypothesis, CDC analyzed reports to the Vaccine Adverse Event Reporting System (VAERS) (*2*) of expired LAIV administered during July 1, 2007, through June 30, 2014.

Of the 4,699 LAIV reports, 866 (18.4%) involved administration of expired vaccine; 97.5% of these reports did not document any adverse health event. In 95.1% of expired LAIV reports, vaccination occurred after the first week in November, which is approximately 18 weeks from July 1. Historically, by early November, most vaccine has been administered for the season (*3*). In contrast, of the 49,695 IIV reports, only 96 (0.02%) involved administration of expired vaccine. VAERS is a national, passive surveillance system that accepts reports from anyone (including vaccine recipients, providers, and manufacturers); because of this, it is not possible to definitively conclude that LAIV is more likely to be administered after its expiration date. However, the magnitude of disproportional reporting for this error in expired LAIV use compared with IIV supports the hypothesis.

As a passive surveillance system, VAERS likely captures only a small fraction of expired LAIV administered, so this error might be more common than VAERS data indicate. Most reports had a vaccination date in November or later. Health care providers need to be aware of the short shelf

life of LAIV and implement measures to avoid administering expired LAIV, especially from November and onward, when this error appears to be more common. Although the data do not indicate that administration of expired LAIV poses a health risk, revaccination with a valid dose is advised (*4*). Replacement options for expired LAIV are available at

Gamma-Knife Surgery for OCD?

Steven Dubovsky, MD reviewing Lopes AC et al. JAMA Psychiatry 2014 Jul 23.
A small study shows benefit for some patients with intractable obsessive-compulsive disorder.
Deep brain stimulation at various locations is approved for the treatment of highly refractory obsessive-compulsive disorder (OCD). Researchers in Brazil examined the benefit of an alternative surgical approach, gamma-knife lesioning of the internal capsule.
The 16 participants had OCD that had failed to respond to multiple serotonin reuptake inhibitors and cognitive-behavior therapy. Patients were randomized to active or simulated bilateral ventral gamma-knife capsulotomy.
During the blinded, first postoperative year, three of eight patients who received active surgery and none in the sham group showed response (≥35% improvement in OCD rating scale scores). Mean OCD-symptom scores were significantly lower in the active-treatment group than in the sham group.
After blinding ended, patients who received sham treatment were offered real surgery, accepted by four patients. During the total follow-up (mean, 55 months), response occurred in two of these patients, and two more active-treatment patients also responded, for an overall 58% response rate. Of the patients who never received active surgery, none responded.

Review of Marijuana's Effects: Relevant Findings for Neurologists

Michael S. Okun, MD reviewing Volkow ND et al. N Engl J Med 2014 Jun 5.
As it becomes more available, be aware of the adverse side of marijuana use.
Many states have recently passed legislation to legalize and to regulate marijuana. In addition, as research increases on the potential uses of marijuana in treating neurological conditions, the guideline development subcommittee of the American Academy of Neurology (AAN) recently published a paper on the state of the evidence base. Spasticity,

central pain syndromes, and bladder dysfunction have all shown positive improvements in neurological symptoms. Now, Nora Volkow, the director of the National Institute on Drug Abuse, and colleagues have reviewed the potential adverse effects of marijuana use.

The authors point out that in the U.S., marijuana is the most commonly used "illicit" drug and that 12% of those aged 12 years or older have used it in the past year. Although smoking is the most common way people use marijuana, this harms lung function. An estimated 9% of users become addicted, and there may be a withdrawal syndrome. Use in adolescence and early adulthood can worsen brain function, decrease connections between brain regions, and decrease IQ. Heavy marijuana use can, rarely, lead to psychosis and hallucinations and can reduce cognitive functioning. Finally, recent use of marijuana before driving doubles the risk for causing a car accident.

The Search for the Perfect Diet Continues

JoAnne M. Foody, MD reviewing Lagiou P et al. BMJ 2012 Jun 26.

A Swedish study suggests that the long-term cardiovascular consequences of a low-carb, high-protein diet are negative.

Short-term, rapid weight loss has made Atkins-type, low-carbohydrate, high-protein diets popular, but concerns about the long-term effects of these diets continue to mount. In a large, population-based sample of 43,396 Swedish women aged 30 to 49 who completed a dietary questionnaire, investigators assessed the impact of low carbohydrate intake, high protein intake, or both on cardiovascular outcomes during an average follow-up of 15.7 years.

Each 10% decrease in carbohydrate intake (20 g — a small roll — per day), each 10% increase in protein intake (5 g — one boiled egg — per day), or each 2-unit increase in low-carbohydrate/high-protein score (scale: 2–20, with 20 representing very low carbohydrate and very high protein intake) was associated with a significant 4%–5% increase in the risk for cardiovascular events. In absolute terms, this represents an additional eight or nine cardiovascular events per 10,000 patient-years in women with low-carbohydrate/high-protein scores of 16 or more, as compared with those with scores of 6 or less.

Teaching Parents How to Nurture May Improve Children's Long-Term Health

Jonathan Silver, MD reviewing Miller GE et al. Proc Natl Acad Sci U S A 2014 Aug 5.
A 7-week intervention for families of low socioeconomic status seems to lead to less low-grade inflammation in the children 8 years later.

Early exposure to stress appears to increase vulnerability to psychiatric and medical conditions years later. Low socioeconomic status during childhood also increases this risk although some children seem less vulnerable, with better parenting apparently modifying the risk. Researchers examined peripheral blood measures of inflammation in children 8 years after a 7-week family intervention to improve parenting, strengthen family relationships, and build youth competencies.

The intervention consisted of weekly group meetings; separate 1-hour parent and youth skill-building sessions were followed by 1-hour family sessions (14 hours total). Parents learned nurturant-involved techniques and other strategies; children were taught the importance of household rules and socially adaptive behaviors. Rural families (667 mothers and their 11-year-old children; 46% were below the federal poverty threshold) were randomized to the intervention or a control (leaflets on child development, stress management, and exercise). Parents completed questionnaires at baseline and 3 months later.

In 272 youths at age 19, blood levels of six cytokines were obtained. The intervention was associated with significantly less inflammation than the control on all indicators. This finding was partially explained by improved parenting, but not by children's obesity or smoking. The more disadvantaged a family was, the more strongly changes in parenting were related to improved inflammatory markers.

Social Media: An Opportunity for Psychiatrists

Holly Peek, MD, MPH
August 04, 2014 | Couch in Crisis, Telepsychiatry
By Holly Peek, MD, MPH

It is essential that we psychiatrists align ourselves with the public and our patients both to disseminate accurate information and to educate. Social media allows us to have this public voice more than ever before.

Psychiatry residents and early-career psychiatrists were among the first to engage in social media while in their college dorm rooms. Facebook began in 2004 as an interactive directory for college students, to share photographs and basic information. Ten years later, the site now boasts over a billion users worldwide and can include anyone 13 years or older as well as businesses, organizations, celebrities, and political figures. Although Facebook was the first popular Web site of its kind, social media now encompasses various forms of media with popular sites such as YouTube, Twitter, Instagram, Pinterest, and LinkedIn.

Along with the exploding popularity of social media over the past decade came the potential pitfalls for many young adults entering graduate schools and their early careers. Personal pictures, posts, and information have become readily available on the Internet, prompting schools, training directors, and employers to screen applicants by searching for them online before offering an interview or a job. Furthermore, it is often even more concerning that a patient may stumble across information on personal social sites. Unfortunately, as the first generation of social media users have entered their early careers, a sense of fear has swept over the online communication scene, with many of these users disengaging altogether.

However, instead of viewing social media as a potential catalyst for` a career downfall, it can be an extremely worthwhile career opportunity for psychiatrists. The current generation of residents and early-career psychiatrists have essentially been engaged in social media for longer than any other generation. This means they are more likely to know how to use the technology and are more accustomed to readily sharing their thoughts and ideas through this very public platform. Re-creating an online presence from personal to professional has several advantages.

Engaging in social media as a psychiatrist is important because our patients spend a significant amount of their time online, and this is where they receive their health information. The average Internet user in the US spends 32 hours a month online, with 22% of this time spent on social media sites. Furthermore, smartphone users average 24 minutes per day using social networking apps.

While spending this time on the Internet, users are doing a lot more than casually socializing with their peers. In fact, according to the Pew Research Center's Internet & American Life Project, 72% of adult online users have searched the Internet for health-related information in the past year. A has also shown that one-third of social media consumers are using it for reading stories on a Web site or blog, signing up to receive alerts and e-mails, or joining a health-related group on a social networking site.

More than traditional Web sites, social media has changed the landscape of how psychiatrists can make use of the Internet. It has unlocked doors for open conversations among physicians, patients, and the general public. We have the ability to disseminate knowledge of evidence-based strategies, provide context to mental health stories in the media, and dispel myths. There are certainly people who are putting false, misleading, and potentially harmful information on the Internet. Therefore we, as mental health professionals, should use social media in a beneficial way by sharing our expertise and knowledge in the field.

Arguably, there is more stigma associated with psychiatric disorders than with any other health problems; this affects patients' mental health outcomes and, on a larger scale, funding and resources available to us and our patients. Social media is our opportunity to give voice to the fight against stigma by educating the public about mental health.

