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ORIGINAL ARTICLE

Comparative fracture risk in vegetarians and nonvegetarians in EPIC-Oxford

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Objective: To compare fracture rates in four diet groups (meat eaters, fish eaters, vegetarians and vegans) in the Oxford cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford).
Design: Prospective cohort study of self-reported fracture risk at follow-up.
Setting: The United Kingdom.
Subjects: A total of 7947 men and 26 749 women aged 20–89 years, including 19 249 meat eaters, 4901 fish eaters, 9420 vegetarians and 1126 vegans, recruited by postal methods and through general practice surgeries.
Methods: Cox regression.
Results: Over an average of 5.2 years of follow-up, 343 men and 1555 women reported one or more fractures. Compared with meat eaters, fracture incidence rate ratios in men and women combined adjusted for sex, age and non-dietary factors were 1.01 (95% CI 0.88–1.17) for fish eaters, 1.00 (0.89–1.13) for vegetarians and 1.30 (1.02–1.66) for vegans. After further adjustment for dietary energy and calcium intake the incidence rate ratio among vegans compared with meat eaters was 1.15 (0.89–1.49). Among subjects consuming at least 525 mg/day calcium the corresponding incidence rate ratios were 1.05 (0.90–1.21) for fish eaters, 1.02 (0.90–1.15) for vegetarians and 1.00 (0.69–1.44) for vegans.
Conclusions: In this population, fracture risk was similar for meat eaters, fish eaters and vegetarians. The higher fracture risk in the vegans appeared to be a consequence of their considerably lower mean calcium intake. An adequate calcium intake is essential for bone health, irrespective of dietary preferences.
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Introduction

Many studies have reported indices of bone health in vegetarians (Marsh *et al*., 1988; Lloyd *et al*., 1991; Tesar *et al*., 1992; Reed *et al*., 1994; Chiu *et al*., 1997; Parsons *et al*., 1997; Barr *et al*., 1998; Lau *et al*., 1998; Outila *et al*., 2000; Siani *et al*., 2003; Fontana *et al*., 2005). Overall, these studies found no differences in bone health indices between lacto–ovo–vegetarians and omnivores (New, 2004). However, three out of four of the studies reported lower bone mineral density or bone mineral content in vegans (who consume no animal products) compared with omnivores or other vegetarians (Chiu *et al*., 1997; Parsons *et al*., 1997; Lau *et al*., 1998; Outila *et al*., 2000), leading one reviewer to conclude that vegans have lower bone mineral density than nonvegans (Smith, 2006).

Several dietary factors known or thought to influence bone health, and possibly also fracture risk, including intakes of calcium, vitamin D, protein (including the ratio of plant to animal protein), potassium, sodium and fruit and vegetables are likely to differ between vegetarians and nonvegetarians and between vegetarians and vegans (New, 2004; Prentice, 2004). For example, data from the Oxford cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford) showed that vegans have a considerably lower mean calcium intake than nonvegans (Davey *et al*.,

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2003). The same study also showed progressive decreases in protein and dietary vitamin D intakes from meat eaters through fish eaters and vegetarians to vegans (Davey *et al*., 2003). Studies in Sweden and Germany have also shown lower than recommended intakes of calcium and vitamin D among vegans (Larsson and Johansson, 2002; Waldmann *et al*., 2003). However, there remains considerable uncertainty over the effects of dietary factors on bone health and fracture risk, leading one expert to conclude that there is insufficient evidence to link intakes of any dietary component with fracture risk among adults, with the exception of calcium and vitamin D (Prentice, 2004). Other lifestyle factors such as physical activity and the use of hormone replacement therapy (HRT) should also be taken into account when comparing fracture rates between different diet groups.

To our knowledge there are no data on fracture rates in identifiably vegetarian populations. We report here results from EPIC-Oxford, a prospective study of men and women in the UK. Recruitment into this cohort was designed to include people over a wide age range with varied dietary patterns (Davey *et al*., 2003). Our principal aim was to examine the association of fracture risk with diet group characterized as meat eater, fish eater, vegetarian or vegan.

