

Perhaps a longer lifespan, certainly a longer 'health span'

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Organisms from yeast to rodents to humans all benefit from cutting calories. In less complex organisms, restricting calories can double or even triple lifespan. It's not yet clear just how much longer calorie restriction might help humans live, but those who practice the strict diet hope to survive past 100 years old.

In a review article in the April 16 edition of *Science*, nutrition and longevity researchers at Washington University School of Medicine in St. Louis, University College in London and the Andrus Gerontology Center at the University of Southern California, report that calorie restriction influences the same handful of [molecular pathways](#) related to aging in all the animals that have been studied.

Aware of the profound influence of calorie restriction on animals, some people have cut their [calorie intake](#) by 25 percent or more in hopes of lengthening lifespan. But first author Luigi Fontana, MD, PhD, is less interested in calorie restriction for longer life than in its ability to promote good health throughout life.

"The focus of my research is not really to extend lifespan to 120 or 130 years," says Fontana, research associate professor of medicine at Washington University and an investigator at the Istituto Superiore di Sanità in Rome, Italy. "Right now, the average lifespan in Western countries is about 80, but there are too many people who are only healthy until about age 50. We want to use the discoveries about calorie restriction and other related genetic or pharmacological interventions to

close that 30-year gap between lifespan and 'healthspan.' However, by extending healthy lifespan, average lifespan also could increase up to 100 years of age."

Fontana and his co-authors write about how cutting calorie intake between 10 percent and 50 percent decreases the activity of pathways involving insulin-like growth factor (IGF-1), glucose and TOR (target of [rapamycin](#)), and considerably increases lifespan in animals. Genetic mutations involved in those pathways have the same effect. Those animals have far fewer problems with diseases related to aging, such as cancer, cardiovascular disease and cognitive problems.

"About 30 percent of the animals on calorie restriction die at an advanced age without any diseases normally related to aging," Fontana says. "In contrast, among animals on a standard diet, the great majority (94 percent) develop and die of one or more chronic diseases such as cancer or heart disease. In 30 percent to 50 percent of the animals on calorie restriction, or with [genetic mutations](#) in these aging-related pathways, healthspan is equal to lifespan. They eventually die, but they don't get sick."

Unfortunately, many humans are moving in the opposite direction. As obesity reaches epidemic rates in Western countries, Fontana says rather than closing the 30-year gap between healthspan and lifespan, the gap is likely to grow. It's even possible [lifespan](#) may decrease as people develop preventable diseases such as atherosclerosis, type 2 diabetes and certain forms of cancer.

Those growing rates of obesity are a reason some scientists think calorie restriction will never catch on, regardless of its potential benefits. But, Fontana says, if researchers who study nutrition and aging can understand how calorie restriction lengthens life and makes people healthier, it may be possible to develop less drastic interventions or

medicines that influence pathways affected by calorie restriction and help keep people healthy as they get older.

Among people now practicing calorie restriction, he says side effects include reduced libido because calorie restriction reduces testosterone levels. They also tend to become cold more quickly because their thermal regulation changes as their metabolism slows and their core body temperature drops.

Fontana says as [calorie restriction](#) research advances on many fronts, it's becoming clear that dietary advice once based on epidemiological data now makes sense from a molecular point of view. In the past, dietitians might recommend more fruits and vegetables or less meat and more whole grains. They based that advice on studies showing people who ate more vegetables or fewer animal products tended to have less cardiovascular disease.

"Now we have moved from epidemiology to molecular biology," he says. "We know that certain nutrients, as well as lower calorie intake, can influence IGF-1 and other pathways. Soon we hope to be able to use that knowledge to help people live longer and healthier lives.

More information: Fontana L, Partridge L, Longo VD. Extending healthy life span — from yeast to humans, *Science*, vol. 328 (5976) April 16, 2010. Manuscript Number: Science.1172539

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