Vegetarian Diet Patterns and Chronic Disease Risk

What We Know and What We Don't

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Vegetarianism continues to increase globally due, in part, to perceived health benefits. Results from observational studies indicate that vegetarian dietary patterns are associated with favorable cardiometabolic risk factor profiles and lower risks of chronic diseases including obesity, diabetes mellitus type 2, cardiovascular disease, and cancer. Aside from avoidance of meat and the compensatory dietary alterations, vegetarians tend to practice lifestyle habits conducive to better health. Well-controlled intervention trials show minimal or no effects of lean meat intake on traditional markers for chronic disease risk, although biologically plausible mechanisms exist through which consumption of meat and other animal products could influence risks of cardiovascular disease and some cancers. Thus, at present, the degree to which favorable health outcomes associated with vegetarian diet patterns are attributable to avoidance of animal products per se is unclear. This issue has major public health implications because more than 95% of the US population are regular consumers of meat and other animal products. This review aims to summarize the evidence regarding vegetarian diet patterns and major chronic diseases, explore possible explanations for these relationships, and identify research gaps and opportunities to better define the health effects of vegetarian dietary patterns. Nutr Today. 2019;54(4):132–140

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Vegetarian diet patterns are characterized by avoidance of meats, poultry, and fish/seafood and are mainly plant based, although several variations are practiced (Table 1). The most commonly practiced form is the lacto-ovo vegetarian pattern in which the individual avoids consumption of meats (eg, beef, pork, veal, lamb, mutton), poultry (eg, chicken, turkey), and fish/seafood, but does consume dairy products and eggs.[1] Vegan dietary patterns avoid all animal products, and intermediate patterns include semivegetarian (also known as flexitarian) and pescovegetarian (includes fish and/or other seafood).

Most people in the United States are omnivores who consume meats and other animal products. Surveys and polls have shown prevalence of 1.4% to 3.3% for vegetarian diets in the United States, including a prevalence of veganism of approximately 0.5%.[1] People choose vegetarian dietary patterns for a variety of reasons. In the National Health Interview Survey in the United States (2012), approximately 2% of the population reported having followed a vegetarian diet pattern within the last 12 months for health reasons, and lifetime history of doing so was 4%.[2] Other reasons for choosing vegetarian diets include religious beliefs, as well as concerns regarding animal welfare and the environmental impact of animal food production.[3,4] Many who choose a vegetarian dietary pattern have a mix of these motivations. The 2015–2020 Dietary Guidelines for Americans (DGA) include a Healthy Vegetarian eating pattern (modeled as a lacto-ovo vegetarian diet), along with Healthy American and Healthy Mediterranean-style eating patterns as examples that can be adapted to promote health and reduce chronic disease risk according to cultural and personal preferences.[5] Most recently, the EAT-Lancet Commission released its report aimed at achieving healthy diets from sustainable food systems by 2050 because food is "the single strongest lever to optimize human health and environmental sustainability on Earth."[6] Primary recommendations of the report were to decrease red meat and added sugars, particularly among wealthier nations, by more than 50% and to double the intake of fruits, vegetables, legumes, and nuts to benefit human health and provide a foundation for environmental sustainability.[6] This equates to target intakes of 14 g/d of meat (beef, lamb, and pork), 29 g/d poultry, 13 g/d egg (56 g/d of combined meat, poultry, and eggs), and 28 g/d of fish. The 2015 DGA's standard

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TABLE 1 Different Types of Vegetarian and Nonvegetarian Dietary Patterns	
Dietary Pattern	
Vegan	Avoids consumption of all animal products
Lacto-ovo vegetarian	Avoids consumption of meats, poultry, fish, and/or other seafood but consumes dairy products and eggs; the most widely practiced form of a vegetarian dietary pattern
Pescovegetarian	Avoids consumption of meats and poultry, but consumes fish and/or other seafood, and most often also consumes dairy products and/or eggs
Semivegetarian (flexitarian)	Consumes small amounts of animal products, which may include dairy, eggs, and/or seafood in a mostly plant-based diet (sometimes referred to as flexitarian)
Omnivore	Consumes animal products, including meats, poultry, and seafood

2000-kcal healthy eating pattern model contains 105 g/d of a combination of meat (beef, lamb, pork) poultry, and eggs and 32 g/d of fish/seafood.[5,6] Based on the 2011–2012 National Health and Nutrition Examination Survey, Americans consume 72 g/d meat (eg, beef, lamb, and pork), 41 g/d poultry, 14 g/d eggs (102 g/d of combined meat, poultry, and eggs), and 19 g/d of fish.[7] Although the EAT report did not specifically advocate for a vegetarian dietary pattern, the significant target reductions in daily animal protein servings and the recommendation to "avoid meat" are attempting to move the population toward vegetarian and vegan dietary patterns.

The aims of this review are to (1) summarize the evidence regarding the relationships of the main vegetarian diet patterns (lacto-ovo vegetarian and vegan) to risks of major chronic diseases, (2) explore possible explanations for the observed associations, and (3) review research gaps that will need to be investigated in order to better define the potential health effects of such dietary patterns. Although a focus of recent plant-based dietary recommendations has been environmental responsibility, this article will focus only on the nutritional and health-related consequences of the dietary patterns, and issues of sustainability and environmental impact are outside its scope.