Subjects and methods

Participants and questionnaires

The EPIC-Oxford cohort was recruited partly by postal methods targeted at vegetarians living throughout the UK and partly through general practice surgeries in Oxfordshire, Buckinghamshire and Greater Manchester (Davey *et al*., 2003). All participants completed a lifestyle and food frequency questionnaire (FFQ), including questions relating to current height and weight, smoking habits, alcohol drinking, physical activity at work and during leisure time (including walking, cycling, other exercise or sport and amount of vigorous physical activity) and marital status. Women were also asked about their reproductive history and use of HRT. Participants' body mass index (BMI) was calculated as their self-reported weight in kilograms divided by the square of self-reported height in meters.

The FFQ required participants to estimate their average frequency of intake of each of 130 foods over the previous 12 months. Nutrient intakes were estimated by multiplying the nutrient content of a specific portion size of each food by the frequency of consumption, using food composition tables (Holland *et al*., 1991). Nutrient intakes estimated and used in this analysis were energy and calcium. Diet group was determined from answers to the following four questions: Do you eat any meat (including bacon, ham, poultry, game, meat pies, sausages)? Do you eat any fish? Do you eat any dairy products (including milk, cheese, butter, yogurt)? Do you eat any eggs (including eggs in cakes and other baked foods)? Subjects who replied that they ate meat were designated meat eaters, subjects who did not eat meat but did eat fish were designated fish eaters, subjects who did not eat meat or fish but did eat either dairy products or eggs were designated vegetarians, whereas vegans were subjects who answered 'no' to each of these questions. Where the answers were incomplete or ambiguous diet group was determined from the reported use of animal foods on the FFQ.

The recruitment questionnaire was completed by 57 450 participants aged 20 and above between 1993 and 2000 (Davey *et al*., 2003). About 5 years after completing the main questionnaire surviving participants were sent a follow-up questionnaire. Participants were asked whether they had suffered any fractured bones over the previous 6 years and to report the month and year of each fracture, the bone(s) affected and the cause, categorized as a fall, road traffic accident, other accident, fracture found only by X-ray or other causes. For this analysis an incident fracture was defined as one occurring after the date of recruitment and involving bones other than the digits or ribs.

Statistical methods

Follow-up questionnaires were available for 36 956 participants. We excluded 240 participants who did not answer the question about fractures, 1360 who reported any type of fracture before recruitment or a fracture of the digits or ribs and 660 whose nutrient intake data were considered to be unreliable ($\geqslant$20% of food frequencies missing or daily energy intakes less than 800 kcal or more than 4000 kcal for men or less than 500 kcal or more than 3500 kcal for women). This left data for 34 696 participants: 7947 men and 26 749 women, including 19 249 meat eaters, 4901 fish eaters, 9420 vegetarians and 1126 vegans.

Fracture incidence in relation to diet group was examined using Cox regression. Fracture-free survival time was calculated as the number of days from recruitment to the earliest incident fracture or the date of completion of the follow-up questionnaire for subjects who did not have an incident fracture. Analyses were stratified by method of recruitment (postal, general practitioners) and adjusted for the following factors: age at recruitment (20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–89 years), smoking (never, former, current cigarette smokers), alcohol consumption ($<$1, 1–7, 8–15, $\geqslant$16 g/day), BMI ($<$20.0, 20.0–22.4, 22.5–24.9, 25.0–27.4, $\geqslant$27.5 kg/m^2), walking, ($<$3, 3–5, 6–9, $\geqslant$10 h/week), cycling (0, 0.5–1.5, 2.0–4.5, $\geqslant$5 h/week), other exercise or sport (0, 0.5–1.5, 2.0–4.5, $\geqslant$5 h/week), amount of vigorous exercise (0, 1–2, $\geqslant$3 h/week), physical activity at work (unemployed or sedentary, standing, manual), marital status (married or living as married, unmarried) and, for women only, number of children (0, 1–2, $\geqslant$3) and use of HRT (never, past, current). Missing values existed for each of the non-dietary factors except for alcohol consumption and method of recruitment. To ensure that all relevant observations were included in each Cox regression analysis 'unknown' categories were