No discussion about social media is complete without talking about maintaining professionalism online. Because social media use for physicians is a relatively new and evolving phenomenon, professional organizations such as the AMA are now creating guidelines for appropriate use. It is essential for any physician using social media to review these guidelines: By following them, any trepidation about entering the social media scene can be alleviated.

Instead of avoiding social media altogether, I encourage mental health professionals to embrace this new and exponentially growing mode of communication. It is essential that we align ourselves with the public and our patients both to disseminate accurate information and to educate. Social media allows us to have this public voice more than ever before. Psychiatry residents and early-career psychiatrists certainly have an advantage in this arena in that many have been using social media for the past decade. However, digital media is not just for younger psychiatrists; medical professionals of all ages are now embracing the social media world. Learning how to use digital tools to teach patients, engage the public, and ultimately advocate for mental health is a skill worth adding to our professional repertoire.

Disclosures:

Dr Peek is a psychiatry resident at Tulane University School of Medicine, department of psychiatry and behavioral sciences, New Orleans. Her Web site iswww.psychgumbo.com and Twitter handle, @psychgumbo. She is the Digital Media in Psychiatry Section Editor for Psychiatric Times and the Media Editor for the American Journal of Psychiatry Residents Journal.

Psychiatric Disorders Are Common in Patients with Dizziness

Jonathan Silver, MD reviewing Lahmann C et al. J Neurol Neurosurg Psychiatry 2014 Jun 24.
Especially when there is no organic etiology

Complaints of dizziness, including vertigo, are common. Almost half are not explained by vestibular or neurologic disorders but are believed to be related to a psychiatric condition. Anxiety and depression also are very common in patients with vestibular migraines (VM), unlike patients with benign paroxysmal positional vertigo (BPPV). These researchers examined records of 547 patients with vertigo/dizziness (mean age, 55; 44% men), who received comprehensive neurological (including neuro-otological and neuro-ophthalmological) and standardized DSM-based psychiatric evaluations at a specialized treatment center.

Organic causes were found in 81% of patients; the most frequent causes were vestibular migraine (n=95), BPPV (n=87), and Meniere disease (n=81). About half of the study population received psychiatric diagnoses. The most common psychiatric disorders were anxiety/phobia (n=158), somatoform disorder (n=136), and affective disorder (n=104). Psychiatric disorders were more common when vertigo/dizziness lacked an organic etiology. Having a psychiatric disorder was associated with greater psychosocial impairment. Half of patients with vestibular paroxysmia and vestibular migraine also had psychiatric disorders.

When Depression Symptoms Remit, Quality of Life Improves — for Some

Joel Yager, MD reviewing IsHak WW et al. Acta Psychiatr Scand 2014 Jun 23.
Still, more than 30% of patients in pharmacologically induced remission reported below-normal quality of life, and 9% reported severe impairment.

Depression treatment studies usually focus on achieving symptom remission (minimal or no symptoms) or response (symptom reduction of ≥50%); few also consider overall quality of life (QOL). Using data from 2280 patients entered into STAR*D, a large, multistep treatment study of major depression (NEJM JW Psychiatry Apr 5 2006), investigators examined how treatment affected patient-rated satisfaction or enjoyment of mood, relationships, living situations, and physical health). Less than 2% of participants had baseline QOL scores within the normal range.

Among 812 patients whose depression remitted in level 1 (citalopram monotherapy), 79% had severely impaired self-rated QOL at entry. At remission, QOL scores were normal in 68% and severely impaired in 9%. Among 193 remitters in a 1-year follow-up, QOL impairment was severe in 14% at start of follow-up and in 13% afterwards.

Level-1 nonremitters generally had lower QOL self-ratings when entering later treatment steps. Among level-1 nonremitters, 89% had severely impaired baseline QOL, which remained severely impaired in 73% at the end of level 1. Among 221 nonremitters in follow-up, QOL was severely impaired in 41% at the start but 68% at 12 months.

A High-Potency Flu Vaccine Improves Protection in Older Adults

Abigail Zuger, MD reviewing DiazGranados CA et al. N Engl J Med 2014 Aug 14.
The new preparation conferred modest benefits and little risk.
Although standard influenza vaccination is moderately helpful in protecting elders from seasonal influenza, the ongoing burden of disease in this age group mandates something better. In 2009, a high-dose inactivated vaccine preparation that contained four times the standard amount of antigen (NEJM JW Gen Med Aug 11 2009) was licensed for use in adults 65 and older on the basis of its safety and promising immunogenicity, with the caveat that clinical benefits had yet to be demonstrated. Now, researchers have provided those data in a manufacturer-supported trial conducted during the 2011–2012 and 2012–2013 flu seasons in 32,000 older adults (mean age, 73; most with ≥1 chronic medical conditions; none seriously ill) at 126 centers in the U.S. and Canada. Flu-like illnesses were diagnosed in similar percentages of those who received standard-dose vaccinations and those who received high-dose vaccinations. However, polymerase chain reaction– or culture-confirmed influenza was significantly less common in the high-dose group (1.4% vs. 1.9%). Hospitalization rates were similar in both groups, but rates of pneumonia after respiratory illness were somewhat lower in the high-dose group; no participant died from the flu. Slightly fewer adverse events were associated with high-dose vaccination, but two high-dose recipients had vaccination-related neurological sequelae (cranial nerve palsy and acute encephalomyelitis), which were complications not seen with standard dosing.

ADHD Stimulant Treatment Does Not Affect Growth

ADHD or treatment with stimulants did not affect final adult height.
To assess the long-term growth effect of stimulant treatment in children with attention-deficit/hyperactivity disorder (ADHD), researchers compared 243 ADHD cases with sex-matched controls from a cohort born between 1976 and 1982. Height measurements during up to 30 years of follow-up were used to calculate height velocity and magnitude. Sex-specific height-for-age z-scores were determined before and after treatment.
The mean age at peak height velocity (PHV), the PHV magnitude, and adult height did not differ significantly between ADHD cases and controls among boys or girls. Among boys with ADHD, the mean age at PHV was later in those treated with stimulants for ≥3 months than in those not treated with stimulants (13.5 vs. 12.9 years). However, among boys and girls with ADHD, the PHV magnitude did not differ between those who were and were not treated with stimulants. Duration of stimulant treatment was not correlated with change in

z-scores. Adult height was similar in ADHD cases with or without stimulant therapy, regardless of duration of treatment.

Comorbidity: Schizophrenia with Obsessive-Compulsive Disorder

Alexandra Bottas, MD
April 15, 2009 | Schizophrenia, Alcohol Abuse, Comorbidity In Psychiatry, Compulsive Personality Disorder, Obsessive Compulsive Disorder, Schizophrenia Psychotic Features
By Alexandra Bottas, MD

The co-occurrence of obsessive-compulsive symptoms (OCS) and psychotic illness has been a challenge for clinicians and investigators for more than a century. Over the past decade, interest in this area has burgeoned because of recognition of higher-than-chance comorbidity rates of schizophrenia and OCD.

The co-occurrence of obsessive-compulsive symptoms (OCS) and psychotic illness has been a challenge for clinicians and investigators for more than a century. Over the past decade, interest in this area has burgeoned because of recognition of higher-than-chance comorbidity rates of schizophrenia and obsessive-compulsive disorder (OCD), and observations of appearance or exacerbation of OCS during treatment of schizophrenia with atypical antipsychotics. Emerging neurobiological and genetic evidence suggests that persons with comorbid OCD and schizophrenia may represent a special category of the schizophrenic population.

The evidence for a putative schizo-obsessive disorder is examined and practical treatment suggestions for this subgroup of patients are outlined in this article.

Comorbidity between OCD and schizophrenia

The lifetime prevalence for schizophrenia is 1% and for OCD it is 2% to 3%. Comorbidity rates for OCD in the schizophrenia population are substantially higher than what would be expected to occur randomly. In the schizophrenic population, the reported prevalence of clinically significant OCS and of OCD ranges from 10% to 52% and from 7.8% to 26%, respectively.

The higher-than-expected comorbidity rate for OCD and schizophrenia suggests a nonrandom association and possibly an integral relation between these 2 conditions. The question is whether this comorbid group with schizo-obsessive disorder represents a more severely ill group with greater brain dysfunction that could, in part, be caused by common neurodevelopmental predisposing factors, or whether the 2 conditions are part of a more complex syndrome that represents a distinct diagnostic entity. The answer could be clarified in part if neurobiological studies were to demonstrate a distinct neuroanatomical substrate in this comorbid group rather than the summation or superimposition of neurobiological lesions observed in the separate disorders.

Clinical and research challenges

Recent studies have aimed to reduce bias and confounding that were often inherent in older studies. Newer studies have used such methods as randomization, prospective and cross-sectional study designs, standardized diagnostic criteria, validated diagnostic tools, age-matched control groups, and stratification of patient populations according to phase of illness to increase the validity of study results.

Notwithstanding these efforts to enhance diagnostic clarity and study validity, the distinction between obsessions and delusions is often difficult to discern. Paradoxically, *DSM-IV* allows for the OCD specifier "with poor insight." This stands in contrast to the definition of an obsession as being recognized by the individual as foreign to him or her (ie, ego-dystonic), and implies the presence of insight. Insel and Akiskal proposed that "OCD represents a psychopathological spectrum varying along a continuum of insight," and that this "obsessional delusion" does not signify a schizophrenia diagnosis. Complicating the matter further is the observation of perceptual disturbances that mimic various types of hallucinations or pseudohallucinations in some persons with OCD.

