

Antidepressants Tied to a Significantly Increased Risk for Death

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Use of antidepressants is associated with an increased risk for death in the general population, but not in patients with existing cardiovascular disease, results of a meta-analysis suggest.

The results support the hypothesis that antidepressants are harmful in the general population but are less so in cardiovascular patients, perhaps owing to their blood thinning effects, investigators note.

"The common wisdom is that antidepressants are safe and effective, and by treating people with depression with antidepressants, we can save lives. However, research over the last decade has shown that antidepressants are much less effective than we had thought. Our research is part of a body of research that suggests that antidepressants are much less safe than we had thought," lead researcher Paul W. Andrews, PhD, JD, of the Department of Psychology, Neuroscience and Behavior, McMaster University, Hamilton, Ontario, Canada, told *Medscape Medical News*.

The study was [published online](#) September 14 in *Psychotherapy and Psychosomatics*.

Similar Risk With Tricyclics, SSRIs

The investigators assessed the effects of antidepressants on all-cause mortality and cardiovascular events in general-population and cardiovascular-patient samples in a meta-analysis that included 17 relevant studies.

"Sample type consistently moderated health risks," the authors report.

In general-population samples, antidepressant use increased the risk for death from any cause by 33% (hazard ratio [HR], 1.33; 95% confidence interval [CI], 1.14 - 1.55) and the risk for new cardiovascular events by 14% (HR, 1.14; 95% CI, 1.08 - 1.21).

Conversely, in patients with preexisting cardiovascular disease, antidepressant use was associated with a nonsignificant decrease in all-cause mortality (HR, 0.90; 95% CI, 0.76 - 1.07) and cardiovascular events (HR, 0.93; 95% CI, 0.82 - 1.06).

The anticlotting properties of antidepressants "may facilitate blood flow to the heart when blood vessels are blocked or constricted, decreasing the likelihood of cardiovascular events in samples exhibiting these types of pathologies, and thereby offsetting the negative effects of antidepressants," the investigators write.

With respect to mortality risk, the selective serotonin reuptake inhibitors (SSRIs) were not significantly different from tricyclic antidepressants (HR, 1.10; 95% CI, 0.93 - 1.31). Antidepressants were a significant moderator of risk only because the risk associated with antidepressants other than SSRIs and serotonin-norepinephrine reuptake inhibitors was significantly higher than that for the tricyclic antidepressants (HR, 1.35; 95% CI, 1.08 - 1.69).

An estimated 1 in 10 Americans use antidepressants. "Our findings highlight the urgent need for more rigorous investigations into the mortality effects of antidepressants. They are too widely used to allow this basic question of safety to remain unanswered," write the investigators.

"We need to understand how antidepressants affect all the mechanisms of the body, not just the brain, to evaluate their safety. By blocking either the serotonin transporter or the norepinephrine transporter, antidepressants prevent cells in crucial organs from taking up these biochemicals the way they normally do. Consequently, these drugs can impair the functioning of many adaptive processes throughout the body," said Dr Andrews.

The researchers note in their article that most antidepressants are prescribed by primary care providers in the absence of a formal psychiatric diagnosis.

"Our results suggest that health care providers should take greater care in evaluating the relative costs and benefits of antidepressants for each individual patient, including an assessment of cardiovascular status," they conclude.

Commenting on the study for *Medscape Medical News*, Scott Krakower, DO, assistant unit chief of psychiatry, Zucker Hillside Hospital, Glen Oaks, New York, said, "Antidepressants help to ameliorate symptoms in patients with depression. They may improve an individual's quality of life and functioning and prevent worsening suicidality.

"Alternatively, antidepressants may come with medical complications and side effects. The placebo effect in trials with depression has also showed improved outcomes. Therefore, it is important for the practitioner to make an informed decision about treatment, taking into consideration the patient's current clinical state and medical comorbidities they may have," said Dr Krakower.

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