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THE FOOD ISSUE

## The Calorie-Restriction Experiment

By JON GERTNER

AS AMERICANS become fatter and fatter — a study published in July revealed that obesity rates increased in 23 states last year and declined in none — a select group of men and women under the watchful care of medical professionals have spent the past few years becoming thinner and thinner. There are 132 of them, located in and around Boston, St. Louis and Baton Rouge, La. All are enrolled in a large clinical trial that is financed by the [National Institutes of Health](#) and known as Calerie, which stands for Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy. A few years ago, researchers at [Washington University](#) in St. Louis, [Tufts](#) in Boston and the Pennington Biomedical Research Center in Baton Rouge began recruiting subjects to examine what happens to people who reduce their daily calories by 25 percent for two years. Admissions are rolling, so not all recruits begin and end at the same time. A few of the early participants, in fact, have just completed their two-year stint. The final recruits began their regimens last month.

In late summer, in St. Louis and Boston, I met with nearly two dozen subjects in the study. At the Washington University medical complex, Doug Hansen was reclining on his hospital bed one afternoon when I walked in to say hello. Hansen, who is 45 and had been in the Calerie study for six months, seemed the picture of good health: tan, tall, friendly, energetic. Maybe a little thin. "Let me pull up some chairs," he said, and he jumped out of bed. He was dressed in jeans that struck me as noticeably baggy. His T-shirt hung loosely on his frame. After checking in 24 hours earlier, Hansen told me, he went through a battery of tests, which were required of participants at the half-year mark. Some of these were cognitive: interviews and questionnaires, administered by a behavioral researcher, that evaluated his memory and

perceptions. Others were mildly invasive. His blood was drawn repeatedly, and his bone-mineral density was measured by scanning equipment that utilized low-levels of radiation. Early that morning, his resting-metabolic rate was calculated by medical technicians who asked him to remain motionless on his bed for 45 minutes as they put a ventilated plastic tent over his head and measured his respiratory output. Also that morning, Hansen swallowed a pink capsule that was slowly passing through his digestive tract. As we spoke, the pill was measuring his core internal temperature and transmitting the information via radio signal to a small, boxlike receiver strapped to his belt. "I've got to wear it until 5 p.m.," he said. Then he shrugged. "It's really not a big deal."

At the start, the recruits taking part in what is called calorie restriction were told they would likely see their weight decrease by around 15 percent during the first year. (A smaller number of recruits were put in a control group and instructed to continue their normal eating habits for two years.) After their weight drop, they would plateau at a "weight stability" level. This was Hansen's experience, as well as that of most of the Calerie subjects I met. After six months in the study, Hansen told me, he dropped to 168 pounds from 198, or near his plateau.

A curious aspect of the Calerie project, though, is that it is not meant to study weight loss or if one type of diet is better than another. Instead, Calerie is investigating how (and if) a spartan diet affects the aging process and its associated diseases. To the Calerie researchers, these are quite distinct. The aging process, which researchers sometimes call "primary" or "intrinsic" aging, refers to the damage that ordinarily accumulates in our cells as we grow older, a natural condition that seems to have limited the maximal lifespan of humans to 120 years. Diseases that accompany the aging process — often called "secondary aging" — are those afflictions increasingly prevalent in the elderly, like cancer, diabetes and cardiovascular disease.

There seems little doubt that calorie restriction can have significant effects on secondary aging. A recent spate of papers in some of the world's leading medical journals demonstrate that in small studies, human subjects following such diets experience astounding drops in cardiovascular risk factors; a

forthcoming review on cancer risks in animals with such diets, moreover, suggests a stark correlation — fewer calories mean fewer tumors. This explains why the stakes for Calerie are high. Essentially, the study asks whether calorie restriction allows people to grow older in better health — with less disease, fewer drugs and shorter hospital stays — through a method that neither medicine nor scientific technology have yet come close to approximating. Meanwhile, the experiment aims to shed some light on the more complex and still-unsettled question of whether calorie restriction affects primary aging, and thus longevity, in humans. Going back more than a half century to an experiment at [Cornell University](#) in the mid-1930s, calorie restriction has been shown again and again to extend the lives of mice, rats and other animals. An ongoing experiment at the [University of Wisconsin](#) on rhesus monkeys, which began in 1989, portends similar results: compared with normal-weight primates on a regular calorie regimen, the monkeys on restricted diets are healthier and more vigorous and seem destined (at least at the moment) for a longer life.

