Antidepressants and Breast Cancer Risk

Results of laboratory studies suggest several mechanisms by which both TCAs and SSRIs might increase breast cancer risk or promote tumor growth. However, a meta-analysis of epidemiologic studies found no association between antidepressant use and breast cancer risk.

Background: Both SSRIs and TCAs are chemically similar to an anti-estrogen binding site that stimulates breast cancer growth in animals. Both types of drug stimulate prolactin secretion and may have other plausibly carcinogenic actions. There have been no randomized controlled trials testing the association.

Methods: A literature search was undertaken to identify all published reports evaluating the association between antidepressant use and breast cancer that reported the outcome as an adjusted odds ratio* or relative risk.* The analysis included a total of 18 case-control and cohort studies.

Results: Of the 18 studies, 11 were conducted in the U.S., 4 in Canada, and 3 in Europe. The reports were published between 1999 and 2011, and 8 of the studies drew their population from large databases. Methodological quality was high for 7 of the studies.

Odds ratios and relative risks ranged from 0.8 to 1.75 in the individual studies. The pooled analysis found no association between antidepressant use and breast cancer risk (adjusted odds ratio, 1.02). No association was found in separate analyses by antidepressant class or for individual agents. Methodologic quality, study funding source, and drug dose did not appear to affect risk estimates. When the analysis was stratified by exposure duration, SSRI exposure of <1–2 years was associated with increased risk (odds ratio, 1.1), but risk was not associated with longer use of SSRIs or with shorter or longer duration of TCA use. The authors found no evidence of publication bias.

Discussion: Depression itself is a known risk factor for breast cancer progression. The authors suggest that the association of breast cancer with a short duration of SSRI use could be
explained by incomplete treatment of depression or by the tendency of adverse effects to appear early in treatment in susceptible individuals.

**Study Rating**—18 (100%): This study met all criteria for a systematic review/meta-analysis.

Eom C-S, Park S, Cho K-H: Use of antidepressants and the risk of breast cancer: a meta-analysis. *Breast Cancer Research and Treatment* 2012; doi 10.1007/s10549-012-2307-y. From Hallym University Chuncheon Sacred Heart Hospital, Chuncheon, South Korea; and other institutions. Funded by the National Research Foundation of Korea. The authors did not include disclosure of potential conflicts of interest.

*See Reference Guide.

### Atomoxetine Improved Driving in Adult ADHD

In a manufacturer-sponsored study, treatment with atomoxetine (*Strattera*) was associated with improved driving performance in a group of adults with ADHD.

**Background:** Studies have consistently shown impaired driving ability in adults with ADHD, and stimulant medications are known to improve driving ability. While atomoxetine has been investigated in simulated driving situations, this appears to be the first trial assessing the effects in an on-road evaluation.

**Methods:** Study participants (aged 18–50 years; n=64) with DSM-IV ADHD as their primary clinical diagnosis were randomly assigned either to receive atomoxetine, titrated to 80 mg/day over 4 weeks and then held at a stable dose for an additional 8 weeks, or to a wait-list control condition. None of the patients had a history of ADHD treatment with atomoxetine or a stimulant. Participants completed baseline and 12-week on-road driving tests, administered by a psychologist who was unaware of treatment assignment. The 45-minute test was taken on weekdays during rush hour in a German city and had 64 pre-defined locations at which the psychologist rated driving performance using a standardized assessment. Driving errors in 4 domains (i.e., orientation, concentration, self-control, and driver skills) were evaluated.

**Results:** A total of 43 participants completed the trial, 22 in the atomoxetine group and 21 in the control group. Error scores in 3 of the 4 domains improved significantly in the participants treated with atomoxetine, but not in the controls. Compared with controls, treated patients had significantly fewer errors in attention (error rate, 2% vs. 7%; p<0.05), risk-related self-control (error rate, 7% vs. 10%; p<0.005), and driver skills (error rate, 6% vs. 13%; p<0.001). Changes in attention did not differ between the groups.

In a driving-related neuropsychological assessment, the treated and comparison groups did not perform differently, either at baseline or endpoint. At baseline, 9 patients in the atomoxetine group and 11 patients in the control group did not fulfill the driving fitness criteria of the German Evaluation Guidelines of Driving Ability. At endpoint, 4 atomoxetine-treated participants and 10 control subjects did not meet these criteria (p<0.05). Self-reported incidents of "critical traffic situations" decreased in the atomoxetine group (p<0.05). Despite the observed improvement in driving performance, participants did not change their coping strategies for driving-related stress—e.g., from confrontive coping and avoidance to task-focused coping and self-reflection. It is possible that such changes could occur after prolonged treatment.

