

UC SANTA BARBARA

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## **Clinical trial shows that the ketogenic diet is effective at controlling polycystic kidney disease**

It's official: The ketogenic diet proved to be effective at controlling polycystic kidney disease (PKD) in the first randomized controlled clinical trial of ketogenic metabolic therapy for PKD.

"I'm really happy about these clinical trial results," said UC Santa Barbara biologist [Thomas Weimbs](#), whose lab was part of an international collaboration to investigate the effect of the fasting response known as ketosis on the cysts that are the hallmark of the disease. "We now have the first evidence in humans that the cysts really don't like to be in ketosis and that they don't seem to grow."

The researchers' study is published in the journal [Cell Reports Medicine](#).

### **Nurture over nature**

For PKD patients, these findings represent an opportunity to control a genetic disease that leads to a progressive condition, causing pain and robbing them of their quality of life, and often resulting in the need for dialysis and kidney transplantation as the cysts destroy the kidneys' ability to effectively filter and remove waste from the body.

“If you have PKD, the dogma is that it’s a genetic disease,” Weimbs said. “And no matter what you do, you progress toward kidney failure and diet doesn’t make any difference, which unfortunately most patients are told to this day.”

This prevailing belief was what the Weimbs Lab and colleagues from various research institutions in Germany set out to challenge with their trial. Sixty-six PKD patients were recruited by the German research team headed by research physician Dr. Roman Müller of the University of Cologne and randomly split into three groups: a control group that received routine PKD counseling, another group that underwent a three-day water fast every month and a third group that observed a low-carbohydrate, high-fat ketogenic diet. The patients were followed closely with blood draws and MRI scans.

At the end of the three-month trial period, the researchers found that while the control group experienced the expected growth in the size of their kidneys, the ketogenic diet patients’ kidneys stopped growing and appeared to show a tendency to shrink somewhat, though the researchers pointed out that the shrinkage over the 90-day trial period failed to meet statistical significance.

The most striking evidence came in the form of measurably improved kidney function in the ketogenic diet patients which was statistically significant.

“To everyone’s great surprise, kidney function actually improved with the ketogenic diet,” Weimbs said. It’s not something one would expect, he added, if PKD was truly something that could only get worse over time. “And that was a hard outcome of statistical significance.”

Kidney function was measured by the concentration of a protein called cystatin C — higher-than-normal concentrations of this protein in the blood indicate a faltering filtration system, a symptom that worsened in the control group.

The ketogenic diet was rated as “highly feasible” by the patients during the study, indicating a strong motivation and ability to control their condition via diet choices alone. “Doctors often assume that their patients cannot adhere to a diet anyway, so they don’t even try. Clearly, this is not true. People with PKD are highly motivated to do something about their condition,” he said.

## **Different kinds of keto**

There is no one ketogenic diet to fit all, however, according to Weimbs. To get the best out of their diet, PKD patients should consult with their physicians and nutritionists as they shift away from the usual carbohydrate and sugar-laden standard diets that are pervasive in industrialized societies.

“A keto diet just means very low carbs,” he pointed out. There are many mainstream applications of this diet which is popular for weight loss. Though a popular version of the ketogenic diet is heavy on meat, that may not be the best option for all people with kidney disease. More plant-focused ketogenic diets are also available such as the [Ren.Nu](#) diet that was developed by Weimbs in collaboration with renal dietitians specifically for people with PKD and has been available to the public for two years.

### **More Trials to Come**

These results represent a significant milestone for the Weimbs Lab, which has for more than two decades been researching the cell mechanisms that underlie PKD and other renal diseases. A chance discovery made by researchers in the lab — kidney cysts had dramatically shrunk in mouse models that had undergone caloric restriction — led them to pursue the idea that the fasting response known as ketosis might have some impact on the growth of the apparently glucose-dependent cysts.

However as any scientist knows, one needs solid evidence to back up any claims of medical benefit for humans. You need clinical trials.

“If you make a discovery in animals, but you don’t check it in actual people, you’ll never quite know if it’s going to be meaningful,” Weimbs said. “There’s always going to be the doubt, and people are going to say animal experiments don’t always translate to humans.” Money to fund these trials became a challenge, thanks to the prevailing notion that PKD was unrelenting because of its genetic origin.

“And, of course, it’s always hard to find funding for diet interventions, because nobody wants to fund diets; they want to fund drug research,” Weimbs added. Drug companies, which fund most clinical trials, have no interest in a diet, he added.

However, Weimbs, together with Dr. Müller, was able to garner additional funding from the PKD Foundation to conduct the clinical trial in Germany.

“Dr. Müller was able to supplement this with some other funding he had, and we essentially designed this trial together based on the animal results,” Weimbs said. “But really the entire trial was run by his team, so they deserve all the credit and they did a fantastic job. They did everything despite the challenges of COVID.”

With these results, Weimbs and his team are looking ahead to further clinical trials slated to start in the coming year, one in Toronto and the other in Tokyo, to assess the efficacy of a medical food they developed specifically to assist PKD patients in reaching ketosis. Called KetoCitra and available through the Weimbs Lab’s spinoff company Santa Barbara Nutrients, it’s a formulation of the ketone beta-hydroxybutyrate (BHB) that is generated during fasting, without the other ingredients and fillers that may be present in drugstore versions of BHB. The studies will involve more people — 80 in Toronto and 200 in Tokyo — and follow patients for a year. These trials will investigate the efficacy of the Ren.Nu plant-focused ketogenic diet in conjunction with KetoCitra.

“We want to investigate the longer-term effects,” Weimbs said. “If this trend of kidney volume change we saw in the three-month study holds true, we would expect to see a larger and statistically significant difference there as well.”

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draw inspiration from the beauty and resources of our extraordinary location at the edge of the Pacific Ocean.