European Journal of Clinical Nutrition (2010) 64, 569–577

0954-3007/10
www.nature.com/ejcn

ORIGINAL ARTICLE

Dairy consumption and patterns of mortality of Australian adults

M Bonthuis[1,2], MCB Hughes[1], TI Ibiebele[1], AC Green[1] and JC van der Pols[1]

[1]*Cancer and Population Studies Group, Queensland Institute of Medical Research, Queensland, Australia and* [2]*Division of Human Nutrition, Wageningen University and Research Centre, Wageningen, The Netherlands*

Background/Objectives: Dairy foods contain various nutrients that may affect health. We investigated whether intake of dairy products or related nutrients is associated with mortality due to cardiovascular disease (CVD), cancer and all causes.
Subjects/Methods: We carried out a 16-year prospective study among a community-based sample of 1529 adult Australians aged 25–78 years at baseline. Habitual intakes of dairy products (total, high/low-fat dairy, milk, yoghurt and full-fat cheese), calcium and vitamin D were estimated as mean reported intake using validated food frequency questionnaires (FFQs) self-administered in 1992, 1994 and 1996. National Death Index data were used to ascertain mortality and cause of death between 1992 and 2007. Hazard ratios (HRs) were calculated using Cox regression analysis.
Results: During an average follow-up time of 14.4 years, 177 participants died, including 61 deaths due to CVD and 58 deaths due to cancer. There was no consistent and significant association between total dairy intake and total or cause-specific mortality. However, compared with those with the lowest intake of full-fat dairy, participants with the highest intake (median intake 339 g/day) had reduced death due to CVD (HR: 0.31; 95% confidence interval (CI): 0.12–0.79; *P* for trend = 0.04) after adjustment for calcium intake and other confounders. Intakes of low-fat dairy, specific dairy foods, calcium and vitamin D showed no consistent associations.
Conclusions: Overall intake of dairy products was not associated with mortality. A possible beneficial association between intake of full-fat dairy and cardiovascular mortality needs further assessment and confirmation.
European Journal of Clinical Nutrition (2010) **64,** 569–577; doi:10.1038/ejcn.2010.45; published online 7 April 2010

Keywords: dairy products; mortality; cardiovascular disease; prospective study; Australia

Introduction

Cardiovascular disease (CVD) and cancer are the leading causes of death in Australia (Australian Bureau of Statistics, 2006) and most other Western countries. Intake of dairy products is suspected to modify mortality from these diseases via several proposed pathways, though the exact relationship remains unclear (Tholstrup, 2006).

Full-fat dairy products such as whole milk, butter and cheese contribute to the intake of saturated fat and cholesterol, and consumption of these products has therefore long been considered a potential risk factor for CVD (Tholstrup, 2006). However, as there is no consistency in the relationship between intake of dairy products and CVD mortality, it has been suggested that there are other factors in dairy products that counterbalance any negative effects (Steinmetz *et al*., 1994; Tavani *et al*., 2002). For example, a pooled estimate of 10 prospective cohort studies suggested that milk drinking may be associated with a reduction in heart disease risk (Elwood *et al*., 2004), possibly through the blood-pressure lowering effect of calcium from dairy products (Jorde and Bonaa, 2000).

Furthermore, there is evidence that intake of dairy products may modify risk of and mortality from a number of different cancers through mechanisms that involve calcium (Cho *et al*., 2004), vitamin D (Giovannucci, 2005), vitamin B_2 (Figueiredo *et al*., 2008), conjugated linoleic acid (Parodi, 1997; Huth *et al*., 2006) or insulin-like growth factor I (Holmes *et al*., 2002; Giovannucci *et al*., 2003; Voskuil *et al*., 2005).

Despite these indications that dairy consumption can influence disease risk and mortality, there is very limited

Correspondence: Dr JC van der Pols, Cancer and Population Studies, Queensland Institute of Medical Research, Herston Road, Brisbane, QLD 4051, Australia.
E-mail: jolieke.vanderpols@qimr.edu.au
Received 20 May 2009; revised 6 December 2009; accepted 13 January 2010; published online 7 April 2010

evidence of the overall association between dairy consumption and mortality. We therefore carried out a 16-year prospective study of dairy intake and mortality due to CVD, cancer, and all causes, in residents of an Australian community whose dietary intakes had been fully characterized.

Materials and methods

Study population

We conducted a prospective cohort study among randomly selected adult residents of Nambour, a subtropical community in Queensland, Australia, who had participated in a skin cancer prevention trial conducted between 1992 and 1996. Details of the trial and its outcomes have been reported earlier (Green *et al*., 1994, 1999). In summary, it was a randomized controlled trial with a 2×2 factorial design that evaluated the effectiveness of daily consumption of a β-carotene supplement and daily application of sunscreen in preventing skin cancer. Self-administered questionnaires on health behaviours and general characteristics were completed by the participants at baseline in 1992. In addition, trained personnel measured height and weight of each participant at baseline. Habitual food intake was assessed in 1992, 1994 and 1996 (see details below).