Whether obsessions can be accurately detected in the presence of psychosis remains a matter of debate. To date, there is no universally accepted method of detecting OCD in the presence of schizophrenia, although most contemporary study designs have used the Structured Clinical Interview for *DSM-IV* Axis I psychiatric disorders and the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). In attempts to ascertain the reliability and validity of the Y-BOCS in this comorbid subgroup, de Haan and colleagues[28]examined the properties of this psychometric tool in patients with recent-onset schizophrenia and comorbid OCS. These investigations found good internal consistency and interrater reliability in this population. However, their findings concerning the divergent validity against depressive and negative symptoms were inconsistent.

Although the phenomenological delineations between obsessions and delusions often remain unclear, there is substantial evidence that OCS in schizophrenia represents more than just an expression of enduring psychosis. This evidence includes observations that conventional antipsychotic medications appear to be of limited use in the treatment of OCS in schizophrenia, the persistence of OCS even after successful treatment of the psychotic symptoms, and the effectiveness of serotonin reuptake inhibitors in the treatment of OCS in patients with schizophrenia.

Clinical relevance of OCS in schizophrenia

Early investigators concluded that the presence of OCS confers protection against cognitive deficits, functional impairment, and negative symptoms associated with schizophrenia. Psychodynamic theories postulated that obsessions constitute a defense against psychosis and prevent progression of the disease. However, more recent studies that used rigorous methods have not tended to replicate these earlier findings. Instead, recent studies have found that this comorbid group is burdened by a greater magnitude of cognitive deficits, negative and positive symptoms, neurological soft signs, distress, dysfunction, hopelessness, depression, suicidal ideation, and suicide attempts. A few studies have not replicated some of these findings.

Pedigree and genetic studies

Pedigree and genetic studies have not found any familial relationship or shared etiology between OCD and schizophrenia in their pure forms. However, specific genotypes of polymorphisms of the same gene may differentially confer risk for the 2 disorders.

The catechol-O-methyltransferase (COMT) gene is a candidate gene for schizophrenia because of its role in the breakdown of dopamine in the prefrontal cortex. Zinkstok and colleagues found that the COMT high activity Val allele is associated with more OCS in young patients with schizophrenia, whereas patients with the Met/Met genotype had the lowest Y-BOCS scores. These results support the hypothesis that the COMT Val-Met polymorphism may be a modifier gene for the symptoms of schizophrenia.

Poyurovsky and colleagues examined familial aggregation of schizophrenia spectrum disorders and obsessive-compulsive–associated disorders in schizophrenia probands with and without OCD. They found that relatives of OCD-schizophrenia probands had significantly higher morbid risks

for OCD-schizophrenia and obsessive-compulsive personality disorder (OCPD); they also found a trend toward higher morbid risk for OCD. When morbid risks for OCD, OCPD, and OCD-schizophrenia were pooled, the significant between-group differences became robust. These data suggest a genetic contribution to the expression of OCS in individuals with schizophrenia. In addition, they lend support for the validity of a putative schizo-obsessive diagnostic entity.

Neurobiology of the schizo-obsessive subgroup

Considerable work has been done to reveal the neurobiological basis of both schizophrenia and OCD.9 This research has focused primarily on elucidating key neurotransmitter systems, structural and functional neuroanatomy, and neuropsychology. However, there is very limited published research that focuses specifically on neurobiological features unique to this putative schizo-obsessive subtype.

Neurotransmitter systems. There is a paucity of published research on unique neurotransmitter involvement in the schizo-obsessive subtype group.

However, serotonin and dopamine have most consistently emerged as the principal neurotransmitters of interest in both disorders. The dopamine hypothesis in schizophrenia has long been regarded as the fundamental neurochemical premise; however, the superior efficacy of the serotonin-dopamine receptor antagonists in the treatment of schizophrenia also supports the importance of the serotonergic system in the pathophysiology of this disorder and may reflect the modulation of dopaminergic systems by serotonin.

Conversely, in OCD a somewhat opposing picture has emerged with respect to neurotransmitter involvement. The serotonin hypothesis of OCD is supported by successful treatment of the disorder with serotonin reuptake inhibitors, pharmacological challenge studies, and cerebrospinal fluid neurotransmitter metabolite studies. However, several lines of evidence suggest that serotonin is not the sole neurotransmitter involved in OCD. Considerable evidence supports the additional role of the dopaminergic system in this disorder. Preclinical evidence of dopamine's reciprocal modulatory effects on the serotonin system and successful treatment of refractory OCD with adjunctive dopamine receptor antagonists and serotonin-dopamine receptor antagonists have provided support for the dopamine-serotonin hypothesis of OCD.

There is a lack of neurotransmitter data in the overlap group. However, one study examined the differences in whole blood serotonin concentrations in healthy volunteers versus patients with OCD, in persons with schizophrenia with and without OCS, and in clozapine-treated schizophrenia in patients with and without clozapine-induced OCS. This study found that the groups with OCD, schizophrenia with OCS, and clozapine-treated schizophrenia with OCS had significantly lower levels of whole blood serotonin than did the healthy volunteers and the schizophrenia-only groups.

Neuroanatomy and neurocircuitry. In contrast to the abundance of neuroimaging studies investigating structural brain abnormalities in persons with OCD and schizophrenia separately, there is a dearth of such studies examining the comorbid subgroup. However, the considerable overlap in the neurocircuitry and specific anatomical structures implicated in each disorder may account for symptom coexpression in this subgroup of patients. The functional circuitry implicated in the pathophysiology of OCD is generally believed to involve a cortico-striatal-thalamic-cortical circuit. Specific structures implicated in this pathway include the basal ganglia, orbitofrontal cortex, and anterior cingulate cortex.

In schizophrenia, the dorsolateral prefrontal cortex circuit contains anatomical substrates similar to those of the OCD orbitofrontal circuit. Thus, the specific neuroanatomical sites identified by structural and functional neuroimaging studies performed in each of these disorders independently show considerable over-lap in implicated structures, including the basal ganglia, thalamus, anterior

cingulum, orbitofrontal cortex, and regions of the temporal cortex, although some of these findings are controversial.

Neuroimaging studies

Neuroimaging studies suggest the presence of specific neuroanatomical abnormalities in the overlap group that may differ from what is observed in the individual disorders. One MRI study of patients with juvenile-onset schizophrenia with OCS found significantly smaller left hippocampi in this group than in schizophrenia-only and control groups.63 In addition, there was an inverse correlation between illness duration and frontal lobe size in the comorbid group but not in the schizophrenia-only group.

Another MRI study of patients with juvenile-onset schizophrenia demonstrated significant enlargement of the anterior horn of the lateral ventricle and the third ventricle in patients with OCS compared with patients who did not have OCS.64 In a different study of patients with schizophrenia and various degrees of OCS, functional MRI found that one subgroup exhibited a negative correlation between activation of the left dorsolateral prefrontal cortex and OCS severity.

Taken together, these findings suggest greater neuroanatomical dysfunction in the comorbid subgroup. Whether these findings reflect a specific pattern of dysfunction unique to this comorbid subgroup or a more severe form of illness with greater brain dysfunction is thus far unclear. The question warrants further study.

Neuropsychological testing

Several studies have compared the profiles of neurocognitive deficits in patients with schizophrenia without OCS with those of the schizo-obsessive subgroup. Most, but not all, of these studies have revealed more severe neuropsychological impairments in the comorbid subgroup. Compared with their schizophrenia-only counterparts, the comorbid subgroup demonstrated greater impairment in nonverbal memory, cognitive shifting abilities, visuospatial skills, and executive function as measured by performance on the Wisconsin Card Sorting Test.

Summary

Epidemiological and biological data strongly suggest an integral relationship between OCD and schizophrenia in the comorbid subgroup of patients. The epidemiological data strongly suggest a unique relationship between these 2 disorders, given the marked degree of comorbidity that has been consistently observed and which appears to represent more than just a spurious association. Although pedigree and genetic studies of this overlap group are limited, preliminary findings suggest intriguing genetic influences on comorbid symptom expression.

The neurobiological data on each disorder suggest the involvement of common brain regions and neurotransmitter systems. However, more neuroimaging studies in the overlap group are required to determine whether specific structural abnormalities unique to this putative subtype are present Neuropsychological testing has generally revealed more severe impairment among patients in this comorbid group, which suggests a specific and active interaction between these 2 disease processes, but it has not identified a unique pattern of impairment.

Hence, despite the growing body of evidence that supports the existence of a specific epidemiological, genetic, and neurobiological relationship between these 2 disorders, the association remains poorly understood. The question of whether this overlap group represents a distinct diagnostic entity or comorbid disorders that result from a greater magnitude of brain involvement, common neurodevelopmental predisposing factors, or other confounding factors is impossible to answer definitively on the basis of existing knowledge.

Further neurobiological and genetic research that focuses specifically on this comorbid group is essential to clarify the nature of this proposed diagnostic entity. The current literature suggests that this comorbid subgroup probably carries a greater overall illness burden and that these patients

have more distress and impairment and worse outcomes—including the possibility of higher suicide risk. These clinical issues highlight the importance of identification and treatment of OCS in schizophrenia (Table) while the biological underpinnings continue to be elucidated.

