

Adults with both anxiety and depression respond poorly to treatment

Clinical question Are adults with both anxiety and depression more difficult to treat than patients with depression alone?

Bottom line Adults with the combination of both anxiety and depression are significantly more difficult to successfully treat than patients with depression alone. (Level of evidence = 1b-)

Synopsis Many patients with major depression also exhibit significant symptoms of anxiety. These investigators initially enrolled 2,876 adults with major depression to receive citalopram (Celexa; maximum of 60 mg/d depending on clinical response) in Level 1 of the STAR*D project. Patients not achieving remission after 14 weeks or with intolerable side effects (n = 1,292) entered Level 2 of STAR*D and randomly received (uncertain allocation concealment) bupropion (Wellbutrin; maximum of 400 mg/d), sertraline (Zoloft; maximum of 200 mg/d), venlafaxine (Effexor; maximum of 375 mg/d), or continued citalopram augmented with bupropion (maximum of 400 mg/d) or buspirone (Buspar; maximum of 60 mg/d). Individuals masked to treatment group assignment administered standard validated instruments to measure the severity of depression and anxiety at baseline and at regular follow-up treatment intervals. At the end of the Level 1 treatment period, both remission and response rates were significantly lower in patients with anxious depression compared to those with depression alone (22.2% vs 33.4% and 41.7% vs 52.8%, respectively). Despite similar citalopram dosages in the two groups, patients with anxious depression also reported significantly more adverse drug effects. Remission rates at

the end of the Level 2 treatment phase were also significantly less in the anxious-depression group than in the depression-only group for all therapeutic modalities (bupropion, 10.2% vs 33.9%; sertraline, 8.3% vs 28.5%; venlafaxine, 12.1% vs 36.4%; citalopram plus bupropion, 17.9% vs 36.7%; and citalopram plus buspirone, 9.2% vs 39.2%).

Fava M, Rush AJ, Alpert JE, et al. Difference in treatment outcome in outpatients with anxious versus nonanxious depression: A STAR*D report. *Am J Psychiatry*. 2008;165(3):342-351.

CV event prediction methods perform equally well

Clinical question Are risk prediction methods using laboratory testing and methods not using laboratory testing comparable in predicting cardiovascular (CV) events?

Bottom line CV prediction models that do not require laboratory testing perform as well as models that use laboratory testing. (Level of evidence = 2b)

Synopsis These researchers sought to determine if CV prediction models that do not use laboratory testing perform as well as those that do. Nearly 6,200 patients with no known heart disease were identified and Framingham-based prediction models were used to estimate CV disease risk. Body mass index replaced cholesterol in the non-laboratory-based model. The patients had completed a comprehensive set of surveys and tests in the 1970s and their vital status was assessed 20 years later. The research team obtained medical records, pathology reports, electrocardiograms, and so forth to confirm diagnoses. Finally, they evaluated the performance of the models on men and on women. During the 21 years of follow up, 38% of the patients died from CV disease and there were more than 1,500 first-time CV events. Both prediction models were 83% accurate for women and 78% accurate for men.

Gaziano TA, Young CR, Fitzmaurice G, et al. Laboratory-based versus nonlaboratory-based method for assessment of cardiovascular disease risk: the NHANES I Follow-up Study cohort. *Lancet*. 2008;371(9616):923-931.

Imiquimod and 5-FU are effective for actinic keratoses

Clinical question What is the best treatment for actinic keratoses?

Bottom line Although more and larger studies are needed, these results suggest that imiquimod and 5-fluorouracil (5-FU) are somewhat more effective than cryotherapy for the treatment of actinic keratoses. (Level of evidence = 1b-)

Synopsis This study enrolled 75 patients with actinic keratoses; their mean age was 73 years and 83% were men. The treatment area could include 5 to 10 lesions in a 5-cm × 10-cm area on any one part of the body. The patients were randomly assigned to treatment with 5% imiquimod (applied 3 times weekly for an 8-hour duration for 4 weeks), cryosurgery (20 to 40 seconds, followed, if necessary, by a second session 2 weeks later), or 5-FU (twice a day for 4 weeks). Cure was evaluated 8 weeks after the last imiquimod application, 6 weeks after the last cryosurgery, and 4 weeks after the last 5-FU application. No patients appear to have been lost to follow-up. Clinical clearance rates were 68% for cryosurgery, 85% for imiquimod, and 96% for 5-FU. Although clinical examination favored the 5-FU group, histologic clearance was highest in the imiquimod group. At 12 months, excellent cosmetic outcome was seen in 4% of patients who received cryosurgery or 5-FU and 81% of the imiquimod group. Adverse effects were not clearly described but appear to have been minor.

Krawtchenko N, Roewert-Huber J, Ulrich M, et al. A randomised study of topical 5% imiquimod vs. topical 5-fluorouracil vs cryosurgery in immunocompetent patients with actinic keratoses: a comparison of clinical and histological outcomes including 1-year follow-up. *Br J Dermatol*. 2007;157(suppl 2):34-40.

Levels of evidence in **Bottom line** are explained at www.essentialevidenceplus.com/levels.html.

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Early diabetes education has little impact on patient self-management

Clinical question Will extensive education for patients with newly diagnosed type 2 diabetes lead to better glucose control?

