



## Conference on ‘The future of animal products in the human diet: health and environmental concerns’ Symposium 3: Alternatives to meat

### The long-term health of vegetarians and vegans

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Vegetarians, who do not eat any meat, poultry or fish, constitute a significant minority of the world’s population. Lacto-ovo-vegetarians consume dairy products and/or eggs, whereas vegans do not eat any foods derived wholly or partly from animals. Concerns over the health, environmental and economic consequences of a diet rich in meat and other animal products have focussed attention on those who exclude some or all of these foods from their diet. There has been extensive research into the nutritional adequacy of vegetarian diets, but less is known about the long-term health of vegetarians and vegans. We summarise the main findings from large cross-sectional and prospective cohort studies in western countries with a high proportion of vegetarian participants. Vegetarians have a lower prevalence of overweight and obesity and a lower risk of IHD compared with non-vegetarians from a similar background, whereas the data are equivocal for stroke. For cancer, there is some evidence that the risk for all cancer sites combined is slightly lower in vegetarians than in non-vegetarians, but findings for individual cancer sites are inconclusive. Vegetarians have also been found to have lower risks for diabetes, diverticular disease and eye cataract. Overall mortality is similar for vegetarians and comparable non-vegetarians, but vegetarian groups compare favourably with the general population. The long-term health of vegetarians appears to be generally good, and for some diseases and medical conditions it may be better than that of comparable omnivores. Much more research is needed, particularly on the long-term health of vegans.

#### Vegetarian: Vegan: Mortality: Morbidity

Vegetarians are defined as people who do not eat any meat, poultry or fish. They may be sub-classified as lacto-ovo-vegetarians who eat dairy products and/or eggs and vegans who do not eat any animal products.

The prevalence of vegetarianism (the practice of following a vegetarian diet) varies widely around the globe. India has the highest proportion of vegetarians of any country with about 30 % of the population following a vegetarian diet<sup>(1,2)</sup>. Elsewhere, vegetarianism is considerably less common, with less than 10 % of the population following a vegetarian diet<sup>(3)</sup>. For example, it has been estimated that vegetarians and vegans represent 5 and 2 %, respectively, of the US population<sup>(4)</sup>.

These figures indicate that vegetarians represent a sizeable minority of the global population, and with calls for a worldwide reduction in consumption of animal products<sup>(5)</sup>, their long-term health is a matter of considerable interest.

Many studies have assessed the nutritional adequacy of vegetarian diets. Overall, these have shown that a well-planned vegetarian or vegan diet can supply all the nutrients required for good health<sup>(6)</sup>. However, some concern remains over the possibility of low intakes of some nutrients such as vitamin B<sub>12</sub>, vitamin D, calcium and *n*-3 fatty acids in poorly selected and/or unfortified vegetarian or vegan diets<sup>(7,8)</sup>; in particular, vitamin B<sub>12</sub> status

Abbreviation: AHS-2, Adventist Health Study-2; EPIC-Oxford, European Prospective Investigation into Cancer and Nutrition-Oxford.  
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**Table 1.** Prospective studies with a high percentage of vegetarian participants

Study	Location	Period of recruitment	Number of participants*	Percentage vegetarian
Adventist Mortality <sup>(11)</sup>	California, USA	1959–60	23000	40
Health Food Shoppers <sup>(14)</sup>	UK	1973–79	11000	40
Adventist Health (AHS) <sup>(12)</sup>	California, USA	1976–80	34000	50
German Vegetarian <sup>(15)</sup>	Germany	1978–81	2000	60
Oxford Vegetarian <sup>(16)</sup>	UK	1980–84	11000	40
EPIC-Oxford <sup>(17)</sup>	UK	1993–99	65000	33
UK Women's Cohort <sup>(18)</sup>	UK	1995–98	35000	29
Adventist Health-2 (AHS-2) <sup>(13)</sup>	USA and Canada	2001–07	96000	36

EPIC, European Prospective Investigation into Cancer and Nutrition.

\* To nearest 1000.

has been widely observed to be relatively low in vegetarians and especially in vegans, and this is associated with relatively high plasma homocysteine<sup>(9)</sup>.

