

EDITOR'S NOTE

This column reflects our commitment to provide you, the primary care physician, with information that will prove helpful in making informed decisions about the care of your patients who suffer from psychiatric disorders. We will highlight abstracts of high interest to you from our sister publication, *The Journal of Clinical Psychiatry*, and summarize pertinent articles from the general scientific literature. We hope that this section is clinically relevant to your practice and that it will encourage you to expand your horizons.

Gender Issues in Depression

Grigoriadis S, Robinson GE

Ann Clin Psychiatry 2007;19:247-255

Background: Until recently, gender differences in depression, which have been documented for many years, were imagined to be insignificant to treatment selection.

Method: Gender differences in the prevalence, presentation, etiology, and antidepressant treatment of depressive disorders are reviewed in this article.

Results: One of the most replicated findings in epidemiology is the high female to male sex ratio in the prevalence of depression, especially during the reproductive years. Women more often have a seasonal component and anxious and atypical depression. Psychological, neurochemical, anatomic, hormonal, genetic, and personality factors have been proposed as explanations for the differences. Gender differences in antidepressant treatment response have not been found consistently. Hormonal status, in addition to the effects of the menstrual cycle, pregnancy, perimenopause, and menopause, may be an important variable.

Conclusions: Rates of depression in women are higher than those in men, and depression often presents differently in women than it does in men. Which combination of factors increases women's risk can be determined by further research. Increased attention should be given to the effect of pregnancy and the impact of the menstrual cycle on the course of all depressive disorders. In order to answer the now-controversial question of gender differences in antidepressant treatment response requires large prospective, randomized, controlled trials, with gender differences in treatment response as the primary endpoint are required.

Homeopathy for Attention-Deficit/Hyperactivity Disorder or Hyperkinetic Disorder

Coulter MK, Dean ME

Cochrane Database Syst Rev 2007;Oct 17:CD005648

Objective: Homeopathy is a type of complementary/alternative medicine said to be a safe and effective form of treatment for children and adults. An estimated 1.9% of the adult population and approximately 11% of children less than 16 years old uses homeopathy within the United Kingdom. There has been increased interest in homeopathy's potential as a nonpharmacologic intervention for attention-deficit/hyperactivity disorder (ADHD) as an alternative to the use of stimulant medications such as methylphenidate. A system of medicine based on the principle of treating "like with like," homeopathy uses different dilutions of natural or man-made substances. Emphasizing the unique elements of each patient's experience and symptomatology, homeopathy uses this information to find the apt prescription for each patient. This study sought to evaluate the safety and effectiveness of homeopathy as a treatment for ADHD.

Data Sources: A wide set of databases were searched from their inception to March 2006, including: CENTRAL, MEDLINE, AMED, BIOSIS, CISCOP, CINAHL, Dissertation Abstracts, ECH (European Committee for Homeopathy thesis database), EMBASE, ERIC, HomInform (Glasgow Homeopathic Hospital Library), LILACS, PsycINFO, Science Citation Index, SIGLE, GIRI-International Congress on Ultra-Low Doses, and Liga Medicorum Homeopathica Internationalis. Experts in the field were contacted regarding continuing or current research.

Study Selection: All trials in which individualized, clinical, or formula homeopathy had been used to treat participants with ADHD or hyperkinetic disorder and in which subjects were randomly or quasi-randomly allocated to either active treatment or a control group were selected. Wait-list, no treatment, medication, placebo homeopathy, and educational or behavioral interventions were included among control groups.

Data Extraction: Data from 4 eligible studies (total N = 168) were extracted and entered into RevMan. Results were synthesized, and estimates of the effect sizes were calculated and presented as appropriate (using standardized mean differences) in both graphical and narrative form. (When no calculation of effect size was possible, narrative only was used.)

Data Synthesis: The types of homeopathy currently assessed do not suggest significant treatment effects for ADHD global symptoms, core symptoms (inattention, hyperactivity, and impulsivity), or related outcomes such as anxiety.