ASSOCIATIONS OF VEGETARIAN DIET PATTERNS WITH INCIDENCE OF MAJOR CHRONIC DISEASES

Several reviews and meta-analyses have been published on the associations between vegetarian diet patterns and disease outcomes.[1,3,8,9] Prospective cohort studies in the United States, the United Kingdom, Europe, and Australia have reported data on vegetarian dietary patterns and their associations with incidence of chronic diseases and/or mortality.[4,10,11]

Table 2 summarizes results from a meta-analysis of the incidence of various health outcomes published by Dinu and colleagues.[3] A total of 86 cross-sectional and 10 cohort prospective studies, which included a mix of population groups from the United States, the United Kingdom, and Germany, were included in the analyses. In pooled analyses, all disease outcomes investigated were numerically lower among vegetarians and vegans compared with omnivores, with relative risks indicating 2% to 25% lower incidence. Among vegetarians, significantly lower incidence was present for ischemic heart disease (25% lower, $P < .001$) and all cancers (8% lower, $P = .002$). No statistically significant differences were observed for all-cause mortality, incidence of all cardiovascular disease (heart disease and stroke), breast cancer, or mortality from any cancer or specific cancer types (breast, colorectal, prostate, lung). A much smaller sample was available to investigate associations in vegans. In this group, incidence of all-cause mortality was lower by 12% (not statistically significant, $P = .10$), and all cancer incidence was significantly lower by 15% ($P = .006$). Of note, subgroup analyses indicate that a vegetarian diet was significantly associated with a lower risk of all-cause mortality and breast cancer mortality in US Seventh Day Adventists with a shorter (<14 years) follow-up; no significant associations were found when assessing non-Adventists living in European countries.[3]

Vegetarian dietary patterns are associated with favorable cardiometabolic risk factor profiles and lower risks of chronic disease, including obesity, diabetes mellitus type 2, cardiovascular disease, and some cancers.

Dinu et al[3] and others have reported that relationships between favorable outcomes with vegetarian diet patterns have generally been stronger in US than non-US cohorts, particularly in data from the Adventist Health Studies, and for the outcome of all-cause mortality.[3,8,10] One possible explanation for this difference is that much of the evidence from US cohorts is from the Adventist Health Studies. Many Seventh Day Adventists consume vegetarian diets

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TABLE 2 Differences in Incidence of Health Outcomes Between Omnivore and Nonomnivore (Vegetarian and Vegan) Comparison Groups in Pooled Analyses From Prospective Cohort Studies Including 72 298 Total Subjects Followed for Periods of 4.1 to 21 Years

Group and Outcome[a-c]	% Lower Incidence vs Omnivore	*P*
Vegetarian diet pattern		
All-cause mortality	6	.24
Cardiovascular disease	7	.07
Ischemic heart disease	**25**	**<.001**
Cerebrovascular disease	7	.39
Cancer	**8**	**.002**
Cancer mortality	2	.76
Breast cancer	6	.31
Breast cancer mortality	6	.81
Colorectal cancer mortality	10	.18
Prostate cancer mortality	10	.56
Lung cancer mortality	14	.36
Vegan diet pattern		
All-cause mortality	12	.10
Cancer	**15**	**.006**

[a]Summarized from data reported in a meta-analysis by Dinu et al.[3] The reference group is omnivore diet pattern (consumes meats, poultry, seafood).

[b]Vegetarian diet pattern is defined as excluding meat, poultry, seafood, and flesh from any animal. Vegan diet pattern is defined as a diet omitting all animal products.

[c]Variables with statistically significant *P* values (<.05) are bolded, and each pooled point estimate includes data from 3 to 7 cohorts, ranging from 6301 to 66 018 participants.

for religious reasons and are characterized by lifestyle practices that are conducive to good health such as avoiding smoking, alcohol, and drug abuse; maintaining relationships; and obtaining regular exercise and adequate rest.[12,13] The degree to which an individual chooses to adhere to a vegetarian diet pattern for religious reasons may correlate with the degree to which other health-promoting lifestyle and other behavioral practices are followed. Therefore, the stronger associations between reduced risks of mortality and chronic disease outcomes may be the result of a range of health-promoting behaviors that differ between US Seventh Day Adventists who consume vegetarian diet patterns and non–Seventh Day Adventist populations consuming vegetarian dietary patterns in other countries.

Dinu and colleagues[3] also found that cross-sectional analyses indicated lower values for several cardiometabolic risk factors among vegetarians compared with omnivores, including significantly lower values for body mass index, total and low-density lipoprotein cholesterol (LDL-C), triglycerides, and blood glucose. Results were similar in magnitude for vegans, although some variables (eg, triglycerides) did not reach statistical significance, likely because of a smaller sample size. In the Adventist Health Study 2 (AHS-2), lower hazards were present for diabetes mellitus type 2 among lacto-ovo vegetarians and vegans compared with regular consumers of meat (omnivores), as well as a lower prevalence of metabolic syndrome[1,14,15]; these associations remained after adjustments for factors such as sex, ethnicity, physical activity, and alcohol intake. These results are consistent with expectations based on cross-sectional results in multiple studies showing a more favorable cardiometabolic risk factor profile among those consuming vegetarian dietary patterns.

