# The Role of Plant-Based Nutrition in Preventing Heart Disease

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**Abstract**

Although there has been a sizeable decrease in death rates from cardiovascular disease over the last 10 years, it remains a leading cause of morbidity and mortality in both developed and undeveloped countries around the world. Results from studies conducted in the last few decades have associated plant-based diets with protection against cardiovascular disease as well as many other chronic disease conditions. Vegetarians have been shown to have decreased risks and prevalence of cardio-metabolic conditions, some cancers, as well as total mortality when compared to those who eat meat. Additionally, vegan diets have been shown to offer further protection against obesity, type 2 diabetes, hypertension, and cardiovascular mortality. To date, this data has primarily come from large prospective cohort studies. Thus, randomized controlled trials are desired to build on and confirm previous findings in order to make better recommendations for nutritional interventions in the prevention, management, and treatment of cardiovascular disease.

## Background

Individuals' dietary patterns can fall into several categories depending on the proportion of animal products consumed. Vegetarians are generally considered those who do not consume any animal flesh products including red meat, poultry, and fish, yet consume animal-derived products such as dairy and eggs.[1] Variety in definition exists, however. Some consider themselves vegetarian if they eat fish and animal-derived products, but not red meat or poultry. These individuals are sometimes referred to as semi-vegetarians, or pescetarians. Lacto-ovo-vegetarians are considered to be "full" vegetarians, where the only animal products consumed are eggs and dairy. Lastly, vegans are those who do not consume animal products of any kind, with their sole food sources being plant-derived.

Numbers of vegetarians and vegans in the population remain small. However, the attitudes towards these lifestyles have gained better acceptance, stemming from various reasons relating to moral and ethical considerations of animal cruelty, environmental impacts of meat and dairy industries, as well as the health and quality of life benefits of plant-based diets.[1,2]

## Introduction

Despite extensions of lifespan and a 40% decrease in mortality rates related to heart disease over the last decade, it remains the leading cause of morbidity and mortality in both developed and undeveloped countries around the world.[3] Cardiovascular disease (CVD) currently affects more than 1.6 million Canadians, with 1 in 12 individuals aged 20 years or older diagnosed with this chronic condition.[4] For these individuals, mortality rates are 3 times higher than those without CVD. Health Canada estimates that 9 in 10 Canadians over the age of 20 have at least one risk factor for heart disease, and 4 in 10 have three or more risk factors. [4] Key metabolic and physiological factors associated with increased risk of CVD include hypertension, diabetes, dyslipidemias, obesity, poor diet, physical inactivity, smoking, and excessive alcohol use.[5,6] Many of these factors are modifiable and can be addressed by lifestyle changes. As a result of the significant health burden of CVD, larger-scale strategies towards prevention and treatment are needed, and nutritional intervention in the form of plant-based diets has the potential to affect this change.

Research into the health effects of plant-based diets is not a novel topic, with considerable evidence from epidemiological studies beginning in the 1950's associating the consumption of animal products with increased risks of CVD, diabetes, certain cancers, as well as all-cause mortality.[7-9] Thus, it is suggested that substitution of animal products with plant-based ones can lower the risk of developing many chronic diseases and increase longevity.[10,11] Past data sources have consisted of large, longitudinal prospective cohort studies, as well as smaller interventional studies. However, little has been done in recent years, and there has yet to be a randomized controlled

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trial (RCT) focusing solely on dietary lifestyle modifications to confirm or build on findings from these studies.

The aim of this report is to provide a review of studies that have investigated the relationship between plant-versus animal-based diets and cardiovascular disease, with the intention of guiding future research.

