

Childhood dairy and calcium intake and cardiovascular mortality in adulthood: 65-year follow-up of the Boyd Orr cohort

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ABSTRACT

Background: Dairy consumption in childhood may have long-term effects on cardiovascular mortality through influencing the development of risk factors or programming effects.

Objective: To investigate whether dairy and calcium consumption in childhood is associated with adult mortality due to coronary heart disease (CHD), stroke and all causes.

Methods: In 1937–9, 4999 children in England and Scotland participated in a study of family food consumption, assessed from 7-day household food inventories. Cause of death was ascertained between 1948 and 2005 in 4374 traced cohort members with complete data. Per capita household intake estimates for dairy products and calcium were used as proxies for individual intake.

Results: No strong evidence that a family diet in childhood high in dairy products was associated with CHD or stroke mortality was found. However, childhood calcium intake was inversely associated with stroke mortality (multivariable adjusted hazard ratio (HR) for highest versus lowest calcium group: 0.41; 95% confidence interval (CI) 0.16 to 1.05; *p* for trend = 0.04), but not CHD mortality. All-cause mortality was lowest in those with the highest family dairy (HR = 0.77; 95% CI 0.61 to 0.98; *p* for trend = 0.04) and calcium intake (HR = 0.77, 95% CI 0.60 to 0.98; *p* for trend = 0.05).

Conclusions: Children whose family diet in the 1930s was high in calcium were at reduced risk of death from stroke. Furthermore, childhood diets rich in dairy or calcium were associated with lower all-cause mortality in adulthood. Replication in other study populations is needed to determine whether residual confounding explains part of these findings.

Atherosclerosis and development of cardiovascular disease risk factors start in childhood¹ and track from childhood to adulthood.² Evidence of the effect of dairy consumption on the early development of cardiovascular disease risk factors in childhood is limited. Some dairy products such as whole milk, butter and cheese have a high content of saturated fatty acids and cholesterol and consumption of these in adulthood has been thought to contribute to cardiovascular disease risk, though evidence for this is not consistent.³ Pooled results of cohort studies show a reduced risk of ischaemic heart disease and stroke associated with relatively high consumption of milk in adulthood.⁴

In children the blood lipid profile is associated with the type of milk consumed. Children who

consume low-fat milk have lower serum saturated fat fractions and higher polyunsaturated fat concentrations than those who drink whole milk.⁵ Furthermore, there is evidence that high calcium intake, of which dairy products are an important dietary source, is associated with lower diastolic and systolic blood pressure in children.⁶ Whether consumption of dairy products in childhood has long-lasting effects on cardiovascular disease risk in adulthood is not known and as far as we are aware, there are no published reports to date that have examined this subject.

Consumption of dairy products in childhood has the potential to affect long-term cardiovascular disease risk through direct effects on early risk factor development. Dairy consumption may also influence cardiovascular disease risk through a long-term programming effect involving insulin-like growth factor I (IGF-I). Milk intake is positively associated with plasma IGF-I levels in cross-sectional^{7,8} and experimental⁹ studies of adults and children. In contrast, inverse associations between milk intake in childhood and IGF-I concentrations in adulthood have been reported in the long-term follow-up of a randomised trial of pre- and postnatal milk supplementation¹⁰ and in 65-year follow-up analysis of participants of the Boyd Orr cohort study.¹¹ In adults, high circulating IGF-I concentrations are associated with reduced heart failure incidence¹² and ischaemic heart disease mortality,¹³ although not all studies show this.¹⁴

The practice of giving extra milk to school children to encourage growth was common in Europe in the 20th century and milk consumption by children is still encouraged in many European countries and world wide. Yet concern has been expressed about the possible long-term health effects of dairy consumption in relation to cancer and cardiovascular disease risk, and safe intake levels are being debated.¹⁵

In the context of this debate we have carried out a 65-year follow-up study of children in Britain to investigate whether childhood dairy intake is associated with mortality due to cardiovascular diseases (coronary heart disease (CHD) and stroke) in adulthood.