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Mechanisms Potentially Linking Consumption of Meat and Other Animal Products With Health Outcomes

There are plausible mechanisms through which consumption of meat and other animal products could adversely impact health. For example, cooking meat at high temperatures, especially charring, has been shown to produce compounds such as heterocyclic amines, aromatic hydrocarbons (eg, benzopyrene), and advanced glycation end-products, the consumption of which has been shown to produce genotoxicity, carcinogenesis, and inflammation/oxidation in animal models.[16–18] Heme iron, which is present in meat, poultry, and seafood, but highest in red meat, can act as an oxidant, which could, theoretically, contribute to the pathogenesis of cardiovascular diseases, diabetes mellitus type 2, and cancers.[19,20] The World Cancer Research Fund released its *Third Expert Report on Diet, Nutrition, Physical Activity and Cancer* in 2018, which reviewed the evidence for various exposures in relation to cancer risk.[21] Based on the mechanistic considerations summarized above, they concluded that there is moderate mechanistic evidence to support a relationship between high consumption of red meat and colorectal cancer risk.[21] Processed meats that are preserved through smoking, curing, salting, and/or the addition of chemical preservatives contribute significantly to dietary intakes of sodium, as well as nitrites and nitrates, excess consumption of which has been associated with vascular dysfunction and impaired glucose tolerance.[22] The World Cancer Research Fund report also stated that "convincing" evidence linked processed meat to colorectum cancer, and "limited" evidence linked processed meat and red meat to other cancers such as lung and nasopharynx, among others.[21] The report cites increased exposure to heterocyclic amines and polycyclic aromatic hydrocarbons formed during high temperature cooking and exposure to potentially carcinogenic N-nitroso–derived compounds present in processed meat as potential mechanisms by which these foods might cause cancer.[21] However, it is important to note that the evidence used to support the report's conclusions is based on observational studies and mechanistic plausibility, because data from dietary intervention studies on cancer incidence in humans are extremely limited.

Randomized controlled trials of the effects of fresh meat consumption have shown minimal or no adverse effects on traditional cardiovascular disease risk factors.[23–26] While red meat, such as beef, is a source of saturated fatty acids, it also contains approximately equal amounts of monounsaturated fatty acids. Furthermore, approximately one-third of the saturated fat in beef is stearic acid, which does not appreciably raise LDL-C.[27] Thus, the predicted effect of red or white meat on blood levels of LDL-C is driven mainly by dietary cholesterol content.[28] Dietary cholesterol appears to have a modest, but statistically significant, effect to raise circulating LDL-C concentration, with linear models showing a rise of ~2 mg/dL in LDL-C for each 100-mg/d increment in dietary cholesterol.[28] Cross-sectional differences between vegetarians and nonvegetarians in circulating levels of lipoprotein lipids, including LDL-C, are likely attributable partially to higher dietary cholesterol and saturated fat intakes in omnivores and to other factors such as lower intakes in omnivores of viscous dietary fibers, plant sterols, and vegetable oils, as well as higher average body mass index.[29,30]

Recently, controlled feeding studies have demonstrated that consumption of red meat, but not white meat, increases circulating and urinary levels of trimethylamine N-oxide (TMAO) compared with a nonmeat diet. This effect was attributable to both increased production of TMAO from carnitine, but not choline, and reduced renal TMAO clearance.[31] Increased circulating TMAO concentration has been associated with higher risks of cardiovascular events and mortality.[32] At present, no data are available from randomized controlled trials to demonstrate that lowering TMAO reduces cardiometabolic risk, but this is expected to be an area of intense investigation in the future.

Egg yolks are high in cholesterol (~186 mg/egg yolk), but also contain other nutrients such as choline and carotenoids.[33] In feeding studies, increasing egg intake has been associated with modestly higher levels of LDL-C, but generally there are no other adverse effects on the cardiometabolic risk factor profile.[34–37]

Dairy products such as milk, cheese, and yogurt contain cholesterol and saturated fatty acids. Despite this, results from observational studies have not shown higher risks of cardiometabolic diseases in those who consume larger amounts of dairy products, including full-fat versions.[38] In feeding studies, low-fat and full-fat dairy product consumption has been associated with favorable effects on some cardiovascular risk factors. For example, the original Dietary Approaches to Stop Hypertension (DASH) trial showed additional blood pressure reduction when low-fat dairy products were included in a diet low in saturated fat with high fruit and vegetable intake.[39] More recently, Chiu et al[40] evaluated the effects of a traditional DASH diet and a high-fat DASH diet that utilized full-fat dairy products. Inclusion of full-fat dairy products did not adversely affect the cardiometabolic risk factor responses. Both the traditional and high-fat DASH diets lowered blood pressure compared with the control (typical American) diet. The high-fat DASH diet also produced a reduction in plasma triglycerides compared with the control and traditional DASH diets without significantly increasing the LDL-C concentration.[40]

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WHY ARE VEGETARIAN DIETARY PATTERNS ASSOCIATED WITH LOWER RISKS FOR CANCER AND CARDIOVASCULAR DISEASE?

