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Calorie Restriction as a Risk Factor for Cardiovascular Disease in the Aged Population

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Abstract

Caloric restriction (CR), a dietary approach that reduces calorie intake without causing malnutrition, has been shown to delay aging and extend lifespan in animals like invertebrates and rodents. Since cardiovascular disease and stroke are leading causes of death in older adults, using CR to slow down atherosclerosis could potentially improve cardiovascular health and increase human longevity. This review explores whether caloric restriction impacts the risk of cardiovascular disease in the aged population. Studies on CR in humans, often focused on obese individuals undergoing short-term calorie reduction for weight loss, have revealed significant improvements in key cardiovascular risk factors. These include reductions in blood pressure (both systolic and diastolic), cholesterol, triglycerides, fasting glucose, and insulin levels. Interestingly, CR has shown similar benefits for non-obese individuals, improving systemic risk factors associated with atherosclerosis. In summary, evidence suggests that caloric restriction can promote better health and potentially extend lifespan by positively influencing cardiovascular risk factors. However, more research is needed to fully understand its long-term effects on cardiovascular health, especially in older adults who are at higher risk for heart disease.

Subject Areas

Cardiology

Keywords

Caloric Restriction, Cardiovascular Disease (CVD), Hypertension, Elderly Population, Diabetes Mellitus, Coronary Heart Disease, Blood Pressure

1. Introduction

Reducing the intake of average daily calories below average or habitual levels without malnourishment or vital loss of nutrients is known as calorie restriction. The only known method to significantly increase lifespan and health in the majority, if not all, living organisms is calorie restriction (CR), which is defined as the chronic reduction of total intake of calories without malnutrition combined with intermittent fasting (which can be thought of as a specific form of CR in which episodes of ad libitum feeding are alternated with episodes of up to zero caloric uptake) [1]. CR mandates that the diet be of good quality, meaning it should be abundant in micronutrients and fiber, and that it must supply enough energy for metabolic equilibrium even when energy intake is restricted [2]. It is a nutritional intervention that involves consuming fewer calories, yet in rodent and monkey models, it has been demonstrated to increase lifespan and health span when combined with proper nutrition. A growing body of research from observational studies and randomized clinical trials indicates that CR induces some of the same molecular adaptations and metabolic effects in humans that have been shown to delay the accumulation of molecular damage and improve health in animal models, thereby increasing longevity [3]. A study by [4] demonstrated that CR can restore some age-related alterations in people. A year's worth of research found that 24 months of continuous CR (15 - 25%) in healthy, non-obese individuals was safe, improved quality of life [5], and led to a 10% - 13% reduction in weight (mostly, but not solely, in fat mass reduction). The following parameters decreased during CR: oxidative stress, thyroid axis activity, resting energy expenditure, body temperature (which may indicate metabolic rate), and fasting insulin levels [6].

It has been shown that calorie restriction (CR) is a proven life-extension strategy that controls both aging and age-related disorders [7]. Numerous age-related ailments, such as cardiovascular disease, metabolic diseases, cancer, and other neurological disorders, can be avoided with CR [8]. The gold standard of aging intervention trials is CR due to its multifaceted effectiveness in preventing age-related illnesses and aging. While CR has been shown to have anti-aging benefits, the precise mechanisms by which it works to prevent aging remain unclear due to its several physiological functions.

2. Cardiovascular Disease (CVD)

Blood vessel illnesses and heart collectively are referred to as cardiovascular diseases or CVDs. The accumulation of fatty deposits on the inner walls of the blood arteries supplying the heart and brain is the most frequent cause of this [9]. Hypertension,

cerebrovascular illness, (stroke) ischemic heart disease, congenital heart disease, rheumatic heart disease, heart failure, valvular heart disease, and peripheral vascular disease are the most prevalent forms of cardiovascular disease (CVD) [10].