added for each of these factors. Results for men and women combined were obtained after further adjustment for sex. Relative risks and 95% confidence intervals were calculated with meat eaters as the reference category. Analyses were performed using STATA version 9.0 (Stata Corporation, 2005).

Previous analysis of these data had shown a strong inverse association between calcium intake and fracture risk in women (Key *et al*., 2007). The influence of calcium intake on the relationship between diet group and fracture risk was examined by further adjustment for energy and calcium intakes and also by restricting the analysis to subjects consuming at least 525 mg/day calcium. Dietary calcium intake was categorized as <525, 525–699, 700–899, 900–1199 and ⩾1200 mg/day. The cut-points for the two lowest intake categories corresponded to the UK estimated average requirement (EAR: 525 mg/day) and reference nutrient intake (RNI: 700 mg/day), respectively (Department of Health, 1991), and the cut-point for the highest intake category corresponded to the US adequate intake for ages 51 and above (1200 mg/day) (Institute of Medicine, 1997). Energy intake was categorized into five groups of similar size based on approximate sex-specific quintiles of intake: <6000, 6000–6999, 7000–8499, 8500–9999, ⩾10 000 kJ/day for women and <7000, 7000–7999, 8000–9499, 9500–10 999, ⩾11 000 kJ/day for men.

Results

The mean age at recruitment was 46.6 years overall: 50.5 years for meat eaters, 43.8 years for fish eaters, 41.0 years for vegetarians and 39.4 years for vegans (Table 1). Meat eaters had the highest mean BMI and tended to be the least active group, with vegans having the lowest mean BMI whilst reporting the highest levels of walking, cycling and vigorous exercise. Current HRT use and parity were highest in the female meat eaters. Mean energy intake was highest in the meat eaters and lowest in the vegans, whereas mean calcium intakes were similar for meat eaters, fish eaters and

Table 1 Baseline characteristics by diet group

Characteristics	*Meat eater*	*Fish eater*	*Vegetarian*	*Vegan*
Number	19249	4901	9420	1126
Female (%)	76.5	82.9	77.2	62.2
Age at recruitment (years)	50.5 (12.1)	43.8 (12.6)	41.0 (13.2)	39.4 (13.3)
Current smoker (%)[a]	10.5	8.3	8.2	9.0
Alcohol consumption (g/day)				
Men	15.8 (17.8)	16.0 (17.9)	13.9 (17.6)	11.4 (17.9)
Women	7.7 (9.4)	8.2 (9.8)	7.5 (9.9)	6.4 (10.1)
Body mass index (kg/m^2)[a]				
Men	24.9 (3.3)	23.5 (3.1)	23.5 (3.3)	22.5 (2.9)
Women	24.3 (4.1)	22.9 (3.5)	22.8 (3.6)	22.0 (3.1)
⩾6 h walking per week (%)[a]	44.3	44.1	45.6	50.4
⩾2 h cycling per week (%)[a]	14.2	19.2	18.1	25.4
⩾2 h other exercise/sport per week (%)[a]	40.4	49.8	47.9	46.5
⩾3 h vigorous exercise per week (%)[a]	25.0	33.6	34.3	38.9
Nonsedentary or manual work (%)[a]	27.7	30.0	31.7	29.6
Current HRT use (%)[a]	19.0	8.5	6.3	3.1
Nulliparous (%)[a]	22.1	40.5	50.4	62.9
Energy intake (MJ/day)				
Men	9.2 (2.4)	9.0 (2.4)	8.8 (2.4)	8.0 (2.4)
Women	8.1 (2.1)	7.8 (2.1)	7.7 (2.1)	7.1 (2.2)
Calcium intake (mg/day)				
Men	1062 (325)	1086 (355)	1085 (402)	603 (232)
Women	995 (303)	1029 (337)	1018 (357)	586 (226)
All subjects				
<525 (%)	4.5	5.2	5.8	44.5
525–699 (%)	10.5	10.7	12.8	31.6
700–899 (%)	22.9	19.8	20.3	15.7
900–1199 (%)	37.3	35.1	31.7	6.1
⩾1200 (%)	24.8	29.3	29.4	2.0

