

Vegetarian diets: what do we know of their effects on common chronic diseases?^{1–4}

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ABSTRACT

A number of studies have evaluated the health of vegetarians. Others have studied the health effects of foods that are preferred or avoided by vegetarians. The purpose of this review is to look critically at the evidence on the health effects of vegetarian diets and to seek possible explanations where results appear to conflict. There is convincing evidence that vegetarians have lower rates of coronary heart disease, largely explained by low LDL cholesterol, probable lower rates of hypertension and diabetes mellitus, and lower prevalence of obesity. Overall, their cancer rates appear to be moderately lower than others living in the same communities, and life expectancy appears to be greater. However, results for specific cancers are much less convincing and require more study. There is evidence that risk of colorectal cancer is lower in vegetarians and in those who eat less meat; however, results from British vegetarians presently disagree, and this needs explanation. It is probable that using the label “vegetarian” as a dietary category is too broad and that our understanding will be served well by dividing vegetarians into more descriptive subtypes. Although vegetarian diets are healthful and are associated with lower risk of several chronic diseases, different types of vegetarians may not experience the same effects on health. *Am J Clin Nutr* 2009;89(suppl):1607S–12S.

INTRODUCTION

The reputation of vegetarian diets and those who eat them has a checkered history. It was not so long ago that the American Dietetic Association (ADA) recorded serious doubts about their nutritional adequacy (1), but recent recommendations have been much more positive (2). Probably, the first serious scientific investigations of these diets were performed by Mervyn Hardinge (3–5) as part of his Harvard doctoral dissertation. His advisors at that time needed some persuasion that this was a serious topic, although to their credit he was allowed to proceed.

The first cohort study of Seventh-day Adventists in California included many vegetarians and was funded by the US Public Health Service and formed in 1958. Although it collected only fatal disease events, it quickly amassed evidence to suggest that Adventists who ate diets emphasizing plant foods experienced much lower coronary disease mortality (6) than did non-vegetarian Adventists. The next cohort of California Adventists was the Adventist Health Study-1 (AHS-1) beginning in 1974–1976 (7), and was approximately concurrent with a small number of other large cohorts designed to evaluate diet-disease associations and to collect all incident events (nonfatal and fa-

tal). These latter studies did not evaluate vegetarian health per se because they enrolled very few vegetarians, but they could compare subjects who ate lesser and greater quantities of animal products. They included such well-known cohorts as the Nurses' Health Study (8), the Physicians' Health Study (9), the Health Professional's cohort (10), and the Iowa Womens' Study (11).

A small number of cohorts did enroll many vegetarians, aside from the California studies of Adventists. These were the Health Food Shoppers' Study (12), the Oxford Vegetarian Study (13), both in the United Kingdom, and the Heidelberg Vegetarian Study (14) in Germany. Those studies observed deaths only and were relatively small so that power for coronary events was moderate but was typically poor for cancers at one site. More recently, the European Prospective Investigation into Cancer and Nutrition–Oxford (EPIC-Oxford) study included many British vegetarians and other “health-conscious” subjects and collected data on all incident cancers and fatal events (15). Other studies have evaluated the nutritional adequacy of vegetarian diets mainly by measuring blood concentrations of vitamins and other key nutrients.

These studies, when taken together, produced compelling evidence that most vegetarian diets were not only nutritionally adequate but also associated with lower risks of certain chronic diseases when compared with effects of a more typical Western diet. Whether this advantage extends to vegans who eat no animal products is still open to question. Thus, more recent official statements from the ADA have clearly described vegetarian diets as healthful, although vegans should take some precautions (2).

WHAT DO THE EXISTING DATA SHOW?

Internal consistency of results in Adventist vegetarians

Briefly, I point out the internal consistency in the results from Adventists about all-cause mortality, risk of certain cancers, and coronary heart disease (CHD) rates. Studies within the Adventist

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group that compared risks of vegetarians with nonvegetarians showed clear benefits to the vegetarians for risks of CHD (16), colon cancer (17), and life expectancy (18). Our results also suggested protection against certain other cancers but are not by themselves conclusive (17, 19).

