

Timing is everything when it comes to weight loss, research shows

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Joint research between the University of Michigan and the Argentina-based National Council of Science and Technology (CONICET) has shed light on one of the most frustrating mysteries of weight loss – why the weight inevitably comes back.

A novel animal model showed that the longer mice remained overweight, the more "irreversible" obesity became, according to the new study that appeared online ahead of print Oct.24 in the [Journal of Clinical Investigation](#).

Over time, the static, obese state of the mice reset the "normal," body weight set point to become permanently elevated, despite dieting that initially worked to shed pounds, authors say.

"Our model demonstrates that obesity is in part a self-perpetuating disorder and the results further emphasize the importance of early intervention in childhood to try to prevent the condition whose effects can last a lifetime," says senior author Malcolm J. Low, M.D., Ph.D., professor of molecular and integrative physiology and internal medicine.

"Our new animal model will be useful in pinpointing the reasons why most adults find it exceedingly difficult to maintain meaningful [weight loss](#) from dieting and exercise alone."

The lead author of the study was Viviana F. Bumashny, M.D., assistant investigator of CONICET.

Obesity affects more than 500 million adults and 43 million children younger than age 5, while related illnesses are the leading preventable cause of death. Individuals who are overweight have a much higher risk of [type 2 diabetes](#), hypertension, and cardiovascular diseases.

One of the major strengths of the research was a new model of obesity-programmed mice that allowed weight loss success to be tracked at different stages and ages by flipping a [genetic switch](#) that controls hunger.

Turning on the switch right after weaning prevented the mice from [overeating](#) and ever becoming obese. Similarly, mice that remained at a healthy weight into young adulthood by strict dieting alone were able to maintain normal weight without dieting after turning on the switch. However, chronically overfed mice with the earliest onset of obesity never completely returned to normal weight after flipping the switch, despite marked reduction in food intake and increased activity.

The new findings may raise questions about the long-term success rate of severe calorie restriction and strenuous exercise used later in life to lose weight, such as the extreme regimens seen in the popular reality television show "Biggest Loser."

"Somewhere along the way, if obesity is allowed to continue, the body appears to flip a switch that re-programs to a heavier set weight," Low says. "The exact mechanisms that cause this shift are still unknown and require much further study that will help us better understand why the regaining of weight seems almost unavoidable."

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