Abbreviation: HRT, hormone replacement therapy.
Values are mean (s.d.), except where indicated.
[a]Unknown for some subjects (percentages are calculated among those with a known value of the factor).

Table 2 Site and cause of first incident fracture

	Meat eater	*Fish eater*	*Vegetarian*	*Vegan*	*Total (%)*
Site of bone broken in first incident fracture					
Wrist/arm	487	96	177	31	791 (41.7)
Ankle	158	47	69	10	284 (15.0)
Foot	117	29	65	5	216 (11.4)
Leg	92	21	41	10	164 (8.6)
Shoulder	28	6	9	4	47 (2.5)
Hip	30	9	14	0	53 (2.8)
Other or unspecified	180	53	96	14	343 (18.1)
Total	1092	261	471	74	1898
Cause of first incident fracture					
Fall	819	172	322	46	1359 (71.6)
Road traffic accident	39	18	23	7	87 (4.6)
Other accident	102	40	65	12	219 (11.5)
Found on X-ray	21	2	6	0	29 (1.5)
Other, unspecified or multiple causes	111	29	55	9	204 (10.7)
Total	1092	261	471	74	1898

Percentages may not sum to 100 due to rounding.

Table 3 Numbers of incident fractures and incidence rate ratios (95% CI) by diet group, showing the effects of progressive adjustment for age, non-dietary factors and intakes of energy and calcium

Sex and diet group	N	*Extent of adjustment*		
		Age alone	*Age and non-dietary factors*[a]	*Age, non-dietary factors, energy and calcium intake*
Men		$P=0.64$[b]	$P=0.69$	$P=0.72$
Meat eater[c]	179	1.00	1.00	1.00
Fish eater	34	0.95 (0.65–1.39)	0.86 (0.59–1.26)	0.87 (0.59–1.27)
Vegetarian	103	1.04 (0.79–1.36)	1.00 (0.76–1.32)	1.01 (0.77–1.33)
Vegan	27	1.30 (0.85–2.00)	1.19 (0.76–1.85)	1.20 (0.73–1.98)
Women		$P=0.35$	$P=0.56$	$P=0.90$
Meat eater[c]	913	1.00	1.00	1.00
Fish eater	227	1.07 (0.92–1.24)	1.04 (0.89–1.21)	1.04 (0.89–1.21)
Vegetarian	368	0.99 (0.87–1.13)	0.98 (0.85–1.12)	0.98 (0.85–1.12)
Vegan	47	1.28 (0.95–1.72)	1.21 (0.89–1.64)	1.05 (0.76–1.44)
Men and women combined[d]		$P=0.10$	$P=0.23$	$P=0.77$
Meat eater[c]	1092	1.00	1.00	1.00
Fish eater	261	1.05 (0.91–1.20)	1.01 (0.88–1.17)	1.01 (0.88–1.17)
Vegetarian	471	1.01 (0.89–1.13)	1.00 (0.89–1.13)	1.00 (0.89–1.13)
Vegan	74	1.37 (1.07–1.74)	1.30 (1.02–1.66)	1.15 (0.89–1.49)

[a]Non-dietary factors were smoking, alcohol consumption, body mass index, walking, cycling, vigorous exercise, other exercise, physical activity at work, marital status and for women parity and use of hormone replacement therapy (see Subjects and methods for details).
[b]The *P*-values relate to tests of heterogeneity between the diet groups.
[c]Reference group.
[d]Incidence rate ratios further adjusted for sex.

vegetarians but were considerably lower for vegans, most of whom had a calcium intake below the UK RNI. The percentage of subjects consuming less than 700 mg/day calcium was 15.0 for meat eaters, 15.9 for fish eaters, 18.6 for vegetarians and 76.1 for vegans.