Hence, the results from within the Adventist group would lead one to predict reduced risk of Adventists as a group when compared with other populations, given the higher proportion of vegetarians. Our findings are exactly as predicted in that California Adventists have lower risks of CHD and many specific cancers and have a greater life expectancy than do non-Adventists living in the same communities (18, 20, 21).

Comparisons with the results from other studies

In the following section, studies that compare risks of certain chronic diseases in vegetarians and nonvegetarians are reviewed. In addition, studies that looked at foods preferred by vegetarians are discussed.

Consistent results

Results about disease risk that largely agree among different studies include those for CHD and perhaps diabetes and colon cancer. In addition, data on other risk factors for chronic diseases, such as overweight, blood lipids, and blood pressure, fit this criterion.

Mortality and incidence rates of coronary disease events are indeed clearly lower in vegetarians. This is true in the 2 previous cohorts of Adventists (16, 22) and in the older cohorts of British and German vegetarians (23–25). A combined analysis of those cohorts (26) confirmed this result with a 32% higher CHD mortality rate in the nonvegetarians. This is not surprising because there is convincing evidence that several important risk factors for CHD have more optimal values in vegetarians.

Regular, moderate nut (16, 27) and whole-grain (11, 16) consumption are associated with lower risk of CHD. These are foods often preferred by vegetarians. Several other studies of nonvegetarians have strongly suggested that dietary patterns emphasizing fruit, vegetables, and less meat are associated with much lower risk of CHD (10, 28) consistent with the CHD mortality data in studies of vegetarians.

Animal fats (largely saturated) raise LDL cholesterol (29) and increase risk; these obviously come from foods eaten less or not at all by vegetarians. Total or LDL cholesterol is typically lower in vegetarians (30, 31). HDL cholesterol is not consistently different (30, 32), although it does tend to be a little lower in Adventists (33), perhaps because of the lack of alcohol consumption. Vegetarians are consistently thinner, or at least less overweight, than are nonvegetarians within the same studies (34, 32). It is also probable that vegetarians have lower blood pressures than others (32, 35, 36), although the reasons are still controversial, and effects are sometimes small as in British vegetarians (37).

Prevalence of diabetes is lower in Adventist vegetarians than in Adventist nonvegetarians (36, 38), and part of this advantage is no doubt due to the lower body weights of the vegetarians. Supporting evidence can be found from a few other studies that have addressed this issue (39). Participants eating more processed meats in the Health Professionals Follow-up Study had a higher risk of developing diabetes (40). Foods with a lower glycemic index predicted lower risk of new diabetes in nurses

(41) and, of course, include such items as vegetables, legumes, grains, and nuts preferred by many vegetarians.

Preliminary results on these risk factors from the new Adventist Health Study-2 cohort are shown in **Table 1**. These results compare prevalence between different types of vegetarians (semi-, pesco-, lactoovo-vegetarians, and vegans; defined further in **Figure 1**) and nonvegetarians. Data on prevalent diabetes and hypertension are those self-reported in the study baseline questionnaire and are ostensibly physician-diagnosed. We used only positive responses when subjects also indicated that they had been treated within the past 12 mo. Body mass indexes (in kg/m²) were calculated from self-reported heights and body weights, which were validated in a validation substudy of 840 representative study subjects in which measurements were taken at a clinic (correlation coefficient: 0.945). Quite dramatic trends are seen in the prevalence of currently treated diabetes, recently treated hypertension, and body mass index, across the spectrum of different types of vegetarian, when compared with Adventist nonvegetarians. Thus, we have a consistent picture for at least CHD, diabetes, and hypertension, in which risks appear to be lower in vegetarians, and some of the mechanisms are clear, which makes causality more plausible.

There is general agreement that red meat consumption increases the risk of colon or colorectal cancer. This was the only food association with cancer that was labeled “convincing” in the recent report from the World Cancer Research Fund, American Institute for Cancer Research (42). The evidence, of course, largely came from studies of meat consumption in nonvegetarians, although data from Adventist vegetarians in California concur (43).