**Study Rating**—17 (100%): This study met all criteria for a randomized controlled trial.

Sobanski E, Sabljic D, Alm B, Dittmann R, et al: Driving performance in adults with ADHD: results from a randomized, waiting list controlled trial with atomoxetine. *European Psychiatry* 2012; doi 10.1016/j.eurpsy.2012.08.001. From the University of Heidelberg, Mannheim, Germany; and other institutions. Funded by Eli Lilly, Germany. Several study authors disclosed financial relationships with commercial sources, including Eli Lilly.

*See Reference Guide.
Risperidone: No Link with Large Pituitary Tumors

Treatment with risperidone (Risperdal) was not associated with increased risk of pituitary tumors with mass effect, according to a study conducted by the drug’s manufacturer, Janssen Research and Development, with oversight by the FDA.¹

Background: The FDA Adverse Event Reporting System has received a disproportionate number of pituitary adenoma reports for risperidone, as has the World Health Organization's reporting system. Risk estimates based on these reports are likely to be biased by the recommendation that MRI be performed on patients with hyperprolactinem ia, a common side effect of risperidone. Most adenomas would not otherwise be detected because they are clinically silent. There is little agreement among radiologists on diagnosing these tumors, and false-positive radiologic diagnoses are common.

Methods: Two large databases, the Department of Veterans Affairs (VA) national patient files and a database of privately insured patients, were analyzed. Eligible patients were those exposed to an antipsychotic since 1999 (the VA population) or since 2002 (the privately insured population) and followed for 10 and 5 years, respectively. Cases of physician-diagnosed pituitary tumor were confirmed by a detailed review of the medical records. For the VA data, each identified case was matched with 4 controls from the same cohort who did not have a pituitary tumor. A case-control analysis of the VA data compared exposures to risperidone vs. other atypical antipsychotics between cases and non-cases. No case-control study was conducted in the other database because only 1 case was identified.

Results: The VA database consisted of about 370,000 patients, most of whom were men and aged 55–60 years. About 42% were taking risperidone at the start of observation, 50% were taking another atypical agent, and 8% were taking a first-generation antipsychotic. There were 20 confirmed cases of pituitary tumor in patients receiving risperidone and 19 in patients receiving other atypicals. Tumors were identified a mean of 47 and 39 months, respectively, after the start of follow-up. The hazard ratio* for risperidone use was 1.0. The case-control analysis also revealed no association of pituitary tumor with any history of risperidone use. Risk could not be further analyzed for patient subgroups or timing of risperidone use because of the small number of cases available for analysis.

Discussion: According to an accompanying editorial,² these findings do not exonerate risperidone or other atypical antipsychotics because these large tumors account for only about 5% of all prolactinomas. In addition, pituitary tumors are particularly slow growing, and risk that could develop with longer term exposure or follow-up was not assessed. Nevertheless, the tumors investigated in this study are among the most clinically important.

More on Safety of Atypicals in Dementia

Atypical antipsychotics are associated with substantial risks and only modest benefits in patients with neuropsychiatric symptoms of dementia. They should be prescribed only when the symptoms pose a risk to the patient or others and when nonpharmacologic treatments have not been effective, according to a review.¹


*See Reference Guide.
All atypical antipsychotics carry a warning about increased mortality and cerebrovascular events in patients with dementia, as do the conventional antipsychotics and some other drug classes that might otherwise be considered. In most cases, there are no effective alternative medications to second-generation antipsychotics for behavioral symptoms of dementia. Guidance for their use can be found in the American Geriatrics Society 2012 Beers consensus criteria for safe medication use in the elderly (available online at www.americangeriatrics.org).²

The absolute risks of mortality associated with short-term use of atypicals in persons with dementia, while elevated, are small—about 1–2%. The mechanisms of death are uncertain, and it is not clear which members of this drug class are associated with highest risk of death. Stroke risk appears to be highest during the initial weeks of treatment and may revert to background levels after 3 months. It seems the metabolic effects of at least some atypicals may be attenuated in the elderly. Risk of extrapyramidal symptoms is highest with risperidone and lowest with quetiapine and clozapine. According to the Beers criteria, all antipsychotics except quetiapine and clozapine are inappropriate in patients with Parkinson’s disease. All antipsychotics are associated with increased risk of falls in the elderly and may be inappropriate for use in patients with a history of falls or fractures, a caution which also applies to many other psychotropic drug classes. Other potential risks of atypicals are cognitive worsening, orthostatic hypotension (especially with olanzapine in patients with previous syncope), QTc prolongation (especially with ziprasidone), and pneumonia.

