Microbiome: Disruption of gut microbial balance is associated with increased mortality after kidney, liver transplants

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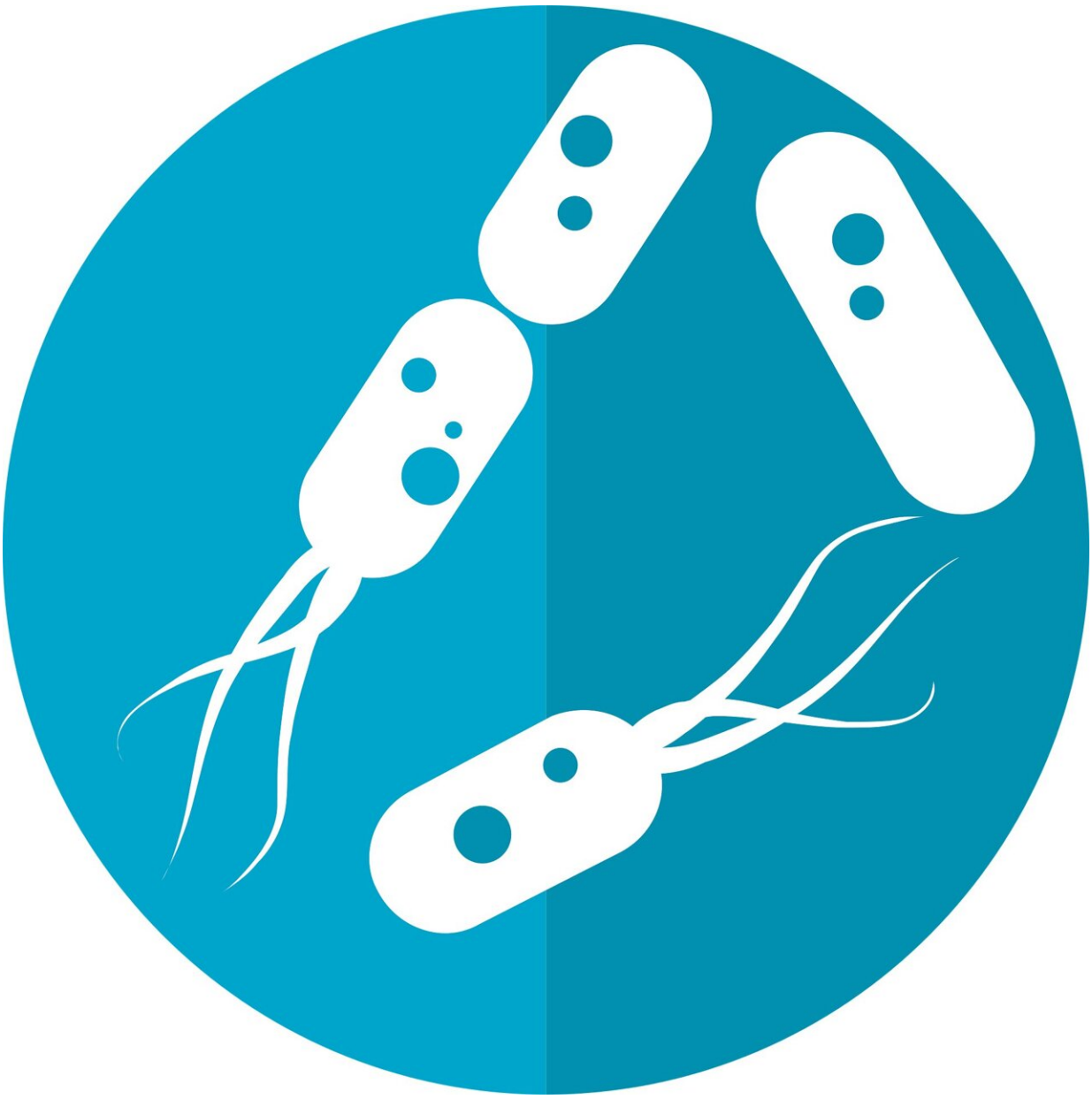

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Disruptions in the gut microbiome have been linked to lower survival rates for people who have undergone kidney and liver transplants, a finding that highlights the critical importance of the vast and complex microbial communities that dwell within us.

