World-first human trial: Experimental hookworm infection led to improvements in type 2 diabetes patients

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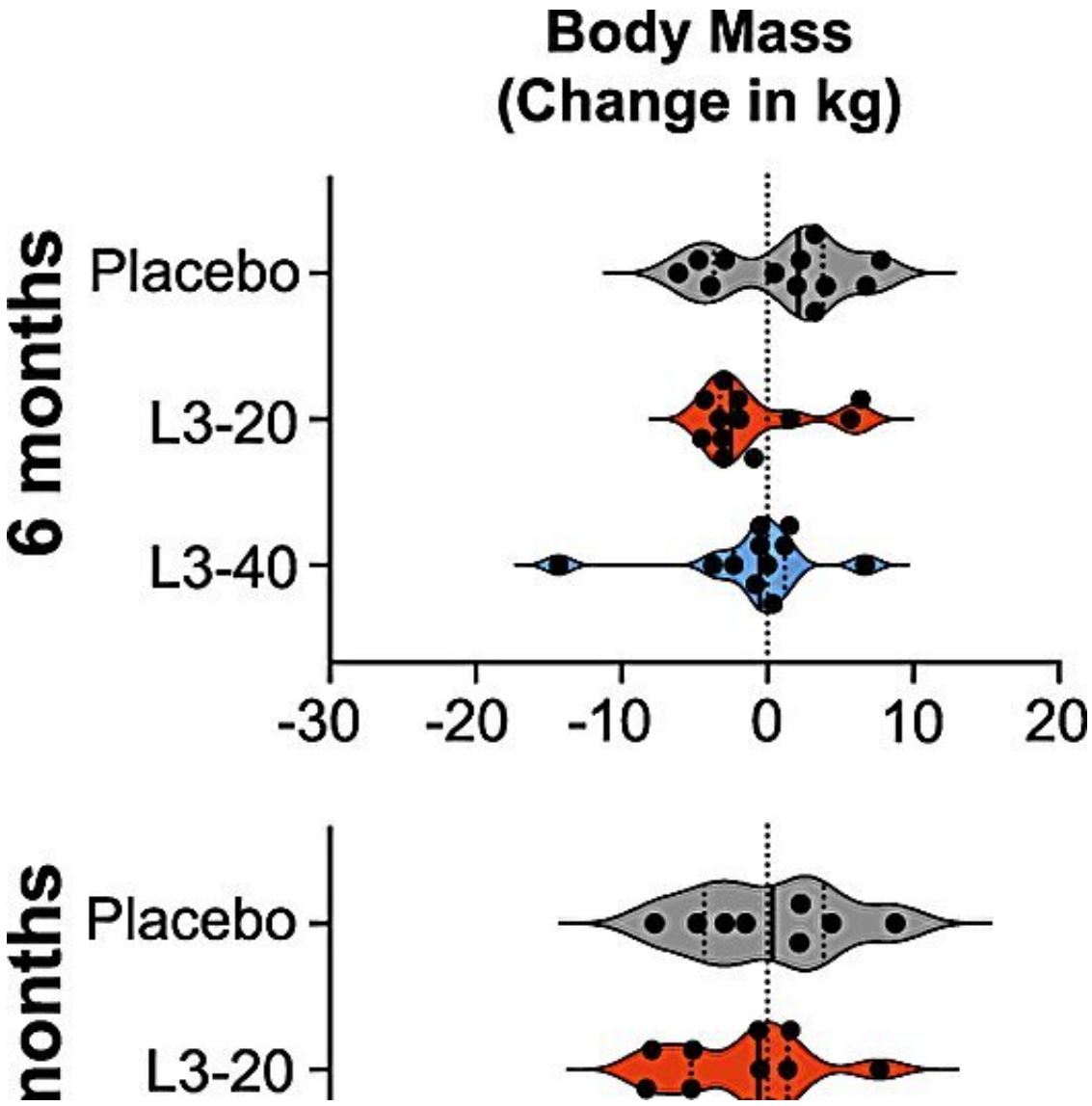

Impact of experimental hookworm infection on body mass. Credit: *Nature*

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A world-first human trial at James Cook University using live hookworms to combat diseases such as type 2 diabetes has proven successful—sparking interest in staging a larger-scale international trial.

Dr. Doris Pierce from JCU's Australian Institute of Tropical Health and Medicine (AITHM) said infecting people with microscopic hookworm larvae was safe and had a beneficial impact on their glucose metabolism, inducing a significant reduction in insulin resistance levels in most trial participants.

Dr. Pierce recruited 40 people—all with early warning signs of future metabolic diseases such as type 2 diabetes—to take part in the two-year clinical trial. The findings are published in the journal *Nature Communications*.

"Participants were inoculated with either 20 or 40 infectious larvae of the human hookworm species Necator americanus or a placebo," said Dr. Pierce.

"Metabolic diseases are characterized by inflammatory immune responses and previous studies have suggested that hookworms release proteins into their host to control the immune system and safeguard their survival," said Dr. Pierce.

Successful efforts to eradicate parasitic worms in developed countries are now linked to increases in human inflammatory and metabolic diseases, including type 2 diabetes.

Dr. Pierce said all participants in the JCU trial received regular clinical

health checks for safety purposes.

"All trial participants had risk factors for developing cardiovascular disease and Type 2 diabetes. The trial delivered some considerable metabolic benefits to the hookworm-treated recipients, particularly those infected with 20 larvae," said Dr. Pierce.

She said it was striking that participants infected with 20 hookworms experienced a median Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) level drop from a pre-trial level of 3.0 units to just 1.8 units within 12 months, restoring their level of insulin resistance to a normal, healthy range.

Worm recipients tended to report feeling better, mood-wise, than those in the placebo group.

"That was an interesting observation as well, given that much of the trial took place during the first waves of the COVID-19 pandemic. I think to see any improvement in mood was remarkable in itself," said Dr. Pierce.

After two years, participants were offered a deworming medication or could elect to stay in the trial for a further 12 months. All but one of the infected participants decided to keep their worms.

Dr. Pierce's Ph.D. supervisor, AITHM Senior Research Fellow and immunologist Dr. Paul Giacomin, said the trial results warranted follow-up studies on a larger scale.

"This early-phase JCU clinical trial provides proof of concept that infection with live hookworms is safe and appears to lead to some improvements in people's metabolic health, which will hopefully be confirmed by larger clinical trials in future.

"Also, if we can learn more about what hookworms release into the body to influence metabolism we may be able to design protein-based treatments that mimic the effect of the live worm," said Dr. Giacomin.

More information: Doris R. Pierce et al, Effect of experimental hookworm infection on insulin resistance in people at risk of type 2 diabetes, *Nature Communications* (2023). DOI: 10.1038/s41467-023-40263-4

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