Many studies have assessed health-related factors such as BMI, plasma cholesterol concentrations and blood pressure in vegetarians, but relatively few studies have been of sufficient magnitude and duration to examine the long-term health of vegetarians and vegans. In this overview, we concentrate our attention on the findings of prospective cohort studies with a high proportion of vegetarian participants, extending and updating those described in a previous review by the authors<sup>(10)</sup>. The present paper is based on the material presented at a conference and is not a full systematic review of the topic. A further caveat is that, because vegetarian diets are defined by the foods that they exclude, the foods included in vegetarian diets can vary substantially and therefore the associations observed may differ between studies; in particular, all the prospective studies we discuss were conducted in western countries, therefore the conclusions in this review may not apply to vegetarians in non-western countries.

### Prospective studies of vegetarians

Table 1 summarises eight prospective studies with a high percentage of vegetarian participants (at least 29% each), the results from which will form the basis of this review. The studies include a total of nearly 280 000 participants, including over 100 000 vegetarians (although there is slight overlap between some of the studies conducted within the same country). Most of the studies were designed with the aim of recruiting a high proportion of vegetarian participants, along with non-vegetarians drawn from the same population. For example, the three North American studies are drawn from members of the Seventh-day Adventist Church, a Christian denomination with a high proportion of vegetarian adherents<sup>(11–13)</sup>. In contrast, the five European studies were all drawn from free-living populations, although recruitment was deliberately targeted at vegetarians and the health-conscious, with the assistance of vegetarian organisations and health-related publications and establishments<sup>(14–18)</sup>. In all these studies the non-vegetarians were recruited with the aim of providing a reasonable comparison group,

in that they were drawn from the same population and had a similar socio-economic status to that of the vegetarians, thus reducing the likelihood that any health differences observed would be due to non-dietary rather than dietary factors.

### Obesity and weight gain

More than one billion adults worldwide are overweight and at least 300 million of these are obese<sup>(19)</sup>. Studies of western vegetarians have consistently shown that vegetarians have a lower BMI than otherwise comparable non-vegetarians, with differences typically in the region of 1–2 kg/m<sup>2</sup> across all adult age groups, vegans generally having the lowest BMI<sup>(17,20,21)</sup>. These differences are reflected in a lower prevalence of obesity among western vegetarians<sup>(22,23)</sup>, and lower weight gain in vegetarians and vegans during adulthood<sup>(24,25)</sup>. Obesity is a major cause of morbidity/mortality, so these findings might be expected to result in a reduced risk of obesity-related diseases and conditions in vegetarians. Some studies have also suggested a role for vegetarian and vegan diets in weight management<sup>(26–28)</sup>. The consistent findings of low BMI in western vegetarians may not apply in non-western populations; for example there was no difference in mean BMI between vegetarians and non-vegetarians in the Indian Migration Study of 7000 participants, 33% of whom were vegetarians<sup>(1)</sup>.

### Diabetes

The risk of type 2 diabetes is very strongly linked to obesity. Diabetes rates have now reached epidemic proportions according to the WHO, mirroring the rapid rise in the prevalence of obesity worldwide<sup>(19)</sup>. It would be expected that, due to their relatively low BMI, western vegetarians would have a lower risk of diabetes than comparable non-vegetarians. Using data from the Adventist Health Study-2 (AHS-2) cohort, Tonstad and colleagues showed a lower risk of self-reported diabetes in semi-vegetarians, lacto-ovo-vegetarians and vegans compared with non-vegetarians, risks in the vegetarian groups being approximately half those of the non-vegetarians overall, after adjusting for BMI<sup>(29)</sup>. These



findings have led some authors to propose a role for vegetarian and vegan diets in the management of type 2 diabetes<sup>(30)</sup>, but more research is needed, ideally with diabetes cases identified through medical records, and further examination of whether the possible lower risk of diabetes in vegetarians is entirely due to their lower BMI. More data are also needed from non-western populations: in a cross-sectional study of Taiwanese Buddhists, Chiu and colleagues found the prevalence of diabetes in vegetarians to be lower than those of non-vegetarians<sup>(31)</sup>, whereas in the Indian Migration Study there was no difference in the prevalence of diabetes between vegetarians and non-vegetarians<sup>(32)</sup>.