## Results

### Longitudinal Prospective Cohort Studies

One of the first investigations into the health effects of plant-based nutrition began in the 1950's, conducted by Mervyn G. Hardinge as his doctoral dissertation at Harvard University.[12-14] His research was initially met with resistance, but opened the door for subsequent investigation into the health benefits of plant-based diets. In 1999, Key and colleagues presented combined data on five of the largest reported prospective studies testing the hypotheses that vegetarians have lower mortality rates from ischemic heart disease (IHD) as well as certain cancers.[15] After adjusting for body mass index (BMI), alcohol use, education level, and exercise level as potential confounders, pooled data were analyzed to compare death rates from these specific causes between vegetarians and non-vegetarians with similar lifestyles.[16-20]

Data for 76,172 men and women were available, of whom 27,808 were vegetarians. There were 8,330 deaths after a mean follow-up of 10.6 years, with mortality rates for IHD shown to be 45% ($p < 0.01$), 31% ($p < 0.01$), and 8% (not significant) lower in vegetarians at ages < 65, 65-79, and 80-89 years, respectively ($p < 0.05$ for trend). Overall pooled mortality from IHD was 24% lower in vegetarians than non-vegetarians, with the effect further amplified in the younger population. The significantly lower death rate for those aged 65 and under is important, given the chronic nature of CVD where predisposing factors/conditions begin earlier in life. Additionally, the protective factor of plant-based diets was mostly confined to those who had been vegetarian for five years or more, suggesting that simply increasing plant consumption in a non-vegetarian diet would not be beneficial in gaining the protective factors that adopting a fully plant-based diet would.

In 2014, Le and Sabaté analyzed data on three large prospective studies of the North American Adventist populations, comparing non-vegetarian, vegetarian, and vegan diets in disease and mortality outcomes.[1] The rationale for using members of this religious community as participants is due to their population characteristics that provide a natural study group well-suited for the topic in question. Their Church doctrines recommend vegetarian practices, thus many individuals are vegetarian or vegan, yet about half are omnivores similar to the general population.[21] Furthermore, strong emphasis is placed on overall health, valuing abstinence from alcohol and tobacco. Therefore, studying these individuals allows for the control of two major non-dietary confounders known to be contributing factors to CVD.[22]

The first Adventist cohort study took place between 1960 and 1976, the second between 1976 and 1988, and the third ongoing study began in 2002.[22-25] In total, data from 153,138 participants from the United States and Canada were collected. In the most recent cohort, 48% of participants were non-vegetarians, 6% were semi-vegetarians, 10% were pescetarians, 28% were lacto-ovo-vegetarians, and 8% were vegans at baseline. Pooled results from all sub-types of plant eaters showed a 55% decreased risk of developing hypertension, a 25-49% decreased risk of developing type-2 diabetes, a 50% risk reduction for the development of metabolic syndrome, and their BMI values were on average 3-5 points lower when compared to non-vegetarians.[1]

Additional comparisons within subgroups of plant eaters showed vegans to have further risk reduction over lacto-ovo-vegetarians, with chances of developing hypertension and type-2 diabetes 75% and 62.5% lower, respectively, compared to 55% and 49.5% in lacto-ovo-vegetarians. For all cardiometabolic-related outcomes, vegans were at lower risk than lacto-ovo-vegetarians, both of which were at lower risk than non-vegetarians. This effect demonstrates that even though vegetarians consume largely reduced amounts of animal products, the animal-based foods that they do consume may still put them at higher risk than vegans who consume solely plant-based foods.

An important observation in gender differences was also obtained from the Adventist study data. According to Health Canada, men are diagnosed with heart disease an average of 10 years younger than women (55-64 vs 65-74 years of age), and are twice as likely to suffer a heart attack.[4] Given the higher burden of CVD in men, it is relevant that findings showed a 23% and 42% risk reduction in CVD-related mortality in lacto-ovo-vegetarian and vegan males, respectively.[1]

### Randomized Controlled Trials

The Lifestyle Heart Trial was the first RCT that investigated the effectiveness and sustainability of comprehensive lifestyle changes, and their effect on the progression of coronary atherosclerosis.[26] Intensive lifestyle modifications included a low-fat vegetarian diet, aerobic exercise, smoking cessation, group psycho-social support, and stress management training. At one year follow-up, subjects in the experimental group maintained lifestyle changes and had a 37.2% reduction in low density lipoprotein (LDL) levels, and a 91% reduction in frequency of angina episodes in comparison to the control group, who were instructed to follow standard care suggested by their primary care physicians. Based on the encouraging findings after one year, the study was extended to allow for a 5-year follow-up to evaluate the feasibility and the effects of long-term lifestyle interventions on CVD risk factors, coronary atherosclerosis, myocardial perfusion, and cardiac events.[27]