METHODS

The Boyd Orr cohort

The establishment of the cohort has been described in detail elsewhere.¹⁶ In brief, the data forming the basis of these analyses were obtained from the original records of the Carnegie (“Boyd Orr”) survey of diet and health in pre-war Britain.¹⁷

The survey was carried out in 1937–9 among 1343 mainly working class families living in 16 rural and urban areas of England and Scotland. Detailed measurements were made of household diet (see below) and the health, growth and living conditions of the children in the households. The name, age and address of the children (mean age 8 years; interquartile range 4–11 years) of the families surveyed were obtained from the original records and used to trace them through the National Health Service Central Register (NHSCR). Ethical approval for the revitalisation of the Boyd Orr study was provided by United Bristol Healthcare Trust Local Research Ethics Committee.

Of the 4999 children identified, 4383 (87.7%) have been successfully traced and were considered for this study; of the remaining 616 participants, 424 could not be identified on the NHSCR, 171 were censored pre-1948 (the NHSCR started in 1948) and 21 were identified but had been lost to follow-up by the NHSCR. The trace rate has increased slightly since earlier publications as a result of further searches of archived records, contacts with surviving study members and additional notifications from the NHSCR. The representativeness of those traced has previously been described. Traced survey participants were almost 1 year younger than their non-traced counterparts but their childhood energy intake, food expenditure or social class were similar.¹⁶ The NHSCR was used to follow up survey members for mortality due to CHD and stroke.¹⁶ Cause of death is ascertained from death certificates and classified according to International Classification of Diseases, 9th (ICD-9) and 10th revisions (ICD-10).

This analysis is based on traced cohort members who were resident in Britain on 1 January 1948 and on deaths occurring up to 31 July 2005. It is limited to the 4374 traced participants (2159 men and 2215 women) for whom full data are available; nine traced participants were excluded because they had missing dietary data.

Dietary assessment

Dietary data in the original Carnegie survey were obtained using a 7-day household inventory method. A weighed inventory of all foods in the household was recorded in a diary at the beginning of the survey period. A weighed record of all subsequent food brought into the home was made and finally, a second inventory was carried out at the end of the survey period. Calculation of the consumption of foods and nutrients for this study was carried out using the DIDO program¹⁸ and McCance and Widdowson's *The Composition of Foods*¹⁹ and supplements. Pre-war food tables were used to adapt the database where composition of 1930s foods was very different from today, or where there was no modern day equivalent. Per capita food and nutrient intake were calculated by dividing daily total intake by the total number of household members, taking into account meals missed by family members and meals consumed by visitors. The food category "dairy products" included all liquid milks (predominantly whole milk), cream, cheese, ice creams and milk puddings.

Statistical analyses

Our two main outcomes were CHD (ICD-9 codes 410–414 and ICD-10 codes I20–I25) and stroke (ICD-9 codes 430–438 and ICD-10 codes I60–I69). Participants with either of these end points listed anywhere on their death certificate were identified. Analyses comparing associations with different causes of death were based on the underlying cause of death (as defined by ICD coding rules).

Intake estimates of total dairy products, dairy subgroups (milk, cheese, cream, milk pudding, ice cream) and calcium were categorised into fourths based on the distribution in the study population.

Hazard ratios for each outcome were calculated by comparing each of the higher exposure groups with the lowest using Cox regression analysis. The proportional hazards assumption was investigated graphically and by formally testing that the log hazard ratio was constant over time for covariates in each model. Emigrants and people dying from other causes were censored at the time of emigration or death.

Clustering effects may have arisen because most participants in the cohort belonged to families that included other cohort members and therefore shared childhood conditions that possibly affect cardiovascular disease risk or they may have shared a genetic predisposition to cardiovascular disease. We therefore used the "id" and "covs" options for PROC PHREG in SAS to allow for a between-family component of variation, and calculated standard errors by using robust sandwich estimates²⁰ for the covariance matrix.