Conclusions: Little evidence currently exists for the effectiveness of homeopathy as a treatment of ADHD. Before additional randomized controlled trials are mounted, the development of optimal treatment protocols is recommended.

Adjunctive Risperidone in the Treatment of Generalized Anxiety Disorder: A Double-Blind, Prospective, Placebo-Controlled, Randomized Trial

Pandina GJ, Canuso CM, Turkoz I, et al.

Psychopharmacol Bull 2007;40:41–57

Background: Symptoms that persist despite treatment are common in generalized anxiety disorders (GAD). The Patient-Rated Troubling Symptoms for Anxiety (PaRTS-A) is a newly created and validated instrument measuring symptoms most troublesome to individual patients. It was used to test the hypothesis that adjunctive risperidone improves residual GAD symptoms.

Method: Adults (N = 417) with GAD and a Clinical Global Impressions-Severity of Illness scale rating ≥ 4 after 8 or more weeks of anxiolytic treatment were enrolled by primary care and psychiatric clinicians. Subjects were randomly assigned to adjunctive risperidone or placebo. The primary outcome measure was change from baseline to week 4 end point on the PaRTS-A.

Results: Improvement from baseline to week 4 end point in PaRTS-A total score (mean \pm SE) was similar between treatment groups (-8.54 ± 0.63 and -7.61 ± 0.64 for adjunctive risperidone and placebo, respectively; $p = .265$). Patients in each treatment group improved significantly from baseline across nearly all patient- and clinician-rated measures. Greater improvement with risperidone than placebo ($p = .04$) was suggested by a post hoc analysis of PaRTS-A symptoms of moderate to severe severity at baseline. Adverse events did not differ between groups, with headache, weight increase, and increased appetite being the most frequently reported.

Conclusions: Either adjunctive risperidone or placebo improved residual GAD symptoms assessed by the PaRTS-A. The ability of the PaRTS-A to provide clinically meaningful information on patient-rated symptoms may be enhanced by alternative analyses or scoring approaches. The potential benefits of risperidone in patients with more severe GAD bear further investigation.

The Lived Experience of Depression in Elderly African American Women

Black HK, White T, Hannum SM

J Gerontol B Psychol Sci Soc Sci 2007;62:S392–S398

Objective: The lived experience of depression in 20 elderly African American women is the focus of this article.

Method: Research that qualitatively explored experiences of depression, sadness, and suffering in 120 community-dwelling persons aged 80 years and older and classified by gender, ethnicity, and self-reported health produced data on depression.

Results: Three general themes of depression emerged from the women's narratives: Depression was (1) connected with

decreased personal strength, (2) associated with sadness and suffering, and (3) avoidable or solvable through personal responsibility. How themes emerged in women's discussion of depression is demonstrated through short reports.

Conclusion: African American women devised a language for depression that was embedded in their personal and cultural history and offered in vivid images through their life stories. Their belief systems and the wording deployed to depict depression are essential parts of the lived experience of depression.

Inconsistent Health Perceptions for U.S. Women and Men With Diabetes

McCollum M, Hansen LB, Ghushchyan V, et al.

J Womens Health (Larchmt) 2007;16:1421–1428

Background: In order to identify gender-based differences between norm-based scores for health status and self-rated health scores, 2 health status measures for adults with diabetes are compared.

Method: The 2001 and 2003 Medical Expenditure Panel Survey (MEPS) provided the data. Self-report or ICD-9 code was used to identify diabetes. The survey included demographic and clinical (e.g., body mass index [BMI], comorbidities) parameters. Norm-based measures of physical and mental health (SF-12 Physical Component Scores [SF-12 PCS] and Mental Component Scores [SF-12 MCS]) and self-rated perception of health status were the outcomes. Univariate analyses and multivariate linear regression for survey data assessed sex-based differences in the 3 outcome measures, SF-12 PCS, SF-12 MCS, and self-rated health scores.