In the experimental group, patients lost an average of 23.9 lbs at one year, sustaining an average loss of 12.8 lbs at five years, compared to little baseline change in the control group. LDL levels decreased by 40% and 1.2 % at one year follow-up in the experimental and control groups, respectively. At five years of follow-up, LDL levels decreased by 20% and 19.3% in the experimental and control groups, respectively. The comparable decrease in LDL levels after five years is attributed to 60% of control group patients taking lipid lowering agents beginning after year one of the study, whereas none of the experimental group patients took lipid-lowering agents.

The degree of reduction in LDL levels of experimental group patients is comparable to effects achieved with lipid-lowering agents. This finding gives preliminary evidence to suggest that lifestyle modifications can be superior or non-inferior to standard pharmacological treatment of dyslipidemias.

Coronary angiography was used to analyze all coronary artery lesions that matched at baseline and five-year follow up. In the experimental group, an average decrease of 4.5% and 7.9% from baseline percentages of coronary artery stenosis were found at 1-year and 5-year follow-up respectively. In contrast, the control group averaged an increase of 5.4% and 27.7% stenosis at one-year and five-year follow-up, respectively. Differences in severity of coronary artery lesions were not statistically different between groups at baseline, and the progression of coronary artery stenosis in the control group occurred even though over half of these participants were prescribed lipid lowering agents during the time of the study. Furthermore, the sustained long-term reduction in severity, frequency, and duration of angina episodes in the experimental group after five years is comparable to the degree of symptom reduction achieved post-angioplasty or coronary artery bypass surgery.[28]

Overall, the trial showed more significant regression of coronary atherosclerosis in the experimental group after five years than one year, whereas disease progression continued in the control group and participants experienced double the frequency of cardiac events (cardiac-related hospitalizations, myocardial infarction, coronary angioplasty, coronary artery bypass surgery). Though the intensive lifestyle changes incorporated more than just dietary modifications, this RCT gives valuable insight into the significant role that various lifestyle factors, including diet, have on the progression and reversal of CVD. Results from this study also demonstrate that lifestyle modifications are possible, sustainable, and can be achieved with sufficient compliance when patients receive adequate education and guidance. If patients were more frequently "prescribed" lifestyle modifications by their physicians in the same way that pharmacological treatments are prescribed, similar results to those found in RCTs could potentially be achieved.

## Plant-Based Diets in the Prevention of Metabolic Syndrome

It is widely accepted that individual physiological factors such as hypertension, diabetes, and dyslipidemias are associated with a higher risk of CVD.[29] In addition to these individual risk factors, patients diagnosed with metabolic syndrome have a three times greater risk of developing CVD, and a five times greater risk for developing type 2 diabetes (a major risk factor for heart disease) within a 5-10 year period.[30] Patients with ≥3 of abdominal obesity, hyperglycemia, hypertriglyceridemia, hypertension, and low levels of high density lipoproteins (HDL) are said to have metabolic syndrome, of which the global prevalence is approximately 25%.[6] Nutritional intervention is a primary aim of lifestyle modification, where evidence shows that high-protein diets are effective in preventing features of metabolic syndrome by increasing HDL levels and reducing fat mass while maintaining lean body mass.[31,32] Furthermore, protein source, in addition to amount of protein in the diet, is considered a contributing factor to developing metabolic syndrome. In 2017, Chalvon-Demersay et al. published a systematic review of 123 studies, comparing the effect of animal and plant protein sources on markers related to metabolic syndrome.[11] Study participants totaled 516,330 and consisted of individuals possessing one of the metabolic syndrome markers, as well as healthy subjects of all ages for controls.