Prescription of an atypical antipsychotic in older patients with dementia should be individualized and, in those with complex medical conditions, is often a "choice between 2 evils." Other options should be exhausted first. Alternative causes of the patient’s behavioral symptoms, including medical symptoms, polypharmacy-induced delirium, and factors in the environment or caregiver interactions, should be ruled out. Suspicion of medical comorbidity should prompt a referral to the primary care physician. The clinician should obtain information about any nonpharmacologic interventions that have been tried. Consultation with a specialist in dementia may be warranted if the use of alternative drugs is under consideration.

If an atypical antipsychotic is prescribed, the initial dose should be the lowest possible. Metabolic tests and an electrocardiogram should be performed at baseline, and metabolic parameters should be re-evaluated at regular intervals, beginning within 1 month, or sooner if the patient is at high risk of adverse events. Because many patients only have a partial response, decisions to increase the dose or switch to another agent should be based on the level of distress caused by the symptoms.


Drug Trade Names: clozapine—Clozaril; olanzapine—Zyprexa; quetiapine—Seroquel; risperidone—Risperdal; ziprasidone—Geodon

Antidepressants Beneficial in Bipolar Disorder

Results of a large, observational study of naturalistic treatment suggest that short-term use of antidepressants is beneficial in patients with bipolar disorder with non-agitated depression. Antidepressants were at least as effective in bipolar depression as in unipolar depression.
**Methods:** The aim of this study was to compare the results of antidepressant drug therapy in patients with unipolar vs. bipolar depression. The investigators analyzed data from 1036 patients treated between 1975 and 2011 by a single specialist practicing at a mood disorders clinic in Sardinia. Depressive symptoms were treated according to contemporary standards of therapy—with MAOIs, SSRIs, SNRIs, TCAs and other older drugs, or with multiple agents. To be eligible for antidepressant treatment, patients were required to have a score of >14 points on the Hamilton Rating Scale for Depression (HAM-D). Response was defined as a ≥50% improvement in HAM-D score and remission as a score of <7. Patients who entered the clinic with agitated depression were given other (not antidepressant) drugs and were not considered in the analysis. Those who switched to mania or hypomania were analyzed separately and not included in the tabulations of response.

**Results:** Of the initial study population, 878 (85%) received antidepressants, with or without a mood stabilizer or antipsychotic drug, and 158 (15%) had clinical evidence of agitation and did not receive an antidepressant. Of the patients receiving antidepressants, 11% had a diagnosis of type I bipolar disorder, 13% type II bipolar disorder, and 76% unipolar depression. The diagnostic groups had similar pretreatment duration and severity of depression.

The mean reduction in HAM-D score was greatest in patients with type II bipolar disorder, followed by type I bipolar disorder, and then unipolar depression. (See table.) Rates of response and remission followed the same pattern. Mean time to remission was shortest for patients with type II bipolar disorder, followed by type I bipolar disorder, and then unipolar depression. More than 8% of patients with bipolar I disorder switched to mania or hypomania during the first 3 months of antidepressant therapy, compared with nearly 16% of those with type II and 0.6% of those with unipolar depression. In a multivariate analysis, response to antidepressants was not influenced by initial depression severity, antidepressant dose, or use of a mood stabilizer or atypical antipsychotic.

<table>
<thead>
<tr>
<th></th>
<th>Bipolar I Disorder (n=93)</th>
<th>Bipolar II Disorder (n=117)</th>
<th>Unipolar Depression (n=668)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean HAM-D reduction</td>
<td>63%</td>
<td>70%</td>
<td>58%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Response</td>
<td>72%</td>
<td>77%</td>
<td>62%</td>
<td>p=0.004</td>
</tr>
<tr>
<td>Remission</td>
<td>51%</td>
<td>54%</td>
<td>41%</td>
<td>p=0.02</td>
</tr>
<tr>
<td>Mean time to remission</td>
<td>9 weeks</td>
<td>6 weeks</td>
<td>7 weeks</td>
<td>p=0.03</td>
</tr>
</tbody>
</table>

**Discussion:** The authors suggest the prevalent belief that patients with bipolar disorder respond poorly to antidepressants may arise in part from the drugs' adverse effects in patients with incipient agitation and irritability or with unrecognized mixed states. The positive response to antidepressants in this study may have been related to the strict exclusion of agitated patients.