Because age is a strong determinant of mortality risk, we controlled for age by choosing age as the time scale for all Cox regression models.²¹ Because dairy intake varied by survey district, all models were evaluated with stratification for this variable. Basic models were further adjusted for sex and energy intake (continuous) because energy intake was associated with dairy intake and mortality in this population.²² In an expanded multivariable model we adjusted for the possible confounding effects of the socioeconomic and dietary characteristics that were associated with dairy consumption and which may affect mortality risk, including the following factors measured in childhood: fruit, vegetable, egg, protein and fat intake, social class (determined from the occupation of the head of the household) and food expenditure of the household. Townsend scores (an area-based measure of deprivation, with high positive values indicating high levels of socioeconomic deprivation) based on health authority area of residence at time of death, emigration or participation in a follow-up study in 1998 were used as a proxy for socioeconomic status in adulthood.²³

We analysed associations between total dairy intake and mortality and associations between individual dairy food groups and mortality to determine whether particular dairy foods could explain the associations. We also repeated the multivariable model with additional inclusion of calcium intake to investigate whether associations between dairy intake and mortality could be explained by the calcium content of dairy foods. Further, because height is a marker for IGF levels²⁴ and childhood dairy intake is associated with taller height²⁵ we added childhood height to the multivariable models to investigate whether associations were partly due to the effect of IGF on all-cause mortality. Because childhood height was available only for a subgroup of 2622 participants, this was modelled only for the outcome variable all-cause mortality owing to lack of statistical power for other outcome variables.

Associations between calcium intake and mortality were assessed after adjustment for confounders to assess whether calcium was associated with mortality independent of dairy intake. Fat and calcium were included in the models without initial adjustment of these variables for energy intake, since the correlation between these nutrients and energy intake was controlled for by inclusion of energy intake as a covariate in all multivariable models.

A test for linear trend was obtained by modelling ordinal numbers ranging from 1 to 4 (for lowest to highest intake

group, respectively) as a continuous term in the regression model. All analyses were performed with SAS statistical software (version 9.1; SAS Institute, Cary, North Carolina, USA). All reported *p* values are two-sided.

RESULTS

The baseline characteristics of the study population by total dairy intake group are shown in table 1. The median daily family intake of dairy products ranged from 89 g/day in the lowest group to 471 g/day in the highest group. On average 94% of dairy intake was due to milk consumption. Children in the highest group of dairy intake were taller and more likely to be in a household with high food expenditure during childhood, more likely to have a father in a high occupational social class and less likely to live in a deprived area or smoke as an adult than were those in the lowest intake group (*p* for trend <0.001 for all), while milk consumption contributed more to the total dairy intake of this group than it contributed to the total dairy intake of the lowest intake group (*p* for trend <0.001). As children the former group also came from families that had higher intakes of fruit, eggs and egg dishes, calcium, protein and total energy (*p* for trend <0.001 for all). Children in the highest group of dairy intake were younger (*p* for trend = 0.004) and their household's intakes of vegetable (*p* for trend = 0.003) and fat (*p* for trend = 0.004) were higher than those in the lowest intake group. Dairy intake was highly correlated with total calcium intake (Spearman correlation coefficient 0.91). Intake of fruit, vegetable, egg and egg dishes, protein, fat and energy intake was

also highest in those with the highest baseline calcium intake (results not shown).

In total 378 deaths due to CHD and 121 deaths due to stroke were identified in 4374 participants of the follow-up study.

Coronary heart disease mortality

There was no clear evidence that intake of dairy products was associated with CHD mortality. Non-proportionality of this model by sex (sex × time interaction *p* = 0.01) was dealt with through stratification by sex (results not shown). The results of this stratification did not change our conclusions because sex-specific estimates were similar.

Milk intake also showed no associations with CHD mortality. CHD mortality was lowest in the group with highest calcium intake but there was little evidence of a linear trend (multivariable-adjusted HR for highest versus lowest calcium group: 0.64, 95% CI 0.38 to 1.07; *p* for trend = 0.26) and this was further attenuated after additional adjustment for intake of dairy products (table 2).

Risk estimates for the groups of cream intake had very wide confidence intervals and there was no clear pattern of association (results not shown). Intake of cheese, milk puddings and ice cream were not associated with CHD mortality (results not shown).