A clinical trial that follows human subjects through their entire lives, much as the primate study in Wisconsin does, would be impossible. For one thing, it would be ethically problematic to restrict calories in children (though with animals, the earlier that calorie restriction begins, the longer they live). For another, we already live a long time now, thanks to advances in medicine, surgery and public health, so “if you wanted to do longitudinal studies in humans, it would take 125 years,” Eric Ravussin, who leads the team doing the Calerie experiment at Pennington in Baton Rouge, told me. Thus the researchers in the two-year study are instead looking at changes in what they call biomarkers. A decline in Doug Hansen’s core internal temperature, for instance, would suggest a slowdown in his primary aging process (data from a respected study on aging shows individuals with lower temperatures generally live longer). Other characteristics related to secondary aging are just as important. As Hansen curtails his calories for the next 18 months, doctors and medical technicians will measure, among other variables, inflammation, insulin levels and blood pressure. Reductions in any of these things would indicate a lessened vulnerability to heart disease and diabetes.

Another problem humans present is their susceptibility to temptation. Primates and mice are kept in cages and eat what they are fed; none have ever had to choose to forswear a spring roll or a cupcake. The medical literature on calorie restriction sometimes cites an experiment conducted in Minnesota in the 1940s to study the effects of starvation, especially with the war-torn populations of Europe in mind. The men — all lean to begin with, all volunteers (they were conscientious objectors to World War II) — were subjected to about a 40 percent decrease in caloric consumption. The state of near starvation led a few of the subjects to the threshold of insanity. They became irritable and depressed; some began to lie and cheat; at least one engaged in acts of self-mutilation. Some of the potential insights of the Calerie study, therefore, are psychological as much as physiological. If ordinary Americans want to cut their energy intake by a more modest 25 percent — whether to slow down the aging process or seek a pharmaceutical-free way to reduce the risks of, say, cardiovascular disease — can they actually do it? The feasibility of long-term food reduction has never been adequately investigated. “Here there are really three things we want to know,” Susan Roberts, a professor of nutrition and psychiatry who is in charge of the Calerie team at Tufts, told me. “The first is, can we really implement human [caloric restriction](#)? The second is, can we really implement it in a way that doesn’t neglect the biology? People can’t walk around hungry, so is hunger a necessary part of the biology of calorie restriction? The third is, are there unacceptable side effects that you wouldn’t pick up in animals that you would pick up in humans?” Roberts went on to say: “And if we found that caloric restriction was healthy and everyone can do it? The goal of the trial is to see if this is ready for prime time.”

THERE’S A JOKE that says calorie restriction may or may not extend your life, but it will most assuredly make your life feel longer. At least in theory, you must accept endless days of grinding asceticism. Starbucks ventis without a breakfast scone (460 calories). Sandwiches without Swiss (106), mayo (57) or potato chips (155). Coffee breaks without a cookie (130). Work parties and weddings that, limited to just a single glass of cabernet (127), become tedious affairs. Some aspects of calorie-deprivation diets may sound familiar because of the Calorie Restriction Society, a group of several hundred men and women who have acquired a degree of notoriety by harshly curtailing their food

consumption. For self-starters, there are now books about calorie-restriction methodology like "The C.R. Way," which favors recipes like Caraway Cabbage. (To prepare, boil for 6-10 minutes one head red cabbage, two tablespoons caraway seeds, one bay leaf; strain; serve.) On a recent "60 Minutes" segment about a group of calorie-restricting Argonauts, a dinner party began with hors d'oeuvres of flour-free bread smeared with baby food.

For the subjects in the Calerie experiment, there was little about their diets that seemed freakish. They ate normal foods, hosted dinner parties for friends and generally went about their lives normally. The subjects do not represent a cross section of American society, however. Whereas 66 percent of Americans are currently classified as overweight or obese, no one allowed into the study was seriously overweight by medical definitions: everyone began the experiment with a body-mass index that fell within a normal to slightly overweight range of 22 to 28. There were scientific reasons for this. The effects of calorie restriction may simply be an evolutionary legacy, "a metabolic, hormonal and molecular adaptation" to a world of sparse resources, as Luigi Fontana, one doctor in charge of the Washington University trial who also holds a position at the National Institute of Health in Italy, described it to me. By slowing aging and increasing resistance to disease during periods of food scarcity, the adaptive responses to fewer calories increased the odds that animals and humans that lived short lives might survive until they could reproduce. In laboratory settings, calorie restriction seems to "work" — that is, it seems to influence primary and secondary aging — when the diet of an animal of normal weight is curtailed by a significant percentage. The degree of calorie restriction can't exceed 50 percent, which is when laboratory animals begin to die. Until that point, however, the more severe the calorie-restriction regimen, the greater the health benefit — a lifespan 50 percent again as long in studies on mice and rats. These results might not apply to the overweight. As Fontana told me, moving a heavysset person's body-mass index from, say, 35 to 29 might increase his longevity by reducing the risk for diseases like diabetes. Yet it is not "triggering the anti-aging pathways" that have been observed at the cellular and molecular levels in animals of normal weight when placed on a calorie-restricted diet.