Self-Reported Memory Complaints and Alzheimer Risk

Jaime Toro, MD reviewing Kryscio RJ. Neurology 2014 Oct 7.
Subjective memory complaints were associated with long-term increased risks for dementia and Alzheimer-type neuropathology in a prospective study.
Elderly people frequently report a decline in memory. These complaints about memory in some cases might be early signs of cognitive decline and, possibly, future dementia. To determine the risk for cognitive decline after subjective memory complaints, researchers prospectively tracked 531 cognitively intact adults (mean baseline age, 73). Participants reported annually whether they perceived changes in memory since their last visit and underwent objective cognitive and physical examinations at periodic intervals. A multistate model estimated when transition to impairment occurred, adjusting for other risk factors and for intervening death. The association between subjective memory complaints and Alzheimer-type neuropathology was studied from autopsies.
Subjective memory complaints were reported by more than 57.7% of the population and were associated with increased risk for cognitive impairment. Smokers with subjective memory complaints took less time to transition to mild cognitive impairment, while women taking hormone therapy took longer to transition directly to dementia. Among 176 participants who died without a diagnosed clinical impairment, subjective memory complaints were associated with elevated levels of neuritic plaques in the neocortex and medial temporal lobe.

Would You Use Marijuana if You Knew This?

Jonathan Silver, MD reviewing Filbey FM et al. Proc Natl Acad Sci U S A 2014 Nov 10.
Chronic use has long-term adverse effects on brain structure and function.
The consequences of long-term marijuana use are increasingly in the spotlight because of marijuana's legalization in many states. Investigators used magnetic resonance imaging to examine brain structure and function (gray-matter volume, functional connectivity, and white-matter integrity) in 42 marijuana users (≥4 times weekly; mean years of use, 9) and 62 nonusing controls matched for age and sex.
Users had lower gray-matter volume in right middle and left superior orbitofrontal gyri, higher connectivity in all orbitofrontal networks (bilateral orbitofrontal cortex and temporal lobe), and greater fractional anisotropy (FA) and lower radial diffusivity (RD) of the forceps minor tract (which connects the orbitofrontal regions). These structural changes correlated with behavioral indicators of marijuana use. Earlier age at onset of use was associated with higher functional

connectivity of the orbitofrontal cortex. Post hoc analysis suggested that FA and RD rose at initiation of heavy use and then fell with chronic use. Controlling for use of tobacco and alcohol did not change the results. Although mean IQ was higher in the control group (111 vs. 106 in users), the observed structural changes did not appear to mediate this effect.

Benefits of the Purposeful Life

Jonathan Silver, MD reviewing Kim ES et al. Proc Natl Acad Sci U S A 2014 Nov 18.
People with a greater sense of purpose use more preventive healthcare services.
Having a purpose in life is associated with lower morbidity and greater longevity (NEJM JW Psychiatry May 22 2014). These researchers examined whether individuals with a stronger sense of purpose are more likely to use preventive healthcare services during a 6-year follow-up. The 7168 participants over age 50 completed seven items on "purpose in life" from the Psychological Well-Being scale. The researchers also tracked self-reported use of six preventive services, overnight hospital stays, and baseline health factors, including psychiatric disorders, and behaviors (smoking, alcohol use, exercise).
Having a greater purpose in life was associated with increased use of five preventive tests (cholesterol test, colonoscopy, mammography, Pap smear, and prostate examination). The number of nights in the hospital was reduced by 17% for every unit increase in purpose. Psychological factors (e.g., anxiety, depression) only modestly decreased the association. Religiosity or positive affect also had only a modest effect. A sense of purpose had a dose–response relationship with preventive services and nights in the hospital.

Bilateral Repetitive Transcranial Magnetic Stimulation for Schizophrenia

Deborah Cowley, MD reviewing Dlabac-de Lange JJ et al. Psychol Med 2014 Oct 30.
Promising results for negative symptoms at 3 months' follow-up
Repetitive transcranial magnetic stimulation (rTMS) has been tried for negative symptoms of schizophrenia, and a few meta-analyses have shown some effects, with subanalyses suggesting greater efficacy when the left dorsolateral prefrontal cortex (DLPFC) is stimulated for ≥3 weeks.
In a two-site, double-blind, randomized, partially industry-funded study, researchers examined the effects of 3 weeks of 10-Hz rTMS or sham rTMS of the bilateral DLPFC in 32 patients with schizophrenia or schizoaffective disorder (81% male). All patients had moderate negative symptoms and were taking antipsychotics (including 12 patients on clozapine and 8 on antipsychotic polypharmacy).
Despite randomization, the sham rTMS group was younger than the active-treatment group (mean age, 32 vs. 42) and had lower negative-symptom and general psychopathology scores at baseline. The regimen involved stimulation of the left DLPFC on weekday mornings and right DLPFC on weekday afternoons (total of 30 treatments).

After adjustment for baseline symptom scores, active versus sham rTMS yielded significant improvement in negative symptoms and insight, which persisted at 3 months' follow-up; semantic verbal fluency, tested at 4 weeks, also improved. No significant group differences were found in other neurocognitive tests, depression, general psychopathology, or self-rated quality of life. No serious adverse effects of rTMS treatment were reported.

Stress During Pregnancy: Impact and Potential Treatment

Anna Wald, MD, MPH reviewing Shaw JG et al. Obstet Gynecol 2014 Dec. Keenan K et al. Obstet Gynecol 2014 Dec.

Two studies highlight the importance of maternal psychological well-being on birth outcomes.

Maternal stress and depression pose risks for preterm delivery. Investigators based at the Veterans Administration used the electronic medical record and data from the compulsory assessment of posttraumatic stress disorder (PTSD) in military personnel to evaluate the association between active PTSD (within 1 year of delivery) or historical PTSD (prior diagnosis) and risk for preterm birth. Among >16,000 deliveries, 19% were to women with PTSD (including 12% with active PTSD). Risk for spontaneous preterm delivery was higher among women with active PTSD (9%) than those with historical PTSD (8%) or no PTSD (7%), and the excess risk persisted after adjustment for potential confounders. Most women with active PTSD had experienced military sexual trauma as well as depressive disorders.

In a different study of prenatal stress, investigators randomized 64 urban, low-income, pregnant black women (gestational range at entry, 16–21 weeks) to receive supplementation with docosahexaenoic acid (DHA; 450 mg daily) or placebo until delivery. Perceived stress at 30 weeks' gestation was lower in the DHA group than the placebo group. DHA recipients also had lower cortisol output in response to arriving at the research laboratory, as well as a better-modulated response to a social stress test.

Anhedonia Plays a Role in Tobacco Withdrawal

Deborah Cowley, MD reviewing Cook JW et al. J Abnorm Psychol 2014 Nov 10.

Focus on pleasurable activities may aid in smoking cessation.

In animal and human laboratory studies, nicotine produces pleasure and increases the reward value of nondrug stimuli. Deprivation of nicotine is associated with decreased reward experiences and with anhedonia. The current researchers examined whether anhedonia is a symptom of tobacco withdrawal that contributes to smoking-cessation outcomes.

The participants were 1175 smokers (≥10 cigarettes daily for the preceding 6 months; women, 58%; white, 85%; mean age, 45) who were motivated to quit and were enrolled in a smoking-cessation study, and who rated pleasure associated with daily activities, negative affect, craving, trouble with concentrating, and hunger. Ratings were completed for the 5 days before the quit date and the 10 days after.

Individuals with heavy drinking or histories of psychosis, bipolar disorder, or eating disorder were excluded. Of the participants, 17% had depression histories; 5% had depression in the previous year. Prequit anhedonia was higher in those with previous-year depression.
Anhedonia increased immediately after smoking cessation and then decreased to prequit levels, consistent with other withdrawal symptoms; it was also associated with severity of nicotine dependence. After adjustment for postquit craving and negative affect, postquit anhedonia was associated with earlier relapse and lower abstinence rates at 8 weeks. Manufacturer-supplied nicotine replacement therapy suppressed postquit anhedonia and other withdrawal symptoms.

Prescribe Family Dinners for Cyberbullying

F. Bruder Stapleton, MD reviewing Elgar FJ et al. JAMA Pediatr 2014 Nov.

Among the nearly 20% of surveyed teens who experienced cyberbullying, family dinners were helpful in protecting them from its harmful effects.
Cyberbullying is known to adversely affect teen health. To assess its effects on mental health and substance use, researchers conducted a survey of Midwestern teens. The number and regularity of family dinners was used as a proxy for family interaction and support. Results were as follows:

- Of 18,834 adolescents surveyed, 18.6% experienced at least one instance of cyberbullying during the previous 12 months; however, only 2.2% experienced it frequently.
- Cyberbullying victimization was more common in girls than in boys (odds ratio, 2.95).
- Girls victimized by cyberbullying were less likely to have substance abuse issues compared with boys but more likely to have internalizing problems of anxiety, depression, suicidal thoughts, and self-harm.
- The frequency cyberbullying was positively associated with risk for mental health problems and substance abuse.
- Family dinners were significantly associated with reduced risks for all mental health and substance use problems (odds ratios ranged from 0.79 for over-the-counter drug use to 0.95 for fighting).
- Cyberbullying frequency had less impact on mental health problems in adolescents reporting ≥4 family dinners weekly versus none.

An Algorithm for Suicide Prediction?

