When the blues won't let you be

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Rini Kramer-Carter has tried everything to pull herself out of her dark emotional hole: individual therapy, support groups, tai chi and numerous antidepressants.

The 73-year-old musician rattles off the list: Prozac, Cymbalta, Lexapro.

"I've been on a bunch," she said. "I still cry all the time."

She has what's known as "treatment-resistant depression." It's commonly defined as depression that doesn't respond to two different medications when taken one after the other, at the right dose and for the right amount of time.

Nearly 16 million adults have major depression, and up to a third do not respond to treatment. The disease afflicts people of all ages, but experts say that as many as half of older adults don't get better with standard treatment.

Mental health experts expect treatment-resistant depression to become more widespread as baby boomers age. Boomers already have been identified as having higher rates of depression than previous generations, and over time their depression may no longer respond to medication.

"We are seeing treatment-resistant depression more, and we are recognizing it more," said Helen Lavretsky, a geriatric psychiatrist at UCLA. "And in older adults, the answer to understanding what it is and what to do about it is more complicated than in younger adults."

The consequences among older adults can be devastating. Persistent depression can raise the risk of early death and suicide, expedite memory decline and lead to a loss of independence.

The phenomenon isn't well studied, but psychiatrists believe there are several reasons why depression in older adults may not respond to treatment. For one thing, if a person has been depressed and taken different medications for a long time, it can diminish their effectiveness. Patients also may neglect to take their medication as prescribed, because they have memory problems or they believe they no longer need it.

"Sometimes people say, 'I'm better. I don't need this,' and stop the medicine," said Anthony P. Weiner, who directs outpatient geriatric psychiatry at Massachusetts General Hospital. "Then the symptoms recur ... and if the person goes back on the medicine, it may not be fully effective."

Seniors are also more likely to have chronic medical illnesses, which raises the risk of depression. Their illnesses may make it more difficult for them to recover from depression. And it can mask whether antidepressants are working, because symptoms of chronic illness can be mistaken for depression - and vice versa.

Poverty, isolation, pain, grief over the loss of a spouse, or being a caregiver can also lead to or intensify a senior's depression. And no matter what medication the patients take, Lavretsky noted, those external factors don't go away.

"Either they change their perspective or they change their circumstances, or the depression just persists," she said.

Antidepressants can help seniors gain some perspective. But Lavretsky and others agree that even if the medications are effective, they shouldn't be used in isolation. "It's an emotional experience," Weiner said. "The whole answer isn't just, 'Oh, here take a pill.' There is such a central role for psychotherapy."

Kramer-Carter, who speaks slowly and hugs everyone she meets, has felt depressed for as long as she can remember. As a young adult, she worked as a secretary and a proofreader but got fired more than once because she had trouble getting out of bed and making it to work on time. She went to the emergency room many times and in her 30s, she was diagnosed with depression.

Now, she spends a few days each week driving her husband, Eugene Carter, to medical appointments. When she feels up to it, she volunteers delivering food to poor families.

Kramer-Carter checks all the boxes for being at high-risk of treatment-resistant depression. She is a long-time caregiver, first for her parents and now for her husband, a stroke survivor with short-term memory problems. Her own list of health problems is long: diabetes, high blood pressure, arthritis, fibromyalgia and gout.

"Who wants to be aching all the time?" she said.

Money problems don't help either. The couple depends financially on Social Security. If she had more money, she said she would go to the theater or see live concerts. She misses both.

"We wouldn't be so stuck," she said. As it is, they spend everything on food, rent and other bills.

"It's a constant struggle," she said. "You have to borrow from Peter to pay Paul."

Despite the prevalence of treatment-resistant depression, few resources exist to help psychiatrists make treatment decisions. Clinical trials have been scant, and there are no universally accepted protocols for the condition. The risks and benefits of different medications for older adults are largely unknown.

Given a shortage of geriatric psychiatrists, decisions on treatment are often left to primary care providers, who may not have relevant training or might be reluctant to take on such complicated care.

Doctors with patients who don't respond to traditional therapies

frequently make ad hoc decisions about whether to change the dosage, add a medication or switch to a new one.

"The clinicians use their best experience and trial and error," said Evelyn Whitlock, chief science officer at the Patient-Centered Outcomes Research Institute. "They try something, and if it doesn't work, they try something else."

Trial and error is not ideal, she said. Many of these people have been living with depression for so many years, and providers need to be able to provide them with effective treatment.

In an effort to produce better medical outcomes for people with treatment-resistant depression, the Patient-Centered Outcomes Research Institute announced in July that it was funding three major studies that will test different approaches to the illness. The goal of the research is to produce tangible evidence that can be used immediately to help patients and their doctors make more informed treatment decisions.

The Washington, D.C. nonprofit, which finances health research, earmarked $40 million for the five-year studies, which it expects to begin this fall. They will include more than 2,500 patients at sites in California, Ohio, New York, Texas, Pennsylvania and elsewhere.

One of the studies will examine electroconvulsive therapy - its impact on quality of life and its potential for relieving the symptoms. Another will compare the effectiveness and safety of three strategies - using magnetic fields to stimulate nerve cells in the brain, adding an antipsychotic medication or switching to a specific antidepressant. The research will assess how these approaches affect the patients' ability to function at home and work.

The third and largest study, with about 1,500 patients, will focus

specifically on older adults, testing different drugs and studying how aging affects the risk and benefits of antidepressants. UCLA, where Kramer-Carter is being treated, is part of the third study, which will weigh life circumstances and disabilities in addition to depression.

The grants represent an "unprecedented opportunity to look at this population," Lavretsky said.

"It will be a comprehensive look at the condition, why it happens and what are the ways of alleviating suffering," she said. "Are there some similarities among all people with treatment-resistant depression? I suspect we will find some."

On a recent afternoon, Rini Kramer-Carter visited Lavretsky at UCLA. She said the only time she truly escapes her sadness is when she plays percussion along with other musicians. But she hasn't been playing lately, and she has been sleeping up to 20 hours a day.

"If I can stay in bed all day, that's what I do," she said.

Sometimes she watches TV comedies to try to dissipate her black moods.

Kramer-Carter said she learned about Lavretsky after seeing a newspaper ad for another research study, of a drug typically used to treat early-stage dementia. During their appointment, Lavretsky went over a list of questions included in the study. "On a scale of zero to 10, where do you place yourself in terms of depression?" the doctor asked her. Nine, she responded.

She told the Lavretsky she sometimes felt restless and anxious, but not suicidal.

"Do you feel full of energy?" Lavretsky asked.

"Do I look like I am full of energy?" she responded with a sigh.

Lavretsky told her that no pill will completely fix her problems, but medication might give her more energy and the ability to cope. Kramer-Carter said she knows a drug won't produce any miracles. She just wants some relief.

"I just want to be able to live my life," she said.