After completion of the trial, participants continued to be followed-up for skin cancer, whereas mortality and cause of death were monitored from baseline in 1992 to the end of 2007 through the National Death Index (NDI) of Australia for all study participants who had provided consent. Causes of death were recorded according to the 10th revision of the International Classification Diseases (ICD-10). All trial participants who provided a reliable assessment of habitual food intake during the trial and provided consent were considered in this follow-up study (Figure 1). This study was approved by the ethics committee of the Queensland Institute of Medical Research.

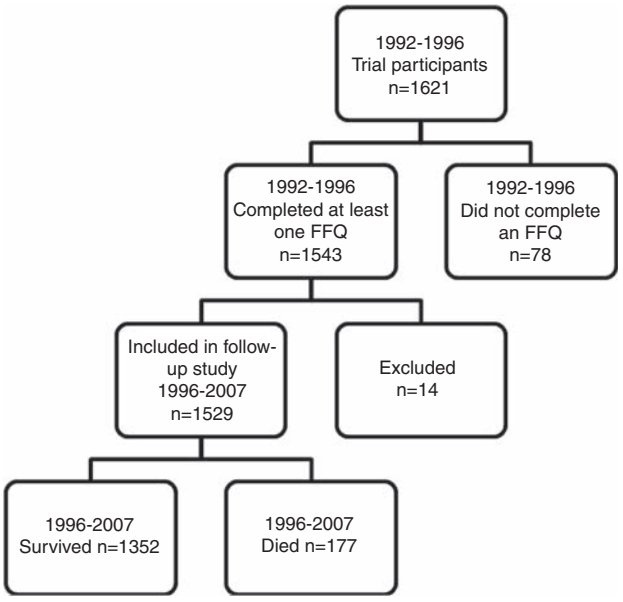

Figure 1 Flowchart of study population selection.

Dietary assessment

Dietary data were obtained from participants by using a self-administered, semi-quantitative food frequency questionnaire (FFQ) in 1992, 1994 and 1996. The FFQ asked about habitual consumption of 129 foods or food groups during the past 6 months. The FFQ was sent to the participant's home for completion before the survey. The completed FFQs were carried back to the skin examination survey clinics where they were reviewed with the respondents face-to-face by nutritionists and any clarifications needed were discussed directly. The FFQ was originally developed for the US Nurses' Health Study. Revisions were made to ensure that the list of foods reflected the Australian diet according to the 1983 National Dietary Survey of Adults (Marks *et al*., 2006b). The FFQ was subsequently validated for nutrient intake (Marks *et al*., 2006a) and food intake (Marks *et al*., 2006b) estimates using weighed food records. Spearman correlation coefficients between FFQ and weighed food records were high for dairy ($r = 0.75$ and $r = 0.73$ for unmodified and modified dairy, respectively) and calcium (energy adjusted $r = 0.67$) intake, whereas vitamin D intake could not be evaluated at that time.

For each food, a commonly used unit or portion size was specified and participants were asked to estimate how often, on average, they had eaten the given amount of food over the past 6 months. The nine response options ranged from 'never' to '4+ times per day'. Food intake in grams was estimated by expressing the consumption frequency as a proportion of daily use and multiplying with the standard serving size of each food specified in the FFQ. To account for seasonal variation, participants were asked to indicate how often seasonal fruits and vegetables were eaten in season. In the calculation of food and nutrient intakes, seasonal foods were weighted according to the proportion of the year that each food was available.

We assessed intake of individual dairy foods as well as dairy food groups. Intake in the food group 'low-fat dairy products' was computed by adding daily servings (in grams) of skim milk, low-fat milk, low-fat yoghurt, cottage or ricotta cheese, whereas the food group 'high-fat/unmodified dairy' included whole milk, cream, ice cream, yoghurt, full-fat cheese and custard. Total dairy intake was the sum of intake of all these dairy foods. Separate analyses of milk intake considered the sum of intake of whole milk, skimmed and low-fat milk.

Intakes of calcium and vitamin D were also considered as these nutrients are found in dairy products and may have independent associations with mortality (although dairy

foods have largely not been fortified with vitamin D in Australia until recently and dairy foods have not been a main source of vitamin D). Calcium and vitamin D intake from food sources were calculated using Australian food composition tables as presented in NUTTAB95 (Marks *et al*., 2006a). The addition of vitamin D to edible oil spreads and margarines has been mandated in Australia since 1987 (Food Standards Australia New Zealand, 2008). Detailed questions about margarine consumption allowed calculation of vitamin D intake from this source. In Australia, voluntary fortification with vitamin D of foods other than margarines has started only recently. Usual intakes of calcium and vitamin D from dietary supplements were estimated from a dietary supplement questionnaire along with other usually consumed supplements by reference to a specially designed database of dietary supplement composition data (Ashton *et al*., 1997).

To obtain more stable longer-term estimates, the means of dairy and nutrient intakes reported in consecutive FFQs (1992, 1994 and 1996, or a combination of these if not all FFQs were completed) were calculated for each participant.

Statistical analysis

The outcomes considered were all-cause mortality, mortality due to CVD, and mortality due to all cancers. Deaths due to CVD were defined by the presence of any ICD code I20–I25 (for coronary heart disease) or I61–I69 (for stroke) anywhere on the death certificate. Cancer as cause of death was derived from the presence of a cancer code anywhere on the death certificate, including ICD codes C00–C97 and D37–D48.