Globally, cardiovascular diseases (CVDs) are the leading cause of death; more people pass away from CVDs each year than from any other cause. WHO research estimates that 17.3 million fatalities worldwide in 2008 were related to CVDs, accounting for 30% of all deaths. By 2030, it is predicted that 23.6 million deaths worldwide will be related to CVDs, primarily stroke and heart disease. More than 75% of deaths from CVD occur in low- and middle-income nations. In 2019, non communicable illnesses accounted for 17 million premature fatalities (deaths under 70 years of age) of which 38% were attributable to CVDs. Cardiovascular disease (CVD) is the primary cause of death in the US, resulting in 35% of adult fatalities [11]. In the United States, CVD mortality is no longer improving, and improvements in life expectancy have slowed for certain groups, despite significant declines in CVD mortality in the late 20th century that were attributed to advancements in public health and health care [12]. As the disease is becoming more common in developing nations as well, the notion that CVD is exclusive to wealthy societies and a disease of affluence is out of date. In terms of NCD-related mortality, cancer ranks second (8.2 million), followed by diabetes mellitus (1.5 million) and respiratory diseases (4 million). Of all NCDs, CVDs cause the greatest number of deaths (17.5 million persons yearly). As over 80% of CVD deaths occur in LMICs, CVD burden remains disproportionately higher there than in high-income countries (HICs) [13]. Furthermore, compared to HICs, CVD affects working-age populations in LMICs far more frequently. For instance, at least ten years earlier than in HICs, 50% of cardiovascular fatalities in Sub-Saharan Africa occur in the 30 - 69 age range [14].

Overall, African Americans exhibit greater rates of severe and common hypertension as well as CVD (including myocardial infarction and stroke) than White people. In addition to having the highest incidence of heart failure without a prior clinical myocardial infarction, African Americans also have the greatest risk of developing heart failure (75%). In 2014, there were 137.5 deaths per 100,000 individuals from coronary heart disease in White males, 150.6 in African American men, 89.4 in African American women, and 72.1 in White women. Furthermore, 5 years after their initial MI, 16% of African American men, 11% of white males, 17% of white women, and a staggering 28% of African American women passed away at the age of 45 to 64 [15]. The prevalence and risks of CVD remain significantly different among African Americans compared to the general US population, with a 30% higher death rate and nearly twice the stroke mortality rate, according to a 2017 government report on healthcare inequalities [16]. **Figure 1** and **Figure 2** illustrate how various CVDs contribute to the burden of CVDs worldwide in both males and females [17].

It has also been shown that the prevalence of CVD, which includes the prevalence of stroke, myocardial infarction, and atherosclerosis, rises with age in both women and men. According to estimates from the World Health Organization

(WHO), lowering risk factors can lessen the increasing burden of CVD on patients and healthcare professionals, and over 75% of premature CVD is avoidable. Numerous risk factors, including hypertension, diabetes, and obesity, have been connected to the onset of CVD [18]. Elevated blood pressure, which causes 13% of all deaths globally, is the main cardiovascular risk factor. In priority order, it is followed by smoking (9%), high blood sugar (6%), not exercising (6%), being overweight (5%), and obesity (6%) (See **Figure 3**).

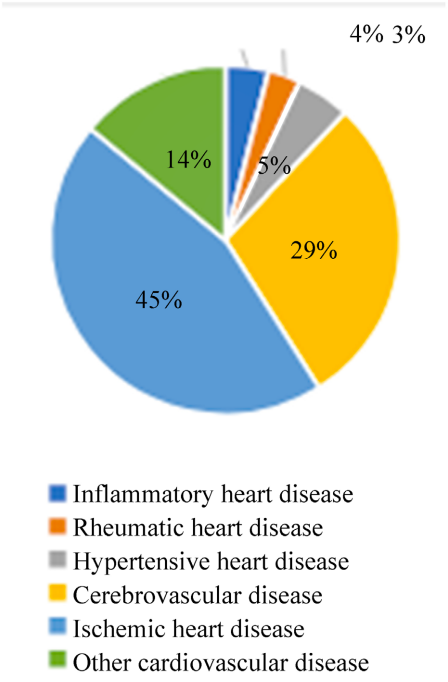

Figure 1. Prevalence of cardiovascular disease among males.