Results: The MEPS identified a cohort of 3640 respondents with diabetes (2037 women, 1603 men). Women were older than men (60.7 vs. 59.3 years, $p < .001$); reported higher mean BMI (31.1 vs. 30.4) and more comorbidities, depression, and physical limitations (all $p < .001$); had poorer SF-12 MCS scores ($p = .01$); and self-rated their health status significantly higher than did men in unadjusted analyses ($p < .01$). Female gender was associated with lower SF-12 MCS scores and higher self-rated health scores in adjusted analyses. Cognitive limitations alone consistently predicted lower health status scores in all 3 measures; no factors were positively associated with higher scores across all 3 measures.

Conclusions: Discrepancies exist in health status measures among adults with diabetes in a nationally representative sample of the U.S. adult population. Women self-rate their own health status higher than do men despite being older, having more comorbidities and physical limitations, and lower norm-based scores for mental functional status. Additional research into the gender-based determinants and clinical implications of self-rated health status is needed.

Recommendations for Treating Depression in Community-Based Older Adults

Steinman LE, Frederick JT, Prohaska T, et al.

Am J Prev Med 2007;33:175–181

Objective: To present recommendations for community-based treatment of late-life depression to public health and aging networks.

Method: In April 2006, an expert panel of mental health and public health researchers and community-based practitioners in

aging met to agree on recommendations. When making recommendations, panelists took into account viability and aptness for community-based delivery, as well as the weight of evidence regarding program effectiveness from a systematic literature review of articles published through 2005.

Results: Depression care management-modeled interventions delivered at home or at primary care clinics were strongly recommended by the expert panel. Individual cognitive behavioral therapy was endorsed by the panel. The panel did not recommend education and skills training, comprehensive geriatric health evaluation programs, exercise, and physical rehabilitation/occupational therapy as primary treatments for late-life depression. Several intervention categories, including group psychotherapy and psychotherapies other than cognitive behavioral therapy, lacked sufficient evidence for the panel to base recommendations on.

Conclusions: While acknowledging the challenges and obstacles involved, this interdisciplinary expert panel decided that recommended interventions should be promulgated throughout the public health and aging networks. Interventions that were rejected or for which there was insufficient evidence often did not treat depression primarily and/or tried to prove efficacy without a clinically depressed sample. While these interventions may provide other benefits, they should not be presumed to effectively treat depression on their own. Panelists also agreed that primary prevention of depression is a much understudied area. These findings should assist individual clinicians and public health decision makers in delivering population-based mental health services in a variety of community settings.

Metareview on Short-Term Effectiveness and Safety of Antidepressants for Depression: An Evidence-Based Approach to Inform Clinical Practice

Cipriani A, Geddes JR, Furukawa TA, et al.

Can J Psychiatry 2007;52:553–562

Objectives: This study investigated the existing scientific literature for answers to clinically relevant questions concerning the effectiveness and tolerability of antidepressant drugs (ADs) for the acute-phase treatment of depression and evaluated the extent to which the literature supports the findings.

Method: Primary reviews were identified through several sources: MEDLINE (1955 to April 2006), EMBASE (1980 to April 2006), PsycINFO (1980 to April 2006), and the Cochrane Library (2006, Issue 1). The following databases of the National Health Service Centre for Reviews and Dissemination were searched: Abstracts of Reviews of Effects, Health Technology Assessment, and Turning Research into Practice. In addition, the National Institute of Health and Clinical Excellence guidance Web site was searched. A metareview of selected high-quality systematic reviews of short-term pharmacologic interventions with ADs for major depression was completed. We adhered to the hierarchy of evidence proposed by the Centre for Evidence Based Medicine (Oxford) to assess efficacy; only reviews of randomized controlled trials were included. When randomized evidence was not available, we also considered observational data in the evaluation of tolerability.

Results: According to the randomized evidence, ADs are efficacious in primary care settings, and there may be small, but clinically important, differences in efficacy between ADs. Robust evidence that an AD combined with an antipsychotic is superior to AD monotherapy in cases of psychotic depression or that intravenous administration leads to more rapid response

was absent. In the treatment of atypical depression, there was evidence that monoamine oxidase inhibitors are superior to tricyclic antidepressants but not to selective serotonin reuptake inhibitors (SSRIs). Some evidence corroborates harm when SSRIs are used during pregnancy but not when they are used during breastfeeding. The use of SSRIs may increase suicidal thoughts, but not actual suicide, in early phase therapy according to some evidence.