We analysed associations between total dairy intake and mortality as well as associations with low-fat and full-fat dairy subgroups and the main individual dairy products to determine whether particular dairy foods could explain the associations. Participants were divided into thirds, ranked according to their intake of each food group or nutrient. Hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated using the Cox proportional hazards model, comparing each higher group to the lowest intake group.

As age is a strong determinant of mortality, we controlled for age by choosing age as the time scale for all Cox regression models (Korn *et al*., 1997). The proportional hazards assumption was investigated both graphically and by formally testing that the log HR was constant over time for covariates in each model.

Age of entry into the cohort was the participant's age at the date on which the first FFQ was completed (1992, 1994 or 1996). Age of exit from follow-up was defined by the end of the study follow-up period (31 December 2007), date of death or lapsed consent, whichever came first.

As energy intake and dairy intake were correlated ($r=0.31$), and energy intake (Fontana and Klein, 2007) and sex (Case and Paxson, 2005) are determinants of mortality, all models included adjustment for sex and energy intake (continuous) in addition to age. The multivariable models further controlled for the confounding effects of body mass index (BMI), alcohol intake, school leaving age (as a measurement of the level of education), physical activity level (sedentary, medium or high level), pack years of smoking (up to 1992), dietary supplement use (yes/no), presence of any medical condition (yes/no) and β-carotene treatment during the trial (yes/no). Other covariates including occupational status, highest education level, intake of fat, fruits, vegetables, fish or meat, whether the participants had ever been told that they have, diabetes, high cholesterol or high blood pressure, and anthropometric indicators did not cause additional confounding.

Subsequently, we repeated the multivariable model with additional inclusion of calcium, vitamin D and total fat intake to investigate whether associations between dairy intake and all-cause mortality could be explained by these components of dairy foods.

Tests for trends were performed by modelling tertiles of intake (1 to 3 for lowest to highest intake group, respectively) as a continuous variable in the regression analyses. All statistical analyses were carried out using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA). All reported *P*-values are two sided.

Results

Of the 1621 participants of the skin cancer prevention trial, 1543 participants completed an FFQ in 1992, 1994 or 1996 (14% of the participants completed one FFQ, 19% completed two and 67% completed all three FFQs). Of these, six participants who did not answer at least 90% of the food items in the FFQ were excluded, together with eight participants who reported energy intakes outside the normal range (Willett, 1998). Thus, 1529 participants were included in this analysis (Figure 1).

Follow-up response (number of person-years included in the analyses) was 90% of the potential follow-up time. During a mean follow-up time of 14.4 years, 177 participants died, including 61 due to CVD (43 due to coronary heart disease and 22 to stroke) and 58 due to cancer (specifically lung cancer (12), breast cancer (5), prostate cancer (3), colorectal cancer (2) and other types (36)).

The baseline characteristics of the study population according to their total dairy consumption are shown in Table 1. Mean daily intake of dairy products ranged from 163 g/day in the lowest group to 628 g/day in the highest group. Compared with participants in the lowest intake group, participants in the highest dairy intake group were younger ($P=0.002$), less likely to be a smoker ($P=0.03$) and more likely to leave school at a higher age ($P=0.001$); they also had higher intakes of total energy ($P<0.0001$), total calcium ($P<0.0001$) and dietary calcium ($P<0.0001$). Intake of dietary vitamin D was lower in the highest compared with the lowest dairy intake group ($P<0.0001$). There was little variability in dairy and nutrient intake between 1992 and

Table 1 Baseline characteristics of participants according to their total dairy intake

	Total dairy intake[a]			
	Lowest (N = *509*)	*Middle* (N = *510*)	*Highest* (N = *510*)	P-*value*
Age at survey (years)[b]	50.8 ± 13.1	50.4 ± 12.7	48.1 ± 13.5	0.002
Male (%)	45	43	42	0.53
Body mass index (kg/m^2)	26.3 ± 4.6	26.1 ± 4.1	26.1 ± 4.2	0.65
Current smoker at baseline (%)	15	10	10	0.03
Mean school leaving age (years)	15.2 ± 1.5	15.5 ± 2.2	15.6 ± 1.4	0.001
Medical condition (%)	40	41	42	0.94
Use of dietary supplements (%)	49	55	55	0.08
Sedentary lifestyle (%)	37	35	35	0.39
Mean daily intakes				
Energy (kJ)	8039.1 ± 2141.1	8919.3 ± 2056.7	9770.1 ± 2260.2	<0.0001
Total calcium (mg)[c]	746.6 ± 239.8	954.6 ± 209.0	1261.0 ± 290.8	<0.0001
Dietary calcium (mg)[c]	697.5 ± 169.9	902.3 ± 152.2	1204.8 ± 241.3	<0.0001
Total vitamin D (μg)[c]	4.4 ± 2.8	4.3 ± 2.5	4.2 ± 2.5	0.51
Dietary vitamin D (μg)[c]	3.7 ± 1.1	3.5 ± 1.0	3.4 ± 1.0	<0.0001
Fat (g)[c]	79.1 ± 10.4	78.8 ± 10.0	77.8 ± 11.9	0.14

[a]Total mean dairy intake was 163, 339 and 628 g/day in the lowest, middle and highest groups, respectively.
[b]Mean ± s.d. (all such values).
[c]Energy adjusted (to 8910.1 kJ/day) with residual method.