And why set the restriction at 25 percent? Why not 20 percent? Or 30 percent? Or why not reduce calorie intake by 10 percent and increase exercise (and calories burned) by 15 percent, so that a subject's calorie deficit still equals about 25 percent? All were viable options. But the study's architects determined that 25 percent was both humanly feasible and, based on data from previous experiments, could have noticeable effects on the rate and diseases of aging. It is possible, meanwhile, that a sustained decrease in calories coupled with a sustained increase in exercise might have a potent effect on aging (at the moment there are no large-scale studies under way, Fontana told me). Such a combination, however, could complicate efforts to understand, in isolation, the effects of calorie restriction on humans.

The researchers in Boston, Baton Rouge and St. Louis screened the Calerie recruits in ways other than body-mass index. They looked for subjects who were motivated and highly organized — desirable traits if you have to keep a journal record for two years of every morsel of food you eat. They sought people who had strong moral support at home. They ruled out anyone who counselors surmised might have a predisposition toward anorexia or bulimia — disorders that might conceivably be triggered by the new diet. They also wanted participants who had stable jobs without too much travel, yet were flexible enough to allow them to visit the hospital centers weekly for weigh-ins, counseling and medical tests. All the subjects are being paid: \$5,000 at Tufts and Pennington, \$2,400 at Washington University. But screeners rejected those who said they were attracted to the study for the money — an unnecessary precaution, perhaps, given that enrollment in Calerie is effectively an arduous part-time job that pays third-world wages. “I figured out that \$5,000 for two years for the 70 times I have to come in here worked out to a dollar an hour,” Tom Jacobs, a participant at Tufts, told me.

Getting someone started on a calorie-restriction diet is far more involved than it might first appear. For the past seven years, Fontana has been collecting data on about 50 members of the Calorie Restriction Society; Fontana estimates that these men and women have cut their calories by 25 to 30 percent. Yet this can't be said with precision or authority. Nor is it clear what their prediet biomarkers or vital signs were. At the start of the Calerie experiment, a first order of business was to rigorously determine how many

calories each recruit ate and burned on a typical day. This required a methodical (and expensive) two-week laboratory test: participants drank water containing rare isotopes that, when excreted and analyzed, allowed researchers to discern a subject's carbon-dioxide production (and his or her calorie burn) to a precise degree. After that, each subject received an individualized target. Most of the subjects I spoke with called this the Number. At the start, researchers determined that Doug Hansen burns (and thus ingests) what he told me was around 2,600 calories a day. So he was put on a diet of 1,950 calories. Jeffrey Peipert, an Ob-Gyn who is nine months into the study in St. Louis, was found to burn 3,300 a day — and thus given a number of just under 2,500. Many of the women, meanwhile, required far fewer calories. Liz Ewen, a molecular biologist who is 18 months into the Tufts study, told me her number was 1,670 calories, down from 2,226. It seemed a common experience that no one had any idea before the study began what his or her caloric requirements were. "My wife and I both took a guess and we both got it wrong," Peipert told me.

At the start, the subjects were informed that although they would receive help with menus and recipes from the study's dieticians, they would be responsible for buying and cooking all their own meals for the next two years. For each participant's first 28 days, however, all meals and snacks are free, custom cooked (based on each individual's calorie requirements) and packaged in large coolers to be picked up every few days and taken home. "That way we can be sure the subjects are getting the exact dietary prescription while they're learning how to do it," Morgan Schram, the study manager in St. Louis, told me. The great challenge, at least for that first month, is to create food for the subjects that is simultaneously satiating, appealing and — most crucially — low in calories. At both Tufts and Washington University, meals for new participants are prepared in facilities that resemble laboratory-kitchen hybrids. The food is not particularly exotic: Mediterranean-style combinations of fish with Greek-style potatoes, for instance, or sweet-and-sour chicken with rice. Whether the meals are bad or good is somewhat beside the point. The meals are precise. When I visited the kitchen in St. Louis, a nutritionist was cooking and weighing, to a tenth of a gram, each ingredient of a dish of farfalle with pesto and diced chicken. Most of the recipes seem to steer participants toward foods that are nutrient-rich but low in calories, or what dieticians refer

to as “low in energy density.” A number of recent experiments — notably by Barbara Rolls at [Penn State](#) — demonstrated that humans tend to eat a consistent weight of food from day to day, but not necessarily a consistent number of calories. For the Calerie study, this has proved a useful tool in the defense against hunger. By building a diet around foods with a low-energy density, especially vegetables, fruits and soups, participants can conceivably ingest the same weight of food as they might on a regular diet while taking in fewer calories.