Amongst studies evaluating dyslipidemias, numerous reports have shown that soy proteins containing isoflavones lead to greater reduction in total and LDL cholesterol in individuals consuming plant rather than animal proteins.[33-35] Additionally, in studies where protein was given as a whole diet rather than supplementation, the degree of differences between plant and animal protein cohorts was amplified.[35-38] This effect is proposed to be a result of factors inherently associated with animal-based diets. Increased consumption of cholesterol and saturated fats, as well as decreased levels of total dietary fibers and polyunsaturated fats, are known to directly cause elevations in plasma cholesterol and triglyceride concentrations.[39] Overall, data presented in this systematic review showed that soy protein with isoflavones, as well as other plant proteins, leads to a greater decrease in both total and LDL cholesterol compared to the ingestion of animal proteins.[11] These results suggest that subjects at high risk of developing CVD could benefit from a plant-based diet.

Furthermore, a 2014 meta-analysis of 7 clinical trials and 32 observational studies showed the consumption of plant-based diets to be associated with lower blood pressure (BP) compared with that of omnivorous diets.[40] Pooled data showed an overall change in systolic BP of -4.8 mmHg and -6.9 mmHg in clinical trials and observational studies, respectively, and diastolic changes of -2.2 mmHg and -4.7 mmHg, respectively. One of the main proposed mechanisms for the changes observed in plant-eaters is said to be related to lower BMI, attributed to less energy-dense foods that are higher in fiber and lower in fat content.[41] However, though weight reduction is an established recommendation towards decreasing BP, in studies controlling for BMI, observed effects of plant-based diets remain.[42] Thus, further mechanisms have been proposed. Meta-analyses of RCTs have shown dietary potassium to contribute to decreases in BP, attributable to its effects on increased vasodilation and glomerular filtration rate, as well as decreasing renin level, renal sodium resorption, reactive oxygen species, and platelet aggregation.[43] Additional contributing factors are various diet and lifestyle characteristics inherent to plant-based diets. Factors known to increase BP (i.e. obesity, sodium intake, alcohol consumption) are lower in plant-eaters, whereas factors that decrease BP (i.e. exercise level, intake of potassium, magnesium, unsaturated fat, protein) are higher.[44-47]

## Plant Proteins

Numerous mechanisms have been proposed to explain the lower risks for CVD seen in vegans, including significantly lower BMI and lower total and LDL cholesterol levels, which are well-established risk factors for CVD.[48-51] The increased

amounts of antioxidants, fibers, folate, phytochemicals, and soy protein in vegan diets have been shown to be associated with lower serum cholesterol, trans and saturated fat, as well as decreased incidence of morbidity and mortality from CVD, diabetes, stroke, and certain cancers.[48-51] In 1999, soybeans received a heart health claim from the U.S Food and Drug Administration, stating that soy protein decreased the risk of CVD via its cholesterol-lowering effect, whereas casein protein from milk was thought to be hypercholesterolemic.[54] Primary mechanisms behind the cardioprotective effects of plant protein include its amino acid pattern and protein structure. Animal protein has a comparatively high ratio of leucine to arginine compared with plant protein, which is suggested to be associated with hyper-cholesterolemia and atherosclerosis.[55] Specific to soybeans, the structure of peptide subunits and lack of excess essential amino acids is proposed to result in decreased stimulation of hepatic cholesterol biosynthesis.[56,57] Furthermore, soy protein contains a 7s globulin protein that has been linked to upregulation of hepatic LDL receptors[58] and reduced plasma tryglicerides.[59] Studies have also shown that diets rich in soy protein, nuts, plant sterols, fibers, and low in saturated fatty acids is equivalent to statin treatment in lowering cholesterol and C-reactive protein in hyperlipidemic subjects.[60,61] Therefore, it is suggested that diets containing soy protein may be a valuable treatment option for dyslipidemic patients, especially in those who can't tolerate or are nonresponsive to pharmacological therapy.[62]

