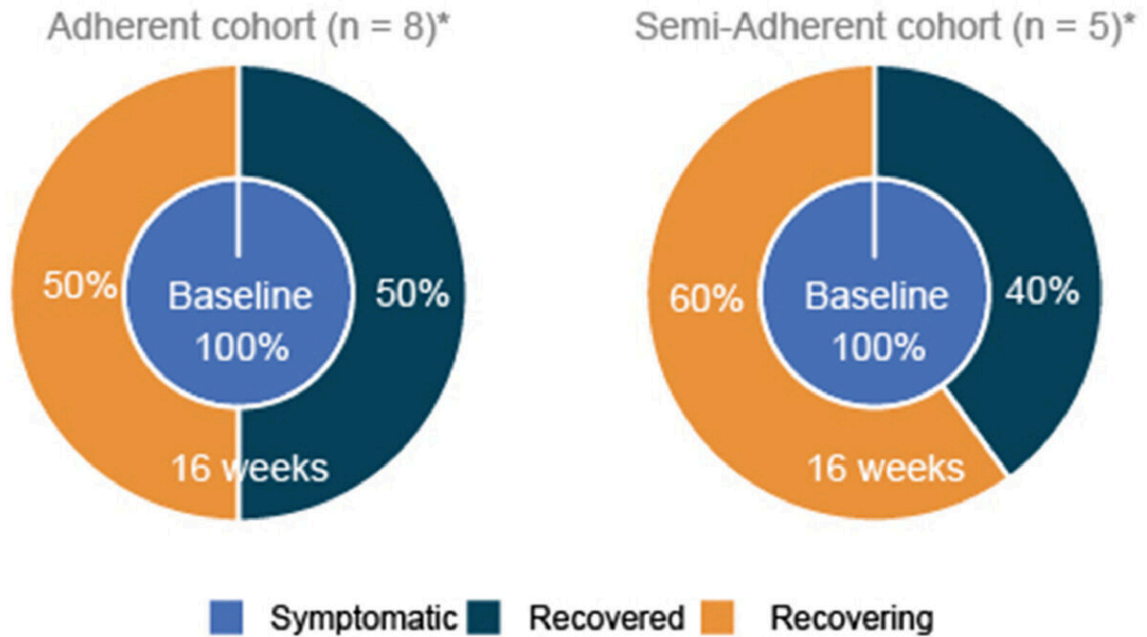


Pilot study shows ketogenic diet improves severe mental illness

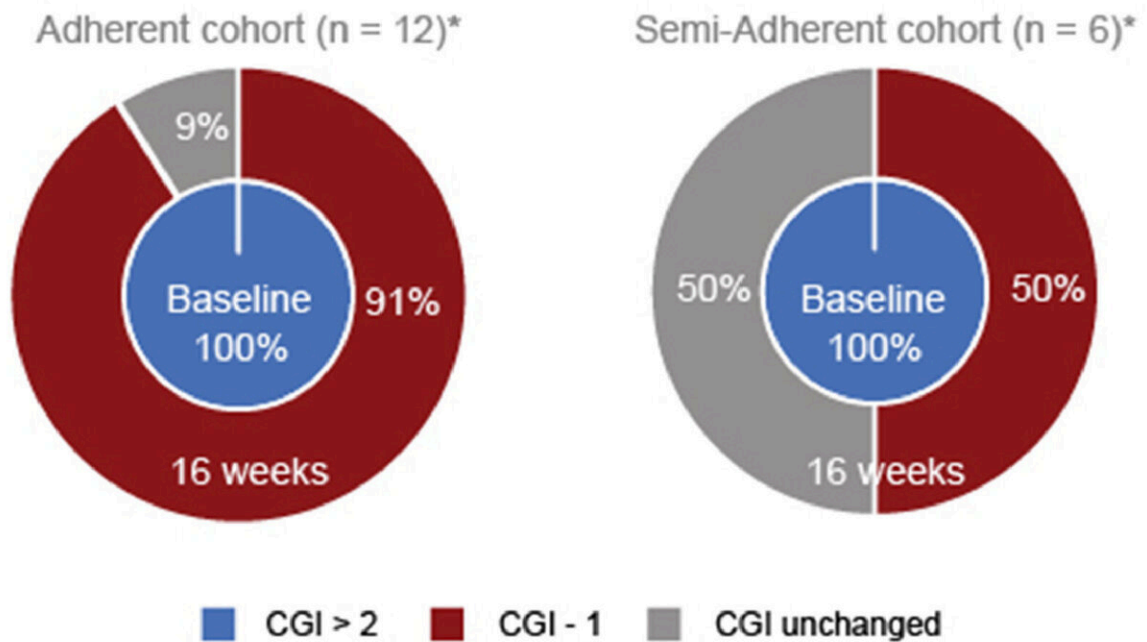
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A Clinical Mood Monitoring (CMM)



*n of patients with CMM not in recovery at baseline

B Clinical Global Impression (CGI)



*n of patients with CGI >2 at baseline

(A,B): Sunburst graph depicting final Clinical Mood Monitoring and Clinical Global Impressions of individual with elevated symptomatology at baseline across adherent and semi-adherent populations (A) Inclusion criteria was baseline Clinical Mood Monitoring assessment of “not in a recovered or recovering state” (B) inclusion criteria was baseline Clinical Global Impressions>2. Credit: *Psychiatry Research* (2024). DOI: 10.1016/j.psychres.2024.115866

For people living with serious mental illnesses like schizophrenia or bipolar disorder, standard treatment with antipsychotic medications can be a double-edged sword. While these drugs help regulate brain chemistry, they often cause metabolic side effects such as insulin resistance and obesity, which are distressing enough that many patients stop taking the medications.

