

Antidepressants may increase risk of stroke and death

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Postmenopausal women who take antidepressants face a small but statistically significant increased risk for stroke and death compared with those who do not take the drugs. The new findings are from the federally-funded, multi-institution, Women's Health Initiative Study sponsored by the National Institutes of Health, and the results are published in the December 14 online edition of *Archives of Internal Medicine*.

Senior author Sylvia Wassertheil-Smoller, Ph.D., is a principal investigator in the Women's Health Initiative and is division head of epidemiology and professor of epidemiology & population health at Albert Einstein College of Medicine of Yeshiva University. In addition to Einstein, other institutions involved in the study were Massachusetts General Hospital, where the lead author of the paper, Jordan W. Smoller, M.D., Sc.D., is based. He is also associate professor of psychiatry in the Harvard Medical School. Also contributing to the study are researchers from the University of California San Diego, the University of Washington, the University of Hawaii, the University of Iowa, the University of Massachusetts Medical School, and Emory University School of Medicine.

The study examined data from 136,293 study participants, aged 50 to 79, who were not taking antidepressants when they enrolled in the study, and who were followed for an average of six years. Data from 5,496 women who were taking antidepressants at their first follow-up visit were compared with data from 130,797 not taking antidepressants at follow-up. The researchers compared the two groups with respect to the

incidence of fatal or nonfatal stroke, fatal or nonfatal heart attack and death due to all causes.

The researchers found no difference in coronary heart disease (defined as fatal and non-fatal heart attacks). However, they did observe a significant difference in stroke rates: antidepressant users were 45 percent more likely to experience strokes than women who weren't taking antidepressants.

The study also found that when overall death rates (all-cause mortality) were compared between the two groups, those on antidepressants had a 32 percent higher risk of death from all causes compared with non-users.

Dr. Wassertheil-Smoller notes that the overall risk for women taking antidepressants is relatively small: a 0.43 percent risk of stroke annually versus a 0.3 percent annual risk of stroke for women not taking antidepressants. However, because antidepressants are among the most widely prescribed drugs in the U.S. - especially among [postmenopausal women](#) - small risk increases can have significant implications for large patient populations.

Dr. Wassertheil-Smoller cautioned that "it remains unclear" from the data whether antidepressants are solely responsible for the greater mortality rate among users. The link observed in this study between antidepressant use and increased stroke risk for older women might partially be due to the underlying depression, since several studies have found that depression itself is a risk factor for cardiovascular problems.

In their analysis, the researchers tried to control for depression's effects, but they couldn't rule out the possibility that underlying depression in the antidepressant group may be contributing to their increased stroke risk. The study found no difference in stroke risk between the two major classes of antidepressants, selective serotonin reuptake inhibitors (SSRIs)

or tricyclic antidepressants (TCAs). However, the SSRIs did appear to convey a higher risk of hemorrhagic [stroke](#) caused by a bleed in the brain.

Antidepressants are valuable drugs for treating a condition that can be debilitating or even fatal. Dr. Wassertheil-Smoller advises women who may be concerned about taking their antidepressants based on this study to discuss the matter with their physicians. "You have to weigh the benefits that you get from these antidepressants against the small increase in risk that we found in this study," she says.

Dr. Jordan Smoller adds, "While this study did find an association between antidepressants and cardiovascular events, additional research needs to be done to determine exactly what it signifies. Older women taking [antidepressants](#), like everyone else, should also work on modifying their other risk factors for cardiovascular disease, such as maintaining a healthy weight and controlling cholesterol levels and blood pressure."

The researchers also pointed out other limitations to their findings. This was an observational study, so the findings are not as conclusive of causality as would be the case for a randomized controlled trial; and since the WHI study is comprised primarily of older white women, the findings might not extend to other groups.

The group's paper, "Antidepressant Use and Risk of Incident Cardiovascular Morbidity and Mortality Among Post-Menopausal [Women](#) in the Women's Health Initiative Study," appears in the December 14 online edition of [Archives of Internal Medicine](#).

Dr. Wassertheil-Smoller is also the Dorothy and William Manealoff Foundation & Molly Rosen Professor of Social Medicine and the principal investigator for the Women's Health Initiative at Einstein.

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