Apples are superb in this regard. At the medical centers running Calerie, you see a lot of people walking around eating apples. Even subjects who disliked apples have discovered that calorie restriction, which generally has the effect of making food taste better, has given them a surprising desire for the fruit. By contrast, alcohol — many calories, not much nutrition — isn’t much use at all. But it isn’t expressly forbidden. If you wish, you can indulge in drinking or in energy-dense foods (nuts or sweets, for instance), but probably not both nor in excess in either case. “I enjoy a regular glass of wine or drink at the end of the day,” Peipert said. “But I think what I’ve learned on this diet is that I enjoy food more. I’d rather have a Häagen-Dazs bar at 190 calories than a gin and tonic at night at 170.”

Subjects willing to re-engineer their eating habits appear to have an easier time on the diet. When I asked Susan Roberts, who runs the Tufts study, if there was a danger in Americans trying calorie restriction on their own, without a dedicated team of medical experts offering advice, she suggested that there are built-in safety mechanisms. Roberts said she didn’t think anyone would be successful by reducing portion size. “If you don’t change your diet to a high-satiety diet, you will be hungry, and you will fail,” she told me. A high-satiety diet, she said, was bound to be a healthful diet with a lot of vegetables, fruits and insoluble fiber — the kind found in some breakfast cereals, like Fiber One — that her research indicates has a unique effect in helping calorie-restriction subjects feel fuller, probably because they activate certain receptors in the lower intestine. Roberts added, “If people are doing this on their own and succeeding, well, I’d be surprised if they’re eating a lot of Hostess Twinkies.”

ONE MORNING in St. Louis, I watched as Peipert, at Week 33, met with his counseling team: a behavioral therapist, Cherie Massmann, and a dietician, Kathleen Obert. "Let's take a look at your weight loss," Obert said, looking at a chart that showed a downward-curving line that was beginning to level off. Peipert began at 174 pounds and had just hit 151; by Week 52, the chart projected he would plateau at 147 pounds, which ideally he would maintain for a full year. Apparently he was a model subject, losing weight right on schedule, just as the research team hoped he would.

In general, the complaints I heard from subjects in Calerie had less to do with raging hunger — most told me they felt hungry for the first few weeks and then acclimated to their diets — than the logistical demands of calorie restriction itself. They were tired of conflating meals and mathematics; they looked forward to a day when they wouldn't need to check the caloric content of every course (usually on a Web site called [calorieking.com](http://calorieking.com)) and record it for the researchers. In his counseling session, however, Peipert told Obert and Massmann that he was struggling with hunger. It was real hunger, the kind that woke him from his sleep. Sometimes he couldn't get through the night unless he went downstairs and had a bowl of cereal.

Massmann asked Peipert to tell them about his daily activities. Peipert happens to have a relatively high calorie prescription, and his diet the day before was surprisingly indulgent. There was no red cabbage or strained peas. Among other things, he consumed two granola bars, a caramel Frappuccino, a bowl of soup, a tuna sandwich and pasta from Pizzeria Uno. While golfing, he also ate a sausage-and-egg sandwich from Burger King.

Massmann asked Peipert about his physical activities. He paused to think for a moment. It had been his day off from work. There were the 18 holes of golf. He biked eight miles to and from his job at the hospital, he told them, because he had to pick something up at the office. He cut the grass in his yard, which was about an acre in size. He and his son spent more than an hour ripping out tree roots. And after dinner he and his wife took a 40-minute walk around the neighborhood. The silence in the room was amusing. Obviously, the day before, Peipert was a calorie-incinerating machine. Massmann gently suggested that perhaps this was why he was hungry. "But it was a beautiful

day," Peipert argued. Massmann nodded and then waited a beat before saying, "But maybe — maybe — you could just try to turn the daytime activities down a notch?"