The favorable outcomes associated with vegetarian dietary patterns are often assumed to be attributable to adverse effects of consuming meat and other animal products. As described previously, some biologically plausible mechanisms have been described for potential adverse effects, although alternative explanations are also possible. Given the low prevalence of veganism, very limited evidence from observational studies is available from which to assess possible differences in health outcomes for those consuming vegan diets compared with other vegetarian diet patterns. Also, it is difficult to evaluate the differences between vegans and vegetarians in other dietary or lifestyle factors that may affect those health outcomes. Therefore, the discussion below will focus mainly on vegetarian dietary patterns generally as defined by the avoidance of meats (ie, vegan and lacto-ovo vegetarian together) compared with omnivorous dietary patterns that include meats and other animal products.

Many lifestyle, behavior, and dietary factors that are independent of meat intake differ between those who follow vegetarian versus omnivore dietary patterns and are difficult or impossible to fully account for completely in statistical models.

Dietary Differences Other Than Meat Consumption

Vegetarians and vegans typically have higher nutrient density and diet quality than omnivores, as assessed by measures such as the Healthy Eating Index and the Mediterranean Diet Score.[41] Vegetarian diet patterns are characterized by higher consumption of whole grains, fruits, vegetables, nuts, seeds, legumes, and vegetable oils compared with omnivores, although considerable variation exists within eating patterns.[41] Vegetarian dietary patterns are typically higher in fiber; magnesium; vitamins C, E, and K; nonheme iron; and phytochemicals (eg, polyphenols and plant sterols) than omnivorous diets.[30] They are also lower in saturated fat, cholesterol, long-chain omega-3 fatty acids, vitamins D and B_{12}, calcium, and zinc.[30] Because vegetarian diet patterns are characterized by greater consumption of foods, nutrients, and dietary components that have been associated with favorable health outcomes,[30] the lower rates of chronic diseases in those consuming vegetarian eating patterns may be attributable, in part, to dietary choices other than avoidance of meats.

Other Lifestyle Factors and Behaviors

Results from large cohort studies in the United States indicate that higher red meat consumption is associated not only with differing dietary habits, but also with numerous lifestyle/behavioral factors that differ markedly from those with low red meat consumption. For example, in the NIH-AARP cohort studies assessing diet, lifestyle, and mortality in more than 500 000 men and women, high red meat consumers, compared with low consumers, had higher average body mass index, a greater prevalence of current smoking, less average physical activity, lower educational achievement, and lower socioeconomic status.[19,42] Similar observations have been reported in other cohorts for vegetarian diet patterns, with vegan and vegetarian diet consumers showing a variety of lifestyle and behavioral characteristics that would be expected to be associated with good health.[43–46] This has been observed in the Adventist Health Study and AHS-2 North American cohorts, the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford) cohort of UK adults, and the NutriNet-Sante Study cohort of French adults.[43-46] Within the AHS-2 cohort, for example, vegetarians and vegans had higher average educational achievement, greater exercise frequency, and lower mean BMI and alcohol consumption and were more likely to be married and less likely to smoke.[43] Among both the EPIC-Oxford and NutriNet-Sante Study cohort participants, vegetarians were less likely to consume alcohol and smoke, and vegans had lower BMI.[44–46]

In observational studies, it may be difficult or impossible to fully account for healthful/unhealthful behaviors other than the exposure under study, which can produce healthy/unhealthy user bias. Healthy user bias was illustrated by the experience with vitamin E supplements. Several large, observational studies showed an association between higher vitamin E intake, including intake from dietary supplements, and lower risk of coronary heart disease.[47,48] These results were strong, consistent, statistically significant after adjustment for many potential confounders, and biologically plausible, given the ability of vitamin E to inhibit oxidative modification of compounds carried by LDL particles.[49] However, subsequent results from randomized controlled trials failed to show a benefit of vitamin E supplementation for reducing coronary heart disease events.[50] The lower risk of coronary heart disease in vitamin E supplement users was likely due to more healthful lifestyle and behavioral patterns of users compared with nonusers that could not

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be fully accounted for in statistical modeling. Unhealthy user bias was recently illustrated by a report of higher covariate-adjusted risks of mortality from several noncancer diseases among those who failed to adhere to cancer screening recommendations in a clinical trial.[51] As an editorial accompanying the paper notes, the most likely explanation is that nonadherence with recommended screening is a marker for behaviors that are associated with increased mortality.[51] Thus, it is possible that the favorable health outcomes associated with vegetarian diet patterns are attributable, at least in part, to healthy user bias in vegetarians and/or unhealthy user bias in high meat consumers.

Results From Randomized Controlled Trials of Disease Outcomes

Minimal long-term data from randomized controlled trials are available to assess disease outcomes associated with abstinence from, or reductions in, meat intake. Randomized controlled trials are less subject to selection bias, such as healthy user bias, because randomization ensures that known and unknown factors related to disease risk are randomly distributed across the groups under study.

Both the Polyp Prevention Trial and the Women's Health Initiative Dietary Modification Trial utilized dietary interventions intended to lower intakes of total fat and increase intakes of fruits, vegetables, and fiber from grains. In the Polyp Prevention Trial (N = 2079 men and women), the subjects assigned to the intervention group had a dietary goal of 20% energy from fat, 18 g fiber/1000 kcal, and 3.5 servings/1000 kcal of fruits and vegetables, whereas the control group received general dietary guidance.[52] After 4 years of follow-up, there was no difference between the groups in the primary outcome variable of recurrence of adenomatous polyps.[52] The intervention group reduced red and processed meat intake by ~20% and increased fruit and vegetable intake. After a median follow-up of ~4 years, 39.7% of the 958 subjects in the intervention group had at least 1 recurrent adenomatous polyp as did 39.5% of the 947 subjects in the control group (no statistically significant difference).

