# For treatment-resistant depression, two drugs may be better than one

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Treating stubborn cases of depression in older adults is challenging, and often requires multiple treatments, says UConn Health psychiatrist David Steffens. His review in the *New England Journal of Medicine*

gives doctors evidence-based advice on how to help depressed patients who don't feel better on the first or second try.

Depression is common in adults, with about 5% suffering from the condition worldwide, according to the World Health Organization. Treatment-resistant depression, when a person with depression doesn't respond to two different treatments each over eight weeks, is also fairly common.

"Estimates range widely that from 20-70% of people don't respond to the first two treatments," says past president of the American Association for Geriatric Psychiatry and current Chair of Psychiatry at UConn School of Medicine David Steffens. "The general response rate to initial treatment is 30-40%, so a lot of people don't fully respond at first," and need to try multiple drugs and psychotherapy before they find a treatment that works, Steffens says.

Steffens, who works primarily with older adults over 60, describes how doctors need to carefully assess baseline symptoms of depression to be able to track improvement. The standard scale, the Patient Health Questionnaire-9 (PHQ-9) goes from 0-27, rating a person's level of depression by their answers to questions such as whether they have low mood, diminished energy, and loss of interest in formerly pleasurable activities. Higher scores indicate worse depression.

People can be reassessed with the PHQ-9 a few weeks after starting treatment to get an objective measure of how their symptoms have changed. Sometimes individuals will respond partially to one drug, but still rate themselves as depressed. Such individuals will need to have their medications adjusted, and some benefit from the addition of psychotherapy.

Steffens also recommends going over a patient's medical history to

identify other conditions they might have that could contribute to the depression. For example, older adults commonly have conditions such as high blood pressure and metabolic diseases such as heart disease or diabetes. These conditions can cause or exacerbate symptoms of depression, and helping patients get those conditions under control can make them feel better overall.

The nature of a patient's symptoms should also influence the choice of antidepressant medications. Some depressed patients suffer from insomnia and agitation; the choice of medication for them would be different than that for a patient who sleeps almost all the time and has trouble motivating to do anything.

Other depressed people suffer from chronic pain, and antidepressant medications known to reduce pain would probably be worth a try for such patients. Coping strategies to manage pain are also helpful.

Steffens also notes that taking two different antidepressant drugs at the same time often helps people with more severe forms of treatment resistant depression. With slow but steady dose increases, older adults can usually tolerate the same therapeutic dose of antidepressant drugs as younger adults, so clinicians should not be afraid to combine two drugs or increase the dose if warranted.

"Depression is really a serious problem in older adults, not just because of how it affects mood and interest in being in the world, but also how it can greatly affect the person as a whole," by affecting how they manage their medical conditions, especially vascular conditions, Steffens says. Depression can increase the risk of heart disease generally and increases the likelihood of death following a heart attack. But appropriate treatment can make a world of difference.

"Depression is not a normal part of aging. Nothing could be further from

the truth."

**More information:** David C. Steffens et al, Treatment-Resistant Depression in Older Adults, *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMcp2305428

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