The session ended in a stalemate. Afterward, Peipert told me he didn't think he would cut down on the exercise. Suffering through a bout or two of hunger was a fair trade-off for doing what he liked on a sunny afternoon. And in any case, he told me, he remained enthusiastic about the study. "My blood pressure when I started was at 130 over 80, and now I think I'm 110 or 115 over 54." He hadn't been at this weight since high school. Other than the nighttime pangs, he did not find the trial nearly as difficult as he imagined. He was eating a lot of apples, he noted — indeed, he was eating one as we spoke.

THE MAJORITY OF subjects in Calerie have so far succeeded in achieving their weight-loss goals. The ones I spoke with seemed to think the most effective tool for sticking with the diet is simply the study's accountability factor: they not only have to produce their food diary each week; they also have to be weighed in. Moreover, once or twice a week they attend individual counseling sessions, like Peipert's, as well as group counseling sessions in which they talk with their fellow dieters about strategies like how to separate food from special events and celebrations. They're also encouraged to "bank" calories if they know they will have a day of excess in the future. "If I'm going to the ballgame on the weekend, I know I'm going to have a bratwurst," Doug Hansen told me. So he eats 100 fewer calories on the days leading up to the game.

People like Hansen and Peipert almost make it sound easy. The question is how many other Americans could do the same. To put it to the medical doctors overseeing the study — could this ever be prescribed to a larger population, either as a preventive tool or a treatment? — is to walk into a wall of skepticism. "Ninety-nine percent can't do it," John Holloszy, a medical doctor who is the lead investigator at Washington University, told me. "The people in the study are not going to stick with it" after they leave. Other medical doctors involved with Calerie told me they were also dubious, believing that a low-calorie regimen requires too much in the way of individual effort and too much in the way of medical resources and counseling to make it practical for

many Americans. When I spoke with Robert Krikorian, a longtime Calorie Restriction Society member who is not in the Calerie study but who happens to be a neuropsychologist, he pointed me to some behavioral studies that showed how inattentive we are in regard to what we ingest on any given day. “I don’t think humans are designed to pay attention to how much they eat,” he said, adding that for most people this natural tendency would chafe against the organizational requirements of calorie restriction, thus limiting its appeal.

Some professors of nutrition and psychology who are involved in Calerie were more optimistic. Most seemed surprised as well as encouraged by the high level of compliance among the subjects. And all of the subjects I spoke with told me they intended to continue with calorie restriction after they were finished. “I think that this can be just as successful as Weight Watchers,” Liz Ewen said — not for everyone, she added, but arguably suitable for larger numbers if there were an infrastructure of online tools, group meetings and dieticians to aid in the process. “It’s really not much more than embarking on a diet that teaches you how to eat normal foods but make better choices.”

Still, a not insignificant number of subjects in the study have struggled to achieve their weight-loss targets. For them, the Calerie team sometimes suggests they go back on the hospital-kitchen meal plan for nine days, so their caloric intake can get back on track. Meanwhile, a few stragglers in the study have not even made it that far. A few have left because of pregnancies and job transfers; a few have been asked to stop because tests showed they were suffering from anemia or because their bone-mineral loss (a known danger of calorie restriction) was becoming substantial. Another negative side effect that subjects share is feeling chilled. This isn’t dangerous — these people are, after all, burning less energy. Counselors tell them to put on a sweater.

I asked Holloszy why he thought some members of the Calorie Restriction Society succeeded for years with a restriction diet. “Fear of death,” he said. The flip side of that, of course, would be love of life, which seemed closer to the sentiments of the Calerie subjects I met. A number of them joined the study not out of a desire for superlongevity, but because they had young children and wanted to maintain their own health as long as they could. In the meantime, they encountered some pleasant surprises. When I sat in on a

group counseling session one day in St. Louis, a participant, Brad Beggs, told the group that he had finally decided to buy new clothes, because his old ones no longer fit. Everyone in Calerie reaches this question at some point: is my lower weight a new normal or just a temporary state? "I've never gotten so much pleasure in my life," Beggs told the group, adding that it only confirmed his resolve. "I'm wearing a medium shirt now. I haven't worn a medium since high school." Mediums are always on sale, he added, which was in fact his point. "It's the stuff nobody in America buys anymore."