Stroke mortality

Mortality due to stroke was lowest in the highest groups of dairy intake but there was only weak evidence of a dose-response

Table 1 Baseline characteristics by total dairy intake group in 4374 children from the Boyd Orr Study cohort (1948–2005)

Characteristics	Total dairy intake groups (showing median g/day)				<i>p</i> for trend*
	89 (n = 1086)	163 (n = 1096)	255 (n = 1096)	471 (n = 1096)	
Age (years) at baseline survey	7.9† (5.0)	7.5 (4.9)	7.3 (4.7)	7.7 (4.6)	0.004
Sex (% male)	48	49	52	49	0.46
Height in childhood (z score)‡	−0.19 (0.95)	−0.14 (0.94)	−0.11 (0.94)	0.38 (0.96)	<0.001
Body mass index in childhood (z score)‡	0.00 (0.95)	0.01 (1.01)	−0.07 (0.97)	0.09 (1.09)	0.14
Household food expenditure in childhood (% high expenditure)	5	6	15	39	<0.001
Occupational social class of the father (% in upper social class, category I–III)	32	35	42	76	<0.001
Townsend deprivation score in adulthood‡	0.37 (4.30)	0.90 (4.69)	0.67 (5.00)	−0.81 (2.95)	<0.001
Smoking status in adulthood (% current smoker)‡ §	27	27	17	12	<0.001
Dietary intake in childhood					
Milk (% of total dairy)	90 (11)	93 (8)	96 (4)	97 (5)	<0.001
Fruit (g/day)	18 (22)	24 (27)	37 (37)	55 (64)	<0.001
Vegetable (g/day)	58 (32)	62 (34)	71 (37)	65 (52)	0.003
Eggs and egg dishes (g/day)	13 (11)	16 (14)	18 (14)	24 (15)	<0.001
Calcium¶ (mg/day)	406 (123)	481 (129)	560 (121)	743 (201)	<0.001
Protein¶ (g/day)	55 (12)	62 (14)	64 (14)	78 (17)	<0.001
Fat¶ (g/day)	76 (11)	80 (14)	82 (14)	78 (22)	0.004
Energy (kJ)	8447 (1877)	9148 (2061)	9302 (1995)	11201 (2362)	<0.001

Results are shown as mean (SD) unless stated otherwise.

**p* Values from Mantel–Haenszel χ^2 test (categorical variables) or linear regression (continuous variables); †mean (SD) (all such values); ‡only available for a proportion of study participants: height *n* = 2632 (60%), body mass index *n* = 2620 (60%), Townsend score for area of residence in 1998 *n* = 4069 (93%), smoking status *n* = 1626 (37%); §smoking status as reported in 1997 follow-up data collection; ¶adjusted for energy intake to 9200 kJ (~2200 kcal) by using the residual method.³¹ Height, body mass index, household food expenditure, social class and dietary intake were measured in childhood; Townsend score (a lower score implies relative affluence) and smoking status were measured in adulthood.

Table 2 Hazard ratios (HRs) and 95% confidence intervals of mortality from coronary heart disease according to dairy and calcium intake in 4374 participants of the Boyd Orr study cohort (1948–2005)

	Intake groups				p for trend
	Group 1	Group 2	Group 3	Group 4	
Total dairy intake*					
Cases (n)	101	92	93	92	
Basic†	1.00	0.89 (0.67 to 1.19)	0.91 (0.68 to 1.22)	0.69 (0.46 to 1.03)	0.33
Multivariable‡	1.00	0.87 (0.63 to 1.18)	0.87 (0.63 to 1.21)	0.74 (0.45 to 1.22)	0.64
Multivariable plus calcium§	1.00	1.00 (0.73 to 1.37)	1.16 (0.81 to 1.67)	1.34 (0.75 to 2.39)	0.69
Milk intake¶					
Cases (n)	95	93	95	93	
Basic†	1.00	0.94 (0.70 to 1.25)	0.96 (0.71 to 1.29)	0.74 (0.50 to 1.10)	0.47
Multivariable‡	1.00	0.93 (0.68 to 1.27)	0.96 (0.70 to 1.33)	0.80 (0.49 to 1.31)	0.83
Multivariable plus calcium§	1.00	1.05 (0.76 to 1.44)	1.25 (0.88 to 1.78)	1.45 (0.83 to 2.54)	0.50
Calcium intake**					
Cases (n)	98	91	100	89	
Basic† HR	1.00	0.93 (0.69 to 1.25)	0.97 (0.70 to 1.35)	0.68 (0.44 to 1.05)	0.23
Multivariable‡	1.00	0.96 (0.70 to 1.36)	0.95 (0.66 to 1.36)	0.64 (0.38 to 1.07)	0.26
Multivariable plus dairy products††	1.00	1.04 (0.76 to 1.44)	1.10 (0.76 to 1.61)	0.89 (0.52 to 1.52)	0.70