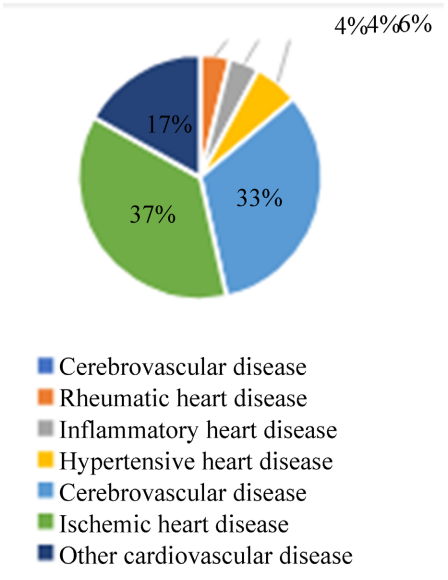

Figure 2. Prevalence of cardiovascular disease among females.

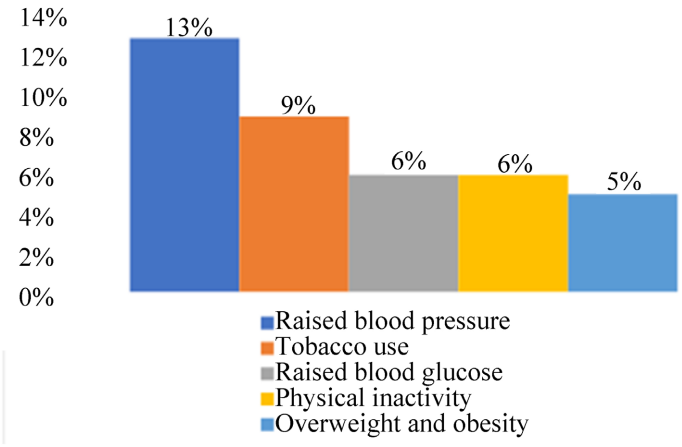

Figure 3. Prevalence of cardiovascular disease risk factors.

3. Hypertension

The most significant threat to African Americans' cardiovascular health is hypertension, which also presents the biggest possibility for disease prevention if properly treated and controlled. African American women (44%) and men (42.4%) who are 20 years of age or older have one of the highest rates of diagnosed and undiagnosed hypertension in the world, with low- to middle-income countries having the greatest rates of population prevalence (29% - 31%) [19]. There is a possibility that the hypertension development in older adults is connected to the vascular changes that accompany physiological aging. These changes result in structural and functional changes to the vascular walls, including increased arterial stiffness and decreased compliance) [20]. This argument is debatable because young patients with hypertension also exhibit the previously described alterations [21]. These aspects make it necessary or crucial to recognize and look into additional risk factors related to the aging process [22].

The US Centre for Disease Control and the American Association for Prevention and Health state that older adults who have comorbidities—such as Type 2 Diabetes Mellitus and obesity—as well as external predisposing factors—such as smoking, a sedentary lifestyle, diet, and stress—are more likely to develop other cardiovascular conditions in addition to hypertension [23]. More than 70% of older persons with kidney disease, aortic syndrome, heart failure, stroke, and acute MI frequently have hypertension [24]. The primary contributing cause to the development of ISH in the elderly is the aging-related increase in arterial wall stiffness brought on by atherosclerosis [25]. However, elderly people who receive excessive hypertension treatment may potentially experience severe complications. In older patients, aggressive BP lowering may be dangerous because of the possibility of target organ hypoperfusion. Hypotension has been linked to acute coronary heart syndrome, dizziness, falls, confusion, and unconsciousness.

4. Diabetes Mellitus

The combination of multiple risk factors, including nutritional, environmental,

and hereditary factors, results in diabetes mellitus, a chronic, silent, multifactorial disease. The World Health Organization (WHO) reported an incredible fourfold increase in the number of people diagnosed with diabetes in 2020, totalling 422 million cases, compared to 1980. Furthermore, estimates indicate that by 2045, over 692 million instances will have been diagnosed [26]. In elderly population, diabetes is a significant risk factor for the development of CVD. Persons 65 years of age and above have a very high prevalence of diabetes [27]. Type 2 diabetes is most common in older people and the general population [28]. In particular, the combined prevalence of diagnosed and undiagnosed prediabetes and diabetes is between 50 - 80% among older persons 65 years of age and above.