### Cardiovascular disease

*Risk factors: plasma cholesterol, hypertension and blood pressure*

Plasma total cholesterol is lower in vegetarians than in non-vegetarians, primarily due to a reduction in LDL cholesterol, with little difference in HDL cholesterol<sup>(33,34)</sup>. This difference in plasma cholesterol is likely to be large due to differences in fat intake, since meat is a rich source of SFA whereas some plant foods such as vegetable oils, nuts and seeds are rich sources of PUFA. In 1987, Thorogood *et al.* concluded that the differences in cholesterol concentration suggested that the incidence of CHD may be 24% lower in lifelong British vegetarians and 57% lower in lifelong vegans than in meat eaters<sup>(33)</sup>.

The main diet-related determinants of hypertension are high salt intake, obesity and excess alcohol consumption<sup>(35)</sup>. Western vegetarians have a lower average BMI than non-vegetarians, but do not necessarily have low intakes of salt and alcohol. Data from the European Prospective Investigation into Cancer and Nutrition-Oxford (EPIC-Oxford) study showed significant differences in age-adjusted prevalence of self-reported hypertension across four diet groups (meat eaters, fish eaters, vegetarians and vegans) with the lowest prevalence in the vegans and the highest prevalence in the meat eaters, although these differences were attenuated by further adjustment for BMI; differences in measured systolic blood pressure between the diet groups were moderate and were non-significant after adjustment for BMI<sup>(36)</sup>. In AHS-2, an analysis of data from 500 white members of the cohort found lower mean systolic and diastolic blood pressure in lacto-ovo-vegetarians and vegans compared with omnivores, these differences translating into significantly lower risks for hypertension, effects that were only partly explained by differences in BMI between the diet groups<sup>(37)</sup>. Vegetarians in the Indian Migration Study also had lower systolic and diastolic blood pressure than non-vegetarians, but the differences were very small (<1 mm Hg) and only statistically significant for diastolic blood pressure<sup>(32)</sup>. Overall the data show small differences in blood pressure and the prevalence of hypertension between vegetarians and non-vegetarians, but are inconclusive as to whether these small differences are partly or wholly attributable to differences in BMI.

### Ischaemic heart disease

IHD is the most common cause of death globally, being responsible for more than 8 million deaths worldwide in 2013<sup>(38)</sup>. Risks for both fatal and non-fatal IHD appear to be lower in vegetarians compared with non-vegetarians. A collaborative re-analysis in 1999 of data from five prospective studies (the first five studies listed in Table 1) showed that IHD mortality was 24% lower (95% CI 6, 38) in vegetarians than in non-vegetarians<sup>(20)</sup>.

More recently, analyses in EPIC-Oxford included non-fatal as well as fatal end points and the risk of hospitalization or death from IHD was 32% (95% CI 19, 42) lower in vegetarians compared with non-vegetarians<sup>(39)</sup>. Thus there is strong evidence that the risk of IHD is lower in vegetarians than in comparable non-vegetarians, and the data suggest that much of this difference may be due to the lower LDL cholesterol of vegetarians, together with their lower BMI and slightly lower systolic blood pressure.

### Stroke

Stroke (cerebrovascular disease) is the second most common cause of death globally, being responsible for more than 6 million deaths worldwide in 2013<sup>(38)</sup>. A collaborative re-analysis in 1999 of data from five prospective studies (the first five studies listed in Table 1) showed that stroke mortality did not differ significantly between vegetarians and non-vegetarians (the death rate ratio in vegetarians *v.* non-vegetarians was 0.93; 95% CI 0.74, 1.17)<sup>(20)</sup>. In a subsequent analysis of data from the EPIC-Oxford study, cerebrovascular disease mortality also did not differ significantly between dietary groups (relative risk in vegetarians compared with meat eaters 1.11; 95% CI 0.76, 1.62)<sup>(40)</sup>. More research is needed, in particular to examine risks of sub-types of stroke and to determine whether dietary factors such as a low intake of vitamin B<sub>12</sub> in vegetarians might have an adverse impact on risk of stroke.