Tondo L, Baldessarini R, Vazquez G, Lepri B, et al: Clinical responses to antidepressants among 1036 acutely depressed patients with bipolar or unipolar major affective disorders. *Acta Psychiatrica Scandinavica* 2012; doi 10.1111/acps.12023. From the McLean Division of Massachusetts General Hospital, Boston; and other institutions. **Funded by the Lucio Bini Private Donors Mood Disorders Research Fund; and other sources. The authors declared no competing interests.**
**Brain Hemorrhage Risk with SSRIs**

Selective serotonin reuptake inhibitors are associated with increased risk of intracerebral bleeding, according to a meta-analysis, but the absolute added risk is extremely small given the low background incidence of strokes.

*Methods:* The investigators identified observational studies of the association of SSRIs with brain hemorrhage, including published articles, conference proceedings, and dissertations. The analysis did not include randomized efficacy trials of antidepressants because these trials do not report intracranial hemorrhage as an adverse event. All other study designs were permitted—prospective and retrospective cohorts, crossover studies, and case-control studies—as long as the study included a control group not exposed to SSRIs.

*Results:* A total of 16 studies with >500,000 subjects were included in the analysis. Bleeding outcomes were reported somewhat differently among the studies. For those reporting intracranial hemorrhage, relative risk* (RR) was increased with SSRIs (adjusted RR, 1.51). Risk of intracerebral hemorrhage was also increased (adjusted RR, 1.42). Risk for subarachnoid hemorrhage or a composite outcome of intracerebral hemorrhage and subarachnoid hemorrhage was not increased with SSRI use. Risks were further increased in patients exposed to oral anticoagulants (RR, 1.56), but this was evaluated in only 5 of the studies.

Increased risk of bleeding was related to duration of SSRI exposure in 6 of the 7 studies that analyzed this factor. Short-term exposure was more strongly associated with bleeding risk than long-term exposure. This finding suggests platelet function may recover after several weeks of SSRI exposure or that high-risk patients are eliminated earlier from the study population.

*Discussion:* Based on the global incidence of stroke, the investigators calculated that 1 additional intracerebral bleeding episode may occur for every 10,000 person-years of SSRI treatment. They suggest that clinicians consider alternate antidepressants in patients with risk factors such as oral anticoagulant therapy, previous intracranial bleeding, cerebral amyloid angiopathy, or severe alcohol abuse.

*Study Rating*–14 (78%): This study met most criteria for a meta-analysis, but individual study quality does not appear to have been assessed and the source of funding was not stated.


*See Reference Guide.*

**Adjunctive Pregabalin for Bipolar Disorder**

In a practice-based, uncontrolled study, adjunctive pregabalin was effective as both acute and maintenance therapy in a group of patients with refractory bipolar disorder.

*Background:* Pregabalin is structurally similar to gabapentin and is approved for treatment of neuropathic pain, partial seizures, and fibromyalgia. It has similar mechanisms to other anticonvulsants used to treat bipolar disorder. While pregabalin was ineffective as monotherapy in a clinical trial of patients with bipolar disorder, there remain several reasons to assess its efficacy as adjunctive therapy.

*Methods:* Open-label pregabalin was investigated in a private psychiatric practice specializing in bipolar disorder. Study participants were adults and adolescents, aged ≥16 years, who had experienced nonresponse or unsatisfactory partial response to numerous standard medications. Mood was compared before and after a 2-month trial of pregabalin, with response defined as a Clinical Global Impression–bipolar version score of 1–3. Patients who experienced response to acute treatment were given the option of continuing pregabalin.
**Results:** Of 58 patients (average age, 47 years; 79% women) who received adjunctive pregabalin, 24 (41%) were rated as responders after 2 months. Responders did not differ in age or gender from nonresponders. Twelve patients with either mixed or rapid cycling symptoms experienced mood stabilization, 5 had an antimanic effect, and 7 had an antidepressant effect. Of the responders, 4 had type I bipolar disorder and 20 had other types—similar proportions to the group as a whole. Responders were taking an average of >3 psychotropic medications when they started pregabalin and had an average of nearly 14 previous unsuccessful drug trials.

Thirty-four patients did not complete acute treatment and were considered nonresponders. Five patients withdrew because of lack of efficacy, and 27 patients withdrew because of adverse effects, most commonly overactivation and weight gain. There were no instances of pregabalin abuse.