The British studies of vegetarians are at variance with this result at present (44); and this is further discussed in the next subsection. However, the results from the combined European cohorts in the EPIC do show increased risk of colon cancer with

TABLE 1
Mean BMI (in kg/m²) and the prevalence of diabetes and hypertension in different types of vegetarians compared with nonvegetarians in California Seventh-day Adventists: preliminary analyses adjusted for age, sex, and race¹

Diet group	BMI ²	Diabetes ³	Hypertension ³
Nonvegetarian	28.26 (28.22, 28.30)	1.00	1.00
Semivegetarian	27.00 (26.96, 27.04)	0.72 (0.65, 0.79)	0.77 (0.72, 0.82)
Pescovegetarian	25.73 (25.69, 25.77)	0.49 (0.44, 0.55)	0.62 (0.59, 0.66)
Lactoovo-vegetarian	25.48 (25.44, 25.52)	0.39 (0.36, 0.42)	0.45 (0.44, 0.47)
Vegan	23.13 (23.09, 23.16)	0.22 (0.18, 0.28)	0.25 (0.22, 0.28)
P ⁴	0.0001	0.0001	0.0001

¹ n = 89,224. The numbers of subjects in each dietary category for each endpoint analysis can be calculated with the proportions given in Figure 1, noting that 5.5%, 6.5%, and 8.2% of subjects in each analysis are excluded because of missing data. For BMI, when calculating means and intervals, covariates are set at age 50 y, sex is 50% male, and race is white. Technically, these are prediction intervals based on the regression. Diabetes and hypertension are self-reported, but physician-diagnosed, and treated within the past 12 mo.

² Values are means; 95% CIs in parentheses.

³ Values are relative risks; 95% CIs in parentheses.

⁴ Tests the null hypothesis of no difference by dietary group. These tests used a partial F test for BMI and likelihood ratio tests for diabetes and hypertension, removing the dietary group terms.

	%	BEEF	POULTRY/FISH	DAIRY/EGGS
VEGAN	4.3	NONE	NONE	NONE
LACTO-OVO	34.0	NONE	NONE	
PESCO-VEGE	9.7	NONE		
SEMI-VEGE	8.3			
NON-VEGE	43.7			

FIGURE 1. A classification of vegetarian diets that is used in the Adventist Health Study-2. Note: Vegans (total vegetarians) eat no red meat, fish, poultry, dairy, and eggs; lactoovovegetarians (LACTO-OVO) eat milk, eggs, or both but no red meat, fish, or poultry; pescovegetarians (PESCO-VEGE) eat fish, milk, and eggs but no red meat and poultry; semivegetarians (SEMI-VEGE) eat red meat, poultry, and fish less than once a week; and nonvegetarians (NON-VEGE) eat red meat, poultry, fish, milk, and eggs more than once a week.

higher meat (mainly processed meat) consumption even though they include the British data (45). Data from US nurses and health professionals, also a very large prospective study of retired persons, support this result further by showing a positive association of risk with meat consumption (46–48). There are several hypotheses about mechanisms for an effect of meat (48), but the evidence is as yet not compelling for any.

The idea that higher consumption of fruit and vegetables is associated with reduced all-cause mortality has a long history. Several recent studies give support to this, including a large US study of women (49), the EPIC Elderly Study in Europe (50), and also a large study of patients with diabetes in Europe (51). In the absence of other confounders it would be expected that vegetarians would benefit from any such effects, because they typically eat more fruit and vegetables than others in the same communities (15, 33). It is also true that to consider vegetables and fruit as single research categories is a broad brush and requires further understanding of the active phytochemical content of these plants. That all fruit and vegetables contribute equally, or at all, seems improbable.

Inconsistent results

Two areas of possible inconsistency in the California and British vegetarian data are the associations between vegetarian diets and total mortality and between vegetarian diets and colon cancer. Although California Adventist vegetarians have lower total mortality and incidence of colon cancer than do Adventist nonvegetarians, such results are not clearly seen in British vegetarians, at least when they are compared with other British subjects who are largely health-conscious persons.