Steven Dubovsky, MD reviewing Kessler RC et al. JAMA Psychiatry 2014 Nov 12.
Despite study flaws, it makes clinical sense to provide careful aftercare to patients discharged with these identified risk factors.
The risk for suicide is increased shortly after discharge from psychiatric hospital, but predicting exactly who is at risk is difficult. Deriving a mathematical algorithm from 38 databases covering 53,769 hospitalizations of 40,820 soldiers between 2004 and 2009, this U.S. Army group examined the risk for suicide within 1 year of hospital discharge (N=68 suicides).

The normalized rates of suicide were 264/100,000 person-years within 12 months of hospitalization, versus 18/100,000 in the overall Army population. Factors associated with a heightened risk for suicide included male sex, criminal offenses, past suicide attempts or ideation, nonaffective psychosis, dissociative disorder, and hearing loss. Post-traumatic stress disorder (PTSD) did not convey an increased suicide risk. Soldiers with greater risk for suicide also had increased risks for suicide attempts, accidental death, and further hospitalizations.

Ultra-High Risk for Psychosis May Mean Ultra-High Risk for Other Disorders

Joel Yager, MD reviewing Lin A et al. Am J Psychiatry 2014 Nov 7.

In 7 years of follow-up, researchers found an assortment of other psychiatric disorders in high-risk but nonpsychotic individuals.

About a third of individuals at high risk for psychosis manifest frank psychosis within 3 years. What about the rest? Investigators in Australia performed a partially industry-funded follow-up study of 331 patients assessed as ultra-high risk between ages 15 and 30. Ultra-high risk was defined as having attenuated psychotic symptoms, brief intermittent psychotic symptoms, or worsening psychosocial function plus trait vulnerability (schizotypal personality disorder or family history of psychosis). At baseline, 90% had at least one comorbid axis I disorder — mood disorders in 71%, anxiety disorders in 40%, and substance use disorders in 22%.

During a mean follow-up of 7 years (range, 2–14 years), 85 individuals developed frank psychosis. At follow-up, of the 226 patients who did not transition to frank psychosis, 28% still showed attenuated psychotic symptoms, but 68% had at least one axis I disorder (mood [mostly major depression], 49%; anxiety, 34%; substance use, 29%), and 10% had all three. Somatoform and eating disorders were also seen (3% and 5%, respectively). Persistent or recurrent disorders were common (initial mood disorders, 54%; initial anxiety disorders, 41%; initial substance use disorders, 52%). Overall, 26% remitted from a nonpsychotic disorder, 37% developed a new disorder, and only 7% never experienced any axis I disorder. Female sex predicted higher risk for anxiety and persistent mood disorders, but initial global functioning scores, IQ, and age poorly predicted course.

SSRIs, Stroke, and Mortality: Should We Be Concerned?

Jonathan Silver, MD reviewing Ayerbe L et al. Neurology 2014 Nov 25. Bartoli F and Paolucci S. Neurology 2014 Nov 25.

Mortality might increase in poststroke patients taking selective serotonin reuptake inhibitors, but the analysis of these data raises many questions.

Risk for stroke can increase with depression (NEJM JW Psychiatry Nov 7 2011), and outcomes and memory after stroke can improve with selective serotonin reuptake inhibitors (SSRIs) even in nondepressed patients (NEJM JW Psychiatry Oct 2 2013 and Feb 22 2010). However, SSRIs may increase risk for intracerebral bleeding (NEJM JW Psychiatry Nov 5 2012). To learn more about

the risks and benefits of using SSRIs in stroke patients, researchers used data from a stroke registry started in 1998. They identified 1354 patients with stroke and follow-up data on depression at 3 months and mortality at 5 years; only 11% were taking antidepressants.
Depression was common (32%). At 5 years, 331 patients (24%) had died. The study involved five separate analyses of different factors (smoking and alcohol use, treatment of hypertension and diabetes, social support, disability, and SSRI use); each analysis controlled for sex, age, ethnicity, and stroke severity.
Mortality was significantly higher in depressed patients than nondepressed patients, but in subanalyses, this difference was restricted to patients aged <65 (hazard ratio [HR], 3.29). Mortality risks also increased with SSRIs initiated after stroke, independent of depression (HR, 1.72), but not with starting SSRIs before stroke.

Adolescent Self-Harm Increases Risk for Poor Young Adult Outcomes

Peter Roy-Byrne, MD reviewing Mars B et al. BMJ 2014 Oct 21.
Even nonsuicidal self-harm predicts higher risk for psychiatric and substance use problems.
Adolescent self-harm, with or without suicidal intent, is relatively common and is alarming to parents and family, who wonder whether this behavior predicts future social and psychiatric difficulties. These researchers used data on 4799 individuals with self-reported self-harm histories at age 16 in a U.K. longitudinal study and tracked their psychiatric diagnoses, substance use, and educational and occupational outcomes through age 21.
After prior depressive symptoms and socioeconomic status were controlled for, self-harm at age 16 predicted increased risk for depression (odds ratios: nonsuicidal self-harm, 2.21; suicidal, 3.94), anxiety (ORs, 2.15 and 4.47), harmful alcohol use (ORs, 1.89 and 1.95), cannabis use (ORs, 2.75 and 5.77), and self-harm by age 21 (ORs, 4.48 and 11.4). Only suicidal self-harm was predictive of poor educational and occupational attainment (ORs, 2.08 and 1.96, respectively). The prevalence of good outcomes (no psychiatric substance use, no educational or occupational problems) was halved with self-harm histories (59% vs. 28%).

For Tension Headache, Combo Rx Tops Acetaminophen

Alisa G. Woods, PhD
News | December 01, 2014 | Headache and Migraine
By Alisa G. Woods, PhD
Pain relief is better with a triple combination medication that includes acetaminophen than with acetaminophen by itself, researchers found, suggesting a new therapeutic option.
Combo therapy works better for headache relief.

A triple combination medication for tension headache that includes acetaminophen is more effective for pain relief than acetaminophen by itself, an international group of researchers has found.

The researchers sought to evaluate whether a combination pain-reliever that includes acetylsalicylic acid (aspirin), acetaminophen (often referred to as Paracetamol in Europe and Tylenol in the United States), and caffeine is more effective for treating patients with tension headache than acetaminophen alone.

Led by Hans-Christoph Diener, MD, of Department of Neurology and Headache Center, University Hospital Essen, Germany, in collaboration with Novartis, the investigators conducted 4 identical randomized, controlled trials in 1900 patients who had episodic tension-type headache. Data were pooled from the 4 studies.

The main end point for this study was the percentage of patients who were pain-free at 2 hours after taking the medication. The researchers also measured headaches at 1 hour after medication, whether patients had mild or no pain at 2 hours after medication, and how much headaches interfered with daily activities.

The combination medication indeed seemed to work better than acetaminophen alone—29% of the patients were pain free at 2 hours after taking the combination medication, compared with 21% who took acetaminophen and 18% who received placebo. This was a statistically significant effect.

Differences among the 3 treatments were even greater for patients who had severe pain at baseline. Of those who received the combination, 20% were pain-free at 2 hours post-medication, compared with 12% who were taking acetaminophen and 11% taking placebo. Combination medication also was superior for the other measurements, including pain relief at 1 hour, pain reduction at 2 hours, and reductions in interference with daily living.

"Clearly, the combination offers an important alternative when acetaminophen alone is not effective enough," the authors noted in this report. "Caffeine, in particular, contributes to the greater efficacy of the combination vs acetaminophen alone; patients with tension-type headache or other pain conditions who take an analgesic without caffeine need about 40% more medication to get the same relief as patients taking the same analgesic with caffeine."

The combination therapy could offer a welcome additional alternative for patients who have tension headaches.

Tension-type headaches are the most common headaches among adults, it was noted. Unlike migraine headaches, they are characterized by nonspecific aching rather than throbbing. About 3% of the US population experiences chronic daily tension headaches. Over-the-counter medication is standard treatment for patients with this type of headache.

The study was published on November 19 in the Journal of Headache and Pain.

Key points

• Combination medication for tension headache, including acetaminophen, aspirin, and caffeine, is more effective for pain relief than acetaminophen alone.

• Combination medication for tension headache may be more effective in patients with severe pain than acetaminophen alone.

• The triple combination therapy could offer an additional alternative for patients with chronic tension headaches.

Recognition and Management of Withdrawal Delirium (Delirium Tremens)

At some time in their lives, 20% of men and 10% of women in most Western societies will have an alcohol-use disorder, which is defined as repetitive alcohol-related problems in at least 2 of 11 areas of life.1,2 These conditions can decrease the life span by a decade and are associated with severe impairments in social functioning, as well as high rates of medical problems. Although alcohol-related conditions occur in persons from all social strata and affect more than 20% of patients in most medical settings,2,3 few physicians have been adequately trained in identifying and treating these serious problems.

About 50% of persons with alcohol-use disorders have symptoms of alcohol withdrawal when they reduce or discontinue their alcohol consumption; in 3 to 5% of these persons, grand mal convulsions, severe confusion (a delirium), or both develop.1 It is essential that clinicians know how to prevent, recognize, and treat these severe withdrawal states to minimize costly hospitalizations and avoidable deaths.