### Cancer

A collaborative analysis of data from the first five studies listed in Table 1, published in 1999, found no significant difference in death rates between vegetarians and non-vegetarians for cancers of the stomach, colorectum, lung, breast or prostate<sup>(20)</sup>. This analysis did not examine overall cancer mortality, but a subsequent analysis of mortality in AHS-2 found no significant difference in overall cancer mortality between vegetarians and non-vegetarians<sup>(41)</sup>.

For cancer incidence, information on site-specific cancer incidence comes from a pooled analysis of nearly 5000 incidence cancers using data from the EPIC-Oxford and Oxford Vegetarian studies<sup>(42)</sup>. In this analysis, the non-vegetarians were subdivided into meat eaters and fish eaters (who ate fish but not meat) and incidence rates compared across the three diet groups. Significant heterogeneity of risk between the diet groups were found for the following cancers: stomach cancer,

with lower risk in vegetarians (relative risk and 95 % CI compared with meat eaters 0.37, 0.19, 0.69); colorectal cancer, with lower risk in fish eaters (0.66, 0.48, 0.92) but not in vegetarians; cancers of the lymphatic and hematopoietic tissues, with lower risk in vegetarians (0.64, 0.49, 0.84), largely due to a significantly lower risk of multiple myeloma in vegetarians (0.23, 0.09, 0.59). There were no significant differences in incidence rates for other common cancer sites including the breast and prostate. Overall cancer incidence rates were significantly lower in both fish eaters (relative risk and 95 % CI compared with meat eaters 0.88, 0.80, 0.97) and in vegetarians (0.88, 0.82, 0.95). When the vegetarians were subdivided into lacto-ovo-vegetarians and vegans, risks for all cancers combined relative to meat eaters were statistically significant (0.89, 0.83, 0.96 for lacto-ovo-vegetarians and 0.81, 0.66, 0.98 for vegans). Further adjustment for BMI made little difference to the relative risks, and the associations remained statistically significant.

Analyses of the incidence of cancer in relation to diet group have also been reported for AHS-2<sup>(43,44)</sup>. Colorectal cancer incidence was compared across five diet groups; the lowest risk was found among fish eaters (described as pescovegetarians in the study), with an adjusted relative risk for all colorectal cancers of 0.57 (95 % CI 0.40, 0.82) compared with non-vegetarians<sup>(44)</sup>. Risks were non-significantly lower than in non-vegetarians for semi-vegetarians (who ate meat at least once per month but not more than once per week), lacto-ovo-vegetarians and vegans (relative risks and 95 % CI 0.92, 0.62, 1.37; 0.82, 0.65, 1.02; and 0.84, 0.59, 1.19, respectively). When the vegetarian groups, including the fish eaters, were combined, the relative risk compared with the non-vegetarians was 0.78 (95 % CI 0.64, 0.95)<sup>(44)</sup>. For all cancers combined, the incidence in comparison with non-vegetarians was 0.98 (95 % CI 0.82, 1.17) for semi-vegetarians, 0.88 (95 % CI 0.77, 1.01) for fish eaters, 0.93 (95 % CI 0.85, 1.02) for lacto-vegetarians and 0.84 (95 % CI 0.72, 0.99) for vegans, with a significantly lower risk for all vegetarian groups combined (relative risk and 95 % CI 0.92, 0.85, 0.99)<sup>(43)</sup>.

Breast cancer incidence was also compared across four diet groups in the UK Women's Cohort study: red meat eaters, poultry eaters (who did not eat red meat), fish eaters (who did not eat meat) and vegetarians<sup>(45)</sup>. In premenopausal women there were no differences in risk between the diet groups. In postmenopausal women fish eaters but not vegetarians had lower risks compared with meat eaters (relative risks and 95 % CI 0.60, 0.38, 0.96; and 0.85, 0.58, 1.25, respectively).

