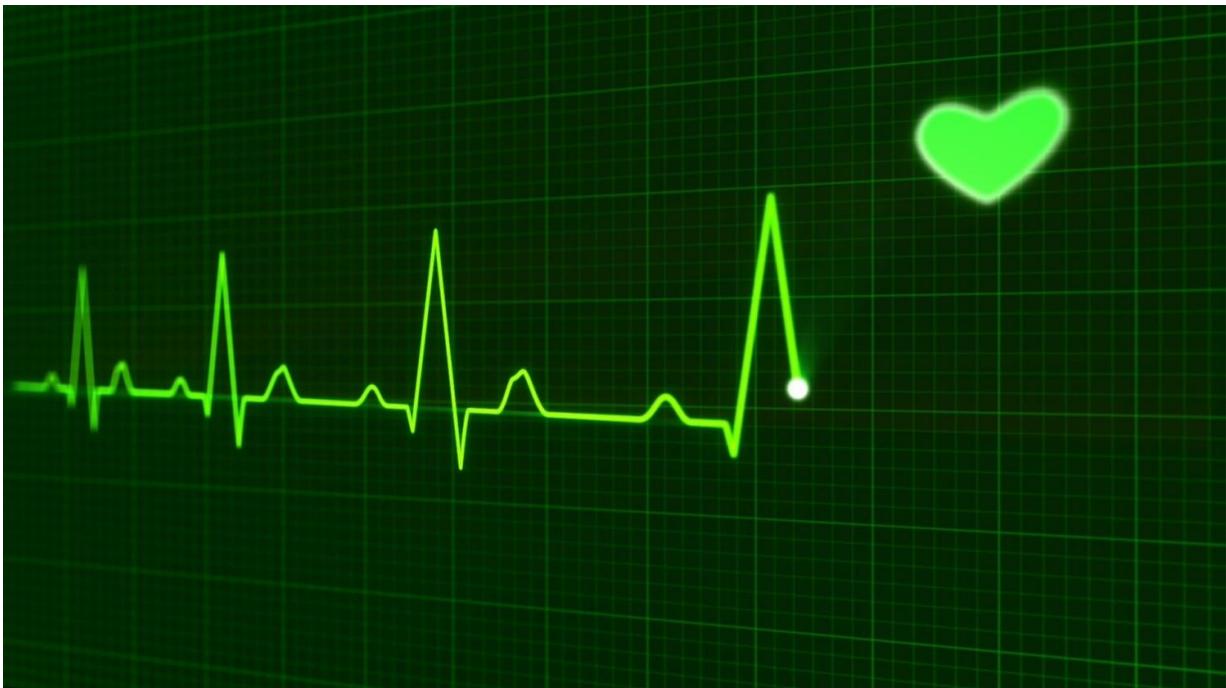


# Study highlights potential for using TMAO—a digestive by-product—to predict heart failure risk

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New Cleveland Clinic and Tufts University research shows that elevated levels of the gut microbiome trimethylamine N-oxide (TMAO) pathway led to a higher risk of heart failure independent of other risk factors, according to a study of two large National Institutes of Health cohorts.

The study was recently [published](#) in the journal *Circulation: Heart Failure*.

"The present studies show that even among apparently healthy subjects at time of enrollment, regular measurement of blood TMAO levels predicted incident risk for [heart failure](#) development during long-term follow up," said senior and corresponding author Stanley Hazen, M.D., Ph.D., chair of Cardiovascular and Metabolic Sciences in Cleveland Clinic's Lerner Research Institute and co-section head of Preventive Cardiology.

"This adds to the growing body of research linking the gut microbial TMAO pathway to cardiovascular and [metabolic diseases](#), and as a potential target for medical therapies."

TMAO is a metabolite that forms when gut bacteria digest certain nutrients abundant in red meat and other animal products. Over the past decade, a Cleveland Clinic research team led by Dr. Hazen has published numerous studies linking high levels of TMAO to increased risk of developing both [cardiovascular disease](#), including adverse events like heart attack and stroke, and chronic kidney disease.

The most recent study further investigated this association by following nearly 12,000 participants who were healthy at the time of enrollment, examining the effects of elevated TMAO over time.

Researchers measured a series of blood level samples over almost 16 years, resulting in over 20,000 evaluations of TMAO levels. Overall, 2,102 cases of heart failure occurred.

Within this group, they found that TMAO served as a strong biomarker for identifying subjects at risk for development of [heart](#) failure, after adjustment for a range of cardiovascular disease risk factors,

sociodemographic, lifestyle, medical and biochemical markers. The findings were generally consistent across cardiovascular disease [risk factors](#) including age, race/ethnicity, BMI and baseline renal function.

"Heart failure is one of the leading causes of death worldwide. These results open a new avenue for potential treatment and prevention," Dr. Hazen said. "I'm hopeful we will someday have medications that target the TMAO pathway and prevent its negative effects from occurring."

TMAO is primarily generated in humans through diet, largely through eating animal products, as the gut microbiome processes these protein sources. Dr. Hazen's team has been developing treatment options that target the TMAO pathway to prevent and treat diseases like cardiovascular disease and [chronic kidney disease](#). His team has found success in the lab and in preclinical models of disease in halting TMAO production as a novel pharmaceutical approach.

The study is part of a collaboration between the Cleveland Clinic research team led by Dr. Hazen and Dariush Mozaffarian, M.D., Dr.PH. from the Food is Medicine Institute at the Friedman School of Nutrition Science and Policy at Tufts University. Wilson Tang, M.D., research director for Heart Failure and Cardiac Transplantation Medicine at Cleveland Clinic, was also a lead author of the study.

**More information:** W.H. Wilson Tang et al, Trimethylamine N -Oxide and Related Gut Microbe-Derived Metabolites and Incident Heart Failure Development in Community-Based Populations, *Circulation: Heart Failure* (2024). [DOI: 10.1161/CIRCHEARTFAILURE.124.011569](https://doi.org/10.1161/CIRCHEARTFAILURE.124.011569)

Provided by Cleveland Clinic

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