Diabetic cardiomyopathy (DCM) is currently the primary cause of death for those with diabetes. DCM refers to heart disease that primarily occurs in patients as a result of diabetes [29]. Even though heart disease is the primary cause of death in people with diabetes and people with diabetes are more likely to die from cardiovascular disease (CVD) than people without diabetes, many elderly diabetic individuals may not be aware that they have heart disease [30]. Diabetes affects persons of all racial and ethnic backgrounds, yet it disproportionately affects those from specific backgrounds. According to the American Diabetes Association (ADA), non-Hispanic Blacks have a higher prevalence of diabetes (11.7%) compared to non-Hispanic Whites (7.5%) (**Figure 4**).

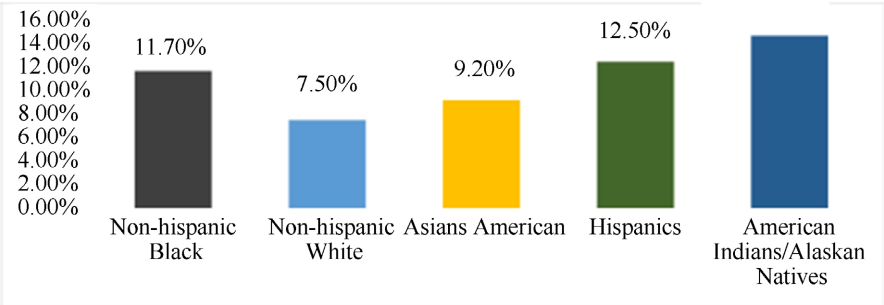

Figure 4. Prevalence of diabetes mellitus among Ethnic groups

While there has been a drop in CHD rates in recent decades, African Americans have experienced a lesser decline in CHD rates than Whites. The ARIC study, which stands for "Atherosclerosis Risk in Communities," found that the incidence of CHD decreased by half (−3.2%/y) in African American men compared to White men (−6.5%/y). White women had a decline of −5.2%/y, whereas African American women experienced a decline of −4.0%/y [31]. The prevalence of self-reported diagnosed CHD in 2010 was 5.8% in White people and 6.5% in African Americans; this difference was not statistically significant. Though rates among men were higher among whites (7.7%) than among African Americans (7.3%), the marginally higher prevalence among African Americans is driven by the excess among African American women (5.9%) compared with White women (4.0%) [32]. That being said, compared to Whites, African American women and men have significantly greater fatal CHD rates (HR, 2.18; 95% CI, 1.24 - 2.56;

women: HR, 1.63; 95% CI, 1.02 - 2.62) [33]. Social determinants of health (SDOH), which include a wide range of factors like access to healthcare, education, socioeconomic status, and environmental factors like a person's residence and interactions with neighbours, have an impact on optimal cardiovascular health [34]. Upstream variables known as SDOH affect cardiovascular risk and health outcomes. Research has demonstrated that the prevalence of heart disease varies by race/ethnicity, with Non-Hispanic Asian adults (7.7%) and Hispanic adults (8.2%) showing notable racial/ethnic differences in heart disease in the US (**Figure 5**). While the overall prevalence of CVD is lowest among Asian Americans, there are significant differences in SDOH among Asian American subgroups, The annual median household income for the Asian population as a whole is $86,000, with the Burmese population having the highest income at $44,000 and the Indian population at $119,000 [35]. As a result, the prevalence of CVD varies greatly among subgroups, with the highest prevalence among Chinese adults being 3.0% and the lowest among Filipino adults being 6.1% [36].