In summary, there is some evidence that the risk for cancer at all sites combined is slightly lower in vegetarians than in non-vegetarians, and that people who eat fish but not meat may have a lower risk of colorectal cancer, but the findings for other individual cancer sites are inconclusive.

### Fracture risk and bone health

The role of diet in bone health is complex. It has been suggested that vegetarians, and especially vegans, may

be at greater risk of low bone mineral density and fracture than non-vegetarians<sup>(8)</sup>. Data from the EPIC-Oxford study showed no differences in self-reported incident fractures between meat eaters, fish eaters and lacto-ovo-vegetarians, but vegans had a 30 % (95 % CI 2, 66) higher risk of fracture compared with meat eaters<sup>(46)</sup>. Among subjects consuming at least 525 mg/d calcium (an amount equal to the UK estimated average requirement) there was no difference in fracture risk between the diet groups, suggesting that the low calcium intakes of many vegans (below the estimated average requirement in almost half of the vegans, compared with less than 6 % below the estimated average requirement in each of the other diet groups) was responsible for the raised risk. In the Adventist studies, risks of self-reported wrist fractures in older women (AHS)<sup>(47)</sup> and hip fractures in men and women (AHS-2)<sup>(48)</sup> were both higher in those who never ate meat than in those who ate meat frequently; there was also evidence suggesting a protective effect of protein, whether of plant or animal origin<sup>(47)</sup>.

A meta-analysis of nine studies found that bone mineral density was 4 % (95 % CI 2, 7) lower in vegetarians than in omnivores at both the femoral neck and the lumbar spine, with a greater difference at the lumbar spine in vegans (6 % lower bone mineral density than omnivores) than in lacto-ovo-vegetarians (2 % lower than omnivores)<sup>(49)</sup>; a subsequent study of 210 postmenopausal women in Vietnam found no difference in femoral bone mineral density between vegans and omnivores<sup>(50)</sup>. More research is needed on bone mineral density in vegetarians, in particular to provide better understanding of the relative importance of dietary factors and body composition.

### Other diseases and conditions

Analyses of the risks for several other diseases and conditions have been reported from EPIC-Oxford. The risk of diverticular disease of the colon was 31 % (95 % CI 14, 45) lower in vegetarians compared with meat eaters<sup>(51)</sup>; when the vegetarians were subdivided into lacto-ovo-vegetarians and vegans the latter group had a 72 % (95 % CI 26, 90) lower risk of diverticular disease compared with meat eaters. This study also found a strong inverse association between dietary fibre intake and diverticular disease risk, but both associations remained statistically significant after mutual adjustment. Other analyses in EPIC-Oxford showed that vegetarians (including vegans) were at lower risk of eye cataract compared with meat eaters (relative risk 0.74, 95 % CI 0.63, 0.86), with a progressive reduction in risk from high (at least 100 g/d) to low (<50 g/d) intake meat eaters, fish eaters, lacto-ovo-vegetarians and vegans<sup>(52)</sup>. Vegetarians in the EPIC-Oxford study also had a 31 % (95 % CI 2, 52) lower risk of kidney stones compared with participants consuming a high meat diet<sup>(53)</sup>.

Analyses from AHS showed that high meat consumption was associated with a higher prevalence of degenerative arthritis and soft tissue disorders<sup>(54)</sup>; compared with



non-meat eaters, multivariate OR for the condition in occasional (<1 x/week) and regular ( $\geq 1$  x/week) meat eaters were 1.31 (95 % CI 1.21, 1.43) and 1.49 (1.31, 1.70) in women, and 1.19 (1.05, 1.34) and 1.43 (1.20, 1.70) in men. A cross-sectional analysis of 773 participants in AHS-2 found that vegetarians had a significantly lower risk of having metabolic syndrome compared with non-vegetarians (OR 0.44, 95 % CI 0.30, 0.64)<sup>(55)</sup>. In the same study, prevalence of self-reported hyperthyroidism was significantly lower in each of fish eaters, lacto-ovo-vegetarians and vegans compared with omnivores (OR and 95 % CI 0.74, 0.56, 1.00; 0.65, 0.53, 0.81; and 0.49, 0.33, 0.72, respectively)<sup>(56)</sup>.