Now, a [pilot study](#) led by Stanford Medicine researchers has found that a ketogenic diet not only restores metabolic health in these patients as they continue their medications but it further improves their psychiatric conditions. The results, [published](#) in *Psychiatry Research*, suggest that dietary intervention can be a powerful aid in treating mental illness.

"It's very promising and very encouraging that you can take back control of your illness in some way, aside from the usual standard of care," said Shebani Sethi, MD, associate professor of psychiatry and behavioral sciences and the first author of the new paper.

The senior author of the paper is Laura Saslow, Ph.D., associate professor of health behavior and biological sciences at the University of Michigan.

Making the connection

Sethi, who is board-certified in obesity and psychiatry, remembers when she first noticed the connection. As a [medical student](#) working in an obesity clinic, she saw a patient with treatment-resistant schizophrenia whose auditory hallucinations quieted on a ketogenic diet.

That prompted her to dig into the medical literature. There were only a few decades-old case reports on using the ketogenic diet to treat schizophrenia, but there was a long track record of success in using ketogenic diets to treat epileptic seizures.

"The ketogenic diet has been proven to be effective for treatment-resistant epileptic seizures by reducing the excitability of neurons in the brain," Sethi said. "We thought it would be worth exploring this treatment in psychiatric conditions."

A few years later, Sethi coined the term metabolic psychiatry, a new field that approaches mental health from an energy conversion perspective.

Meat and vegetables

In the four-month pilot trial, Sethi's team followed 21 adult participants who were diagnosed with schizophrenia or bipolar disorder, taking [antipsychotic medications](#), and had a metabolic abnormality—such as [weight gain](#), [insulin resistance](#), hypertriglyceridemia, dyslipidemia or impaired glucose tolerance. The participants were instructed to follow a ketogenic diet, with approximately 10% of the calories from carbohydrates, 30% from protein and 60% from fat. They were not told to count calories.

"The focus of eating is on whole non-processed foods including protein and non-starchy vegetables, and not restricting fats," said Sethi, who shared keto-friendly meal ideas with the participants. They were also

given keto cookbooks and access to a health coach.

The research team tracked how well the participants followed the diet through weekly measures of blood ketone levels. (Ketones are acids produced when the body breaks down fat—instead of glucose—for energy.) By the end of the trial, 14 patients had been fully adherent, six were semi-adherent, and only one was non-adherent.

Feeling better

The participants underwent a variety of psychiatric and metabolic assessments throughout the trial.

Before the trial, 29% of the participants met the criteria for metabolic syndrome, defined as having at least three of five conditions: abdominal obesity, elevated triglycerides, low HDL cholesterol, elevated blood pressure and elevated fasting glucose levels. After four months on a ketogenic diet, none of the participants had metabolic syndrome.

On average, the participants lost 10% of their body weight, reduced their waist circumference by 11% percent, and had lower blood pressure, body mass index, triglycerides, blood sugar levels, and insulin resistance.

"We're seeing huge changes," Sethi said. "Even if you're on antipsychotic drugs, we can still reverse the obesity, the metabolic syndrome, the insulin resistance. I think that's very encouraging for patients."

The psychiatric benefits were also striking. On average, the participants improved 31% on a psychiatrist rating of mental illness known as the clinical global impressions scale, with three-quarters of the group showing clinically meaningful improvement. Overall, the participants also reported better sleep and greater life satisfaction.

"The participants reported improvements in their energy, sleep, mood, and quality of life," Sethi said. "They feel healthier and more hopeful."

The researchers were impressed that most of the participants stuck with the diet. "We saw more benefit with the adherent group compared with the semi-adherent group, indicating a potential dose-response relationship," Sethi said.

Alternative fuel for the brain

There is increasing evidence that psychiatric diseases such as schizophrenia and [bipolar disorder](#) stem from metabolic deficits in the brain, which affect the excitability of neurons, Sethi said.

The researchers hypothesize that just as a ketogenic diet improves the rest of the body's metabolism, it also improves the brain's metabolism.

"Anything that improves [metabolic health](#) in general is probably going to improve brain health anyway," Sethi said. "But the [ketogenic diet](#) can provide ketones as an alternative fuel to glucose for a brain with energy dysfunction."

Likely, there are multiple mechanisms at work, she added, and the main purpose of the small pilot trial is to help researchers detect signals that will guide the design of larger, more robust studies.

As a physician, Sethi cares for many patients with both serious mental illness and obesity or metabolic syndrome, but few studies have focused on this undertreated population.

She is the founder and director of the metabolic psychiatry clinic at Stanford Medicine

"Many of my patients suffer from both illnesses, so my desire was to see if metabolic interventions could help them," she said. "They are seeking more help. They are looking just to feel better."

More information: Shebani Sethi et al, Ketogenic Diet Intervention on Metabolic and Psychiatric Health in Bipolar and Schizophrenia: A Pilot Trial, *Psychiatry Research* (2024). [DOI: 10.1016/j.psychres.2024.115866](https://doi.org/10.1016/j.psychres.2024.115866)

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