*Daily intake of dairy products was 89 g/day, 163 g/day, 255 g/day and 471 g/day in groups 1, 2, 3 and 4, respectively. All HRs were from Cox regression; †adjusted for age, sex, survey district and energy intake; ‡adjusted for age, sex, survey district, intake of fruit, vegetable, egg and egg dishes, protein, fat and energy intake, household food expenditure in childhood and Townsend deprivation score in adulthood; §adjusted for same confounders as in multivariable model plus calcium intake; ¶daily milk intake was <0.5 cup (<118 ml), 0.5–0.8 cup (118–188 ml), >0.8–<1.2 cups (>188–282 ml) and ≥1.2 cups (>282 ml) in groups 1, 2, 3 and 4, respectively. 1 cup milk = ~235 ml; **daily intake of calcium was 150–397 mg, 398–513 mg, 513–683 mg, 683–2198 mg in groups 1, 2, 3 and 4, respectively; ††adjusted for same confounders as in multivariable model plus dairy products.

relationship (p for trend = 0.16) (table 3). Associations with milk intake were similar.

Calcium intake was inversely associated with stroke mortality in the second through to the highest compared with the lowest intake group (p for trend = 0.04), with a 60% lower risk of stroke mortality in those with the highest family calcium intake (multivariable-adjusted HR for highest versus lowest calcium group: 0.41, 95% CI 0.16 to 1.05) but also a 40–55% reduced risk of stroke mortality in the middle calcium intake groups. This association was attenuated (p for trend = 0.11) after additional adjustment for intake of dairy products (table 3).

Risk estimates for the groups of cream intake had very wide confidence intervals and there was no clear pattern of association (results not shown). Intake of cheese, milk puddings

and ice cream was not associated with mortality due to stroke (results not shown).

Total mortality and non-cardiovascular disease mortality

By the end of follow-up in 2005, in total 1468 (34%) of the participants had died, including 497 (34%) from cancer, 366 (25%) from CHD, 120 (8%) from stroke, 143 (10%) from diseases of the respiratory system, 77 (5%) from external causes (including accidents and suicide) and 265 (18%) from other causes.

Dairy intake was inversely associated with all-cause mortality (p for trend = 0.04). Compared with those with the lowest family intake of dairy, all-cause mortality was lower in participants in the highest group of dairy intake (multivariable-adjusted HR for

Table 3 Hazard ratios (HRs) and 95% confidence intervals of mortality from stroke according to dairy and calcium intake in 4374 participants of the Boyd Orr study cohort (1948–2005)

	Total dairy intake groups (showing median g/day)				p for trend
	Group 1	Group 2	Group 3	Group 4	
Total dairy intake*					
Cases (n)	38	33	22	28	
Basic† HR	1.00	0.90 (0.56 to 1.45)	0.56 (0.32 to 0.96)	0.70 (0.36 to 1.33)	0.18
Multivariable‡	1.00	0.96 (0.58 to 1.59)	0.54 (0.30 to 0.97)	0.61 (0.27 to 1.38)	0.16
Multivariable plus calcium§	1.00	1.01 (0.60 to 1.71)	0.59 (0.30 to 1.16)	0.74 (0.24 to 2.22)	0.35
Milk intake¶					
Cases (n)	38	30	25	28	
Basic† HR	1.00	0.82 (0.51 to 1.33)	0.62 (0.37 to 1.04)	0.70 (0.37 to 1.33)	0.33
Multivariable‡	1.00	0.84 (0.50 to 1.41)	0.59 (0.34 to 1.01)	0.60 (0.28 to 1.33)	0.26
Multivariable plus calcium§	1.00	0.88 (0.52 to 1.51)	0.65 (0.34 to 1.25)	0.76 (0.26 to 2.19)	0.59
Calcium intake**					
Cases (n)	44	21	30	26	
Basic† HR	1.00	0.45 (0.26 to 0.79)	0.61 (0.37 to 1.03)	0.48 (0.23 to 1.00)	0.03
Multivariable‡	1.00	0.44 (0.24 to 0.79)	0.61 (0.34 to 1.07)	0.41 (0.16 to 1.05)	0.04
Multivariable plus dairy products††	1.00	0.46 (0.25 to 0.85)	0.68 (0.35 to 1.34)	0.52 (0.15 to 1.72)	0.11