### Plant-Based Nutrition in Children

Canada, like many nations, is currently in the midst of a health crisis surrounding obesity in both adults and children. Based on current data, 59% of adults and 25% of children in Canada are either overweight or obese, with numbers expected to increase in the coming decades if current trends continue.[63,64] In addition to studies showing the benefits of plant-based proteins on cardiovascular health in adults, similar effects have been demonstrated in children. Studies have shown that the consumption of animal-sourced protein at one year of age is positively associated with increased BMI and body fat by the ages of 6-7 years.[65-67] Excess weight in early life has been linked to insulin resistance, type 2 diabetes, and hypertension, which can predispose children to early onset of CVD.[68] In the absence of interventions, overweight children and adolescents tend to become overweight adults. Therefore, it is important to develop preventative measures that begin in childhood in order to decrease the risk of premature onset of CVD and related health conditions.

### Official Dietary Recommendations

According to a 2013 Canadian Diabetes Association publication,[69] a 2015 report from the World Heart Foundation,[70] the 2015-2020 Dietary Guidelines for Americans[71], and the 2016 Canadian Cardiovascular Society guidelines,[72] vegetarian and vegan diets are recommended as dietary patterns that promote health and prevent disease. A 2009 randomized controlled trial showed a vegan diet to be as beneficial as conventional American Diabetes Association dietary guidelines in promoting weight loss, improving fasting blood glucose, total cholesterol, and LDL in adults with type-2 diabetes.[73] Another study showed that participants on a calorie-restricted vegetarian diet had a greater improvement in BMI and LDL levels, and a greater decrease in the need for diabetes medications than those following a conventional diabetes diet (43% and 5%, respectively).[74] Therefore, in counselling patients at risk of developing or being treated for conditions such as diabetes, dyslipidemia, hypertension, and CVD, recommendations for adopting a plant-based diet should be considered.

## Discussion

In summary, data from large, longitudinal, prospective studies paints a consistent picture showing significant correlations between diet and health status, emphasizing that vegetarians and vegans live longer and have a greatly lowered risk of developing most chronic diseases.

There have been doubts about the nutritional adequacy of plant-based diets in past decades. However, national dietetic associations have since changed their position statements on dietary recommendations, resulting from increased research on vegetarian and vegan nutrition as well as better understanding of the connections between diet and disease.[80-82] Though numerous assumptions exist in regards to the health of vegans, suggesting that significantly greater challenges exist in meeting nutritional requirements for elements such as vitamin B12, protein, and calcium, vegans can avoid deficiencies with appropriate food choices just as non-vegans can.[83] With vegan diets gaining popularity as an alternative to the "norm" of omnivorous diets, it can be easy to make assumptions based on a lack of knowledge. It could be thought that vegans must be missing key nutritional elements since plant-based diets are not as common, vegan foods are not advertised in the same way that animal products are, and veganism is not the way that humans have traditionally lived. Humans began as omnivores, restricted in their dietary intake, necessitating hunting and fishing for survival. However, we are no longer restricted to the same way of living and thinking about food. In today's society, many of the world's populations now have the resources, the options, and the privilege to have a larger array of food possibilities and to choose what we consume. Just because something has always been done a certain way, doesn't mean that it is the way it always has to remain.

Nonetheless, it can be difficult to convey these ideas and challenge the assumptions and dietary habits of individuals. In order for messages to be heard, it takes time, money, and resources. Large dairy and meat companies have long had the resources to advertise their products, whereas those promoting vegan lifestyles have only recently begun to compete on that level. Just as the truths of animal cruelty in factory farming are not often shared with the public, neither are the significant health benefits of adopting a plant-based diet.[84-86]

An important issue impeding changes in societal dietary patterns is considering the way in which dietary advice is conveyed. Canada's Food Guide serves as the country's nutritional backdrop, underlying policies and programs in areas ranging from publicly- funded school programs to hospitals. Its information is taught to Canadians of all ages, as well as to future health professionals, and is used by food industries

to promote their products. Large cohort studies have presented data reporting that approximately 82% and 91% of the risk for CVD and diabetes, respectively, can be prevented by dietary and lifestyle modifications.[87,88] However, despite efforts to encourage more plant-based nutritional practices, including recommendations by the Canadian Cardiovascular Society, Canadian Diabetes Association, and World Heart Foundation outlined above, changes have been slow.[70] Potential factors contributing to this delayed effect include the well-established popularity and accessibility of Canada's Food Guide, versus the relative lack of availability and easy access to concise resources with alternative recommendations outlined by large health societies.