### All-cause mortality and life expectancy

In the pooled analysis of mortality in five prospective studies in 1999, the death rate ratio in vegetarians compared with non-vegetarians, based on a total of 8330 deaths, was 0.95 (95 % CI 0.82, 1.11)<sup>(20)</sup>. However, the death rate ratios for vegetarians compared with non-vegetarians varied between studies from 0.80 to 1.17, and the test for heterogeneity between studies was highly significant ( $P < 0.0001$ ). When the diet groups were subdivided, all-cause mortality was significantly lower in occasional meat eaters (death rate ratio and 95 % CI 0.84, 0.77, 0.90), fish eaters (0.82, 0.77, 0.96), and lacto-ovo-vegetarians (0.84, 0.74, 0.96), but not in vegans (1.00, 0.70, 1.44) compared with regular meat eaters (defined as those eating meat at least once per week)<sup>(20)</sup>. Subsequent analyses of mortality data from the EPIC-Oxford and AHS-2 studies, based on 1513 and 2570 deaths, respectively, produced contrasting results. In EPIC-Oxford, there was no significant difference in all-cause mortality between vegetarians and non-vegetarians (death rate ratio and 95 % CI 1.05, 0.93, 1.19)<sup>(40)</sup>. When the non-vegetarians in this study were subdivided as meat eaters and fish eaters (who ate fish but not meat) the death rate ratios compared with meat eaters were 0.89 (95 % CI 0.75, 1.05) in fish eaters and 1.03 (95 % CI 0.90, 1.16) in vegetarians. Analyses in both AHS and AHS-2 have shown lower mortality in vegetarians and semi-vegetarians combined than in non-vegetarians<sup>(57,41)</sup>; in AHS-2, death rate ratios in semi-vegetarians, fish eaters, lacto-ovo-vegetarians and vegans compared with non-vegetarians were 0.92 (95 % CI 0.75, 1.13), 0.81 (0.69, 0.94), 0.91 (0.82, 1.00), and 0.85 (0.73, 1.01), respectively<sup>(41)</sup>.

In the analysis of mortality data from the EPIC-Oxford study, standardised mortality ratios relative to the UK population for all causes of death were 52 % for both vegetarians and non-vegetarians<sup>(40)</sup>. Low mortality relative to the general population is a common finding in prospective cohort studies owing to the 'healthy volunteer effect', partly as a consequence of healthy lifestyle choices such as the avoidance of tobacco<sup>(17,13)</sup>, but the strikingly low mortality of both vegetarians and non-vegetarians in EPIC-Oxford does suggest that the general health of both groups is good.

### Conclusions

The amount of data available is not large, but the results so far suggest that the long-term health of vegetarians is good, and may be better than that of comparable non-vegetarians for some conditions and diseases such as obesity and IHD. Stroke mortality has not been shown to differ between vegetarians and non-vegetarians. Overall cancer rates may be slightly lower in vegetarians, but the data are inconclusive for most common individual cancers. Bone fracture rates in lacto-ovo-vegetarians may be similar to those in non-vegetarians, but more data on this are needed; fracture rates are higher in vegans if they have inadequate intakes of calcium. Vegetarians have also been found to have lower risks for diabetes, diverticular disease, eye cataract, degenerative arthritis, hyperthyroidism and the metabolic syndrome, but these findings need to be further investigated in other studies. Overall mortality is similar for vegetarians and comparable non-vegetarians, but vegetarian groups compare favourably with the general population.

More data are needed, for example on stroke and subtypes of stroke, bone health and diseases and conditions not yet studied, as well as for vegetarians and others with a low intake of animal products in non-western populations. For vegans, the current data are insufficient to draw any strong conclusions and much more research is required.

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### Conflicts of Interest

T. J. K. is a member of the Vegetarian Society and the Vegan Society.

### Authorship

P. N. A. and T. J. K. wrote the paper.

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