In more than 182 000 person-years of follow-up 343 (4.3%) of the men and 1555 (5.8%) of the women reported having had one or more incident fractures. The most common fracture sites were wrist/arm and ankle, accounting for 42 and 15% of the incident fractures (Table 2). More than 70% of the fractures were caused by a fall. A total of 1092 meat eaters, 261 fish eaters, 471 vegetarians and 74 vegans reported having had one or more incident fractures.

Table 3 shows the numbers of incident fractures and the incidence rate ratios by diet group relative to meat eaters in men, women and men and women combined, showing the

Table 4 Numbers of incident fractures and incidence rate ratios (95% CI) by diet group among subjects consuming at least 525 mg/day calcium

Diet group	*Men*		*Women*		*Men and women*	
	N	*IRR (95% CI)*[a]	N	*IRR (95% CI)*	N	*IRR (95% CI)*
Meat eater[b]	172	1.00	851	1.00	1023	1.00
Fish eater	34	0.90 (0.61–1.32)	214	1.07 (0.91–1.25)	248	1.05 (0.90–1.21)
Vegetarian	101	1.04 (0.79–1.38)	341	0.98 (0.86–1.13)	442	1.02 (0.90–1.15)
Vegan	11	0.80 (0.42–1.51)	20	0.96 (0.61–1.51)	31	1.00 (0.69–1.44)
		$P=0.77$[c]		$P=0.82$		$P=0.95$

[a]Incidence rate ratios are stratified by method of recruitment and adjusted for age, smoking, alcohol consumption, body mass index, walking, cycling, vigorous exercise, other exercise, physical activity at work, marital status and for women parity and use of hormone replacement therapy (see Subjects and methods for details). Results for men and women combined are further adjusted for sex.
[b]Reference group.
[c]The *P*-values relate to tests of heterogeneity between the diet groups.

effects of progressive adjustment for age, non-dietary factors and intakes of energy and calcium. Fracture rates were similar for meat eaters, fish eaters and vegetarians and, overall, there was no significant heterogeneity in fracture risk between diet groups. However, fracture risk was highest among vegans for both men and women, an association that was attenuated by adjustment for non-dietary factors in both sexes and for intakes of energy and calcium in women. Compared with meat eaters, fracture incidence rate ratios in men and women combined adjusted for sex, age and non-dietary factors were 1.01 (95% CI 0.88–1.17) for fish eaters, 1.00 (0.89–1.13) for vegetarians and 1.30 (1.02–1.66) for vegans. After further adjustment for energy and calcium intake the incident rate ratio was unchanged for fish eaters and vegetarians but decreased to 1.15 (0.89–1.49) for vegans.

Table 4 shows the numbers of incident fractures and the incidence rate ratios by diet group relative to meat eaters in men, women and men and women combined among subjects who consumed at least 525 mg/day calcium, a quantity equal to the UK EAR. This analysis included 18 376 meat eaters, 4645 fish eaters, 8872 vegetarians and 625 vegans (7475 men and 25 043 women), of whom 1023, 248, 442 and 31, respectively, reported having had one or more incident fractures. Again, there was no significant heterogeneity in fracture risk between the diet groups. For men and women combined, fracture incidence rate ratios adjusted for sex, age and non-dietary factors compared with meat eaters were 1.05 (95% CI 0.90–1.21) for fish eaters, 1.02 (0.90–1.15) for vegetarians and 1.00 (0.69–1.44) for vegans.