Another significant challenge hindering the availability of resources on plant-based diets is in the knowledge of those providing information and nutritional recommendations. Physicians are often the first point of contact for those seeking nutritional consultation. However, nutrition and its relation to health and disease is seldom included in medical school curricula in a way that adequately addresses the importance of this concept and its centrality to the processes of disease prevention, management, and treatment. Whether one has a chronic disease or not, health literacy is an important concept to consider, both for health professionals and members of the general public. If appropriate resources are not provided, or are not available and easily accessible, society will continue to be burdened with the epidemics of obesity, type 2 diabetes, and CVD. Therefore, society-wide improvements in knowledge, education, and delivery of information are needed in order to foster meaningful improvements in the health status of populations.

This subject shares similarity to the way in which cigarette smoking was not originally viewed as detrimental to one's health. Lung cancer, now responsible for 1.5 million annual deaths around the world, was considered a rare disease until the 1900's.[89] Cigarette smoking dates back to at least the 18th century, its popularity rising dramatically in the 19th century, and it wasn't until the mid-20th century when evidence began to establish it as the leading cause of lung cancer.[90,91] However, despite results from studies, cigarette manufacturers continued to argue against evidence in efforts to protect sales,[91,92] and even physicians remained unconvinced. In reports as late as 1960, only 1/3 of doctors in America agreed that smoking should be considered a cause of lung cancer, with 48% reporting to be smokers themselves.[93] Therefore, even though the cigarette is considered to be the deadliest artefact in the history of human civilization,[94] efforts to generate and facilitate ignorance long prevented the now well-established awareness of its health dangers. The observation of a similar trend is beginning to emerge in the area of plant-based nutrition, where research results showing its health benefits have existed since the 1950's, although society and physicians remain largely uninformed.

Though there has yet to be a randomized control trial investigating the health benefits of plant-based diets and the health detriments of animal-based ones, the value of prospective cohort studies should not be discounted. Findings that show the benefits of plant-based nutrition can be used to guide shifting views and practices until the time that randomized control trials are realized. Thus, in addition to the current increased environmental impact of animal proteins and the emerging awareness of the cruelty involved in factory farming, plant-based diets are likely to be favored in the future due to their numerous health benefits.

## Limitations of Current Evidence

Choice of participants has been a critique of cohort studies that have shown plant-based diets to decrease the risk of CVD. Participants were from populations that place great emphasis on healthy living and comprised a high proportion of vegetarians, thus results may not be generalizable.[10] However, the validity of this concern is questionable, given that investigators deliberately recruited a large proportion of vegetarians, since this is the population desired for study.[16-20] In their report of the 3 Adventist cohorts, Le and Sabaté acknowledged the higher prevalence of vegetarians and vegans as the reason for studying these individuals.[15]

Authors also noted that due to emphasis on personal health, Adventists tend to live longer than their counterparts in the general population. In interpreting their data and its generalizability from the isolated study population, it was found that although both male and female Adventists lived an average of 7.3 and 4.4 years longer, respectively, vegetarian Adventists had a further increase in life expectancy (1.5-2.4 years) over non-vegetarian Adventists.[75] Additionally, the non-vegetarian Adventists used as reference cohorts in the reported comparisons consumed much less meat than the general population. Therefore, it could be hypothesized that the relatively low intake of meat by this reference group would have resulted in smaller observed effects, limiting conclusions that could be made based on the data. However, there were significant observed effects, suggesting that even within a controlled health-focused population, considerable differences existed between the health status of vegans, vegetarians, and meat eaters. This finding indicates a potentially stronger association between plant-based diets and improved health and longevity, rather than an insignificant correlation that may not be generalizable.