*Daily intake of dairy products was 89 g/day, 163 g/day, 255 g/day and 471 g/day in groups 1, 2, 3 and 4, respectively. All HRs were from Cox regression; †adjusted for age, sex, survey district and energy intake; ‡adjusted for age, sex, survey district, intake of fruit, vegetable, egg and egg dishes, protein, fat and energy intake, household food expenditure in childhood and Townsend deprivation score in adulthood; §adjusted for same confounders as in multivariable model plus calcium intake; ¶daily milk intake was <0.5 cup (<118 ml), 0.5–0.8 cup (118–188 ml), >0.8–<1.2 cups (>188–282 ml) and ≥1.2 cups (>282 ml) in groups 1, 2, 3 and 4, respectively. 1 cup milk = ~235 ml; **daily intake of calcium was 150–397 mg, 398–513 mg, 513–683 mg, 683–2198 mg in groups 1, 2, 3 and 4, respectively; ††adjusted for same confounders as in multivariable model plus dairy products.

Table 4 Hazard ratios (HRs) and 95% confidence intervals for all-cause mortality according to dairy and calcium intake in 4374 participants of the Boyd Orr study cohort (1948–2005)

	Intake groups				p for trend
	Group 1	Group 2	Group 3	Group 4	
Total dairy intake*					
Deaths	412	377	345	334	
Basic†		0.93 (0.81 to 1.08)	0.82 (0.71 to 0.95)	0.69 (0.57 to 0.84)	0.001
Multivariable‡	1.00	0.92 (0.79 to 1.07)	0.81 (0.69 to 0.95)	0.77 (0.61 to 0.98)	0.04
Multivariable plus calcium¶	1.00	0.95 (0.82 to 1.11)	0.87 (0.73 to 1.03)	0.90 (0.68 to 1.19)	0.44
Milk intake**					
Deaths	408	369	354	333	
Basic†	1.00	0.92 (0.80 to 1.06)	0.83 (0.72 to 0.96)	0.69 (0.57 to 0.84)	0.002
Multivariable‡	1.00	0.90 (0.78 to 1.05)	0.82 (0.70 to 0.95)	0.77 (0.61 to 0.97)	0.05
Multivariable plus calcium¶	1.00	0.93 (0.80 to 1.08)	0.87 (0.73 to 1.03)	0.89 (0.68 to 1.17)	0.43
Calcium intake††					
Deaths	423	353	360	332	
Basic†	1.00	0.83 (0.72 to 0.96)	0.85 (0.73 to 1.00)	0.70 (0.56 to 0.86)	0.005
Multivariable‡	1.00	0.82 (0.70 to 0.96)	0.87 (0.74 to 1.04)	0.77 (0.60 to 0.98)	0.05
Multivariable plus dairy‡‡	1.00	0.85 (0.73 to 1.00)	0.94 (0.78 to 1.13)	0.89 (0.68 to 1.16)	0.25

*Daily intake of dairy products was 89 g/day, 163 g/day, 255 g/day and 471 g/day in groups 1, 2, 3 and 4, respectively. All HRs were from Cox regression; †adjusted for age, sex, survey district and energy intake; ‡adjusted for age, sex, survey district, intake of fruit, vegetable, egg and egg dishes, protein, fat and energy intake, household food expenditure in childhood and Townsend deprivation score in adulthood; §adjusted for same confounders as in multivariable model plus calcium intake; ¶daily milk intake was <0.5 cup (<118 ml), 0.5–0.8 cup (118–188 ml), >0.8–<1.2 cups (>188–282 ml) and ≥1.2 cups (>282 ml) in groups 1, 2, 3 and 4, respectively. 1 cup milk = ~235 ml; **daily intake of calcium was 150–397 mg, 398–513 mg, 513–683 mg, 683–2198 mg in groups 1, 2, 3 and 4, respectively; ††adjusted for same confounders as in multivariable model plus dairy products.

highest versus lowest dairy group: 0.77, 95% CI 0.61 to 0.98) (table 4). This association was attenuated after additional controlling for calcium.