STATES OF ALCOHOL WITHDRAWAL

Mild and Moderate Withdrawal

Alcohol is a central nervous system depressant. Like benzodiazepines, barbiturates, and drugs that have similar action, it rapidly increases the release of γ-aminobutyric acid (GABA) in the brain, with prominent effects on GABA type A ($GABA_A$) receptors, and it inhibits postsynaptic N-methyl-d-aspartate glutamate-receptor activity.4,5 With repeated exposure, the brain adapts to the effects of alcohol through changes in receptors and other proteins. These adaptations result in decreased effects of the depressant, with the result that higher doses of the agent are required to achieve similar results.5,6 Subsequent reductions in blood alcohol levels lead to symptoms that are, in general, the opposite of the acute effects of the drug. Withdrawal symptoms associated with depressants such as alcohol include insomnia, anxiety, and increased pulse and respiration rates, body temperature, and blood pressure, as well as a hand tremor.1,4 Because of the short action of ethanol (beverage alcohol), withdrawal symptoms usually begin within 8 hours after blood alcohol levels decrease, peak at about 72 hours, and are markedly reduced by day 5 through 7 of abstinence.4,7

The time course of alcohol withdrawal and the severity of symptoms associated with it must be closely monitored to identify the most effective treatments. Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised.describes a withdrawal rating instrument that is commonly used by trained clinicians — the Clinical Institute Withdrawal Assessment of Alcohol Scale, revised (CIWA-Ar).4,8 Scores on the CIWA-Ar range from 0 to 67; scores lower than 8 indicate mild withdrawal symptoms that rarely require the use of medications, scores from 8 to 15 indicate moderate withdrawal symptoms that are likely to respond to modest doses of benzodiazepines, and

scores higher than 15 indicate severe syndromes that require close monitoring to avoid seizures and alcohol withdrawal delirium (delirium tremens).

Withdrawal Delirium (Delirium Tremens)

The criteria for withdrawal delirium, described in Criteria for Withdrawal Delirium (Delirium Tremens)., are delirium (a rapid-onset fluctuating disturbance of attention and cognition, sometimes with hallucinations) plus alcohol withdrawal. 1,7,9 Clinicians differ in how well they adhere to these criteria, so it is difficult to determine the prevalence of withdrawal delirium, and rates depend on whether persons with this condition were treated as outpatients, as general medical or psychiatric inpatients, or as patients in an intensive care unit (ICU). Most studies estimate that 3 to 5% of patients who are hospitalized for alcohol withdrawal meet the criteria for withdrawal delirium. 7,10,11 Retrospective chart reviews based on diagnoses made by general clinicians show higher but less reliable rates.

Withdrawal delirium usually begins about 3 days after the appearance of symptoms of alcohol withdrawal and lasts from 1 to 8 days or more (usually 2 or 3 days).7,9,12Approximately 1 to 4% of hospitalized patients who have withdrawal delirium die; this rate could be reduced if an appropriate and timely diagnosis were made and symptoms were adequately treated.7,9,11,13 Death usually results from hyperthermia, cardiac arrhythmias, complications of withdrawal seizures, or concomitant medical disorders. 14,15

Delirium during alcohol withdrawal is predicted by the following: CIWA-Ar scores above 15 (especially in association with a systolic blood pressure >150 mm Hg or a pulse rate >100 beats per minute), recent withdrawal seizures (seen in 20% of persons with delirium), prior withdrawal delirium or seizures, older age, recent misuse of other depressant agents, and concomitant medical problems.7,10,11,13,16,17 The latter include electrolyte abnormalities (e.g., low levels of potassium, magnesium, or both), low platelet counts, and respiratory, cardiac, or gastrointestinal disease.7,10,11,17

TREATMENT OF WITHDRAWAL DELIRIUM

The best approach to the prevention of withdrawal delirium is the identification and treatment of preexisting concomitant medical problems and withdrawal syndromes.4 Perhaps because of the low prevalence of withdrawal delirium and the high treatment costs, and because pharmaceutical companies lack profit motives associated with research into new treatments for this condition, few double-blind, controlled, prospective trials of treatments exist. The best evidence is provided in a 2004 review of nine prospective, controlled trials that were conducted between 1959 and 19789 and in subsequent noncontrolled studies that were identified in a PubMed search.

The major treatment goals for withdrawal delirium are to control agitation, decrease the risk of seizures, and decrease the risk of injury and death with the use of the methods outlined in Suggested Treatment of Alcohol Withdrawal Delirium (Delirium Tremens)..7,9,13,18-23 Because of the high prevalence of agitation among patients with withdrawal delirium and the potential lethal outcomes, treatment is best carried out in a locked inpatient ward or an ICU.

The approach to the management of withdrawal delirium includes a careful physical examination and appropriate blood tests to identify and treat medical problems that may have contributed to the severe withdrawal state.9,17 The same general types of support needed for any patient with delirium should be used for the patient with withdrawal delirium, including helping to reorient the

patient to time, date, and place, evaluating and treating the patient in a well-lit room, providing reassurance, performing frequent monitoring of vital signs, and ensuring adequate hydration. A functioning intravenous line should be established; care should be taken when administering glucose to avoid precipitating Wernicke's encephalopathy or thiamine-related cardiomyopathies and to circumvent overhydration in patients who have temporary, alcohol-related, compromised cardiac functioning.18,23 Although thiamine (e.g., 500 mg infused intravenously over the course of 30 minutes once or twice daily for 3 days) and multivitamins are recommended, there is little support for routine administration of magnesium.9,19,20,24 In patients in whom Wernicke's encephalopathy is suspected, recommended doses of thiamine are even higher (e.g., 500 mg intravenously three times daily for 5 days), in addition to daily parenteral multivitamins.24

The mainstay of the pharmacologic treatment of withdrawal delirium is depressants such as benzodiazepines.7,9,12 No single drug of this class has been shown to be superior to another. The doses needed to control agitation and insomnia vary dramatically among patients and can be prodigious (e.g., >2000 mg of diazepam in the first 2 days in some patients); this underscores the advisability of providing treatment in a hospital, preferably in an ICU. The severity of symptoms requires that care be directed by clinicians who are well trained in the treatment of this disorder.

Alternative depressant-like drugs have been proposed for uncomplicated withdrawal, but data are lacking regarding their use in persons who have withdrawal delirium. These agents include phenobarbital (up to 1500 mg to 2000 mg administered orally or intravenously on day 1 in patients with delirium13); clomethiazole (not available intravenously, but for uncomplicated withdrawal, up to 2304 mg (12 capsules) can be administered orally in divided doses on day 17,25); midazolam (one study indicated a dose of up to 2800 mg over 50 days); carbamazepine (approximately 800 mg per day); and oxcarbazepine (approximately 900 mg per day). 7,26-28

In patients who do not have a response to high doses of benzodiazepines (especially patients who are intubated), propofol may be administered (e.g., 0.3 to 1.25 mg per kilogram of body weight, up to 4 mg per kilogram per hour, for up to 48 hours).20,26 Another adjunctive medication is dexmedetomidine, an α_2-adrenergic agonist that is used in ICUs to produce a state in which the patient is sedated but arousable, with decreased sympathetic tone. Doses up to 0.7 μg per kilogram per hour have been administered in patients who do not have a good response to benzodiazepines.29,30 This drug cannot be used in patients with a heart block, and the patient's blood pressure and heart rate must be closely monitored. None of these regimens have been as well studied as the benzodiazepine regimen, and each has additional dangers and few advantages over benzodiazepines for most patients.21,31-33 lists the potential adjunctive use of haloperidol for severe agitation or hallucinosis, but antipsychotic drugs can prolong the QT interval and can increase the likelihood of seizures.

CONCLUSIONS

Withdrawal delirium is an uncommon, serious complication of alcohol withdrawal that is best treated with intravenous benzodiazepines. All the doses described in this review are approximations based on uncontrolled studies. Data on the most effective care for patients with withdrawal delirium are lacking. Since the low potential of profit from this research may undercut interest from pharmaceutical companies, treatment trials sponsored by the National Institutes of Health are warranted.

Malpractice Risk According to Physician Specialty

Despite tremendous interest in medical malpractice and its reform,1-10 data are lacking on the proportion of physicians who face malpractice claims according to physician specialty, the size of payments according to specialty, and the cumulative incidence of being sued during the course of a physician's career.11-13 A recent American Medical Association (AMA) survey of physicians showed that 5% of respondents had faced a malpractice claim during the previous year.14 Studies estimating specialty-specific malpractice risk from actual claims are much less recent,15,16including a Florida study from 1975 through 1980 showing that 15% of medical specialists, 34% of obstetricians and anesthesiologists, and 48% of surgical specialists faced at least one claim that resulted in an associated defense cost or payment to a claimant (an indemnity payment) during the 6-year study period.17

Each of these earlier studies has limitations, including the use of older data15-17 with limited geographic coverage,17 reliance on self-reports with limited sample size and low response rates,14limited information on physician specialty,13,14 and a lack of information on the size of payments.14 Although the National Practitioner Data Bank includes most cases in the United States in which a plaintiff was paid on behalf of a licensed health care provider,18 it does not report the specialties of physicians and does not record information on cases that do not result in a payment.

Using physician-level malpractice claims obtained from a large professional liability insurer, we characterized three aspects of malpractice risk among physicians in 25 specialties: the proportion of physicians facing a malpractice claim in a given year, the proportion of physicians making an indemnity payment, and the size of this payment. In addition, we estimated the cumulative career risk of facing a malpractice claim for physicians in high- and low-risk specialties.