1996. Total dairy intake increased 2%, calcium intake increased 3% and vitamin D intake decreased 3%.

All-cause mortality

Multivariable HRs for all-cause mortality by dairy intake group are given in Table 2. Although the inverse association between total dairy intake and all-cause mortality in the middle group of intake was significant after additional adjustment for calcium, a similar reduction in the highest intake group was not significant. There was no association between low-fat or full-fat dairy intake and all-cause mortality, and no individual dairy product (milk, yoghurt, full-fat cheese (Table 2) or custard, cream or ice cream (results not shown)) was associated with all-cause mortality.

Cardiovascular mortality

There was no association between overall intake of dairy products and mortality due to CVD (Table 3). However, full-fat (but not low-fat) dairy consumption was significantly and inversely associated with cardiovascular mortality. Compared with participants in the lowest intake group, participants in the highest full-fat dairy intake group had a multivariable HR of 0.33 (95% CI: 0.13–0.81; *P* for trend = 0.05). Additional adjustment for dietary intake of calcium slightly strengthened the association (highest versus lowest intake group HR: 0.31; 95% CI: 0.12, 0.79; *P* for trend = 0.04). Additional adjustment for dietary vitamin D did not influence the association (data not shown). Milk, yoghurt and full-fat cheese intakes were not significantly associated with cardiovascular mortality though all HR estimates were below 1.0 (Table 3). Participants in the highest but not the middle tertile of custard intake had a reduced risk of cardiovascular mortality (HR of highest versus lowest intake group: 0.48; 95% CI: 0.24–0.96; *P* for trend = 0.11); cream and ice cream intake were not associated cardiovascular mortality (data not shown).

Cancer mortality

There were no associations between total dairy intake or any of the dairy groups considered and all-cancer mortality (data not shown). The multivariable HR for the highest compared with the lowest group of total dairy intake and all-cancer mortality was 0.94 (95% CI: 0.42–2.11; *P* for trend = 0.83) and similar results were found for intakes of low- and full-fat dairy products. Intakes of individual dairy food groups were also not associated with cancer mortality (data not shown).

Calcium and vitamin D intake

Results of the associations between calcium and vitamin D intake and mortality from all causes and from CVD are presented in Table 4. There was a significant inverse relationship between dietary calcium intake and CVD mortality for the middle intake group compared with the lowest intake group but mortality in the highest calcium intake group was not associated with calcium intake. A similar pattern of association was seen for total calcium intake and CVD mortality. Dietary and total vitamin D intakes were not associated with cardiovascular mortality.

Table 2 Multivariable hazard ratios (HRs) and 95% confidence intervals (CIs) of dairy intake and all-cause mortality (1992–2007)

	Median intake in grams (min, max)	*No. of deaths/No. of participants*	*Multivariable HR (95% CI)*[a]	*Multivariable plus calcium HR (95% CI)*[b]
Total dairy, tertiles				
1	174 (8, 270)	68/509	1.00 (referent)	1.00 (referent)
2	332 (271, 429)	54/510	0.69 (0.44, 1.07)	0.60 (0.37, 0.99)
3	599 (430, 1580)	55/510	0.82 (0.51, 1.32)	0.60 (0.29, 1.23)
P-value for trend			0.26	0.13
Low-fat dairy, tertiles				
1	1 (0, 24)	62/509	1.00 (referent)	1.00 (referent)
2	119 (25, 240)	56/510	0.99 (0.64, 1.54)	0.98 (0.63, 1.53)
3	383 (240, 1431)	59/510	0.99 (0.64, 1.52)	0.94 (0.55, 1.59)
P-value for trend			0.99	0.97
Full-fat dairy, tertiles				
1	34 (0, 66)	58/509	1.00 (referent)	1.00 (referent)
2	123 (66, 216)	62/510	1.00 (0.64, 1.55)	1.00 (0.64, 1.55)
3	339 (217, 1174)	57/510	0.95 (0.59, 1.52)	0.94 (0.59, 1.51)
P-value for trend			0.97	0.96
Milk, tertiles				
1	109 (0, 198)	65/512	1.00 (referent)	1.00 (referent)
2	250 (198, 328)	55/506	0.85 (0.54, 1.33)	0.82 (0.51, 1.32)
3	500 (329, 1500)	57/511	0.93 (0.59, 1.48)	0.85 (0.46, 1.56)
P-value for trend			0.78	0.71
Yoghurt, tertiles				
1	0 (0, 2)	80/499	1.00 (referent)	1.00 (referent)
2	11 (3, 29)	38/519	0.84 (0.53, 1.35)	0.85 (0.53, 1.35)
3	76 (30, 700)	59/511	1.20 (0.79, 1.83)	1.22 (0.77, 1.93)
P-value for trend			0.36	0.36
Full-fat cheese, tertiles				
1	4 (0, 9)	62/490	1.00 (referent)	1.00 (referent)
2	13 (10, 19)	64/543	1.17 (0.76, 1.79)	1.16 (0.76, 1.79)
3	30 (19, 120)	54/496	0.93 (0.59, 1.46)	0.91 (0.57, 1.45)
P-value for trend			0.60	0.56

[a]From a multivariable model adjusting for age, sex, total energy intake, body mass index, alcohol intake, school leaving age, physical activity level, pack years of smoking, dietary supplement use, β-carotene treatment during trial and presence of any medical condition.
[b]As the multivariable model with additional adjustment for dietary calcium intake.