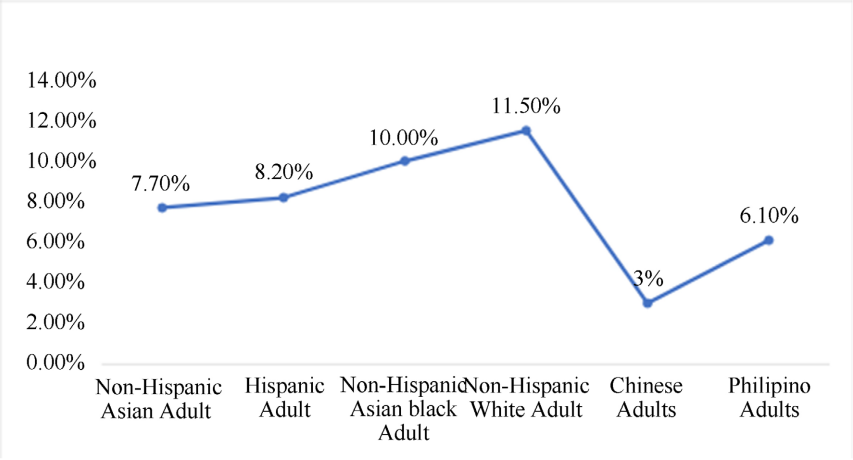

Figure 5. Graphical description of the prevalence of heart disease among ethnic groups.

5. Heart Failure

The larger burden of traditional risk factors among African Americans is largely responsible for the prevalence, lower incidence, and worse prognosis of heart failure among this population. According to CARDIA (Coronary Artery Risk Development in Young Adults), there are significant disparities in the incidence of heart failure at early ages. Of the 27 incident cases of heart failure in people under 50 years old, 26 of the participants were black [37].

6. Sudden Cardiac Arrest/Sudden Cardiac Death

Outside of medical settings, sudden cardiac arrest (also known as sudden cardiac death) has a high fatality rate. It is a sudden, pulseless state that is often caused by underlying cardiac problems. African Americans have a greater incidence of both classic and nontraditional (such as sickle cell trait) CVD risk factors than White people. This is the main reason why African Americans experience both sudden

cardiac death and sudden cardiac arrest more frequently than White people [28]. African Americans had a twofold higher risk of experiencing sudden cardiac death in the Oregon Sudden Unexpected Death Study, a community-based epidemiological study that was started in 2002 to gather data about out-of-hospital cardiac arrest. Between 2002 and 2012, African American men experienced 175 sudden cardiac arrests per 100,000, while white men experienced 84 per 100,000 cases. The rate of sudden cardiac death among African American women was 90 per 100,000, while the rate for white women was 40 per 100,000 cases of sudden cardiac arrest. Compared to their white counterparts, African American women and men who suffered from sudden cardiac arrest were, on average, more than six years younger. The National Registry on Cardiopulmonary Resuscitation reports that African Americans have a lower discharge rate (25.2%) compared to White patients (37.4%) after being hospitalized for sudden cardiac arrest [38].

6.1. Calorie Restriction as a Risk Factor for Cardiovascular Disease in the Aged Population

A study [39] having diabetes dramatically raised the chance of both dying from CVD (hazard ratio: 1.7 for men and 2.2 for women) and acquiring CVD (hazard ratio: 2.5 for women and 2.4 for men). In comparison to their non-diabetic counterparts, diabetic men and women aged 50 and above lived an average of 7.5 (95% confidence interval, 5.5 - 9.5) and 8.2 (95% confidence interval, 6.1 - 10.4) years shorter lives. Life expectancy without cardiovascular disease varied by 7.8 and 8.4 years, respectively. A study by [40] found that although the differences were not consistent or clinically relevant, they did attain statistical significance for certain groups in the individual risk factors for CVD. Using the Framingham or SCORE algorithms, there were no statistically significant variations in the risk of CVD between never-smokers, recent quitters, and former smokers (7.5%, 7.4%, 8.1% for males; 3.3%, 3.0%, 3.2% for women; $p < 0.001$).

Report that between 2009 and 2010, 49.6% of women and 54.0% of men might have avoided cardiovascular death due to the complete elimination of high blood pressure, diabetes, obesity, smoking, and elevated cholesterol [41]. The more practical objective of reducing risk factors to the best levels obtained in the states was taken into consideration, and among men and women, smoking (5.1% and 4.4%) hypertension (3.8% and 7.3%), and diabetes (1.7% and 4.1%), were individually connected to the largest avoidable fractions. The South of the state had the largest avoidable proportion with both criteria, while the west of the state had the lowest. The total elimination of risk factors might save 54.0% of cardiovascular deaths in males, while the metabolic syndrome's constituent parts could prevent 39.6% of cardiovascular deaths in men. The comparable percentages for women were 49.6% and 56.5%, respectively. For each of the two groups, the highest avoidable fractions were linked to smoking (36.4%) and hypertension (30.4% and 38.0%), respectively. Calorie restriction was examined in seven randomized controlled studies that considered the effects of exercise treatments. All things

considered; the research indicates that burning calories while exercising can help people lose weight.