METHODS

Malpractice-Claims Data

We obtained physician-level data on malpractice claims from a large, physician-owned professional liability insurer that provided coverage to physicians in every U.S. state and the District of Columbia. The procedures for safeguarding these data were approved by the institutional review board at RAND. The data included records on closed malpractice claims for 40,916 physicians who were covered for at least one policy year from 1991 through 2005. The number of physicians grew steadily from 12,498 in 1991 to 17,376 in 2005. We identified 24 specialties that had at least 200 physicians represented in our sample. Physicians belonging to other, smaller specialties were grouped together in an "other specialty" category. Across specialties, there were 233,738 physician-years of coverage, with an average duration of coverage of 5.7 years (range, 4.6 in pediatrics to 7.3 in thoracic–cardiovascular surgery). The most common specialties in our data were anesthesiology, family general practice, and internal medicine.

Claims were available for all years during which a physician was covered by the insurer. Claims that were not yet closed by the insurer were not available. Indemnity payments that were associated

with a claim reflected payments to a claimant that arose from either a settlement with the claimant or a jury verdict.

Although the data included physicians from all 50 states, California was overrepresented in our data, accounting for 16,076 physicians (39.3%). We corrected for this oversampling by weighting each physician in our data by the relative number of physicians who are not employed by the federal government reported in the Area Resource File of the Department of Health and Human Services. After weighting, the share of physicians in California was 12.2%, which by construction matches the share reported in the Area Resource File. Because we relied on data from a single insurer, we verified that the average number of indemnity claims per physician and payment levels in our data matched similar numbers in the National Practitioner Data Bank. In a previous study, investigators also relied on claims from a single insurer.19

We included physicians between the ages of 30 and 70 years in the study. The average age of physicians in all specialties was 49.0 years (range, 43.2 for emergency medicine to 53.0 for gynecology). Data on other demographic characteristics (e.g., sex and race) were not available.

Describing Malpractice Risk

For each specialty, we began by calculating the proportion of physicians who faced a malpractice claim in a given year. We distinguished between claims leading to indemnity payments versus overall claims (those with a defense cost but not necessarily a payment). In sensitivity analysis, we adjusted for physician age, year, and state to examine whether these adjustments would affect our reported estimates.

Given the long period studied, we separated our sample into three periods (1991–1995, 1996–2000, and 2001–2003) in order to investigate how claims rates varied over time for high- and low-risk specialties, which were defined as the five specialties with the highest and lowest proportions of physicians with a claim in a year, respectively. We did not include 2004–2005, since many claims that had been filed during that period might not have been closed by the end of 2005.

We then characterized the size of malpractice payments for each specialty by computing mean and median annual payments. We also determined how many payments exceeded $1 million to characterize specialties with outlier awards. Payments were normalized to 2008 dollars on the basis of the Consumer Price Index.

Finally, we analyzed data on physician age to estimate the cumulative career malpractice risk of being sued at least once by a given age for both high- and low-risk specialties. We first estimated a multivariate regression model of the probability of facing at least one claim in a given year as a function of physician age, physician random effects, physician specialty, state of practice, and county–year demographic variables (per capita income, age distribution, and the proportions of residents who were white or male). We allowed the effect of age to vary according to specialty. Physician random effects were included to account for unobserved differences among physicians that might have led some physicians to have been sued more frequently than others. This estimation yielded predicted annual rates of facing a claim at every age of a physician's career and for each specialty. These estimated lifetime risk profiles were then used to compute cumulative career malpractice risks for physicians in high- and low-risk specialties, as well as in each of the largest specialties in our data (internal medicine and its subspecialties, general surgery and surgical subspecialties, anesthesiology, obstetrics and gynecology, and pathology).

Our model assumes that the probability of being sued was unrelated to the duration of coverage by the insurer and that the probability of being sued at a given age was independent of being sued at

an earlier age (after adjustment for physician random effects). To ensure that estimates of the cumulative risk of being sued in each specialty were not determined by the experience of a few idiosyncratic physicians, we conducted two sensitivity analyses: we excluded physicians after their first claim (consequently ignoring the subsequent experiences of physicians who were sued repeatedly) and estimated fixed-effects specifications that allow for correlation between physician characteristics (such as age) and unobserved propensities to be sued.

RESULTS

Malpractice Claims According to Specialty

Figure 1FIGURE 1Proportion of Physicians Facing a Malpractice Claim Annually, According to Specialty. shows the proportion of physicians who faced a malpractice claim in a year according to specialty. Across specialties, 7.4% of physicians annually had a claim, whereas 1.6% made an indemnity payment. There was significant variation across specialties in the probability of facing a claim, ranging annually from 19.1% in neurosurgery, 18.9% in thoracic–cardiovascular surgery, and 15.3% in general surgery to 5.2% in family medicine, 3.1% in pediatrics, and 2.6% in psychiatry. Specialties in which physicians were most likely to face claims were not always specialties in which indemnity claims were most prevalent. Our estimates of rates of overall and paid claims were unaffected by adjustment for physician age, year, and state of practice.

Another measure of risk is the likelihood of a payment conditional on a claim. The payment rate can be inferred as the proportion of physicians making a payment divided by the proportion facing a claim. The proportion of physicians with a claim was not well correlated with the payment rate (Pearson's correlation, 0.17; P=0.42). For example, gynecology alone had the 12th highest average annual proportion of physicians with a claim, but it had the highest payment rate (>38%).

Trends in Claims

The proportion of physicians facing a malpractice claim varied moderately across the study period (Figure 2FIGURE 2Trends in Overall Claims and Claims with an Indemnity Payment, According to Risk of Specialty.). Between the 1991–1995 and 2001–2003 periods, the average annual proportion of physicians in low-risk specialties with a claim decreased from 8.3% to 5.8%. Among high-risk specialties, the proportion of physicians with a claim was highest during the 1996–2000 period. Claims with an indemnity had similar patterns, and the differences between periods were significant (P<0.001 for all comparisons). Differences in overall and indemnity claims were stable between high-risk and low-risk specialties over time.

Size of Malpractice Indemnity Payments

Figure 3FIGURE 3Amount of Malpractice Payments, According to Specialty. shows mean and median indemnity payments per physician for each specialty after the exclusion of claims that did not result in an indemnity payment. Across specialties, the mean indemnity payment was $274,887, and the median was $111,749. The difference between the mean and median payment reflects the right-skewed payment distribution. Specialties that were most likely to face indemnity claims were often not those with the highest average payments. For example, the average payment for neurosurgeons ($344,811) was less than the average payment for pathologists ($383,509) or for pediatricians ($520,924), even though neurosurgeons were several times more likely to face a claim in a year. The estimated correlation between the proportion of physicians with a claim and the average payment amount was 0.13 (P=0.52). The correlation between the proportion of physicians with an indemnity payment and the average payment was similar and was not

significant. This suggests that factors driving the likelihood of a claim are largely independent of factors that drive the size of a payment.

Outlier awards, which were defined as those exceeding $1 million, were infrequent, in part because the full size of outlier awards would not have been recorded if they had exceeded individual policy limits. Among all physician-years, 66 payments exceeded this amount, accounting for less than 1% of all payments. Obstetrics and gynecology accounted for the most payments (11), followed by pathology (10), anesthesiology (7), and pediatrics (7).

Cumulative Career Malpractice Risk

The projected proportion of physicians facing a malpractice claim by the age of 65 years was high (Figure 4FIGURE 4Cumulative Career Probability of Facing a Malpractice Claim or Indemnity Payment, According to Risk of Specialty and Age of Physician.). Among physicians in low-risk specialties, 36% were projected to face their first claim by the age of 45 years, as compared with 88% of physicians in high-risk specialties. By the age of 65 years, 75% of physicians in low-risk specialties and 99% of those in high-risk specialties were projected to face a claim. The projected career risk of making an indemnity payment was also large. Roughly 5% of physicians in low-risk specialties and 33% in high-risk specialties were projected to make their first indemnity payment by the age of 45 years; by the age of 65 years, the risks had increased to 19% and 71%, respectively. Specialty-specific projections of career malpractice risk were also calculated. Roughly 55% of physicians in internal medicine and its subspecialties were projected to face a malpractice claim by the age of 45 years, and 89% by the age of 65 years. In contrast, 80% of physicians in surgical specialties (including general surgery) and 74% of physicians in obstetrics and gynecology were projected to face a claim by the age of 45 years. The results were unchanged after the exclusion of data for physicians after their first claim or in models that allowed for a correlation between physician characteristics and an unobserved propensity to be sued.

DISCUSSION

There are few recent estimates on the likelihood of malpractice claims and the size of payments according to physician specialty. Using physician-level malpractice claims from a nationwide liability insurer, we found substantial variability across specialties in each of these descriptors of liability risk. Specialties in which the largest proportion of physicians faced a claim were not necessarily those with the highest average payment size. For example, physicians in obstetrics and general surgery — both fields that are regarded as high-risk specialties — were substantially more likely to face a claim than pediatricians and pathologists, yet the average payments among pediatricians and pathologists were considerably greater. The same pattern was noted in a national analysis that was performed more than two decades ago.15

For many high-risk specialties, our estimates of annual and career malpractice rates match self-reported claims rates reported in a recent AMA survey of physicians.14 For several low-risk specialties, however, our findings suggest that the proportion of physicians facing claims is consistently higher than that reported in the AMA survey. This finding suggests underreporting by physicians in low-risk specialties, perhaps because these physicians did not report a claim or because those with previous claims were less likely to respond to the survey. Such a trend could be because the stigma of a claim is worse in specialties in which such claims are less common or because recall bias is more severe for rare events.