Discussion

As far as we know, ours is the first study to report fracture rates in identified categories of non-meat eaters including vegetarians and vegans. We observed similar fracture rates among meat eaters, fish eaters and vegetarians. A 30% higher fracture rate among vegans compared with meat eaters was halved in magnitude by adjustment for energy and calcium intake and disappeared altogether when the analysis was restricted to subjects who consumed at least 525 mg/day calcium, a quantity equal to the UK EAR.

Fractures in this large study were self-reported; previous studies have shown that self-report is relatively accurate for several important fracture sites, including those of the hip, wrist and humerus (Chen *et al*., 2004). The dietary questionnaire has been shown to provide valid estimates of energy and calcium intake when compared with estimates from weighed food intakes: Spearman's rank correlations between the two estimates were 0.52 for energy intake and 0.50 for calcium intake (Bingham *et al*., 1994).

The similarity in fracture rates among meat eaters, fish eaters and (nonvegan) vegetarians may reflect the similarity in mean calcium intakes in these three groups, and is consistent with previous studies that have not shown any clear differences in bone health indices between vegetarians and omnivores (New, 2004). With more than 19 000 meat eaters and over 9000 vegetarians in this study the results provide good evidence that omnivores and vegetarians do not differ with respect to bone fracture risk.

The higher fracture rate among vegans in this study appears to reflect their markedly lower mean calcium intake. Three studies have reported lower bone mineral density or bone mineral content in vegans compared with omnivores or other vegetarians (Chiu *et al*., 1997; Parsons *et al*., 1997; Outila *et al*., 2000). Another study found no difference in bone mineral density between vegans and lacto–vegetarians, although the researchers noted a positive correlation between calcium intake and bone mineral density (Lau *et al*., 1998). A small, short-term intervention study found that calcium balance remained positive after 10 days consuming a vegan diet as well as after 10 days consuming a lacto–vegetarian diet, despite a significantly lower mean calcium intake on the vegan diet (Kohlenberg-Mueller and Raschka, 2003). However, the experimental vegan diet included a calcium-rich mineral water and the mean calcium intake of 843 mg/day in that study substantially exceeded the UK EAR of 525 mg/day, a level above which we found no increase in fracture rate among vegans.

Although the lower mean calcium intake among the vegans in this study seems to be the most likely explanation for their higher fracture rate other dietary factors need to be considered. Cross-sectional data from the EPIC-Oxford study showed that the vegans have the lowest mean intake of protein (Davey *et al*., 2003). Increasing protein intake raises the circulating level of insulin-like growth factor-1, which promotes osteoblast formation and bone growth (Dawson-Hughes, 2003), and vegans in EPIC-Oxford have previously been observed to have significantly lower mean serum insulin-like growth factor-1 concentrations than both meat eaters and vegetarians (Allen *et al*., 2000, 2002). However, previous analysis of the current data showed no association between protein intake and fracture risk (Key *et al*., 2007). It is also recognized that the effects of total dietary protein and the ratio of plant to animal protein on bone health are unclear (Dawson-Hughes, 2003; Ginty, 2003). Vegans in the EPIC-Oxford study also have the lowest mean intake of vitamin D (Davey *et al*., 2003), a nutrient of recognized importance for bone health (Prentice, 2004). However, dietary vitamin D intake is a poor indicator of overall vitamin D status because the majority of vitamin D is produced by the action of sunlight on the skin, and previous analysis of the current data showed no association between dietary vitamin D and fracture risk (Key *et al*., 2007).

In conclusion, fracture risk was similar for meat eaters, fish eaters and vegetarians in this study. The higher fracture risk among vegans appeared to be a consequence of their considerably lower mean calcium intake. Vegans, who do not consume dairy products, a major source of calcium in most diets, should ensure that they obtain adequate calcium from suitable sources such as almonds, sesame seeds, tahini (sesame paste), calcium-set tofu, calcium-fortified drinks and low-oxalate leafy green vegetables such as kale (American Dietetic Association; Dietitians of Canada, 2003).

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