

Suicide Care Insights: Depression

Hope for Treatment Resistant Depression

George is no stranger to depression. A seventy-five-year-old married man, father of three adult children, and grandfather of five, he was first diagnosed with depression in his twenties. He was trying to get through college while adjusting to marriage and civilian life after four years of active military service. He took the prescription his doctor gave him and was grateful for the relief it provided.

Like everyone, George's life was stressful with job changes, a move, the death of a family member, and juggling family and marital stressors. In his forties he developed heart problems, which his doctor told him was related to anxiety and stress. He went to see a psychiatrist who prescribed different medications to help him manage his depression and anxiety. He saw a therapist to talk about his stressors and his childhood trauma. He learned skills. He and his wife went to marriage counseling. Medications were added and changed. He leaned into his strong Christian faith. He took up running and cycling. For quite a while, George felt good. That combination helped him, and he wasn't depressed

But then, in his late sixties, something changed. He had some significant life changes, including an accident. That triggered an episode of depression that was more intense than he had ever previously had. He started to have thoughts of suicide, and he and his family spent the next several years attempting to help George break free of his suffering. There were new medications and new combinations of medications. They caused a lot of problematic side effects that affected his physical well-being. He also had more frequent therapy, in-patient hospitalizations, and intensive outpatient programs.





No one told George that he had treatment-resistant depression, but in hindsight, that's what it was.

While treatment-resistant depression (TRD) isn't an official diagnosis in the Diagnostic & Statistical Manual (DSM), to a person like George—who has tried every medication and therapy and still feels depressed—the name might make a lot of sense. "There is no consensus definition in the field of mental health or psychiatry for TRD," said Linda Carpenter, M.D. a psychiatrist, researcher and director of the Butler TMS Clinic and Neuromodulation Research Facility.



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Some people's brains respond to some medications and not to others, and science can't definitively answer why. A recent article in *Nature* magazine reported that, while serotonin-reuptake inhibitors (SSRIs)—a common type of anti-depressant medication—reduce symptoms of depression for some people, researchers can't figure out exactly how they work (Moncrieff et al., 2022). They don't know what the mechanism is between the person's brain and the medicine that reduces symptoms of depression—or doesn't reduce them. So, it makes sense that for some people, typical anti-depressants don't work at all. They need something different.

This understandably frustrates individuals who try many different medications for months or years at a time with little to no lasting relief from their symptoms. "Most people know when they have TRD because they have tried multiple medications. Maybe they couldn't take them long enough at high enough doses [for them to be effective], or the medications worked and then stopped working," Carpenter said.

There are adjunct treatment options for TRD, but to get to them individuals often have to try many medications and suffer through side effects and inadequate relief before insurance companies approve therapies such as electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), or vagus nerve stimulation. Esketamine, another treatment for depression, isn't covered by insurance at all. And some people aren't aware of these treatments.



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"I'd really like people experiencing TRD and their doctors to have more awareness and understanding of adjunct treatment options," said Carpenter. "It's not uncommon to have a patient contact us who has been working with the same doctor for a decade or more, trying different medications and combinations of medications, maybe seeing slight improvements from time to time, but never really experiencing relief from their depression," said Carpenter. "They may be nervous to bring up the possibility of TMS, or another adjunct treatment, to their doctor because they feel uncomfortable or guilty for going around their doctor."

Eventually, after a suicidal crisis and in-patient hospital stay, a friend suggested George look into TMS. George's TMS treatments were in an outpatient office close to his home. George's depression symptoms decreased. He was able to stop some of his medications and reduce the doses of others. This reduced the side effects considerably. Also, he didn't experience any side effects from the TMS treatments.



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- George's Grandson

these days.

He finally started to feel like himself again. Even his grandchildren noticed the difference. "It's really nice to have Grandpa back," said George's grandson. He asked me a lot of questions, really listened to my answers and shared ideas. It was like the old Grandpa. I think he must be feeling a lot better these days."

Stories like George's are what keep Carpenter and her team hopeful and energized to do this work. "When somebody's gone through decades of struggle, and then finally something [like TMS] turns it around for them. They're so grateful, and they're so they're so exuberant and that's just a huge boost for all of us," said Carpenter. It keeps her going.

Unfortunately, one problem with treatments like TMS or vagus nerve stimulation is access and availability. Providers aren't always aware of the treatments, their efficacy, or how they work in conjunction with medications. Individuals might not know about them or how to access them, much less how to determine if they are right for them. Often insurance companies make people go through multiple trials of different (and sometimes similar) treatments—either pharmacological or talk therapy—before they will approve coverage of a "non-traditional" treatment. Some individuals, particularly impoverished or minoritized people have additional difficulty with access to these kinds of treatments.





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(Greenburg et al., 2021)

TRD is a chronic disorder that is difficult and sometimes overwhelming to live with. And it isn't cheap either. It robs people and families of hours, days, and years of life. It's difficult for people to hold onto hope. It isn't only the individual or family that struggles with the "costs" of TRD. Across the country depression costs the economy \$326.2 billion with the biggest identified economic burden on workplaces (Greenburg et al., 2021).

This is one reason why Carpenter remains connected with research into treatments like TMS, esketamine, and vagus nerve stimulation. The research into treatments that help people with TRD continues to evolve and she has hope that there will be better treatments in the future. "I keep myself active in the research world because we need to keep developing newer, better, smarter treatments in mental health," said Carpenter. "That's an area that is exciting for me. There is so much talent that is being applied to come up with new insights and new treatments. It is extremely encouraging and seeing people get better who never thought they could. All of this makes me very hopeful."

REFERENCES

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DISCLOSURES

In the past 3 years, Dr. Carpenter has served as a paid scientific advisor to Neuronetics Inc, Nexstim PLC, Affect Neuro Inc, Neurolief LTD, Sage Therapeutics, Otsuka, Sunovion, Magnus Medical, and Janssen Pharmaceuticals Inc. She has received research support (to Butler Hospital) from Neuronetics Inc, Neosync Inc, Nexstim PLC, Affect Neuro Inc, and Janssen Pharmaceuticals Inc.

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