Our study uncovered an important aspect of malpractice liability: the high likelihood of claims that do not result in payments to a plaintiff. Annual rates of claims leading to indemnity payments

ranged from 1% to 5% across specialties, whereas rates of all claims ranged from 5% to 22%. Our projections suggest that nearly all physicians in high-risk specialties will face at least one claim during their career; however, a substantial minority will not have to make an indemnity payment.

Our results may speak to why physicians consistently report concern over malpractice and the intense pressure to practice defensive medicine,20 despite evidence that the scope of defensive medicine is modest.4,21,22 Concern among physicians over malpractice risk varies far less considerably across states than do objective measures of malpractice risk according to state (e.g., rates of paid claims, average payment sizes, malpractice premiums, and state tort reforms).1 For example, 65% of physicians practicing in states in the bottom third of rates for paid malpractice claims (5.5 paid claims per 1000 physicians) express substantial concern over malpractice, as compared with 67% of physicians in the top third (14.6 claims per 1000 physicians).1 Although these annual rates of paid claims are low, the annual and career risks of any malpractice claim are high, suggesting that the risk of being sued alone may create a tangible fear among physicians.

The perceived threat of malpractice among physicians may boil down to three factors: the risk of a claim, the probability of a claim leading to a payment, and the size of payment. Although the frequency and average size of paid claims may not fully explain perceptions among physicians,1one may speculate that the large number of claims that do not lead to payment may shape perceived malpractice risk. Physicians can insure against indemnity payments through malpractice insurance, but they cannot insure against the indirect costs of litigation, such as time, stress, added work, and reputational damage.23 Although there is no evidence on the size of these indirect costs, direct costs are large. For example, a Harvard study of medical malpractice suggested that nearly 40% of claims were not associated with medical errors and that although a low percentage of such claims led to payment of compensation (28%, as compared with 73% of claims with documented medical errors), they accounted for 16% of total liability costs in the system.19

Our study has several limitations. As in a previous study,19 we used data from a single insurer, which may not be nationally representative, even though it is one of the largest in the United States and covers physicians in every state. Whether the claims rates in our study are representative of those nationwide depends on whether physicians who were covered by the insurer that we studied were more or less likely to be sued than physicians who were insured elsewhere. To assess the representativeness of the data, we compared our weighted estimates with the probability and size of indemnity claims reported by the National Practitioner Data Bank. The results are reassuring: the weighted number of indemnity claims per 1000 full-time, nonfederal physicians during the period from 1991 through 2005 was 17.1 in our sample, as compared with 19.6 in the federal database. The weighted average payment in our sample was $274,887 (in 2008 dollars), which is only 4.8% less than the average in the database. These small differences may reflect the fact that the mix of specialties in our sample may not be nationally representative.

Our estimates provide a glimpse into U.S. malpractice risk among physician specialties. High rates of malpractice claims that do not lead to indemnity payments, as well as a high cumulative career malpractice risk in both high- and low-risk specialties, may help to explain perceived malpractice risk among U.S. physicians.

Is Diet a Viable Adjunctive Treatment for Adults with Epilepsy?

Robert C. Knowlton, MD, MSPH reviewing Klein P et al. Neurology 2014 Nov 18.

The ketogenic and modified Atkins diets may have sustained efficacy in some adults with medically refractory epilepsy, but long-term adherence is often challenging.

Most studies of efficacy and tolerability of diet modification as an alternative treatment for epilepsy are in children. The ketogenic diet (KD) has demonstrated effectiveness, in some instances dramatically so, in young children with catastrophic epilepsies. In adults, much less is known about the effectiveness of such diets, despite increasing interest.

Researchers conducted this review to cull as much data as possible from published studies of both KD and the modified Atkins diet (MAD) as adjunctive treatment for adults with medically intractable epilepsy. A meta-analysis was not possible because no common statistical measures could be shared between the available studies. Data regarding status epilepticus were insufficient to evaluate.

Efficacy measured with the responder rate (percentage of cases with a ≥50% reduction in seizures) was approximately 30% for both diets. The main adverse effects were increased cholesterol and triglycerides, which were greater with KD than with MAD. Other adverse effects of both diets were gastrointestinal problems (diarrhea, constipation, bloating) and weight loss. Ketosis, achieved in all patients who were on either diet for at least one week, declined over time and was not associated with efficacy.

Higher BPA Levels Associated with Prostate Cancer

By Amy Orciari Herman

Higher urinary levels of bisphenol A (BPA) are linked to early-onset prostate cancer, according to a PLoS ONE study.

Researchers measured urinary BPA concentrations in 60 urology patients, about half of whom had prostate cancer. Concentrations were significantly higher in patients with than without cancer, particularly among those younger than 65.

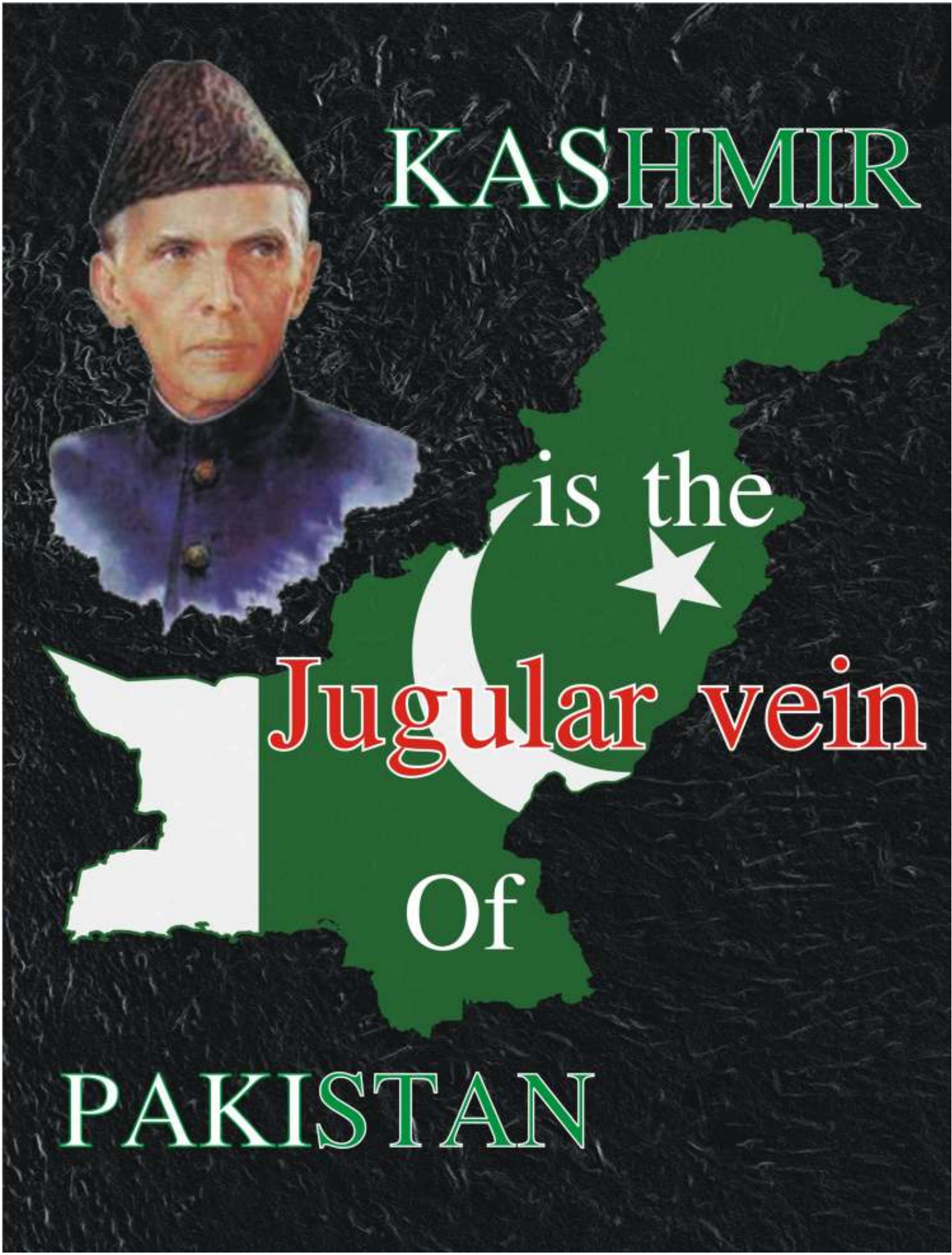
In addition, when prostate cancer cells were treated in vitro with low doses of BPA, there was a significant increase in the proportion of cells with three or more centrosomes (untreated cells showed no such increase). This "centrosome amplification," the researchers say, commonly occurs in human tumors and "may contribute to neoplastic transformation of the prostate."

BPA, found in many plastics and food and beverage containers, is detectable in the urine of over 90% of Americans, the researchers note.

FREE WORKSHOP FOR DOCTORS
On
Psychiatric Illness

Karachi Psychiatric Hospital held the monthly workshop.

Topic: The problems of married life and their solution


KASHMIR
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