In the much larger Women's Health Initiative Dietary Modification Trial, like the Polyp Prevention Trial, reductions in saturated fat and red meat intake and increases in fruits, vegetables, grains, and related nutrients were observed by the first year in the intervention group compared with the control group.[53] However, there were no differences between the intervention (n = 19 451) and usual diet control (n = 29 294) groups for incidence of the main prespecified outcomes of colorectal cancer, breast cancer, or cardiovascular events, although there were small but statistically significant decreases in body weight, LDL-C, and diastolic blood pressure in the diet intervention group.[53] Despite the ~20% reduction in red and processed meat consumption (poultry intake was stable or increased slightly) along with other dietary changes, no effects of dietary changes were observed on the primary outcome variables.[52,53]

Thus, while the available data from randomized controlled trials of disease incidence are very limited, the available results do not show favorable effects on health outcomes of reducing red and processed meat intakes by ~20%. To the authors' knowledge, no large-scale, randomized controlled trial evidence is available for vegetarian or vegan dietary pattern interventions and chronic disease incidence.

Well-controlled intervention trials show minimal or no effects of lean meat intake on traditional markers for chronic disease risk.

Results from randomized controlled trials of vegan or vegetarian diet interventions for periods of several weeks to several months have shown improvements in several cardiometabolic risk factors, including lipoprotein lipids (total and LDL-C), body weight, and indices of carbohydrate homeostasis, which is consistent with differences that have been reported in observational studies between those who consume vegetarian or vegan diets and omnivores.[54–60] Because these interventions generally included multiple dietary changes, it is difficult to determine the degree to which effects on the cardiometabolic risk factor profile may have been attributable to reductions in the intakes of meat and other animal products versus changes in intakes of other dietary components such as higher consumption of dietary fibers, unsaturated fatty acids, and magnesium.[55,56] Additional studies are needed in which overall diet quality is matched to more clearly isolate the impacts of the presence or absence of meats and other animal foods in diets that are otherwise of similar overall quality.

SUMMARY AND CONCLUSIONS

The facts are clear regarding what we know: vegetarian diet patterns (lacto-ovo and vegan) are associated with favorable cardiometabolic risk factor profiles and improved health outcomes in observational studies, particularly lower risks of incident cancer (8%-15%) and ischemic heart disease (25%) compared with an omnivorous dietary pattern.[3] What we don't know, or fully understand, is the degree to which these favorable health outcomes can be attributed to avoiding consumption of meats and/or other animal

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products. Vegetarian dietary patterns are generally associated with higher overall diet quality and other lifestyle and behavioral habits that have been linked with good health, which may be difficult or impossible to fully account for in statistical models, resulting in residual confounding regarding intake of meat and other animal products as a potentially causal factor. In addition, recent publications have pointed out that not all plant-based diets are healthful and not necessarily synonymous with vegetarianism.[61] For example, "unhealthy" plant-based diets, rich in refined grains, sweets, soft drinks, juice, French fries, and so on, are linked to a higher risk of cardiovascular disease compared with a "healthy" plant-based diet, rich in whole grains, fruits, vegetables, nuts, seeds, and legumes.[61] Thus, even within plant-based diets, the wide spectrum of dietary choices makes it difficult to account for all potential confounding.

There are biologically plausible mechanisms through which consumption of meats could increase risks of cardiometabolic diseases and cancers. However, at present, very limited data are available from randomized controlled trials in which meat intake has been modified to assess effects on clinical outcomes. The DGA 2015–2020 recommend consuming up to 26-oz equivalents of protein foods, including meats, poultry, and eggs, and limiting red meat consumption to 3 to 4 servings per week (2–3 oz per serving) as part of a healthy dietary pattern. Examples of healthy eating patterns modeled in the DGA 2015–2020 include Healthy American, Mediterranean, and Vegetarian approaches. For those who opt to consume a vegetarian (including vegan) eating pattern, strategies are needed to ensure adequate intakes of some nutrients, such as long-chain omega-3 fatty acids, vitamins D and B_{12}, calcium, and zinc. For those who consume meats, fresh choices should generally be preferred over processed versions to limit intakes of sodium and nitrites/nitrates. Dietary saturated fat and cholesterol levels should not be excessive (<10% of energy and <300 mg/d, respectively). Also, it is ideal to minimize consumption of meats that have been charred or cooked at very high temperatures, which can generate potentially carcinogenic compounds.

Additional research is needed to more clearly quantify the health effects of vegetarian dietary patterns and to assess the degree to which favorable clinical outcomes associated with such patterns in observational studies (ie, what we know) are attributable to avoidance of meat and/or other animal products, as opposed to other characteristics of those who choose to follow such patterns, including higher overall diet quality and other lifestyle/behavioral factors that promote good health (ie, what we don't know, at present). Given that more than 95% of the US population regularly consumes meats and other animal products, answers to these questions have important public health implications.