At the final follow-up, 10 of the 24 acute-phase responders were still taking adjunctive pregabalin after an average of 45 months. Five patients were lost to follow-up, and 9 discontinued adjunctive treatment, in 3 cases because of loss of efficacy.

**Discussion:** Pregabalin appears to have mood stabilizing, antimanic, and antidepressant activity when combined with other medications to treat bipolar disorder. The average dosage taken by the patients who continued with pregabalin, about 90 mg/day, is far lower than that recommended for the drug’s indicated uses. Adverse effects did not result in serious medical complications and were rapidly reversed with dosage reduction or discontinuation.

Schaffer L, Schaffer C, Miller A, Manley J, et al: An open trial of pregabalin as an acute and maintenance adjunctive treatment for outpatients with treatment resistant bipolar disorder. *Journal of Affective Disorders* 2012; doi 10.1016/j.jad.2012.09.005. From Sutter Community Hospitals, Sacramento, CA; and other institutions. **Source of funding not stated; however, the authors did state that the study was not funded by the manufacturer of pregabalin. The authors declared no conflicts of interest.**

**Drug Trade Names:**
- gabapentin—Neurontin
- pregabalin—Lyrica

### Benzodiazepines and Dementia Risk

Use of benzodiazepines was associated with a 50% increase in risk of dementia in a cohort of elderly people.

**Methods:** Subjects for this study were randomly selected from a cohort of patients enrolled in a brain aging study in France. Community-dwelling adults, aged ≥65 years in the late 1980s, were followed every 2 or 3 years for up to 20 years. In order to minimize the inclusion of persons who may have had benzodiazepines prescribed for insomnia, depression, or anxiety (all prodromal syndromes for dementia), participants were included in the present analysis only if they had not taken benzodiazepines before the 3-year follow-up and were free of dementia at the 5-year follow-up. Subjects were screened for dementia by trained psychologists using DSM-III-R criteria, and diagnoses were confirmed by neurologists. For the primary analysis, onset of dementia after the 5-year visit was compared in patients who began using benzodiazepines between the 3- and 5-year visits and nonusers. A separate, secondary analysis was carried out in different cohorts who began using benzodiazepines before the follow-up visits at years 8, 10, 13, and 15. The analysis further included a nested case-control study, with up to 4 controls per case of dementia, to assess risk more precisely.

**Results:** The sample for the primary analysis included 1063 participants, of whom 95 first reported benzodiazepine use at the 5-year visit. During the 15-year risk period, dementia was diagnosed in 32% of persons exposed to benzodiazepines and in 23% of controls. After adjustment for potential confounding factors (e.g., age; gender; wine consumption; change in the Mini-Mental State Exam between years 0 and 3; and use of various medications) risk remained elevated (adjusted hazard ratio,* 1.60 ). The risk estimate was unchanged by adjust-
ment for depressive symptoms. The secondary analysis, in which additional benzodiazepine exposure was considered, added 116 persons who began benzodiazepine use after the 5-year follow-up. This analysis did not change the results appreciably (hazard ratio, 1.40). The nested case-control study also produced similar risk estimates and found associations in both past and recent users.

Discussion: These results support previous observations of an association between benzodiazepine use and risk of dementia. The study improves on previous research by including a larger sample size, long follow-up, and design features to minimize the risk of biases. A causal association can not be proven by this research. The excess risk observed during the early phase of exposure could indicate that benzodiazepine use may be an early risk marker for dementia without playing any causal role in the occurrence of the disease.

In France, 30% of people aged ≥65 years take benzodiazepines. Use is less widespread but still high in the U.S. Use is often chronic, contrary to good practice guidelines. Physicians should carefully assess the benefits of benzodiazepines and, when possible, should limit prescriptions to a few weeks as recommended.

Billioti de Gage S, Begaud B, Bazin F, Verdoux H, et al: Benzodiazepine use and risk of dementia: prospective population-based study. British Medical Journal 2012;345:e6231: doi 10.1136/bmj.e6231. Published online September 27, 2012. From the Universite Bordeaux Segalen, France; and other institutions. Funded by INSERM (Institut National de la Sante et de la Recherche Medicale); the Universite Bordeaux Segalen; and other sources. The study authors declared no conflicts of interest.

Memantine in Parkinson's Disease

Axial signs, poor balance, and falls are a serious consequence of late-stage Parkinson's disease for which there is currently no treatment. Dopaminergic depletion in Parkinson's induces glutamatergic hyperactivity, and memantine (*Namenda*), an NMDA receptor antagonist, reduced akinesia and improved locomotion in an animal model of this process. The present pilot study found no improvement in gait with memantine treatment but suggested a possible benefit for axial motor symptoms and dyskinesia.

