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Low-calorie diet may not prolong life: study (Update)

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Scientists have found that calorie restriction—a diet comprised of approximately 30 percent fewer calories but with the same nutrients of a standard diet—does not extend years of life or reduce age-related deaths in a 23-year study of rhesus monkeys. However, calorie restriction did extend certain aspects of health. The research, conducted by scientists at the National Institute on Aging (NIA) at the National Institutes of Health, is reported in the August 29, 2012 online issue of *Nature*.

Calorie restriction research has a long history. The first finding came in the 1930s, when investigators observed laboratory rats and mice lived up to 40 percent longer when fed a calorie-restricted diet. Subsequent research has cited calorie restriction as extending lifespan of yeast, worms, flies and some strains of mice. But other studies have not shown a longevity benefit. For example, in studies of certain strains of mice, calorie restriction on average had no effect on lifespan. Some of these mice actually had a shorter lifespan when given a calorie-restricted diet. To date, research does not provide evidence that calorie restriction is an appropriate age regulator in humans, the NIA investigators point out. Currently, limited human studies are under way to test the effectiveness and safety of calorie restriction in people.

The survival results in the study reported today by NIA researchers differ from those published in 2009 by NIA-supported investigators at the University of Wisconsin-Madison. The Wisconsin study followed two groups of rhesus monkeys for 20 years and found that monkeys on a calorie-restricted diet lived longer than those on a standard diet.

Beyond longevity, the parallel NIA and Wisconsin studies have reported similar beneficial health effects of calorie-restriction. Both studies found that certain age-related diseases—including diabetes, arthritis, diverticulosis and cardiovascular problems—occurred at an earlier age in monkeys on the standard diet compared to those on calorie restriction. However, this observation was not statistically significant in the NIA study. NIA researchers did find that monkeys started on calorie restriction at an early age had a statistically significant reduction in cancer incidence.

NIA researchers also found that while calorie restriction had a beneficial effect on several measures of metabolic health and function in monkeys who were started on the special diet regimen during old age (at 16 to 23 years), it did not have the same positive outcome for monkeys started on calorie restriction at a young age (less than 14 years). In the Wisconsin study, all the monkeys were 7 to 14 years when started on calorie restriction.

"These results suggest the complexity of how calorie restriction may work in the body," said NIA Director Richard J. Hodes, M.D. "Calorie restriction's effects likely depend on a variety of factors, including environment, nutritional components and genetics."

Differences in the monkeys' meal and other nutritional factors were cited as possible explanations for NIA's and Wisconsin's different outcomes. Both studies used a similar percentage of calorie restriction with their intervention groups; however, the Wisconsin monkeys in both the calorie restricted and control groups were eating more and weighed more than the matched NIA monkeys.

NIA's food had a natural ingredient base, while Wisconsin opted for a purified diet. Purified diets generally lack trace dietary chemicals and minerals that could affect an animal's health. Each ingredient of a

purified diet provides a specific nutrient and minerals or vitamins must be added separately. Natural-ingredient diets have risk of variation between batches, but are considered by some to be more complete than purified diets. NIA and Wisconsin also used different sources for proteins, fat and carbohydrates, as well as different approaches to vitamin and mineral supplementation.

"There is no right or wrong nutritional approach to calorie restriction, but the differences should be considered as we try to understand the dissimilar effects of calorie restriction between the two studies," said first author Julie A. Mattison, Ph.D., facility head of NIA's Nonhuman Primate Studies Unit, part of the Laboratory of Experimental Gerontology.

NIA researchers cited genetics as another possible reason for their differing results. NIA monkeys had a greater genetic diversity, originating from China and India. Wisconsin's monkeys came only from an Indian colony.

"We've learned more by having two concurrent and independent studies of calorie restriction in monkeys than would have been possible by just the NIA or Wisconsin study alone. While the two studies share many of the same findings, the differences will be particularly important for helping us better understand this aging intervention," said Felipe Sierra, Ph.D., director of NIA's Division of Aging Biology.

As scientists measure the possible outcomes of calorie restriction, research is also focusing on finding the mechanisms and pathways by which calorie restriction may influence longevity and the risk of age-associated disease. "My laboratory and other researchers are looking at calorie restriction's effects on cell metabolism, gene expression, insulin signaling pathways and other basic biological processes to pinpoint how reducing calorie intake may attenuate the negative consequences of

aging. We are looking at whether compounds can mimic the effects of calorie restriction via these mechanisms," said senior author, Rafael de Cabo, Ph.D., chief of the Mechanisms and Interventions of Aging section of NIA's Laboratory of Experimental Gerontology.

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