REFERENCES

1. Segovia-Siapco G, Sabate J. Health and sustainability outcomes of vegetarian dietary patterns: a revisit of the EPIC-Oxford and the Adventist Health Study-2 cohorts [published online ahead of print October 2, 2018]. *Eur J Clin Nutr*. 2018.
2. Cramer H, Kessler CS, Sundberg T, et al. Characteristics of Americans choosing vegetarian and vegan diets for health reasons. *J Nutr Educ Behav*. 2017;49(7):561–567. e561.
3. Dinu M, Abbate R, Gensini GF, Casini A, Sofi F. Vegetarian, vegan diets and multiple health outcomes: a systematic review with meta-analysis of observational studies. *Crit Rev Food Sci Nutr*. 2017;57(17):3640–3649.
4. Appleby PN, Key TJ. The long-term health of vegetarians and vegans. *Proc Nutr Soc*. 2016;75(3):287–293.
5. US Department of Health and Human Services and US Department of Agriculture. *2015-2020 Dietary Guidelines for Americans*. 8th ed. December 2015. http://health.gov/dietaryguidelines/2015/guidelines/. Accessed November 14, 2018.
6. Willett W, Rockström J, Loken B, et al. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. *The Lancet*. 2019;393(10170):447–492.
7. Rehm CD, Penalvo JL, Afshin A, Mozaffarian D. Dietary intake among US adults, 1999-2012. *JAMA*. 2016;315(23):2542–2553.
8. Kwok CS, Umar S, Myint PK, Mamas MA, Loke YK. Vegetarian diet, Seventh Day Adventists and risk of cardiovascular mortality: a systematic review and meta-analysis. *Int J Cardiol*. 2014;176(3):680–686.
9. Le LT, Sabate J. Beyond meatless, the health effects of vegan diets: findings from the Adventist cohorts. *Nutrients*. 2014;6(6):2131–2147.
10. Mihrshahi S, Ding D, Gale J, Allman-Farinelli M, Banks E, Bauman AE. Vegetarian diet and all-cause mortality: evidence from a large population-based Australian cohort—the 45 and Up Study. *Prev Med*. 2017;97:1–7.
11. Key TJ, Appleby PN, Crowe FL, Bradbury KE, Schmidt JA, Travis RC. Cancer in British vegetarians: updated analyses of 4998 incident cancers in a cohort of 32,491 meat eaters, 8612 fish eaters, 18,298 vegetarians, and 2246 vegans. *Am J Clin Nutr*. 2014;100(suppl 1):378S–385S.
12. Phillips RL. Role of life-style and dietary habits in risk of cancer among Seventh-Day Adventists. *Cancer Res*. 1975;35(11 Pt. 2):3513–3522.
13. Montgomery S, Herring P, Yancey A, et al. Comparing self-reported disease outcomes, diet, and lifestyles in a national cohort of black and white Seventh-Day Adventists. *Prev Chronic Dis*. 2007;4(3):A62–A62.
14. Tonstad S, Butler T, Yan R, Fraser GE. Type of vegetarian diet, body weight, and prevalence of type 2 diabetes. *Diabetes Care*. 2009;32(5):791–796.
15. Rizzo NS, Sabate J, Jaceldo-Siegl K, Fraser GE. Vegetarian dietary patterns are associated with a lower risk of metabolic syndrome: the adventist health study 2. *Diabetes Care*. 2011;34(5):1225–1227.
16. Cross AJ, Sinha R. Meat-related mutagens/carcinogens in the etiology of colorectal cancer. *Environ Mol Mutagen*. 2004;44(1):44–55.
17. Jagerstad M, Skog K. Genotoxicity of heat-processed foods. *Mutat Res*. 2005;574(1–2):156–172.
18. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 114: IARC Working Group on the Evaluation of Carcinogenic Risk to Humans*. Lyon, France: International Agency for Research on Cancer; 2018.
19. Etemadi A, Sinha R, Ward MH, et al. Mortality from different causes associated with meat, heme iron, nitrates, and nitrites in the NIH-AARP Diet and Health Study: population based cohort study. *BMJ*. 2017;357:j1957.