Methods: The study enrolled 25 patients (mean age, 65 years; mean illness duration, 14 years) with a severe gait disorder and an abnormal forward-leaning stance despite optimal levodopa treatment. Enrollment included 16 patients (8 in each treatment group) undergoing subthalamic nucleus stimulation who had a ≥50% improvement in motor symptoms with the treatment. Study participants received randomly assigned memantine (titrated over 1 month to 20 mg/day) or placebo for a total of 90 days. The primary efficacy criterion was stride length during dopaminergic treatment.

Results: Stride length did not improve during the course of memantine treatment. However, memantine was associated with a beneficial effect on axial motor symptoms and levodopa-induced axial dyskinesias (p=0.014 and p=0.003, respectively, compared with placebo). Dynamometer measurements of axial rigidity and strength were also improved with memantine. Treatment was well tolerated and apparently safe.

Discussion: The negligible effect of memantine on gait suggests that a clinical trial with a larger sample size would be unlikely to show a clinically significant effect. However, the study authors recommend confirmation of the effect on other motor symptoms with a larger study.

Vortioxetine for GAD: Ineffective in U.S. Trial

In a randomized clinical trial conducted at 36 U.S. sites, the investigational antidepressant vortioxetine (Lu AA21004) failed to show superiority to placebo in generalized anxiety disorder.¹ This finding contrasts with the positive results of a parallel trial of identical design, conducted outside the U.S.² Multiple possible explanations for the disparity exist, but no single factor accounts for the difference.

Methods: Vortioxetine is a member of a new class of antidepressants, the bis-aryl-sulfanylamines, that work via serotonin reuptake inhibition and receptor activity. The present phase III study tested a 5-mg/day dosage, previously shown to be effective in antidepressant trials. Study participants were 299 adults with a primary diagnosis of GAD, a score of ≥20 on the Hamilton Rating Scale for Anxiety (HAM-A), and low levels of depression. Change from baseline in the HAM-A after 8 weeks of treatment was the primary efficacy outcome.

Results: Study participants had a mean age of 41 years, and 66% were women. The mean baseline HAM-A score was 25. By week 8, average scores decreased by about 13 points in both the active treatment and placebo groups. The effects of vortioxetine did not differ from placebo for any secondary outcome or in any subgroup.

Discussion: The results of the non-U.S. trial suggest that vortioxetine does have an anti-anxiety effect and that the 5-mg dose is not too low. Sample sizes of the 2 trials were the same, and a larger sample would not have changed the outcome of the U.S. study. Factors that may have had a small effect on the results include: a higher discontinuation rate in the U.S. study; a smaller percentage of U.S. subjects with prior treatment for GAD; and more racial diversity and higher body weight in the U.S. sample. Antianxiety drugs, even those with FDA approval, do not show superiority to placebo in nearly half of published clinical trials. Design issues involved in patient recruitment or rater consistency may have produced bias against a positive result. The authors suggest that further study is needed to confirm or refute the present results.


Reference Guide

Hazard Ratio: A measure of the risk of an event relative to exposure, or the probability of an event occurring in an exposed group versus a non-exposed group. A hazard ratio of 0.5 indicates that one group has half the risk of the other group.

Odds Ratio: A comparison of the probability of an event in two groups. An odds ratio of 1 implies that the event is equally likely in both groups. An odds ratio greater than 1 indicates that the event is more likely to occur in that group than in the comparison group.

Relative Risk: The risk of an event (or of developing a disease) relative to exposure. Relative risk is a ratio of the probability of the event occurring in the exposed group versus the control (non-exposed) group.

Study Rating: A measure of how well a study conforms to quality standards. The study rating uses a checklist system based on the comprehensive Strength of Evidence Report from the Evidence-based Practice Center Program of the Agency for Healthcare Research and Quality (AHRQ). The rating checklists have been posted at www.alertpubs.com.
Superstorm Sandy Double Issue

Production delays associated with power and communications outages in New Jersey from the storm prompted the editors at MJ Powers & Co. Publishers to make the decision to combine the November and December issues this year. The index (normally included in the December issue) for 2012 will be available as a printable document on our web site and through email. If you currently receive issues by email, you will automatically receive the index that way. If you do not currently receive issues by email but would like to receive the index, send an email to Krista@alertpubs.com and put “Index” in the subject line.

Thank you for your understanding, and Happy Holidays.

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