Conclusions: Although a substantial body of evidence exists regarding the benefit and harm of ADs in the treatment of depressive disorder, there remains considerable residual uncertainty. Generally applicable recommendations are not supported by adequate evidence; in most cases, clinicians should be guided by the balance between risks and benefits for individual patients. The recommendations and warnings issued by drug-regulatory authorities should also be considered by clinicians.

Cost-Effectiveness of Interpersonal Psychotherapy for Elderly Primary Care Patients With Major Depression

Bosmans JE, van Schaik DJ, Heymans MW, et al.

Int J Technol Assess Health Care 2007;23:480–487

Objectives: Major depression is common in elderly patients and may be treated effectively in this population with interpersonal psychotherapy (IPT). This study compared the cost-effectiveness of IPT provided by mental health workers in primary care settings with care as usual (CAU) for depressed patients ≥ 55 years who were identified by screening.

Method: In conjunction with a randomized, controlled trial comparing IPT with CAU, a complete economic assessment was conducted. Depressive symptoms, presence of major depression, and quality of life were outcome measures. Cost diaries kept over a 12-month period tracked resource use from a societal perspective. Data were assessed with multiple imputation and bootstrapping.

Results: The differences in clinical outcomes between IPT and CAU, measured at 6 and 12 months, were small and nonsignificant. Total costs at 12 months were €5753 in the IPT group and €4984 in the CAU group (mean difference = €769; 95% CI = –2459 to 3433). Much uncertainty around the cost-effectiveness ratios was indicated by cost-effectiveness planes.

Conclusions: These results indicate that providing IPT to elderly depressed patients in a primary care setting was not cost-effective in comparison with CAU. Improvement of patient selection and treatments with more robust effects in the acute and maintenance phases of treatment should be the target of further studies.

Atomoxetine Treatment for Pediatric Patients With Attention-Deficit/Hyperactivity Disorder With Comorbid Anxiety Disorder

Geller D, Donnelly C, Lopez F, et al.

J Am Acad Child Adolesc Psychiatry 2007;46:1119–1127

Objective: Research indicates that 25% to 35% of children with attention-deficit/hyperactivity disorder (ADHD) have comorbid anxiety disorders. This double-blind study compared atomoxetine with placebo for treating pediatric ADHD with comorbid anxiety. Outcome measures were the ADHD Rating Scale-IV-Parent Version: Investigator Administered and Scored (ADHDRS-IV-PI) and the Pediatric Anxiety Rating Scale (PARS).

Method: Patients (aged 8–17 years) who met DSM-IV criteria for ADHD and generalized anxiety disorder, separation anxiety disorder, and/or social phobia were randomly assigned to receive 12 weeks of atomoxetine (N = 87) or placebo (N = 89). Analysis of covariance and last-observation-carried-forward and repeated-measures analyses were used to analyze ADHDRS-IV-PI and PARS total scores.

Results: The study was completed by 66 patients in each group. Mean ADHDRS-IV-PI total score improved significantly for patients taking atomoxetine (N = 55; mean = -10.5, SD = 10.6) compared with those taking placebo (N = 58; mean = -1.4, SD = 8.3; $p < .001$). Mean PARS total score also improved significantly for patients taking atomoxetine (N = 55; mean = -5.5, SD = 4.8) compared with those taking placebo (N = 58; mean = -3.2, SD = 5.0; $p = .011$).

Conclusions: Atomoxetine effectively reduced ADHD symptoms in patients who had ADHD with comorbid anxiety, and it was well-tolerated. A significant reduction in independently assessed anxiety symptoms, using both clinician-rated and self-rated measures, was also seen, a finding that merits further investigation. Atomoxetine should be considered for the treatment of ADHD in children and adolescents who have ADHD with comorbid anxiety disorder.

Integration of Mental Health Services Into Primary Care Overcomes Ethnic Disparities in Access to Mental Health Services Between Black and White Elderly

Ayalon L, Areán PA, Linkins K, et al.