The choice and definitions of study populations, as well as the length of the study period are further factors to consider in interpreting contradictory evidence. First, it is difficult to derive meaningful conclusions from self-report data, since individual definitions of vegetarian tend to vary. Some might self-identify as vegetarian if only eating meat on occasion, or if red meat is not consumed but poultry and fish are. Others may describe themselves as lacto-ovo-vegetarian if the only animal products consumed are eggs and dairy. This bias potentially explains conflicting evidence between studies, with some studies showing that vegetarians have no significant differences in disease states and mortality, whereas others have reported considerable health benefits of vegetarian diets. For example, results from cohorts in the EPIC-Oxford study reported no differences in rates of vascular disease, stomach cancer, colorectal cancer, lung cancer, breast cancer, prostate cancer, or all-cause mortality related to diet.[76] Conversely, in addition to the aforementioned data relating to cardiovas-

cular health in the Adventist studies, vegetarian participants experienced an 8% risk reduction from overall cancer, 50% from colon cancer, 23% from cancer of the gastrointestinal tract, 35% from prostate cancer, and 48% from breast cancer compared to non-vegetarians.[1]

Lastly, though there have been some interventional studies examining the health-related outcomes of plant-versus animal-based diets, most involved meal replacements for trial periods ranging from 4-12 weeks, where it was unclear if additional food was consumed, and whether it was of plant or animal origin.[77-79] Furthermore, data from short-term interventional studies is not representative of the potential health benefits of adopting a plant-based diet. The decreased mortality from ischemic heart disease seen among vegetarians in Key and colleagues' analysis was present in those who had followed their current diet for >5 years.[15] It is possible that if populations were followed for more than five years or if study participants consisted of individuals who have been vegetarian or vegan since early life, these results would be further amplified.

## Future Perspectives

Given the consistency of results associating vegetarian diets with decreased risks of developing CVD, further randomized interventional trials are warranted. These trials would validate existing findings and further investigate the health effects of these diets in order to make meaningful recommendations and implement guidelines for nutritional planning, assessment, and counseling.

Future studies should focus on comparing meat-eaters to vegans rather than vegetarians. Using vegans as study participants would provide for improved identification and isolation of the relationships between plant-based diets and CVD, since these individuals consume solely products of plant origin. This study population would also eliminate the ambiguity and inherent risk of bias that has existed in studies to date, based on differing definitions of 'vegetarian'. Additionally, studies should focus on those who have followed vegan dietary practices for a significant amount of time, given that the majority of differences between health outcomes in plant-versus meat-eaters were found in individuals who had been vegetarian for more than five years.

Another possible area to explore would be in comparing the current standards for management of CVD and its risk factors with nutritional interventions in the form of vegan diets. Studies could aim to assess the comparative effectiveness of medical therapies such as antihypertensives, cholesterol-lowering agents, and diabetes medications with specific dietary management. If vegan diets are shown to be superior, or equal to standard pharmacological therapy, perhaps they would be the preferred intervention. Though compliance could remain a challenge with dietary interventions as with pharmacological interventions, issues related to drug side effects or adverse reactions would not be of concern. For example, though clinical trials have shown antihypertensive drugs to be effective in preventing cardiovascular death, poor blood pressure control is not infrequent, and drug nonadherence is considered a primary contributing factor.[95-97] Since significant evidence from both observational studies and RCT's exist showing an association between the intake of plant protein and decreased blood pressure,[40] investigations comparing vegan nutritional interventions with antihypertensives could be valuable.

Lastly, though challenges in design and execution would exist, it might be of interest for observational studies to evaluate the prevalence of vegans amongst patients undergoing procedures related to CVD. For example, a comparison between vegans and meat-eaters undergoing angioplasty or coronary artery bypass surgery could provide valuable information in ascertaining how many vegans versus meat-eaters suffer from severe CVD requiring procedural intervention.

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