IT MAY TURN OUT that the medical doctors are right and the trial subjects are wrong. Calorie restriction — or simply living a life of less in a culture of more — is extremely difficult to achieve and even more difficult to maintain. Americans' seemingly inexorable slide toward obesity tends to indicate as much: for the majority of us, the desire to eat can easily overwhelm personal willpower and (so far) any messages from public-health campaigns. At the same time, debates over the viability of calorie restriction might ultimately seem academic. Why spend time worrying over whether normal-weight subjects or slightly overweight subjects should lose weight, anyway? These are generally the healthiest of Americans. Perhaps the dollars would be better spent on cancer or heart research.

Of course, calorie research is now intimately related to all those other kinds of disease research. When I sat down with Holloszy and Fontana, the Calerie investigators at Washington University, they pointed out that Holloszy had conducted some of the pioneering experiments on exercise, health and weight. In a study on rats, he compared animals that were lean because of exercise with those that were equally lean from calorie restriction. "Both had an increase in average life span," Fontana said, but only calorie restriction was able to slow down aging and increase maximal life span. That suggested that "leanness" was not in and of itself determining the rate of aging. "Speaking of humans," Fontana added, "if you are lean because you are exercising, of course you are doing good, because you're preventing types of diabetes, some kinds of cardiovascular disease and maybe some types of cancers. But the data suggest that calorie restriction is more powerful. And the people on C.R. are more powerfully protected from diseases than the exercisers."

Fontana connected his point to his continuing observations of some Calorie Restriction Society members. "In terms of cardiovascular diseases — the No. 1 cause of death; 4 out of 10 people die of it in the U.S. and Europe — we know that they will not die of cardiovascular death," Fontana said. His subjects have cholesterol around 160, blood pressure around 100 over 60, high HDL, low triglycerides and very low levels of inflammation. "So these people won't develop these diseases," he said. "And I think that's an important finding. Because every day doctors are publishing hundreds of papers on circulation research and medications that are lowering blood pressure or cholesterol by a small bit. And here we have such a powerful intervention that is basically cleaning out the arteries." At Tufts, Susan Roberts, the lead investigator, echoed this position, saying that the study will probably have greater effects than the average clinical trial. "I don't know why anyone would take drugs when they could do something like this," Roberts said, referring to Calerie.

You could spin that around, however. Why should you do something like calorie restriction if you could take a pill that somehow reproduces its effects? Nothing of the kind exists at the moment. Yet the development of such a drug would almost certainly be an immense medical advance. Instead of trying to seek cures and treatments for the individual diseases of aging, it would conceivably address all of them in one grand application. The hope of some people involved in the Calerie study — Eric Ravussin, for instance, who heads the research team in Baton Rouge — is that a better understanding of the mechanisms of calorie restriction will hasten the development of a drug. This is why, in addition to taking measurements, the researchers are collecting blood, muscle and fat samples from the subjects. "If you find the mechanism, you can mimic the mechanism" is how Ravussin put it to me.

Fontana is doubtful. "My perception right now is the effects of calorie restriction are multiple," he said, "so I think it's highly difficult to find one, or two or three drugs that will mimic such a complex effect." And to say that in five years a cocktail of calorie-restriction mimetics will increase maximal lifespan? "I don't believe that," he said. Fontana also wasn't optimistic that a diet involving a 25 percent reduction in calories could find much traction in the general population. While he said a more modest caloric-reduction diet might enjoy some popularity, he believes the larger lesson to come out of his

research might be fairly simple, if perhaps a bit conventional: eating less is better than eating more, especially if it's a nutritious mix of whole grains, fruits, vegetables and the like. "The evidence is overwhelming now that it will improve your health and will improve your chances of living healthier and probably longer," he said.

In the meantime, this fall will be the first time that some of the Calerie subjects, their two-year regimen completed, will go out on their own — without weigh-ins, without counseling, without nutritionists at their beck and call. There are no immediate plans to continue collecting data on those who have finished the experiment — the N.I.H. budget did not provide financing for a follow-up study — yet the investigators told me they hope to check in with the subjects in the future to see how they fared. As it happened, I ran into several participants in St. Louis who were in the homestretch. None planned on an ice-cream binge. Instead, they told me, they would continue with their diets while looking forward to estimating, rather than counting, their calories. "I'll probably do that for a week or two," Josh McMichael told me. About a month later, in late September, I sent McMichael a note to see how he was faring. He gained eight pounds in the weeks after finishing, he said, but later shed most of that weight. "I tried the new massive burgers from Burger King," he said. "Twice. Wasn't worth the side effects."

Then he added: "I think I've gotten over things like that. For the most part."

Eating much, much less helped rats live longer. Will it work on humans?

*Jon Gertner, a contributing writer, last wrote about high-speed rail for the magazine.*