In the subgroup of participants for whom anthropometric data were available (60% of the study population), the inverse association between dairy intake and all-cause mortality remained, albeit with wider confidence intervals owing to loss of statistical power (multivariable adjusted HR for highest versus lowest dairy group = 0.75, 95% CI 0.55 to 1.03; p for trend = 0.14) (results not shown in table). Additional adjustment for childhood height in the multivariable model did not change these estimates.

Milk intake showed a similar inverse association with all-cause mortality, but the association was abolished after additional control for calcium (table 4). Intake of other dairy products was not associated with all-cause mortality (results not shown).

A family diet in childhood rich in calcium was inversely associated with all-cause mortality. Compared with those with the lowest intake of calcium, all-cause mortality was lower in participants in the highest group of calcium intake (multivariable-adjusted HR for highest versus lowest dairy group = 0.77, 95% CI 0.60 to 0.98; p for trend = 0.05) (table 4). After adjustment for dairy intake this association was attenuated. The inverse association between calcium intake and all-cause mortality was independent of childhood height (results not shown).

Mortality due to diseases of the respiratory system was lowest in the highest group of family dairy intake after basic adjustment, though there was no clear trend (basic-adjusted HR for highest versus lowest dairy group: 0.59, 95% CI 0.31 to 1.09; p for trend = 0.39) (results not shown in table) and attenuated after full covariate adjustment. Deaths due to external causes (mostly accidents and suicide) and deaths due to other causes were not associated with family dairy intake. Calcium intake was not associated with mortality due to respiratory diseases, external causes, or to other causes (full results not shown). Previous analyses have suggested that overall cancer risk in this study population was lowest in those with the highest

childhood dairy intake (multivariable adjusted odds ratio for highest versus lowest dairy group = 0.84, 95% CI 0.64 to 1.10; p for trend = 0.09)²⁵

DISCUSSION

In this 65-year follow-up study of children born in the 1920s or 1930s, a family diet in childhood relatively high in calcium was associated with reduced risk of mortality caused by stroke, with calcium intakes above ~400 mg/day associated with 40–60% lower mortality due to stroke compared with those with daily calcium intakes below ~400 mg/day. Neither milk nor calcium intake showed clear associations with CHD mortality but for all three of these intercorrelated aspects of diet CHD mortality was lowest in the highest intake group. Our results also showed an inverse association between intakes of dairy (in particular, milk) or calcium and all-cause mortality, with 25% lower mortality in those in the highest groups of childhood dairy or calcium intake. As far as we know, this is the first study to provide evidence for an association between childhood dairy and calcium intake and mortality due to stroke or all-causes in adulthood.

In adults, observational studies have quite consistently shown an inverse association between intake of calcium and cardiovascular mortality, although results from clinical trials of calcium supplementation are equivocal.²⁶ Evidence of mechanisms such as a reduction in blood pressure following high calcium intake,²⁷ as well the lowering effect of calcium on plasma cholesterol levels²⁸ add support to a role for calcium intake in reduction of cardiovascular disease risk in adults.

Our observation that such inverse associations are also seen between calcium intake in childhood and stroke mortality later in life may indicate that calcium intake already starts its protective influence on risk factor development early in life, possibly through a lifelong accumulative effect. In particular, the lowering effect of calcium intake on diastolic and systolic blood pressure in children may be relevant here.⁶

All-cause mortality was lowest in those with the highest family intake of dairy or calcium. It is unclear which cause of death is driving these inverse associations. Mortality was generally lowest in those with the highest childhood dairy

intakes for most causes of death, including deaths from cancer,²⁵ though after multivariable adjustment none of these associations reached conventional levels of statistical significance. This apparent non-specificity of the inverse associations may indicate that these may be due to residual confounding, although there was no evidence of confounding by most of the measured covariates, including dietary and socioeconomic exposures in childhood and adulthood. The group of “other deaths” contained a broad mix of different causes of death and conclusions about associations with specific causes included in these “other deaths” could not be made.