All-cancer mortality was not associated with calcium and vitamin D intake from foods only or from foods plus supplements (results not shown).

Discussion

In this prospective study, we found no evidence of a positive association, and no consistent evidence for an inverse association, between total dairy intake and mortality due to all causes, CVD, or cancer.

Full-fat dairy intake was inversely associated with cardiovascular mortality but showed no associations with all-cause mortality. As dairy products, and in particular the full-fat varieties, contribute to the intake of saturated fatty acids, dairy products have generally been suggested to increase CVD risk, although some studies found no association (Tholstrup, 2006) and others found an inverse association between dairy intake and the risk of CVD (Ness *et al*., 2001) or its risk factors (Samuelson *et al*., 2001; Pereira *et al*., 2002; Sjogren *et al*., 2004). We found no strong evidence that any of the individual full-fat dairy foods was underlying the inverse association between full-fat dairy intake and CVD mortality. Although the participants in the highest group of custard intake had a reduced risk of CVD mortality compared with those in the lowest intake group, the HRs for those in the highest intake groups of most other full-fat dairy products tended to be below one, and thus it seems likely to have been the cumulative effect of all full-fat dairy products that resulted in the significant inverse trend for total full-fat dairy intake.

In support of our observation of an inverse association between full-fat dairy intake and CVD mortality, there are some earlier studies that have reported inverse associations between specific dairy fats and risk factors for CVD. For example, fatty acids typically found in milk were associated

Table 3 Multivariable hazard ratios (HRs) and 95% confidence intervals (CIs) of dairy intake and cardiovascular disease (CVD) mortality (1992–2007)

	Median intake in grams (min, max)	*No. of deaths/No. of participants*	*Multivariable HR (95% CI)*[a]	*Multivariable plus calcium HR (95% CI)*[b]
Total dairy, tertiles				
1	174 (8, 270)	27/509	1.00 (referent)	1.00 (referent)
2	332 (271, 429)	16/510	0.50 (0.21, 1.16)	0.43 (0.15, 1.22)
3	599 (430, 1580)	18/510	0.77 (0.32, 1.85)	0.28 (0.06, 1.34)
P-value for trend			0.27	0.20
Low-fat dairy, tertiles				
1	1 (0, 24)	23/509	1.00 (referent)	1.00 (referent)
2	119 (25, 240)	17/510	1.04 (0.48, 2.22)	0.99 (0.46, 2.12)
3	383 (240, 1431)	21/510	1.35 (0.62, 2.93)	1.45 (0.56, 3.77)
P-value for trend			0.73	0.69
Full-fat dairy, tertiles				
1	34 (0, 66)	23/509	1.00 (referent)	1.00 (referent)
2	123 (66, 216)	24/510	0.75 (0.36, 1.57)	0.73 (0.35, 1.54)
3	339 (217, 1174)	14/510	0.33 (0.13, 0.81)	0.31 (0.12, 0.79)
P-value for trend			0.05	0.04
Milk, tertiles				
1	109 (0, 198)	23/512	1.00 (referent)	1.00 (referent)
2	250 (198, 328)	22/506	0.82 (0.38, 1.80)	0.73 (0.32, 1.67)
3	500 (329, 1500)	15/511	0.81 (0.35, 1.87)	0.60 (0.20, 1.81)
P-value for trend			0.84	0.63
Yoghurt, tertiles				
1	0 (0, 2)	32/499	1.00 (referent)	1.00 (referent)
2	11 (3, 29)	14/519	0.70 (0.32, 1.50)	0.70 (0.33, 1.52)
3	76 (30, 700)	15/511	0.71 (0.31, 1.65)	0.65 (0.26, 1.58)
P-value for trend			0.58	0.52
Full-fat cheese, tertiles				
1	4 (0, 9)	26/490	1.00 (referent)	1.00 (referent)
2	13 (10, 19)	19/543	1.00 (0.45, 2.20)	0.96 (0.43, 2.14)
3	30 (19, 120)	16/496	0.69 (0.31, 1.56)	0.64 (0.27, 1.49)
P-value for trend			0.63	0.54

[a]From a multivariable model adjusting for age, sex, total energy intake, body mass index, alcohol intake, school leaving age, physical activity level, pack years of smoking, dietary supplement use, β-carotene treatment during trial, and using medications for hypertension, diabetes mellitus, or cardiac disorder and use of β-adrenergic blocking agents.
[b]As the multivariable model with additional adjustment for dietary calcium.

with a more favourable low-density lipoprotein cholesterol profile in men (Sjogren *et al*., 2004), and were inversely associated with total serum concentrations of cholesterol and apolipoprotein B in healthy adolescents (Samuelson *et al*., 2001). Therefore, it has been suggested that milk fat may contain components that counterbalance the expected negative effect of saturated fatty acids on CVD (Samuelson *et al*., 2001; Tholstrup, 2006). Conjugated linoleic acid might be one of such components (Corino *et al*., 2002; Mitchell *et al*., 2005).