In the EPIC-Oxford study (44), there was no clear evidence that vegetarians had rates of colorectal cancer lower than those of average British citizens (standardized incidence ratio: 101; 95% CI: 79, 128). It may be relevant that in this relatively health-conscious cohort the pattern of the diet (excepting meats, fruit, and vegetables) was relatively similar to the UK population in most other respects, with high consumption of tea, sauces, cakes, soft drinks (women), butter, and margarine (52).

Overall, differences in nutrient intake between British vegetarians (the few vegans excepted) are modest compared with nonvegetarians in the EPIC-Oxford study (15). The amount of meat consumption in the largely health-conscious nonvegetarian comparison group is also unclear and may affect the interpretation of results.

One could also consider the possibility that some other factor confounds the meat–colon cancer association in the United Kingdom and is not present in other parts of Europe or the United States. The identity of such a factor is not at all clear, however. It is also possible that there may be differences in the composition of beef at various locations. The meat from largely corn-fed cattle in the United States may have different characteristics that influence health (53).

For all-cause mortality there appeared to be a strong age modification of the effect of vegetarianism in the Adventist data, in that meat consumption was strongly associated with increased mortality during the sixth decade and younger, with a weakening effect thereafter (54). In the data from British vegetarians compared with other health-conscious subjects, there was little overall difference in total mortality (55). Both groups, however, experienced much less mortality than did average British subjects. One interpretation is that British vegetarians have an advantage compared with the general population but that other health-conscious subjects manage equal benefits without totally removing meat from the diet.

Could the usually mild (56) healthy volunteer effect in most cohort studies produce these results? One form of healthy volunteer effect results when those who volunteer to participate in a cohort study are systematically less likely to be chronically ill. Trends of increasing risk on follow-up because of the initial lack and subsequent development of acute illness in the cohort disappear after 3–4 y as a new steady state is reached. If stable differences in risk compared with some hypothetical parent population still remain, these may reasonably be attributed to differences on average in environmental factors, including the long-term health habits that we are investigating (56). This a different form of healthy volunteer effect that does not in itself bias effect estimates within the cohort.

It seems probable that the British and California Adventist vegetarian diets are rather different. In this case, effects on risk may not perfectly agree. For instance, health-conscious British subjects in the EPIC study are relatively high consumers of fruit and vegetables compared with British nonvegetarians, but they consume considerably less fruit and vegetables than some nonvegetarian Mediterranean cohorts in the EPIC study (52, 57). How the diets of British vegetarians compare with those of California vegetarians will be of interest to explore further as data from the latter group become available. This introduces the idea that using "vegetarian" as a single dietary label in research is probably inadequate.

IS "VEGETARIAN" A SATISFACTORY LABEL FOR RESEARCH PURPOSES?

Although the word "vegetarian" implies an emphasis on vegetables in the diet, in practice it has been traditionally interpreted to mean an absence of meat. It is not usual to define a dietary pattern based on one food category such as this. The problem is a lack of control on intake of all other food groups that may make up a large proportion of total calories even in vegetarians. Thus, it unfortunately allows the possibility of grouping together subjects under the one label who may eat in quite different ways, although all choose to exclude meats. If these other foods influence risk, they confound analyses evaluating effects that use a simple definition of vegetarianism.

It seems that the only solution is to insist on more detail. The vegan dietary category may be more comparable across countries and cultures, because avoiding all animal products allows little choice but to include large quantities of vegetables, fruit, nuts, and grains for nutritional adequacy. Admittedly, the identity of those vegetables and fruit may also vary widely at different locations.