Scientists in the Netherlands studied fecal samples from more than 1,000 recipients of kidney and liver transplants to learn how the balance of microbes in the gut microbiome impact post-transplant survival. Gut microbiome dysbiosis—disruptions in microbial diversity—is associated with increased mortality after solid organ transplantation, researchers found.

The gut microbiome is made up of both "good" and "bad" microbes: bacteria, viruses and fungi. Health benefits throughout the body are derived from the healthy balance of these microbial communities in the gut. However, the living communities are not static; they fluctuate in response to diet, emotions, exercise, surgery, and exposure to medications.

Past studies demonstrated that recipients of stem cell transplants had a higher mortality risk when faced with disruptions in their gut microbiome. It has taken until now to pose the same question, based on a large sample size, whether microbiota disruption negatively impacts recipients of solid organ transplants.

Going into their research the Dutch team was well aware that the health of the microbiome influenced the fate of patients who had undergone

stem cell transplants, infusions that are sometimes referred to as bone marrow transplants. The procedure provides the recipient with a donor's healthy progenitor cells to generate a new blood supply. But scientists also were aware that a successful stem cell transplant wasn't enough unless the gut microbiome was also flourishing with a diverse population of beneficial microbes.

Writing in *Science Translational Medicine*, researchers from various divisions of the University of Groningen's medical center in Groningen, Netherlands, reported on the need for microbial variety to ensure a healthy transplant outcome.

"Organ transplantation is a life-saving treatment for patients with end-stage disease, but survival rates after transplantation vary considerably," wrote J. Casper Swarte, first author of the report. Working with a large team of collaborators in the Netherlands, Swarte and colleagues emphasized that stem cell transplants had long stood alone as evidence that gut health played a role in transplant success.

"There is now increasing evidence that the gut microbiome is linked to the survival of patients undergoing hematopoietic cell transplant, yet little is known about the role of the gut microbiome in solid organ transplantation.

"We analyzed 1,370 fecal samples from 415 liver and 672 renal transplant recipients using shotgun metagenomic sequencing to assess microbial taxonomy, metabolic pathways, antibiotic resistance genes, and virulence factors," Swarte added.

The Dutch research—which also included a two-year follow-up of some of the kidney transplant recipients—underpins the important role of gut microbiota in transplant outcomes and suggests that microbiota-based therapies might help improve outcomes for more patients.

To gain further data on the importance of the microbiome in post-transplant health, Swarte and colleagues also studied fecal samples from 1,183 controls. Overall, transplant recipients showed classic signs of gut microbiome dysbiosis, evidence of a disrupted microbiota that, for some, persisted as long as 20 years. This included less diverse gut bacteria and a higher prevalence of genes linked to antibiotic resistance. Patients with the lowest bacterial diversity also had the poorest survival rates.

On average, patients with evidence of gut microbiome dysbiosis had a 3-year survival of 77% compared with 96% among patients with high bacterial diversity. The team's analysis also showed that the use of immune-suppressing drugs—which are needed to prevent organ rejection—were the most critical factor driving disruptions of patients' gut microbiome.

While the research suggests a link between solid organ transplants and dysbiosis of the gut microbiome, Swarte and colleagues caution that their study doesn't demonstrate a causal link. They also hope that future work will expand their research to recipients of heart and lung transplants.

"Our data showed that both liver and kidney transplant recipients suffered from gut dysbiosis, including lower microbial diversity, increased abundance of unhealthy microbial species, decreased abundance of important metabolic pathways, and increased prevalence and diversity of antibiotic resistance genes and virulence factors," Swarte emphasized.

"Last, we demonstrated that the use of immunosuppressive drugs was associated with the observed dysbiosis and that the extent of dysbiosis was associated with increased mortality after transplantation. This study represents a step toward potential microbiome-targeted interventions that might influence the outcomes of recipients of solid organ

transplantation."

More information: J. Casper Swarte et al, Gut microbiome dysbiosis is associated with increased mortality after solid organ transplantation, *Science Translational Medicine* (2022). DOI: 10.1126/scitranslmed.abn7566