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## Survival in good health? Part I - Longevity and diet

**A low-calorie diet has been suggested to increase lifespan due to a decrease in oxidative stress. This article presents the rationale and impact of such an approach on longevity in humans.**

The number and proportion of elderly are increasing worldwide among almost all populations.<sup>1</sup> Nowadays, most persons over 65 years old are healthier, more active, and mentally better off compared with those of previous generations. Although the frail and disabled are only a small percentage of the total, due to the marked increase in elderly and old people, those with some functional deficits are likewise increasing in number.<sup>2</sup>

The greatest life expectancy at birth occurs in Japan and Sweden, with 77.1 years for Japanese men, and 84.0 years for Japanese women, and 77.1 years for Swedish men and 81.9 years for Swedish women. India and Ecuador, for example, have shorter life expectancy at birth with only 67.3 and 61.9 years for men, and 72.5 and 62.6 years for women. In Japan, Sweden, and Norway, more than 15% of the population is aged 65 and over, and more than 75% of men and 85% of women are in the seventies or older.<sup>3</sup>

Age-related losses are suggested to be slower prior to the age of 65 than beyond this age.<sup>4</sup> Self-reported difficulties in basic activities of living—eg, bathing, dressing, feeding, etc—were reported in 15% and 18% of US men and women aged 65 to 74 years. It rises to 20% and 31% among those aged 75 to 84 years, and to 40% and 53% at the age of 85 and older. The functional deficiencies are associated with risks for injury, disability, and death. With increasing age, decline in motor coordination, spatial perception, visual and auditory acuity, gait, muscle and bone strength, mobility, and sensory perception is likewise well documented. In addition, chronic degenerative diseases—such as coronary heart disease, heart failure, hypertension, diabetes etc—and their disabling sequels increase with age. Despite the inherent risks the proportion living alone increases with age from 24% at age 65 to 74, to 40% at age 75 to 84, and to 47% at  $\geq 85$  years.<sup>3</sup> It is, therefore, a scientific goal not only to find measures to prolong human life, but likewise to reduce and/or postpone chronic age-associated diseases.

In rodents and other short-lived species, it has been shown that caloric restriction increases life span. These antiaging effects were hypothetically explained by a reduced energy expenditure

and as a consequence of reduced production of reactive oxygen species (ROS). Calorie-restricted monkeys have lower body temperatures and insulin concentrations than controls; both parameters are surrogate biomarkers for longevity in rodents. The concentrations of dehydroepiandrosterone sulfate (DHEAS) are elevated, which is considered a marker for longevity in humans.<sup>4</sup>

Episodes of caloric restriction in humans were not uncommon in the past in all countries, and are still present in many parts of the world. However, the diets for these populations are generally lacking in protein and micronutrients. In a randomized controlled trial, the effects of 6 months of caloric restriction were studied in overweight, nonobese men and women (body mass index 25 to 30). The participants were randomized to four groups: I. control; II. caloric restriction (=25% restriction of baseline energy requirements); III. caloric restriction with exercise (=12.5% restriction plus 12.5% increase in exercise expenditure); IV. Very low caloric diet (890 kcal/d until 15% weight reduction is achieved, followed by a weight-maintenance diet). Weight changes after 4 months were as follows: Group I: -1%; group II: -10.4%, group III: -10.0%, and group IV: -13.9%. After 6 months, fasting insulin levels were significantly reduced in all intervention groups, whereas DHEAS and glucose levels were unchanged. Body temperature and DNA damage were reduced in the intervention groups, as was sedentary 24-hour energy expenditure, indicating metabolic adaptation.<sup>5</sup>

**According to these results in humans, with prolonged caloric restriction two biomarkers of longevity (fasting glucose levels and body temperature) are decreased. However, these are surrogate end points. In order to document an antiaging effect and an attenuation of chronic degenerative diseases in humans, studies of longer duration with high power would be required. However, such a diet would have low acceptance in the general population. Therefore, instead of such a diet, small molecules that safely mimic the beneficial effects of caloric restriction are now under investigation (see part II).**

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