A control randomized trial by [4] showed the benefits of exercise in addition to calorie restriction for weight reduction. The risk-benefit ratio of calorie restriction in older adults is yet unclear. Further efficacy research and more comprehensive long-term follow-up are needed to identify the interventions that obese older people in community settings are currently employing. In the CALERIE trial, there was no change in Biological Age between the adlibitum and caloric restriction groups at baseline, according to separate research by [42] (p-value for difference = 0.777). Each participant's biological age was a little older than their chronological age. The baseline mean chronological age (SD = 7) for CALERIE participants was 38 years. KDM biological age mean (SD = 7) was 37 years. There are several possible explanations for this discrepancy, such as volunteer bias, sampling frames used for both the NHANES and CALERIE, and the fact that the CALERIE individuals were selected based on their good health while the NHANES sample, which was used to estimate KDM Biological Age parameters, represented the general population.

6.2. Influence of Race on Calorie Restriction (CR)

According to [43], a cross-sectional study comprised black people who were born in Africa and those who were born in the United States. We made a comparison between African Americans and African immigrants in terms of the age-standardized prevalence of hypercholesterolemia, overweight/obesity, diabetes mellitus, hypertension, physical inactivity, and current smoking by sex using the census data from 2010. 27,749 African Americans and 1345 African immigrants made up the overall participants in the survey, which was 29,094. Compared to African Americans, African immigrants had a lower insurance coverage rate ($p < 0.05$) but a higher employment, education, and age probability. Regardless of gender, African immigrants exhibited lower rates of age-standardized hypertension (22% against 32%), diabetes mellitus (7% compared to 10%), high cholesterol (4% versus 5%), overweight/obesity (61% versus 70%), and current smoking (4% versus 19%) than African Americans.

6.3. Gender Differences in Calorie Restriction (CR)

Gender plays a significant role in physiological and metabolic reactions to Calorie restriction. Studies have suggested that men and women vary in response to CR based on hormonal regulations, fat distribution, and energy metabolism. Women tend to have higher fat storage due to higher levels of estrogen, potentially as an evolutionary mechanism for reproductive health. This can, however, reduce weight loss in comparison to men on the same diet. During CR men rapidly lose visceral fat which may contribute to their quicker metabolic improvement. These variations underline the necessity of tailored CR strategies that take gender-specific health issues into account, guaranteeing the treatment's effectiveness and safety.

6.4. General Measures to Realize Calorie Restriction (CR)

By eliminating processed foods and added sugars and consuming nutrient-dense foods such fruits, vegetables, lean meats, and healthy fats, calorie restriction (CR) can be attained, with the primary aim of cutting caloric intake by 15 - 25% without sacrificing vital nutrients. In order to prevent nutritional deficiency, implementation must be gradual, with portions controlled, meals tracked, with or without vitamin supplementation. Intermittent fasting may also be implemented. Benefits of CR are increased when moderate exercise is included, with precautions put in place to avoid physical exertion. CR should be tailored to suit individual requirements, with regular health monitoring under physician supervision set in place for patients with chronic conditions. The aim is to adopt sustainable lifestyle modifications that enhance general health and stave against age-related illnesses.

7. Conclusion

In conclusion, it has been demonstrated that calorie restriction, which entails cutting daily calories without causing malnutrition, lengthens an animal's life and improves its health. Further research is necessary to confirm the potential benefits of weight loss and blood pressure management on cardiovascular health in humans, particularly in older people who are more susceptible to cardiovascular disease. Research is required to determine how CR affects the risk of CVD in this cohort as well as the best length and level of intensity for heart health promotion in older persons. Further research is warranted, given the great potential of CR for cardiovascular health, especially with its application in this high-risk population.

Conflicts of Interest

The authors declare no conflicts of interest.

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