DIFFERENT TYPES OF VEGETARIAN

The categories that we have used to distinguish different types of vegetarians in Adventist Health Study-2 (58) have also proven to be categories that have markedly different risks of common diseases such as diabetes and hypertension (Table 1). These categories are somewhat similar to those used previously in the United Kingdom (34). Previous comparisons of disease rates among vegetarians in different countries have not taken advantage of this greater amount of detail, however. The categories are as follows: vegans who eat no animal products; lactoovo-vegetarians who eat no meat but do eat eggs or dairy foods, or both; pescovegetarians who eat fish, but other meats <1 time/mo; semivegetarians who eat meats aside from fish occasionally but less than weekly; and nonvegetarians who eat meats aside from fish ≥ 1 time/wk. Operational definitions that we have used are shown in Figure 1. It is possible that the more-refined categories may provide better comparability when combining subjects from different countries in a pooled analysis.

IMPORTANT QUESTIONS AND TOPICS FOR FURTHER RESEARCH RELATED TO PLANT-BASED DIETS

- 1) Define the health experience of vegans compared with other vegetarians. Although certain risk factors appear to take

more favorable values in vegans, the limited data for risk of cancer and total mortality do not yet suggest a benefit in vegans (59).

- 2) Somewhat related to this are the effects of dairy foods on health, both cancer and cardiovascular disease. Effects on risk may point in different directions for colon and prostate cancers.
- 3) Are the n-6 (omega-6) fatty acids consumed preferentially by many vegetarians proinflammatory outside the laboratory, ie, in the intact person?
- 4) Clarify whether α -linolenic acid (eg, flax seed, soy) increases the risk of prostate cancer as some data suggest.
- 5) What are the advantages and risks of soy consumption (if any)?
- 6) Do all meats increase risk of CHD, colon cancer, and possibly other chronic diseases equally? Do processed meats have greater effects?
- 7) The decreased risk of several chronic diseases in vegetarians is probably not only due to reduced or absent meat consumption. The possible effects of particular families of vegetables, fruit, nuts, and grains should be evaluated to gain greater specificity.
- 8) Report descriptive details of vegetarian diets in different countries. Are these diets comparable, and how are pooled analyses best conducted?
- 9) When evaluating effects of specific foods or food groups, the difficulties imposed by dietary measurement errors are severe. Identification of additional biomarkers of intake for different families of fruit and vegetables should reduce this problem when they are used in biomarker-guided analyses of diet-disease associations (60).
- 10) Further basic science work is needed to identify and clarify mechanisms of biologically active phytochemicals. May some of these alter gene expression, for instance?

CONCLUSIONS

Much remains to be understood. However, it seems clear that vegetarians experience less CHD than do others. Their risk factor status would lead us to expect this result. The evidence that risk of diabetes is less in vegetarians is highly suggestive, although as yet it comes from cross-sectional work and mainly from California vegetarians. Again, what is known of causal factors in diabetes would lead us to expect this result. Body weight is lower in vegetarians and much lower in California Adventists. LDL cholesterol is lower in vegetarians, and this is probably true for blood pressure and risk of treated hypertension. The reasons for the blood pressure association are not well understood, and more research may refine our understanding of this.

Studies in both California and the United Kingdom are fairly consistent in finding at least moderate reductions in all-cause mortality in vegetarians, in comparison to other subjects living in the same communities. This would be expected on the basis of reduced cardiovascular mortality, unless some other presently unrecognized cause of death is increased in vegetarians. As suggested by the British work, it is also likely that there are other ways to similarly decrease mortality (the health-conscious nonvegetarians) aside from a dietary habit that is fully vegetarian.

Both British and California data are also fairly consistent in showing a reduction in total cancer incidence among vegetarians. In the British study there is, again, little difference between vegetarians and mainly health-conscious nonvegetarians, but large differences are seen when comparing with rates in the general population. These differences are most likely due to

environmental differences (including health habits) rather than to an acute healthy volunteer effect, which usually resolves in the early years of follow-up. The clear stand-out where the differences are stark is the relation between colon cancer and red meat consumption. The reasons for the lack of association in the United Kingdom are quite unclear and demand explanation.

Our understanding will probably be advanced by using more refined dietary categories than simply vegetarian and non-vegetarian in the future, because diets may differ greatly even when all lack meat. Nonmeat foods may be quite different in different countries, and pooling of data should be done with great care. (Other articles in this supplement to the Journal include references 44, 55, and 61–85.)

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