Intake in the middle tertile group of dietary calcium intake was associated with reduced CVD mortality, but there was no association for the highest calcium intake group and associations with total calcium intake followed a similar pattern. There is some evidence for a protective effect of calcium on risk factors of CVD (Elwood *et al*., 2004; Huth *et al*., 2006; Tholstrup, 2006), but this does not seem to be the case in our study population.

Major strengths of this study are its prospective nature (16 years of follow-up) and cause of death confirmation by the NDI. The high rate of follow-up in this study reduced the potential bias from loss to follow-up. Average food intake over a 4-year period was used instead of a single measure, to reduce within-subject variation and improve representation of long-term diet (Hu *et al*., 1999). There was sufficient variability in levels of dairy intake and the distribution of intake levels in our study population was comparable with that of other, similar studies.

However, despite the plausible explanations for an inverse association between full-fat dairy intake and CVD mortality (as discussed above), it is important to take into account the large number of comparisons considered in this study and thus we cannot rule out the possibility that the protective association between full-fat dairy intake and cardiovascular mortality was due to chance. Also, participants in the highest intake group of full-fat dairy may have been at

Table 4 Multivariable hazard ratios and 95% confidence intervals of mortality from all causes and from cardiovascular disease (CVD) (1992–2007) according to categories of calcium and vitamin D intake

	Median intake (min, max)	*All-cause mortality*[a]	*CVD mortality*[b]
Dietary calcium (mg), tertiles			
1	606 (157, 763)	1.00 (referent)	1.00 (referent)
2	886 (763, 1043)	0.81 (0.51, 1.48)	0.27 (0.10, 0.75)
3	1267 (1045, 2596)	0.86 (0.50, 1.48)	0.99 (0.38, 2.56)
P-value for trend		0.66	0.03
Total calcium (mg), tertiles			
1	636 (157, 796)	1.00 (referent)	1.00 (referent)
2	932 (796, 1102)	1.11 (0.70, 1.77)	0.41 (0.16, 1.05)
3	1351 (1103, 3575)	1.27 (0.74, 2.17)	1.31 (0.52, 3.29)
P-value for trend		0.68	0.06
Dietary vitamin D (μg), tertiles			
1	2.4 (0.0, 2.9)	1.00 (referent)	1.00 (referent)
2	3.4 (2.9, 3.9)	1.01 (0.63, 1.60)	0.87 (0.40, 1.90)
3	4.7 (3.9, 13.6)	0.78 (0.46, 1.31)	0.55 (0.21, 1.45)
P-value for trend		0.50	0.45
Total vitamin D (μg), tertiles			
1	2.5 (0.0, 3.1)	1.00 (referent)	1.00 (referent)
2	3.7 (3.1, 4.4)	0.89 (0.56, 1.40)	0.69 (0.30, 1.58)
3	5.6 (4.4, 33.5)	0.86 (0.53, 1.42)	1.08 (0.43, 2.68)
P-value for trend		0.82	0.51

[a]From a multivariable model adjusting for age, sex, total energy intake, body mass index, alcohol intake, school leaving age, physical activity level, pack years of smoking, dietary supplement use, β-carotene treatment during trial and medical condition.
[b]From a multivariable model adjusting for sex, total energy intake, body mass index, alcohol intake, school leaving age, physical activity level, pack years of smoking, dietary supplement use, β-carotene treatment during trial, and using medications for hypertension, diabetes mellitus, or cardiac disorder and use of β-adrenergic blocking agents.

generally lower risk of CVD: compared with participants in the lowest and medium-level intake groups of full-fat dairy, participants in the highest intake group were younger, had a lower BMI, were less likely to have any medical condition and were more likely to leave school at an older age (all $P<0.01$), whereas physical activity levels did not vary by full-fat dairy intake groups ($P=0.29$). At baseline in 1992 they were also less likely to have been told in the past that they had high cholesterol or high triglycerides levels. The inverse association between full-fat dairy intake and CVD mortality was independent of all these factors. Some incomplete confounding may have occurred, because the covariates that we have measured can, for example, only partially capture socioeconomic status, which may be an indicator of better health care. However, this is unlikely to fully explain the inverse association observed.

All-cancer mortality is a heterogeneous group of cancers that each have a different pathogenesis, and this may have limited our ability to study these associations. We were, however, not able to distinguish between different types of cancer in our analyses because of too small number of deaths for each cancer type.