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20. Sasso A, Latella G. Role of heme iron in the association between red meat consumption and colorectal cancer. *Nutr Cancer*. 2018; 70(8):1173–1183.
21. World Cancer Research Fund/American Institute for Cancer Research. *Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective. The Third Expert Report*. Washington, DC: American Institute for Cancer Research; 2018.
22. O'Connor LE, Campbell WW. Red meat and health: getting to the heart of the matter. *Nutr Today*. 2017;52(4):167–173.
23. Maki KC, van Elswyk ME, Alexander DD, Rains TM, Sohn EL, McNeill S. A meta-analysis of randomized controlled trials that compare the lipid effects of beef versus poultry and/or fish consumption. *J Clin Lipidol*. 2012;6(4):352–361.
24. Maki KC, Palacios OM, Wilcox ML, Dicklin MR, Bell M, Maki CE. Effects of lean beef intake, as part of a healthful dietary pattern, on cardiometabolic risk markers in subjects at risk for diabetes mellitus: a controlled feeding trial. Presented at the American Society for Nutrition 2019 in Baltimore, MD, June 8-11, 2019.
25. Roussell MA, Hill AM, Gaugler TL, et al. Beef in an Optimal Lean Diet study: effects on lipids, lipoproteins, and apolipoproteins. *Am J Clin Nutr*. 2012;95(1):9–16.
26. Roussell MA, Hill AM, Gaugler TL, et al. Effects of a DASH-like diet containing lean beef on vascular health. *J Hum Hypertens*. 2014;28(10):600–605.
27. McNeill SH, Harris KB, Field TG, van Elswyk ME. The evolution of lean beef: identifying lean beef in today's U.S. marketplace. *Meat Sci*. 2012;90(1):1–8.
28. Jacobson TA, Maki KC, Orringer CE, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 2. *J Clin Lipidol*. 2015;9(6 suppl): S1–122.e1.
29. Wang F, Zheng J, Yang B, Jiang J, Fu Y, Li D. Effects of vegetarian diets on blood lipids: a systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc*. 2015;4(10): e002408.
30. Melina V, Craig W, Levin S. Position of the Academy of Nutrition and Dietetics: vegetarian diets. *J Acad Nutr Diet*. 2016;116(12): 1970–1980.
31. Wang Z, Bergeron N, Levison BS, et al. Impact of chronic dietary red meat, white meat, or non-meat protein on trimethylamine N-oxide metabolism and renal excretion in healthy men and women. *Eur Heart J*. 2019;40(7):583–594.
32. Heianza Y, Ma W, Manson JE, Rexrode KM, Qi L. Gut microbiota metabolites and risk of major adverse cardiovascular disease events and death: a systematic review and meta-analysis of prospective studies. *J Am Heart Assoc*. 2017;6(7).
33. Lonn E, Bosch J, Yusuf S, et al. Effects of long-term vitamin E supplementation on cardiovascular events and cancer: a randomized controlled trial. *JAMA*. 2005;293(11):1338–1347.
34. Maki KC, Palacios OM, Buggia M, Dicklin MR, Bell M, Maki CE. The effect of replacing carbohydrate-based breakfast foods with eggs on cardiometabolic risk factors in adults at-risk for type 2 diabetes. Presented at the American Society for Nutrition 2019 in Baltimore, MD, June 8-11, 2019.
35. Xu L, Lam TH, Jiang CQ, et al. Egg consumption and the risk of cardiovascular disease and all-cause mortality: Guangzhou Biobank Cohort Study and meta-analyses. *Eur J Nutr*. 2019; 58(2):785–796.
36. Blesso CN, Fernandez ML. Dietary cholesterol, serum lipids, and heart disease: are eggs working for or against you? *Nutrients*. 2018;10(4).
37. Alexander DD, Miller PE, Vargas AJ, Weed DL, Cohen SS. Meta-analysis of egg consumption and risk of coronary heart disease and stroke. *J Am Coll Nutr*. 2016;35(8):704–716.
38. Drouin-Chartier JP, Cote JA, Labonte ME, et al. Comprehensive review of the impact of dairy foods and dairy fat on cardiometabolic risk. *Adv Nutr*. 2016;7(6):1041–1051.
39. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med*. 1997;336(16):1117–1124.
40. Chiu S, Bergeron N, Williams PT, Bray GA, Sutherland B, Krauss RM. Comparison of the DASH (Dietary Approaches to Stop Hypertension) diet and a higher-fat DASH diet on blood pressure and lipids and lipoproteins: a randomized controlled trial. *Am J Clin Nutr*. 2016;103(2):341–347.
41. Clarys P, Deliens T, Huybrechts I, et al. Comparison of nutritional quality of the vegan, vegetarian, semi-vegetarian, pesco-vegetarian and omnivorous diet. *Nutrients*. 2014;6(3): 1318–1332.
42. Sinha R, Cross AJ, Graubard BI, Leitzmann MF, Schatzkin A. Meat intake and mortality: a prospective study of over half a million people. *Arch Intern Med*. 2009;169(6):562–571.
43. Orlich MJ, Singh PN, Sabate J, et al. Vegetarian dietary patterns and mortality in Adventist Health Study 2. *JAMA Intern Med*. 2013;173(13):1230–1238.
44. Key TJ, Appleby PN, Spencer EA, Travis RC, Roddam AW, Allen NE. Mortality in British vegetarians: results from the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford). *Am J Clin Nutr*. 2009;89(5):1613S–1619S.
45. Key TJ, Appleby PN, Spencer EA, Travis RC, Roddam AW, Allen NE. Cancer incidence in vegetarians: results from the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford). *Am J Clin Nutr*. 2009;89(5):1620S–1626S.
46. Allès B, Baudry J, Méjean C, et al. Comparison of sociodemographic and nutritional characteristics between self-reported vegetarians, vegans, and meat-eaters from the NutriNet-Santé Study. *Nutrients*. 2017;9(9).
47. Kushi LH, Folsom AR, Prineas RJ, Mink PJ, Wu Y, Bostick RM. Dietary antioxidant vitamins and death from coronary heart disease in postmenopausal women. *N Engl J Med*. 1996;334(18): 1156–1162.
48. Rimm EB, Stampfer MJ, Ascherio A, Giovannucci E, Colditz GA, Willett WC. Vitamin E consumption and the risk of coronary heart disease in men. *N Engl J Med*. 1993;328(20):1450–1456.
49. Suzukawa M, Ayaori M, Shige H, Hisada T, Ishikawa T, Nakamura H. Effect of supplementation with vitamin E on LDL oxidizability and prevention of atherosclerosis. *Biofactors*. 1998;7(1–2):51–54.
50. Yusoff K. Vitamin E in cardiovascular disease: has the die been cast? *Asia Pac J Clin Nutr*. 2002;11(suppl 7):S443–S447.
51. Grady D, Parks M. Why is nonadherence to cancer screening associated with increased mortality? [published online ahead of print December 28, 2018]. *JAMA Intern Med*. 2018.
52. Schatzkin A, Lanza E, Corle D, et al. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. Polyp Prevention Trial Study Group. *N Engl J Med*. 2000;342(16): 1149–1155.
53. Beresford SA, Johnson KC, Ritenbaugh C, et al. Low-fat dietary pattern and risk of colorectal cancer: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *JAMA*. 2006; 295(6):643–654.
54. Wright N, Wilson L, Smith M, Duncan B, McHugh P. The BROAD study: a randomised controlled trial using a whole food plant-based diet in the community for obesity, ischaemic heart disease or diabetes. *Nutr Diabetes*. 2017;7(3):e256.
55. Yokoyama Y, Levin SM, Barnard ND. Association between plant-based diets and plasma lipids: a systematic review and meta-analysis. *Nutr Rev*. 2017;75(9):683–698.
56. Kahleova H, Levin S, Barnard N. Cardio-metabolic benefits of plant-based diets. *Nutrients*. 2017;9(8).