Bottom line A 6-hour, well-constructed educational intervention given to patients with newly diagnosed diabetes was no better than usual care in improving their overall glucose control over 1 year of evaluation. However, the intervention resulted in a greater average weight loss and prompted more patients to quit smoking, though these results were not the primary goal of the intervention. (Level of evidence = 1b-)

Synopsis The study took place in 207 UK general practices. The practices were randomized so that all patients in each practice received either the education program or usual care (cluster randomization). The 824 participants were adults who received a new diagnosis of type 2 diabetes. Patients receiving the intervention attended 6 hours of education taught in a nondidactic fashion by two educators over 1 day or 2 half-days. The education consisted of a discussion of lifestyle factors, such as food choices, physical activity, and cardiovascular risk factors. The goal of the education program was for participants to understand their own risk factors and to choose a specific behavior change to work on. Patients in the control group received the diabetes education normally provided at the practice. Diabetes education was ongoing in both groups. At 12 months following diagnosis, A1C levels had decreased by 1.21% to 1.49% in both groups from a baseline of 7.9% to 8.3%. The intervention group experienced greater weight loss (an average 2.98 kg as compared with an average 1.86 kg in the control group; $P = .027$) and were, on average, slightly less likely to be smokers. The lack of effect on A1C may be because, as patients with newly diagnosed disease, patients in both groups were high-

ly motivated to achieve good control independent of the education they received. Studies of the effect of education on patients with established diabetes have shown a decrease in A1C. Also, the lack of masking of both the patients and the clinicians may have prompted clinicians in the control practices to try harder.

Davies MJ, Heller S, Skinner TC, et al; Diabetes Education and Self-Management for Ongoing and Newly Diagnosed Collaborative. Effectiveness of the diabetes education and self management for ongoing newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trial. *BMJ*. 2008;336(7642):491-495.

Complex interventions help elderly patients maintain independence

Clinical question Do community-based complex interventions help elderly patients maintain their physical function and independence?

Bottom line In general, complex interventions prevent nursing home admissions, hospitalizations, and falls in the elderly. However, depending on the outcome of interest, some interventions are ineffective. (Level of evidence = 1a)

Synopsis These authors searched multiple databases for randomized controlled trials of complex interventions designed to preserve physical function and independence in community-dwelling elderly patients. Additionally, they tried to identify unpublished studies. Only one investigator determined which studies to include. Two investigators extracted data from the included studies and independently assessed methodologic quality. They settled disagreements by consensus. They evaluated 89 interventions in nearly 98,000 patients. Twenty-eight interventions targeted "general elderly" people; 24 addressed geriatric assessment of frail elderly; 21 were community-based care after hospital discharge; 13 were fall-prevention programs; and 3 were group education or counseling interventions. For each of these types of interventions, the researchers assessed

the effect on mortality, nursing home admission, hospital admission, and falls. First, they found that death was prevented by fall-prevention programs but no other interventions (number needed to treat [NNT] = 51; 95% CI 28-255). General elderly (NNT = 66; 51-94) and community-based care after discharge (NNT = 39; 22-162) interventions prevented nursing home admissions. Hospitalizations were averted by geriatric assessment of frail elders (NNT = 42; 22-551) and community-based care after discharge (NNT = 35; 19-201). Finally, falls were prevented with general elderly interventions (NNT = 12; 9-19) and fall-prevention programs (NNT = 36; 21-149). In general, group education and counseling were ineffective. Finally, the researchers assessed the net effectiveness of all types of interventions on these outcomes, finding improvements in all except mortality.

Beswick AD, Rees K, Dieppe P, et al. Complex interventions to improve physical function and maintain independent living in elderly people: a systematic review and meta-analysis. *Lancet*. 2008;371(9614):725-735.

Quality of life varies after different prostate cancer treatments

Clinical question What is the outcome of different approaches to the treatment of prostate cancer?

Bottom line Quality of life is significantly affected by treatment for prostate cancer, and it varies with the type of treatment. Randomized trials that directly compare treatments are still needed. (Level of evidence = 2b)

Synopsis Direct comparisons of different approaches to the treatment of prostate cancer are uncommon in the literature. This study identified patients undergoing brachytherapy ($n = 306$), external beam radiation ($n = 292$), and radical prostatectomy ($n = 603$). Some patients underwent more than one treatment (ie, 35 patients received brachytherapy and radiation or androgen suppression) and most

patients undergoing surgery had nerve-sparing procedures. A range of quality-of-life and satisfaction outcomes were measured at 2, 6, 12, 24, and 30 months by asking both patients and their spouses. A clinically meaningful change was defined as a change of at least one-half standard deviation. Patients had a median age of 59 years and 9% were black. Groups differed in a number of ways: white patients were more likely to choose surgery; black patients had more comorbidities, a larger mean prostate size, and a higher mean prostate-specific antigen (PSA). Patients choosing brachytherapy were

more likely to have a low-risk cancer and a Gleason score of less than 7 points. The results are fairly complex, and the graphs of symptoms versus time since treatment may be helpful when counseling patients. A few patterns emerged, though. Nerve-sparing surgery was significantly better than nonnerve-sparing surgery with regard to sexual and urinary incontinence scores. Patients receiving radiation plus neoadjuvant hormone therapy had significantly worse sexual outcomes than those receiving radiotherapy only. Although sexual function and urinary incontinence scores declined precipi-

tously after surgery, some recovery occurred over the next 2 years. Worse outcomes were associated with obesity, black race, a larger prostate volume, and a higher pretreatment PSA. Spousal and patient concerns over urinary and sexual adverse effects were correlated, as were outcome satisfaction among patients and symptoms related to sexual function, vitality, and urinary function. The study is limited by the relatively short (2-year) follow-up period.

Sanda MG, Dunn RL, Michalski J, et al. Quality of life and satisfaction with outcome among prostate-cancer survivors. *N Engl J Med.* 2008;358(12):1250-1261.