Am J Geriatr Psychiatry 2007;15:906–912

Objective: This study assessed whether the ethnic disparities in access to and participation in mental health (MH) and substance abuse (SA) treatment can be overcome when mental health is integrated into primary care.

Method: Participation of black and white elderly patients in an integrated model of care (all MH/SA services are provided at primary care clinics) versus an enhanced referral model of care (all MH/SA services are provided at specialized MH clinics) was compared in a site-specific analysis of a multisite clinical trial. In all, 183 elderly patients (56% black) diagnosed with depression (82%), anxiety (32%), and/or problem drinking (22%) were randomly assigned to an arm of the trial.

Results: Compared with blacks in the enhanced referral arm (22%, adjusted odds ratio [OR] = 14.13, CI = 4.76 to 41.95, Wald $\chi^2 = 22.75$, $df = 1$, $p < .0001$), blacks in the integrated arm were significantly more likely to have at least 1 MH/SA visit (77.5%). The difference between the participation of whites in the integrated treatment arm (66.6%) and whites in the enhanced referral arm, on the other hand, was not significant (46.9%, adjusted OR = 2.98, CI = 0.98 to 9.06, Wald $\chi^2 = 3.72$, $df = 1$,

$p = .05$). In the enhanced referral arm, compared with whites (mean [SD] = 5.31 [7.76], adjusted incident rate ratio [IRR] = 2.87, CI = 1.06 to 7.73, Wald $\chi^2 = 4.37$, $df = 1$, $p = .03$), blacks had a significantly smaller number of overall MH/SA visits (mean [SD] = 2.08 [5.28]). There was no statistically significant difference between blacks (mean [SD] = 3.22 [3.71]) and whites (mean [SD] = 2.75 [4.29], adjusted IRR = 0.58, CI = 0.25 to 1.33, Wald $\chi^2 = 1.64$, $df = 1$, $p = .20$) in the integrated arm. Time between baseline evaluation to first MH/SA visit was significantly shorter in the integrated treatment arm (for blacks: mean [SD] days = 31.06 [28.66]; for whites: mean [SD] days = 22.18 [33.88]) than in the enhanced referral arm (mean [SD] = 62.45 [43.53], adjusted hazard ratio [HR] = 7.82, CI = 0.65 to 16.75, Wald $\chi^2 = 28.02$, $df = 1$, $p < .0001$ and mean [SD] = 63.46 [32.41], adjusted HR = 2.48, CI = 1.20 to 5.13, Wald $\chi^2 = 6.02$, $df = 1$, $p = .01$, respectively).

Conclusion: Among black primary care patients, an integrated model of care is particularly effective in improving access to and participation in MH/SA treatment.

Light Therapy for Bipolar Disorder: A Case Series in Women

Sit D, Wisner KL, Hanusa BH, et al.

Bipolar Disord 2007;9:918–927

Objectives: To perform a dose-ranging safety and efficacy study of bright light therapy for depression in women with bipolar disorder.

Method: Nine women in the depressed phase of DSM-IV bipolar disorder I or II received 50 lux (illuminance at the receiving surface) red light therapy for 2 weeks and 7000 lux light therapy for 2-week epochs of 15, 30, and 45 minutes daily thereafter. Mood symptoms were evaluated with the Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement and the Mania Rating Scale. Morning light was administered to 4 patients, and midday light was administered to 5 patients.

Results: Mixed states were developed by 3 of the 4 subjects treated with morning light. The fourth subject achieved a full, sustained response. The time of light exposure was changed to midday to lessen the risk of inducing mixed episodes. Two of the 5 women who received midday light therapy achieved full response, and 2 showed early improvement but required a dose increase to sustain response. One woman remained depressed with 45 minutes of midday light but responded fully to a switch to morning light, 30 minutes daily.

Conclusions: Because women with bipolar illness are very sensitive to morning bright light treatment, the risk of inducing mixed states is high. It is advisable to initiate treatment with midday light of brief duration (15 minutes) for bipolar depression.