The inverse association between dairy and calcium intake and all-cause mortality was independent of childhood height (a marker for IGF levels in childhood²⁴), thus these results do not suggest that the IGF pathway is involved as an underlying mechanism. Childhood diet may, however, also have long-term programming effects on adult IGF-I levels,^{10 11} which differ from the acute effects and which may not be reflected by childhood height.

This study has a number of strengths. First, diet was measured in childhood long before the occurrence of disease, thus avoiding the problem of recall bias encountered in studies based on remembering childhood diet. Second, all foods consumed in the home were assessed, allowing consideration of other dietary factors—such as fruit and vegetable intake—as potential confounders of the relation between dairy intake and cancer risk. A previous repeatability study has shown good reliability of milk and calcium intake estimates in this study population.²⁹

It is important though to interpret these results in light of the study limitations. First, childhood diet was based on household rather than individual consumption. Misclassification resulting from imprecise diet measurements would, however, probably have been non-systematic, attenuating rather than explaining the associations observed. We expect that dairy products more so than other foods were consumed by the children of the families in the Boyd Orr study, thus we have greater confidence in attributing this exposure to our cohort members. The analyses are based on the traced participants only. Study participants who were excluded from this analysis were older, more often of lower socioeconomic class and had higher intakes of fat and total energy in childhood than those who were included ($p < 0.05$, data not shown). However, it is unlikely that the small group of excluded participants (13% of the original cohort) would have substantially altered the estimates presented here.

Because repeat assessments of diet during the life-course are not available for the majority of participants, we are unable to tell whether some of these associations are confounded by dietary habits in adulthood, which may have been correlated with childhood diet³⁰ but could not be accounted for in these analyses. Data from the 1997 follow-up study in a subgroup of the study participants showed that the correlation between milk intake in childhood and that in adulthood was very low (Pearson correlation coefficient 0.07; unpublished observation) and thus these results are unlikely to be explained by similar dairy and calcium consumption patterns in adulthood and probably point to a childhood-specific effect.

The macroenvironment of participants has varied considerably between the time of participation in the study at baseline, as children in 1930s pre-war Britain and the time of their death. Conditions during the second world war and participants' environment as adults in the second half of the 20th century will have been considerably different from those in the 1930s. Food

availability, general income and health and housing standards have varied considerably during the study period, but such changes could not be considered in the analyses. Townsend score was included in our models as a proxy indicator for adulthood environment, but this is a crude measure.

Competing risks could have occurred in this population, since, for example, people who had died of CHD were no longer at risk of death due to stroke. Given the small difference in average age at which people died of CHD or stroke (63 years and 65 years of age, respectively) we could not separate the competing risk through modelling, but these are unlikely to have had a substantial effect on the results.

This study included a relatively large study population and a long follow-up time. However, the widths of the confidence intervals for hazard ratio estimates are dependent on the number of events that occurred in each group. For example, the widths of the confidence intervals for stroke mortality were wider than those for CHD mortality owing to the smaller number of events. Nevertheless, our results indicated a substantial, up to 60% lower probability of death due to stroke in groups with a higher calcium intake than in the group with lowest calcium intake.

We attempted to investigate whether the reported inverse associations were confounded by smoking status in adulthood. However, follow-up data were available for 1626 participants only and confidence intervals were too wide to establish whether there was evidence of confounding by smoking.

In conclusion, this study showed that a family diet in childhood relatively high in calcium is associated with reduced stroke mortality and that a childhood diet high in dairy or calcium is inversely associated with total mortality in adulthood. As far as we are aware this is the first study to investigate the long-term associations between childhood dairy and calcium intake and cardiovascular and all-cause mortality. Dairy products are important contributors to children's intake of protein, vitamins and minerals and they play an important role in the maintenance of bone health. The beneficial effects of dairy and calcium intake suggested by this study were seen at estimated intake levels that are similar to the currently recommended intake amount for dairy and calcium in children. Further evidence is needed to replicate these findings, in particular of studies that involve a more complete life-course assessment of dairy intake and cardiovascular disease outcomes.

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