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57. Kahleova H, Tura A, Hill M, Holubkov R, Barnard ND. A plant-based dietary intervention improves beta-cell function and insulin resistance in overweight adults: a 16-week randomized clinical trial. *Nutrients*. 2018;10(2).
58. Ornish D, Scherwitz LW, Billings JH, et al. Intensive lifestyle changes for reversal of coronary heart disease. *JAMA*. 1998; 280(23):2001–2007.
59. Lee YM, Kim SA, Lee IK, et al. Effect of a brown rice based vegan diet and conventional diabetic diet on glycemic control of patients with type 2 diabetes: a 12-week randomized clinical trial. *PLoS One*. 2016;11(6):e0155918.
60. Kahleova H, Dort S, Holubkov R, Barnard ND. A plant-based high-carbohydrate, low-fat diet in overweight individuals in a 16-week randomized clinical trial: the role of carbohydrates. *Nutrients*. 2018;10(9).
61. Hemler EC, Hu FB. Plant-based diets for cardiovascular disease prevention: all plant foods are not created equal. *Curr Atheroscler Rep*. 2019;21(5):18.

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HIGH INTAKES OF VITAMINS B_6 AND B_{12} ASSOCIATED WITH INCREASED RISK OF HIP FRACTURE

Vitamin supplementation far exceeding recommended doses is popular in many segments of the population. However, adverse effects can and do occur. In a previous secondary analysis of combined data from 2 double-blind randomized clinical trials, investigators found an unexpected increased risk of hip fracture was found among those treated with high doses of vitamin B_6 in combination with vitamin B_{12}. To study if high intakes of vitamins B_6 and B_{12} from food and supplements were associated with a risk of hip fracture in the Nurses' Health Study, researchers investigated whether combined high intakes of both vitamins conferred a particularly increased fracture risk. In the prospective cohort study, 75 864 postmenopausal women in the United States were followed up from June 1984 through May 2014. Information on hip fracture and a wide range of potential confounders was collected at baseline and with biennial follow-up questionnaires. Extensive dietary information was collected approximately every 4 years with a semiquantitative food frequency questionnaire. The analysis was done from July 2016 to June 2018. Relative risks were calculated by Cox proportional hazards regression, with cumulative average intakes of vitamins B_6 and B_{12} as main exposures, adjusting for potential confounders. During follow-up, 2304 of 75 864 women had a hip fracture. Among the women with hip fractures, the median age at hip fracture was 75.8 years, and the mean body mass index was 24.3 kg/m^2, Median cumulative average intakes of total vitamins B_6 and B_{12} were 3.6 mg/d and 12.1 μg/d, respectively. Both vitamin B_6 and vitamin B_{12} were associated with increased fracture risk. Risk was highest in women with a combined high intake of both vitamins (B_6 ≥35 mg/d and B_{12} ≥20 μg/d), who had an almost 50% increased risk of hip fracture compared with women with a low intake of both vitamins (B_6 <2 mg/d and B_{12} <10 μg/d). Thus, the combined very high intake of vitamins B_6 and B_{12}, much higher than the recommended dietary allowances was associated with an increased risk of hip fracture. These findings add to previous studies suggesting that vitamin supplements should be used cautiously because adverse effects can occur. If replicated, these findings will provide another reason for going easy on massive amounts of vitamins.

Source: Meyer HE, Willett WC, Fung TT, Holvik K, Feskanich D. Association of high intakes of vitamins B_6 and B_{12} from food and supplements with risk of hip fracture among postmenopausal women in the Nurses' Health Study *JAMA Netw Open.* 2019;2(5): e193591.

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