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## Risk of Seizures Associated with Antidepressant Use in Patients with Depressive Disorder – a Nested Case-control Analysis

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### Objective

To assess the risk of first-time seizures in association with exposure to antidepressants in patients with depressive disorders.

### Methods

We conducted a retrospective follow-up study with a nested case-control analysis using data from the U.K.-based Clinical Practice Research Datalink. We estimated incidence rates (IRs) with 95% confidence intervals (CIs) of seizures in depressed patients who used no antidepressant treatment or who used selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), or 'other antidepressants'. To better adjust for potential confounding, we estimated odds ratios (ORs) of antidepressant drug use among cases with seizures and matched controls in a nested case-control analysis.

### Results

Of 151,005 depressed patients, 619 had an incident seizure during follow-up. IRs per 10,000 person-years were 9.33 (95% CI, 6.19-12.46) in non-users of antidepressants, 12.44 (95% CI, 10.67-14.21) in SSRI users, 15.44 (95% CI, 8.99-21.89) in SNRI users, 8.33 (95% CI, 4.68-11.98) in TCA users, and 5.05 (95% CI, 4.49-5.62) in past users of antidepressants. Across single antidepressants, the highest IR per 10,000 person-years (17.06 [95% CI, 7.41-26.72]) was observed in mirtazapine users. In the case-control analysis we observed the highest risks of seizure in male users of other antidepressants (OR 3.90, 95% CI 1.85-8.26), and in female users of SNRIs (2.70, 95% CI 1.33-5.48) compared with non-use.

### Conclusion

With the exception of TCAs, antidepressant use in depressed patients was associated with an increased risk of seizures compared to non-use. Risk estimates differed across antidepressants and depended on timing of therapy, dose, and sex.