As dietary intakes were assessed by self-reports, misclassification of exposure might have occurred. However, comparisons with intake estimated from weighed food records in our study population have shown relatively high validity for assessment of dairy and calcium intake (Marks *et al*., 2006b) (Marks *et al*., 2006a) in our study population, Furthermore, our estimates of dairy and nutrient intake are comparable to those obtained from the 1995 National Nutrition Survey of Australia, which used a different dietary assessment method (24-h recall) (Cook *et al*., 2001).

However, like all methods of dietary assessment, FFQs have limitations, which have been discussed in detail by others (Kristal *et al*., 2005; Kristal and Potter, 2006; Freedman *et al*., 2007; Willett and Hu, 2006, 2007). For example, the issue of whether use of FFQ results in attenuation of the actual associations remains disputed (Willett and Hu, 2006, 2007). We have attempted to minimize any misclassification by tailoring a previously well documented and evaluated FFQ to our specific study population, by validating it for foods and nutrients in our study population against weighed food records as well as biomarkers by using the methods of triangulation (McNaughton *et al*., 2005, 2007), and based our intake estimates on the average of up to three repeated FFQ assessments.

The dairy products that we combined to obtain estimates of total intake on a 'weight consumed' basis, differ in their concentration of components; for example the amount of saturated fat in a gram of cheese is much greater than that in a gram of milk. However, for the majority of our participants, milk was the main contributor to total dairy intake: for

almost 50% of the participants, milk constituted ⩾80% of their total dairy intake.

Butter was not included in our analyses but inclusion of butter in the total intake of high-fat dairy would have resulted in quite similar conclusions in relation to CVD mortality (HR of highest versus lowest intake group with adjustment for calcium: 0.33; 95% CI: 0.14–0.82; *P* for trend = 0.06). In conclusion, our results show no harmful effects of dairy intake on mortality from all causes, from CVD or from all cancers. In fact, intake of full-fat dairy foods was associated with a lower risk of cardiovascular mortality. It is not clear which pathway underlies this protective association and our observational study cannot confirm cause-effect relations. Further research should particularly consider the relevance of high and low-fat dairy products and their unique fatty-acid compositions.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

We thank all the participants of the Nambour skin cancer study for their participation. This study was supported by the National Health and Medical Research Council of Australia.

References

Ashton BA, Ambrosini GL, Marks GC, Harvey PW, Bain C (1997). Development of a dietary supplement database. *Aust N Z J Public Health* **21**, 699–702.

Australian Bureau of Statistics Leading causes of death in Australia 2006.

Case A, Paxson C (2005). Sex differences in morbidity and mortality. *Demography* **42**, 189–214.

Cho E, Smith-Warner SA, Spiegelman D, Beeson WL, van den Brandt PA, Colditz GA *et al*. (2004). Dairy foods, calcium, and colorectal cancer: a pooled analysis of 10 cohort studies. *J Natl Cancer Inst* **96**, 1015–1022.

Cook T, Rutishauser IHE, Allsopp R. *The Bridging Study—Comparing the Results from the 1983, 1985 and 1995 Australian National Nutrition Surveys*. Australian Food and Nutrition Monitoring Unit, Commonwealth Department of Health and Aged Care: Canberra 2001.

Corino C, Mourot J, Magni S, Pastorelli G, Rosi F (2002). Influence of dietary conjugated linoleic acid on growth, meat quality, lipogenesis, plasma leptin and physiological variables of lipid metabolism in rabbits. *J Anim Sci* **80**, 1020–1028.

Elwood PC, Pickering JE, Hughes J, Fehily AM, Ness AR (2004). Milk drinking, ischaemic heart disease and ischaemic stroke II Evidence from cohort studies. *Eur J Clin Nutr* **58**, 718–724.

Figueiredo JC, Levine AJ, Grau MV, Midttun O, Ueland PM, Ahnen DJ *et al*. (2008). Vitamins B2, B6, and B12 and risk of new colorectal adenomas in a randomized trial of aspirin use and folic acid supplementation. *Cancer Epidemiol Biomarkers Prev* **17**, 2136–2145.

Fontana L, Klein S (2007). Aging, adiposity, and calorie restriction. *JAMA* **297**, 986–994.

Food Standards Australia New Zealand. *Australia New Zealand Food Standards Code Standard 2 4.2*. ANSTAT: Melbourne 2008.

Freedman LS, Schatzkin A, Thiebaut AC, Potischman N, Subar AF, Thompson FE *et al*. (2007). Abandon neither the food frequency questionnaire nor the dietary fat-breast cancer hypothesis. *Cancer Epidemiol Biomarkers Prev* **16**, 1321–1322.

Giovannucci E, Pollak M, Liu Y, Platz EA, Majeed N, Rimm EB *et al*. (2003). Nutritional predictors of insulin-like growth factor I and their relationships to cancer in men. *Cancer Epidemiol Biomarkers Prev* **12**, 84–89.

Giovannucci E (2005). The epidemiology of vitamin D and cancer incidence and mortality: a review (United States). *Cancer Causes Control* **16**, 83–95.

Green A, Battistutta D, Hart V, Leslie D, Marks G, Williams G *et al*. (1994). The nambour skin cancer and actinic eye disease prevention trial: design and baseline characteristics of participants. *Control Clin Trials* **15**, 512–522.

Green A, Williams G, Neale R, Hart V, Leslie D, Parsons P *et al*. (1999). Daily sunscreen application and betacarotene supplementation in prevention of basal-cell and squamous-cell carcinomas of the skin: a randomised controlled trial. *Lancet* **354**, 723–729.

Holmes MD, Pollak MN, Willett WC, Hankinson SE (2002). Dietary correlates of plasma insulin-like growth factor I and insulin-like growth factor binding protein 3 concentrations. *Cancer Epidemiol Biomarkers Prev* **11**, 852–861.

Hu FB, Stampfer MJ, Rimm E, Ascherio A, Rosner BA, Spiegelman D *et al*. (1999). Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. *Am J Epidemiol* **149**, 531–540.

Huth PJ, DiRienzo DB, Miller GD (2006). Major scientific advances with dairy foods in nutrition and health. *J Dairy Sci* **89**, 1207–1221.

Jorde R, Bonaa KH (2000). Calcium from dairy products, vitamin D intake, and blood pressure: the Tromso Study. *Am J Clin Nutr* **71**, 1530–1535.

Korn EL, Graubard BI, Midthune D (1997). Time-to-event analysis of longitudinal follow-up of a survey: choice of the time-scale. *Am J Epidemiol* **145**, 72–80.

Kristal AR, Peters U, Potter JD (2005). Is it time to abandon the food frequency questionnaire? *Cancer Epidemiol Biomarkers Prev* **14**, 2826–2828.

Kristal AR, Potter JD (2006). Not the time to abandon the food frequency questionnaire: counterpoint. *Cancer Epidemiol Biomarkers Prev* **15**, 1759–1760.

Marks GC, Hughes MC, van der Pols JC (2006a). The effect of personal characteristics on the validity of nutrient intake estimates using a food-frequency questionnaire. *Public Health Nutr* **9**, 394–402.

Marks GC, Hughes MC, van der Pols JC (2006b). Relative validity of food intake estimates using a food frequency questionnaire is associated with sex, age, and other personal characteristics. *J Nutr* **136**, 459–465.

McNaughton SA, Marks GC, Gaffney P, Williams G, Green A (2005). Validation of a food-frequency questionnaire assessment of carotenoid and vitamin E intake using weighed food records and plasma biomarkers: the method of triads model. *Eur J Clin Nutr* **59**, 211–218.

McNaughton SA, Hughes MC, Marks GC (2007). Validation of a FFQ to estimate the intake of PUFA using plasma phospholipid fatty acids and weighed foods records. *Br J Nutr* **97**, 561–568.

Mitchell PL, Langille MA, Currie DL, McLeod RS (2005). Effect of conjugated linoleic acid isomers on lipoproteins and atherosclerosis in the Syrian Golden hamster. *Biochim Biophys Acta* **1734**, 269–276.

Ness AR, Smith GD, Hart C (2001). Milk, coronary heart disease and mortality. *J Epidemiol Community Health* **55**, 379–382.

Parodi PW (1997). Cows' milk fat components as potential anticarcinogenic agents. *J Nutr* **127**, 1055–1060.

Pereira MA, Jacobs Jr DR, Van Horn L, Slattery ML, Kartashov AI, Ludwig DS (2002). Dairy consumption, obesity, and the insulin resistance syndrome in young adults: the CARDIA Study. *JAMA* **287**, 2081–2089.

Samuelson G, Bratteby LE, Mohsen R, Vessby B (2001). Dietary fat intake in healthy adolescents: inverse relationships between the estimated intake of saturated fatty acids and serum cholesterol. *Br J Nutr* **85**, 333–341.

Sjogren P, Rosell M, Skoglund-Andersson C, Zdravkovic S, Vessby B, de Faire U *et al*. (2004). Milk-derived fatty acids are associated with a more favorable LDL particle size distribution in healthy men. *J Nutr* **134**, 1729–1735.

Steinmetz KA, Childs MT, Stimson C, Kushi LH, McGovern PG, Potter JD *et al*. (1994). Effect of consumption of whole milk and skim milk on blood lipid profiles in healthy men. *Am J Clin Nutr* **59**, 612–618.

Tavani A, Gallus S, Negri E, La Vecchia C (2002). Milk, dairy products, and coronary heart disease. *J Epidemiol Community Health* **56**, 471–472.

Tholstrup T (2006). Dairy products and cardiovascular disease. *Curr Opin Lipidol* **17**, 1–10.

Voskuil DW, Vrieling A, van't Veer LJ, Kampman E, Rookus MA (2005). The insulin-like growth factor system in cancer prevention: potential of dietary intervention strategies. *Cancer Epidemiol Biomarkers Prev* **14**, 195–203.

Willett W (1998). *Nutritional Epidemiology* 2nd edn Oxford University Press: New York. xiv 514 pp.

Willett WC, Hu FB (2006). Not the time to abandon the food frequency questionnaire: point. *Cancer Epidemiol Biomarkers Prev* **15**, 1757–1758.

Willett WC, Hu FB (2007). The food frequency questionnaire. *Cancer Epidemiol Biomarkers Prev* **16**, 182–183.